A consensus on outcome measures for device-based interventions that seek to restore bilateral and binaural hearing in adults with single-sided deafness

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Abstract

Objectives: Unilateral severe-to-profound sensorineural hearing loss (single-sided deafness, SSD) often has functional, psychological, and social consequences. Interventions for adults with SSD include hearing aids and auditory implants. Benefits and harms of these interventions (outcome domains) are until now reported inconsistently in clinical trials involving adults with SSD. Inconsistency in reporting of outcome measures prevents meaningful comparisons or syntheses of trial results. The Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) international initiative used structured communication techniques to achieve consensus among healthcare users and professionals working in the field of SSD. The product is a set of core outcome domains that experts agree are critically important to assess in all clinical trials of SSD interventions. An assessment of the available measurement instruments for relevance and comprehensiveness has implications on how the outcome domains should be measured in clinical trials assessing the benefits and harms of SSD interventions.

Methods: A long list of candidate outcome domains was compiled from a systematic review of outcome domains and measurement instruments used in designs of clinical trials for SSD interventions, and published qualitative data on the psychological and social consequences of SSD in adulthood; to inform the content of a two-round online Delphi survey. Overall, 308 participants from 29 countries were enrolled. Of those, 233 participants completed both rounds of the survey and scored each outcome domain on a 9-point scale: 1-3 = *not important in deciding whether an SSD intervention is effective*, 4-6 = *important but not critical*, and 7-9 = *critically important to measure in all trials*. A domain was considered for inclusion if ≥70% of participants in all stakeholder groups (healthcare users, healthcare professionals, and clinical researchers) scored 7-9 and <15% in any stakeholder group scored 1-3. The set of core outcome domains was finalised via a web-based consensus meeting with 12 participants. Votes involved all stakeholder groups, with an approximate 2:1 ratio of professionals to healthcare users participating in the Delphi survey, and a 1:1 ratio participating in the consensus meeting. Subsequent focus groups were conducted to

help with domain conceptualisation, to identify themes or conceptual elements, to inform an assessment of the relevance of available measurement instruments for the core outcome domains.

Results: The first round of the survey listed 44 potential outcome domains, organised thematically in ten categories: factors related to the treatment being tested, health-related quality of life, hearing disability, other effects, physical effects, psychological effects, self, sound quality, spatial hearing, and tinnitus. A further five outcome domains were included in Round 2 based on participant feedback. The structured voting at Round 2 identified 17 candidate outcome domains which were voted on at the consensus meeting. Consensus was reached for a core outcome domain set including three outcome domains: *Spatial orientation* (knowing where you are in relation to the position of a sound source), *Group conversations in noisy social situations* (listening and following a conversation between a group of people, when others are talking in the background), and *Impact on social situations* (your hearing loss or device limiting your ability to fully participate in the social world). Seventy-seven percent of the remaining Delphi participants agreed with this core outcome domain set. Three conceptual elements were identified for each outcome domain that were used to assess 76 available patient reported outcome measurement instruments. The relevance and comprehensiveness to the conceptual elements and detailed operational definitions of the outcome domains were assessed independently by three coders. The Speech, Spatial and Qualities (SSQ) scale, the Nijmegen Cochlear Implant Questionnaire (NCIQ), the Spatial Hearing Questionnaire (SHQ), the Hearing Implant Sound Quality Index (HISQUI-NL), and the Monaural auditory capacity assessment scale (MACAS) match several operational definitions in the *Spatial orientation* and *Group conversations in noisy social situations* outcome domains. The Communication profile for hearing impaired (CPHI) questionnaire was the only identified patient reported outcome measure (PROM) suitable for assessing the *Impact on social situations* outcome domain.

Conclusions: Adoption of the core outcome domain set will promote consistent assessment and reporting of outcomes that are meaningful and important to all stakeholders. This consistency will in turn enable comparison of outcomes reported across clinical trials comparing SSD interventions in adults and reduce research waste

in clinical trials of SSD interventions. Further prospective validation of measurement instruments will provide validation data and help finalise the core outcome set for clinical trials of SSD interventions in adults.

Declaration

I declare that this thesis and the work contained herein is my own work, except where indicated by referencing, and that no part of this thesis has been submitted elsewhere for any other degree or professional qualification.

Roulla Katiri

Funding statement

The main body of work for this thesis was funded by the National Institute for Health Research (NIHR) Nottingham Biomedical Research Centre (BRC), funding reference number BRC-1215-20003. Additional grants obtained were the Graham Fraser Foundation Travel Grant to attend the 15th International Conference on Cochlear Implants and other Implantable Auditory Technology (Ci2018.org), where the study was launched; and Oticon Medical™ provided funding (Appendix 1) to purchase the DelphiManager software from the COMET (Core Outcome Measures in Effectiveness Trials) initiative, University of Liverpool. The funding bodies had no role in the study design, implementation, writing, or resulting peer reviewed publications.

Other grants and awards received:

- NIHR Nottingham BRC (Hearing) PPI/E funding (**£385**) for development of the study summary dissemination infographic poster (Appendix 2) and animated infographic[1] (March 2022).
- NIHR Nottingham BRC (Hearing) PPI/E funding (**£180**) to support two PPI collaborators' expenses and honorary payments for their contributions to the patient reported outcome measures steering group meeting (March 2022).
- NIHR Nottingham BRC (Hearing) PPI/E funding (**£1100**) to support development of the core outcome set dissemination video[2] and reimbursement of two PPI collaborators (**£180**) for their contributions in the video development process (February 2022).
- NIHR Nottingham BRC (Hearing) PPI/E funding (**£110**) to support two PPI collaborators' expenses and honorary payments for their contributions to the measurement instruments steering group meeting (September 2021).
- NIHR Nottingham BRC (Hearing) PPI/E funding (**£160**) to support two PPI collaborators' expenses and honorary payments for their contributions to the post-consensus meeting focus groups organisation (October 2020).

[1] https://youtu.be/2sA8QxhYQlE
[2] https://youtu.be/BcUy_2bzHZw

- University of Nottingham School of Medicine Sue Watson postgraduate oral presentation event, 2nd prize (**£50**) winner (October 2019).
- NIHR Infrastructure SPARC (Short Placement Award for Research Collaboration), reference: SPARC-05-18-10 (Appendix 3), to cover travel and other expenses (**£642.46**) whilst on a week's placement at the BRC Central Manchester University Hospitals NHS Foundation Trust, Manchester (July 2019).
- NIHR Nottingham BRC (Hearing) PPI/E funding (**£1024.80**) to support two PPI collaborators' expenses and honorary payments for their contributions to the pre-Delphi outcome domain organisation during a 2-day workshop, Dublin (June 2019).
- NIHR Nottingham BRC (Hearing) PPI/E funding (**£850**) for development of the participant recruitment video[3] (June 2019).
- Oticon Medical™ open competition research grant (**£850**) to purchase the COMET (Core Outcome Measures in Effectiveness Trials) initiative DelphiManager software (Appendix 1) from the University of Liverpool (October 2018).
- NIHR Nottingham BRC (Hearing) PPI/E funding (**£304.75**) to reimburse two PPI collaborators' expenses who attended the ShareBank 'Health research and getting involved in funding applications' training event, University of Nottingham, Nottingham (June and July 2018).
- The 2017 Graham Fraser Foundation Travel Grant (**£500**) to attend the 15th International Conference on Cochlear Implants and other Implantable Auditory Technology (Ci2018.org), Antwerp, Belgium (June 2018).

[3] https://youtu.be/CFBC3Wv5_8s

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Secondly, I would like to thank the CROSSSD study steering group we have been honoured to collaborate with, Professor Jill B. Firszt, Professor Paul H. Van de Heyning, and Professor Iain A. Bruce; the patient and public involvement collaborators, Nóra Buggy and Nicholas Hogan, for so generously sharing their everyday experience of living life with single-sided deafness, and Dr Adele Horobin for her wealth of knowledge and guidance on how to conduct and disseminate research that is relevant to those the research is conducted for.

A huge thank you to everyone who contributed to all the aspects of the project described in this thesis: all the healthcare users, healthcare professionals, clinical researchers, commercial representatives, journal editors, reviewers, research and development facilitators, participant identification site coordinators, and last but not least, all my colleagues at the University of Nottingham Hearing Sciences. This work would not have been possible without you.

On a personal note, I would like to thank my family for their continuous care throughout the peaks and troughs of PhD life, mum and dad for teaching me that hard work and generosity do pay off, my siblings Sophia, Constantinos, Kyriaki, Elisavet, and Chara for being so encouraging, understanding and for cheering me on. Thank you also to my work colleagues for seeing me through five years of PhD!

Dedication

I would like to dedicate this work to those with hearing and balance disorders whom I have encountered throughout my audiology career and this project. You inspire and motivate me daily, your life stories and wisdom have shaped me into the clinician I am today, and guide my future professional aspirations.

Relevant peer reviewed publications

Katiri, R., Hoare, D.J., Smith, S., Adams, B., Fackrell, K., Hall, D.A., Horobin, A., Hogan, N., Buggy, N., & Kitterick, P. T. (*in preparation*). Measurement instruments for core outcome domains in single-sided deafness intervention clinical trials.

Katiri, R., Hall, D. A., Hoare, D. J., Fackrell, K., Horobin, A., Hogan, N., Buggy, N., Van de Heyning, P., Firszt, J. B., Bruce, I. A., & Kitterick, P. T. (2022). The Core Rehabilitation Outcome Set for Single-Sided Deafness (CROSSSD) study: international consensus on outcome measures for trials of interventions for adults with single-sided deafness. *Trials*. 23(1), 764. doi: 10.1186/s13063-022-06702-1.

Katiri, R., Hall, D. A., Hoare, D. J., Fackrell, K., Horobin, A., Buggy, N., Hogan, N., & Kitterick, P. T. (2021). Redesigning a web-based stakeholder consensus meeting about core outcomes for clinical trials: formative feedback study. *JMIR Form Res*, 5(8), e28878. doi: 10.2196/28878.

Katiri, R., Hall, D. A., Killan, C. F., Smith, S., Prayuenyong, P., & Kitterick, P. T. (2021). Systematic review of outcome domains and instruments used in designs of clinical trials for interventions that seek to restore bilateral and binaural hearing in adults with unilateral severe to profound sensorineural hearing loss ('single-sided deafness'). *Trials*, 22(1), 220. doi: 10.1186/s13063-021-05160-5.

Katiri, R., Hall, D. A., Buggy, N., Hogan, N., Horobin, A., Van de Heyning, P., Firszt, J. B., Bruce, I. A., & Kitterick, P. T. (2020). Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) study: protocol for an international consensus on outcome measures for single sided deafness interventions using a modified Delphi survey. *Trials*, 21(1), 238. doi: 10.1186/s13063-020-04240-2.

Other relevant publications

Katiri, R., Fackrell, K. & Hoare D. J. (2023). Working together to overcome the challenges of evaluating treatments for single-sided deafness. British Society of Audiology (BSA) Audacity magazine. Issue 21, page 42. Accessible: https://cloud.3dissue.net/30176/30074/30346/88198/.

Gorst, S. L., Barrington, H., Brookes, S. T., Chalmers, J. R., Devane, D., Fledderus, A. C., Grosskleg, S., Hall, D. A., Harman, N. L., Hoffmann, C., **Katiri, R.**, Maeso, R., Saldanha, I. J., Tong, A., & Williamson, P. R. (2021). Online consensus meetings for COS development: issues to consider. Accessible: https://www.comet-initiative.org/Resources.

Katiri, R., Hall, D.A., & Kitterick, P.T. (2020). Developing an international core outcome set for SSD interventions. *Hearing Journal*. 73(4): 41. doi: 10.1097/01.HJ.0000661612.83232.57.

Katiri, R., Hall, D.A., & Kitterick, P.T. (2020). Developing outcome measures for Single-Sided Deafness (SSD) research. British Society of Audiology (BSA) Audacity magazine Issue 15, page 40. Accessible: https://cloud.3dissue.com/2883/3774/241465/Audacity-issue15/.

Conference presentations

Katiri, R., Hall, D.A., Hoare, D.J., Fackrell, K., Horobin, A., Hogan, N., Buggy, N., Van de Heyning, P.H., Firszt, J.B., Bruce, I.A., Kitterick, P.T. **(2022)**. Core Rehabilitation Outcome Set for Single-Sided Deafness (CROSSSD) study update. Irish Society of Hearing Aid Audiologists (ISHAA) education day, Dublin. Ireland.

Katiri, R., Hall, D.A., Hoare, D.J., Fackrell, K., Horobin, A., Hogan, N., Buggy, N., Van de Heyning, P.H., Firszt, J.B., Bruce, I.A., Kitterick, P.T. **(2021)**. The CROSSSD study: Development of a core outcome domain set for single-sided deafness interventions. Implantable Acoustic Devices (IAD) meeting, Oxford. UK.

Katiri, R. and Banerjee, A. **(2020)**. It is a better use of resources to implant people unilaterally rather than bilaterally. Cochlear Symposium debate 'Together towards tomorrow'. York. UK.

Katiri, R., Hall, D. A. and Kitterick, P. T. **(2019)**. The Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) case study. British Academy of Audiology (BAA) Clinical Research Network (CRN) session. Liverpool. UK.

Katiri, R., Hall, D. A. and Kitterick, P. T. **(2018)**. Core rehabilitation outcome set for single-sided deafness in adults: A systematic review. British Otorhinolaryngology & Allied Sciences Research Society (BOARS) autumn research meeting. Nottingham. UK.

Poster presentations

Katiri, R. (2022). The CROSSSD study infographic poster. Hearing Sciences student day. University of Nottingham, Nottingham. UK.

Katiri, R., Hall, D. A., Hoare, D.J., Fackrell, K., Horobin, A., Hogan, N., Buggy, N., Van de Heyning, P.H., Firszt, J., Bruce, I.A. & Kitterick, P. T. **(2021)**. The CROSSSD study: Working together to overcome the challenges of evaluating treatments for SSD. British Academy of Audiology (BAA) conference, Manchester. UK.

Katiri, R., Hall, D. A. & Kitterick, P. T. **(2020)**. The Core Rehabilitation Outcome Set for Single-Sided Deafness (CROSSSD) study. School of Medicine research Impact forum. University of Nottingham, Nottingham. UK.

Katiri, R., Hall, D. A., Killan, C. & Kitterick, P. T. **(2020)**. International Consensus on Outcome Measures for Single Sided Deafness Interventions. Improving Hearing Healthcare in the 21st Century British Cochlear Implant Group (BCIG) meeting. Nottingham. UK.

Katiri, R., Hall, D. A., Killan, C. & Kitterick, P. T. **(2019)**. International Consensus on Outcome Measures for Single Sided Deafness Interventions. 7th International Congress on Bone Conduction Hearing and Related Technologies (OSSEO). Miami Beach, FL. USA.

Katiri, R., Hall, D. A. & Kitterick, P. T. **(2019)**. An international consensus on outcome measures for single-sided deafness interventions. British Society of Audiology (BSA) eConference. UK.

Katiri, R., Kitterick, P. T., Killan, C. & Hall, D. A. **(2019)**. International consensus on outcome measures for single-sided deafness interventions. Hearing Sciences summer event. University of Nottingham, Nottingham. UK.

Katiri, R., Hall, D. A. & Kitterick, P. T. **(2018)**. Core rehabilitation outcome set for single sided deafness in adults: An international consensus. Audiological Research Centres in Europe (ARCHES) Conference. University of Nottingham, Nottingham. UK.

Katiri, R., Hall, D. A. & Kitterick, P. T. **(2018)**. Towards an International Consensus on Core Outcome Measures for Clinical Trials in Adult Single Sided Deafness. 15th International Conference on Cochlear Implants and Other Implantable Auditory Technology (Ci2018). Antwerp, Belgium.

Meetings and conferences attended

The following relevant local, national and international meetings and conferences have been attended, to engage with relevant stakeholders, launch the study, promote healthcare user and professionals' recruitment, distribute outputs, network, and disseminate outcomes.

Date(s)	Meeting	Location	Contribution
06/12/2022	Vestibular education seminar for vestibular physiotherapists and audiologists in Ireland	e-Seminars, Ireland	Oral presentation: Core outcome sets- what are they and why do we need them?
17/11/2022	NIHR Nottingham BRC conference 2022	East Midlands Conference Centre, Nottingham	CROSSSD infographic poster (Appendix 2) and study outcomes poster at exhibition
13/10/2022-14/10/2022	British Academy of Audiology (BAA) conference	Manchester Central Convention Complex, Manchester	CROSSSD infographic poster (Appendix 2) and study outcomes poster at exhibition
24/09/2022	Irish Society of Hearing Aid Audiologists (ISHAA) education day	Raddison Blu Hotel, Dublin	Oral presentation: How do we know what treatment is best for SSD?
07/06/2022	Manchester University NHS Foundation Trust ENT and Audiology journal club	Web based, Manchester	Oral presentation: Working together to overcome the challenges of evaluating treatments for SSD
24/05/2022	Hearing Sciences Student Day event	University of Nottingham, Nottingham	Oral presentation: The CROSSSD study: Where are we at, where are we going?; Infographic poster (Appendix 2)

12/04/2022	Belfast Health and Social Care Trust ENT and Audiology audit meeting	Web-based, Belfast	Oral presentation: The Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) initiative
28/02/2022	Research on Research (RoR): Challenges of setting up implementation research	Web-based, Southampton	Contribution to discussions
19/02/2022	Irish Academy of Audiology (IAA) educational day	Web-based, Ireland	Oral presentation on CROSSSD study core outcome set
10/01/2022	MED-EL® corporation: New SSD testing protocol	Web-based, US-led webinar	Online attendance and discussions
09/12/2021-10/12/2021	University College London (UCL) Auditory Implants masterclass	Ear Institute, University College London, London	Oral presentation on study methods and outcomes
18/11/2021-19/11/2021	British Academy of Audiology (BAA) 17th annual conference	Central Convention Centre, Manchester	Poster presentation at exhibition space for study outcomes dissemination
09/10/2021	Ménière's disease society annual conference	Web-based, National UK conference	Oral presentation on working with stakeholders to gain consensus
04/10/2021	MSc Clinical (Neurosensory) Sciences teaching session on single-sided deafness	Web-based, Aston University, Birmingham	Oral presentation on SSD interventions, outcome measures and the COS concept
30/09/2021	Implantable Acoustic Devices (IAD) conference	University of Oxford, Oxford	Oral presentation on CROSSSD core outcome set development
18/03/2021	HEARRING group: Unilateral hearing loss roundtable	Web-based	Contribution to discussions
23/02/2021	COMET: Issues to consider for web-based consensus meetings	Web-based workshop	Discussion and guidance document contribution
14/02/2021	CROSSSD overview: Outcome measures for single-sided	South Warwickshire	Web-based recorded

	deafness interventions in adults	NHS Trust, Warwick	presentation for audiologists
26/11/2020	The Victorian Childhood Hearing Impairment Longitudinal Databank (VicCHILD) meeting	Web-based, organised by Dr Robert H. Pierzycki, University of Nottingham	Slide on CROSSSD study aim and outputs
30/10/2020	Division of Clinical Neuroscience: PGR student research meeting	Web-based	N/A
25/10/2020-27/10/2020	PROMIS (Patient-Reported Outcomes Measurement Information System) international conference	Web-based	N/A
08/10/2020-03/12/2020	COMET initiative webinar series (6 seminars)	Web-based	Submitted abstract for contributed session (not accepted)
18/09/2020	PGR Research impact forum	Web-based	Poster and oral presentation
18/03/2020	Cochlear® Hear on the other side meeting on implantable solutions	Web-based	N/A
10/03/2020-11/03/2020	British Cochlear Implant Group (BCIG) annual conference: Improving Hearing Healthcare in the 21st century	Crowne Plaza, Nottingham	Poster presentation, and elevator pitch oral presentation
08/03/2020	Standardising Outcome Reporting in Gastric Cancer Surgery Research (GASTROS) consensus meeting	Web-based	International stakeholder consensus meeting observer
27/02/2020	Cochrane training event: No outcomes about us without us	Web-based	N/A
30/01/2020-31/01/2020	Cochlear® Together Towards Tomorrow symposium	Principal Hotel, York	Debate participant: 'It is a better use of resources to implant people unilaterally rather than bilaterally'

11/12/2019-14/12/2019	Osseo 2019 7th International congress on bone conduction hearing and related technologies	Miami Beach, Florida, USA	Poster presentation
01/12/2019-31/12/2019	British Society of Audiology (BSA) e-Conference	Web-based	Poster presentation
29/11/2019	OMERACT: Introduction to the Outcome measures in Rheumatology Delphi methods	Web-based	N/A
14/11/2019-15/11/2019	British Academy of Audiology (BAA) conference	ACC Exhibition Centre, Liverpool	Oral presentation at NIHR CRN session: How to get involved in clinical research and NIHR Hearing BRC exhibition support
06/11/2019	Cochlear® week workshop: Asymmetric hearing loss and cochlear implantation	Buenos Aires, Argentina	Poster and slide contribution to Jill Firszt's presentation
29/10/2019	School of Medicine Sue Watson postgraduate oral presentation event	City Hospital, Nottingham	Oral presentation
12/10/2019	Ménière's disease society annual conference	Avonmouth House, London	Poster and slide contribution to Natasha Harrington-Benton's presentation
12/10/2019	British Acoustic Neuroma Association (BANA) annual conference	Salford Royal Hospital, Manchester	Poster and slide contribution to Julie Dixon's presentation
08/10/2019	Manchester BRC Hearing Health showcase	Whitworth Gallery, Manchester	N/A, networking, study promotion
08/10/2019	Innsbruck binaurality conference by MED-EL®	Innsbruck, Austria	CROSSSD awareness slide contribution to Catherine Killan's presentation
07/10/2019	Nottingham Otology and Audiology updates course	Queen's Medical Centre, Nottingham	CROSSSD awareness slide contribution to

			Doug Hartley's presentation
18/09/2019	Withington Community Hospital audiology team presentation	Web-based	Recorded presentation: Study promotion and participant recruitment
17/09/2019	Mater Misericordiae University Hospital (MMUH) ENT weekly journal club meeting	MMUH, Dublin	Oral presentation: Study promotion and participant recruitment
09/09/2019	Queen's Medical Centre (QMC) ENT team monthly research forum	QMC, Nottingham University Hospitals NHS Trust, Nottingham	Oral presentation: Study promotion and participant recruitment
19/08/2019-23/08/2019	NIHR infrastructure Short Placement Award for Research Collaboration (SPARC) placement (Appendix 3)	NIHR Manchester BRC, Manchester	N/A, networking with other COS developers
29/07/2019	Manchester Royal Infirmary (MRI) monthly Audiology and ENT teams journal club	MRI, Manchester University NHS Foundation Trust, Manchester	Oral presentation: Study promotion and participant recruitment
24/07/2019	Hearing sciences annual summer event	University of Nottingham, Nottingham	Poster presentation
11/07/2019	NIHR Nottingham BRC annual conference	East Midlands Conference Centre, Nottingham	CROSSSD study promotion at exhibition space
10/07/2019	COMET webinar: No choice of outcomes about us without us	Wed-based	N/A
28/01/2019	INVOLVE seminar: What's new for training, learning and development in PPI?	Web-based	N/A
12/11/2018-13/11/2018	Audiological Research Centres in Europe (ARCHES) conference	University of Nottingham, Nottingham	CROSSSD study Elevator Pitch and Poster presentation

26/10/2018	ENT UK British Otorhinolaryngology and Allied Sciences Research Society (BOARS) autumn meeting	Hearing Sciences, The Ropewalk, Nottingham	Oral presentation
05/09/2018	PubhD Dublin: Can you explain your PhD in the pub?	J. T. Pim's, Dublin	CROSSSD study presentation to the general public
27/06/2018-30/06/2018	Ci2018.org 15th International Conference on Cochlear implants and implantable auditory technology	Antwerp, Belgium	Poster presentation / CROSSSD study launch
19/06/2018-20/06/2018	NIHR Nottingham BRC anniversary conference	East Midlands Conference Centre, Nottingham	Workshop session 'Now hear this!' Advancing Hearing Science through collaborative research
04/06/2018-06/06/2018	Advances in auditory implants course	Ear Institute, University College London, London	Networking
14/12/2017	Introduction to Good Clinical Practice (GCP): A practical guide to ethical and scientific quality standards in clinical research	University of Nottingham, Nottingham	N/A
12/12/2017	NIHR webinar: How clinical academic careers can benefit the whole NHS	Web-based	N/A
11/10/2017	NIHR Manchester BRC Hearing Health showcase	University of Manchester, Manchester	Healthcare professionals and clinical researcher engagement

Dissemination activities

- NIHR Clinical Research Network (CRN) East Midlands regional updates. **Study in the spotlight: CROSSSD** https://mailchi.mp/e2f40a0b3dd2/new-and-updates-from-nihr-crn-east-midlands?e=%5bUNIQID%5d (August 2022).
- British Society of Hearing Aid Audiologists **(BSHAA) People magazine article** Audiology News section. 'Single-sided deafness: Measuring the effects of treatments' https://www.flipsnack.com/bshaa/bshaa_people_summer_2022_web/full-view.html (July 2022).
- British Acoustic Neuroma Association **(BANA) Headline News** Summer 2022 edition, magazine article: 'Research -CROSSSD study' https://bana-uk.com/account/ (July 2022).
- **Hearing Sciences newsletter** Research News section: CROSSSD Study Outcomes promotion week! https://sway.office.com/epPUf9tkXxSFxCK6?ref=email (May 2022).
- **Hearing Link** news 'Single sided deafness research' https://www.hearinglink.org/news/202204/single-sided-deafness-research/ (April 2022).
- **University of Nottingham** communications **press release** 'Study looks at effects of single-sided deafness treatments on patients' https://www.nottingham.ac.uk/news/study-looks-at-effects-of-single-sided-deafness-treatments-on-patients (March 2022).
- **Evidently Cochrane** sharing health evidence you can trust **blog**, 'Single-sided deafness: Working together to improve research into treatments' https://www.evidentlycochrane.net/single-sided-deafness-working-together-to-improve-research-into-treatments/ (March 2022).
- **Ménière's disease society news** 'Update on research into SSD treatments' https://www.menieres.org.uk/news/entry/3568/update-on-research-into-single-sided-deafness-treatments (March 2022).

- NIHR **Nottingham BRC news story** 'BRC Study develops a core outcomes set for single-sided deafness' https://nottinghambrc.nihr.ac.uk/about-nottingham-brc/news/3781-brc-study-develops-a-core-outcomes-set-for-single-sided-deafness (February 2022).
- British Cochlear Implant Group **(BCIG) newsletter** article 'The CROSSSD study: Development of a core outcome set for single-sided deafness interventions' https://www.bcig.org.uk/the-crosssd-study-development-of-a-core-outcome-set-for-single-sided-deafness-interventions-2/ (February 2022).
- University of Nottingham **Hearing Matters blog**, compiled post 'Helping research improve treatments for single-sided deafness more quickly: An agreement on what is important to measure' https://blogs.nottingham.ac.uk/hearingloss/2022/02/25/helping-research-improve-treatments-for-single-sided-deafness-more-quickly-an-agreement-on-what-is-important-to-measure/ (February 2022).
- Composed a week long daily reflection thread on **Twitter @CROSSSD_** account on the study's background, aim, methods, results, learning, implications of adoption of the core outcome set, a thread of 25 tweets published https://twitter.com/CROSSSD_/status/1495657540201246720?s=20&t=_9PEwnbOa9q3I_sr4XuPCg (February 2022).
- CROSSSD study outcomes general public core outcome set **promotional video** development https://youtu.be/BcUy_2bzHZw (ScienceSplained, 2022b) (February 2022).
- **Ménière's disease society website** contribution 'Non-surgical treatments information and support' https://www.menieres.org.uk/information-and-support/treatment-and-management/other-non-surgical-treatments (May 2021).
- University of Nottingham **Hearing Matters blog**, supported study participant Chris Parker to compile post 'Acoustic neuroma 20 years on in 2021' https://blogs.nottingham.ac.uk/hearingloss/2021/05/27/acoustic-neuroma-20-years-on-in-2021/ (May 2021).
- **Sudden Hearing Loss Support website**, compiled information on hearing interventions section 'What if your hearing does not recover?'

https://suddenhearingloss.support/2021/03/21/what-if-your-hearing-does-not-recover/ (April 2021).

- University of Nottingham **Hearing Sciences newsletter** Issue 3 post 'CROSSSD study systematic review: A substantial contribution to the SSD literature' https://uniofnottm.sharepoint.com/sites/o365-ms-hearing-sciences/SitePages/Newsletters.aspx (April 2021).
- **My Hearing Loss story blog**, supported study participant Carly Sygrove to compile public awareness post 'Working together to develop the research of treatments for single-sided deafness' https://myhearinglossstory.com/2020/08/03/working-together-to-develop-the-research-of-treatments-for-single-sided-deafness/ (August 2020).
- **Cochlear® Atlantics clinical bulletin** 'The Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) study' independent research article. For Cochlear® internal use only (June 2020).
- **My Hearing Loss story blog**, supported study participant Carly Sygrove to compile participant recruitment post 'CROSSSD Study: You can help with vital research!' https://myhearinglossstory.com/2019/09/26/crosssd-study-you-can-help-with-vital-research/ (September 2019).
- CROSSSD study Delphi participant **recruitment video** development https://youtu.be/CFBC3Wv5_8s (ScienceSplained, 2019) (June 2019).
- CROSSSD study dedicated **Twitter account @CROSSSD_** https://twitter.com/CROSSSD_ (December 2017).
- University of Nottingham Hearing Sciences dedicated **CROSSSD study website** www.nottingham.ac.uk/go/CROSSSD (November 2017).

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List of abbreviations

ABI	Auditory Brainstem Implant
ACIA	American Cochlear Implant Alliance
AHL	Asymmetric Hearing Loss
APHAB	Abbreviated Profile of Hearing Aid Benefit
APSQ	Audio Processor Satisfaction Questionnaire
ARCHES	Audiological Research Centres in Europe
ARIG	Adult Rehabilitation Interest Group
BAA	British Academy of Audiology
BAHA	Bone Anchored Hearing Aid
BBSS	Bern Benefit in Single-Sided Deafness
BCIG	British Cochlear Implant Group
BKB-SIN	Bamford-Kowal-Bench Sentence in Noise test
BOARS	British Otolaryngology & Allied Sciences Research Society
BRC	Biomedical Research Centre
BSA	British Society of Audiology
BSHAA	British Society of Hearing Aid Audiologists
CENTRAL	Cochrane Central Register of Controlled Trials
CES-D	Center for Epidemiologic Studies Depression
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
CI	Chief investigator
CI	Cochlear implant
CID	Central Institute for the Deaf
CINAHL	Cumulative Index of Nursing and Allied Health Literature
CNC	Consonant-Nucleus-Consonant
CNC	Consonant-Noun-Consonant
COMET	Core Outcome Measures in Effectiveness Trials
COMiT'ID	Core Outcome Measures in Tinnitus, International Delphi
CONSORT	Consolidated Standards of Reporting Trials
COPE	Coping Orientation to Problems Experienced
COS	Core outcome set
COSI	Client Orientated Scale of Improvement
COSMIN	Consensus-based Standards for the selection of health Measurement Instruments
COS-STAD	Core Outcome Set-STAndards for Development
COS-STAR	Core Outcome Set-STAndards for Reporting
COVID-19	COrona VIrus Disease
CPHI	Communication Profile for Hearing Impaired
CPMS	Central Portfolio Management System
CRF	Case Report Form
CRN	Clinical Research Network
CROS	Contralateral Routing of Signals

CROSSSD	Core Rehabilitation Outcome Set for Single-Sided Deafness
CROWN	CoRe Outcomes in Women's and Newborn health
CVA	Cerebrovascular accident
DHI	Dizziness Handicap Inventory
ECHO	Expected Consequences of Hearing aid Ownership
EMA	European Medicines Agency
EMBASE	Excerpta Medica dataBASE
EMSQ	Entific Medical System Questionnaire
ENT	Ear, Nose, Throat
EQ-5D/ EuroQol-5	European Quality of life five dimension
EU	European Union
FDA	Food and Drug Administration
fMRI	functional Magnetic Resonance Imaging
GAD	Generalized Anxiety Disorder
GASTROS	Standardising Outcome Reporting in Gastric Cancer Surgery Research
GBI	Glasgow Benefit Inventory
GCP	Good Clinical Practice
GHABP	Glasgow Hearing Aid Benefit Profile
GHSI	Glasgow Health Status Inventory
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HADS	Hospital Anxiety and Depression Scale
HCRW	Health and Care Research Wales
HHIA	Hearing Handicap Inventory for Adults
HINT	Hearing in Noise Test
HISQUI-NL	Hearing Implant Sound Quality Index
HIV	Human immunodeficiency virus
HOME	Harmonising Outcome Measures for Eczema
HRA	Health Research Authority
HSM	Hochmair-Schulz-Moser
HTA	Health Technology Assessment
HU	Healthcare User
HUI	Health Utilities Index
ICER	Incremental Cost-Effectiveness Ratio
ICH	International Conference on Harmonisation
ICTRP	International Clinical Trials Registry Platform
IMMPACT	Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials
IOI-HA	International Outcome Inventory for Hearing Aids
IRAS	Integrated Research Application System
ISRCTN	International Standard Randomised Controlled Trials Number
MACAS	Monaural Auditory Capacity Assessment Scale
MEDLINE	Medical Literature Analysis and Retrieval System Online
MEI	Middle Ear Implant

mOMEnt	management of Otitis Media with Effusion in children with cleft palate
MRC	Medical Research Council
MYMOP	Measure Yourself Medical Outcome Profile
NCIQ	Nijmegen Cochlear Implant Questionnaire
NF1	Neurofibromatosis type 1
NF2	Neurofibromatosis type 2
NHANES	National Health and Nutrition Examination Survey
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NSA	Non-substantial amendment
OlSa	Oldenburg Sentence Test
OMERACT	Outcome Measures in Rheumatoid Arthritis Clinical Trials
PAC	Primary auditory cortex
PI	Principal investigator at a local centre
PIC	Participant identification centre
PICOS	Population, Intervention, Comparator / Control, Outcomes, Setting
PIS	Participant Information Sheet
PONCHO	Prioritising Outcomes iN Childhood Hearing lOss
PoPPIE	People and Patient Participation, Involvement and Engagement
PPI	Patient and Public Involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROM(s)	Patient Reported Outcome Measure(s)
PROSPERO	International prospective register of systematic reviews
PSQ	Perceived Stress Questionnaire
PTA	Pure Tone Audiometry
QALY	Quality-Adjusted Life Year
QoL	Quality of Life
QuickSIN	Quick Speech-in-Noise
R&D	Research and Development
REC	Research Ethics Committee
SADL	Satisfaction with Amplification in Daily Life
SF-36	36-Item Short Form Survey Instrument
SHQ	Spatial Hearing Questionnaire
SNHL	Sensorineural Hearing Loss
SNR	Signal-to-Noise Ratio
SPARC	Short Placement Award for Research Collaboration
SPIN	Speech Intelligibility In Noise
SPSS	Statistical Package for Social Sciences
SRQR	Standards for Reporting Qualitative Research
SRT(s)	Speech Reception Threshold(s)
SSD	Single-sided deafness
SSNHL	Sudden Sensorineural Hearing Loss
SSQ	Speech, Spatial and Qualities hearing scale

STSS	Subjective Tinnitus Severity Scale
TBQ	Tinnitus Burden Questionnaire
TFI	Tinnitus Functional Index
THI	Tinnitus Handicap Inventory
THQ	Tinnitus Handicap Questionnaire
TM	Trademark
TMRP	Trials Methodology Research Partnership
TQ	Tinnitus Questionnaire
TRQ	Tinnitus Reaction Questionnaire
TRS	Tinnitus Rating Scale
UCL	University College London
UHL	Unilateral hearing loss
UK	United Kingdom
UNITI	Unification of Treatments and Interventions for Tinnitus Patients
UoN	University of Nottingham
US(A)	United States (of America)
VAS	Visual Analogue Scale
WHO	World Health Organization
WHOQOL-BREF	World Health Organization Quality of Life short form survey

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Thesis outline

Measuring the therapeutic benefit(s) or harm(s) of interventions in clinical trials, or clinical practice, has historically been challenging in the field of single-sided deafness (SSD). This thesis assembles the background, and a series of studies, that work towards a common goal: forming a stakeholder consensus on outcome measurement for device-based interventions that seek to restore bilateral and binaural hearing in adults with single-sided deafness (SSD). The thesis comprises of six chapters, illustrated in the schematic outline in Figure 0-1.

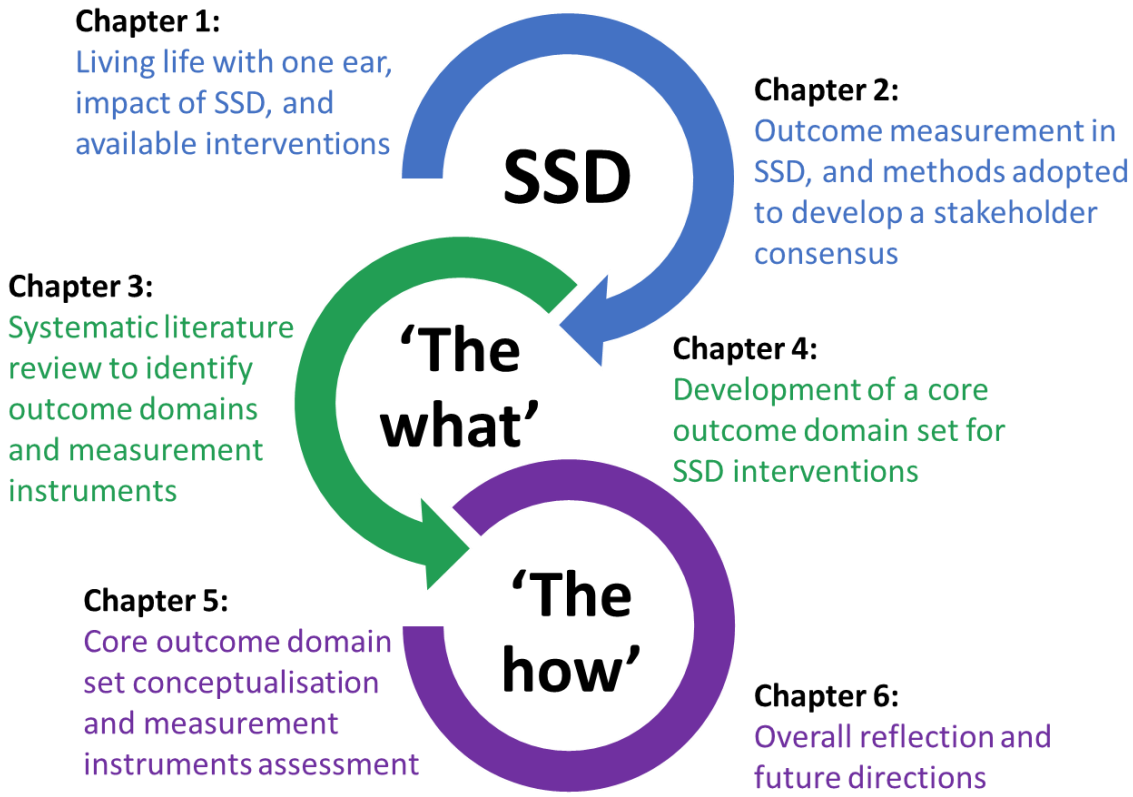

Figure 0-1. Schematic outline of the thesis.

Chapter 1 outlines the aetiologies of SSD in adulthood, the associated functional, psychological, social, and other related consequences. The available device-based interventions for SSD are also listed in this chapter, alongside a brief overview of the measurement methods adopted by clinicians or researchers to date to define their

benefits or harms. This chapter sets the scene and provides a rationale for the thesis aims and objectives.

Chapter 2 describes the methods adopted, the theoretical background, and detailed rationale for adopting the chosen methodology. This chapter focuses on the development of the Core Outcome Set for Single-Sided Deafness (CROSSSD) initiative, and the design of an international consensus process to develop a core outcome set for SSD interventions, comprising an agreed minimum set of outcome domains relevant to both patients and professionals.

Chapter 3 encompasses the systematic review which aimed to identify outcome domains and measurement instruments reported in published clinical studies evaluating rerouting and/or restoring interventions in adults with SSD.

Chapter 4 describes how the systematic review findings were used to generate a 'long list' of candidate outcomes to be rated by relevant stakeholders, according to whether each is important and critical to determine the benefit(s) or harm(s) of an SSD intervention. The purpose of the studies described in Chapter 4 was to define an agreed minimum standard for 'the what' is critically important to assess in all clinical trials evaluating SSD interventions: a core outcome domain set.

Chapter 5 describes a qualitative study that concentrates on developing an in-depth understanding of each concept of each outcome domain in the core outcome domain set. The second study discussed in this chapter describes how the outcome domains were operationalised to help with the assessment of candidate measurement instruments. This chapter suggests 'the how' the core outcome domain set should be measured.

Chapter 6 concludes the thesis. The chapter summarises the objectives of the CROSSSD study, recaps the contributions made to the field, and suggests future directions.

The thesis closes with a reflective statement by the author.

A high-level Gantt chart that illustrates the project schedule can be found on Figure 0-2. The chart lists the tasks performed during the project on the vertical axis, and time intervals on the horizontal axis.

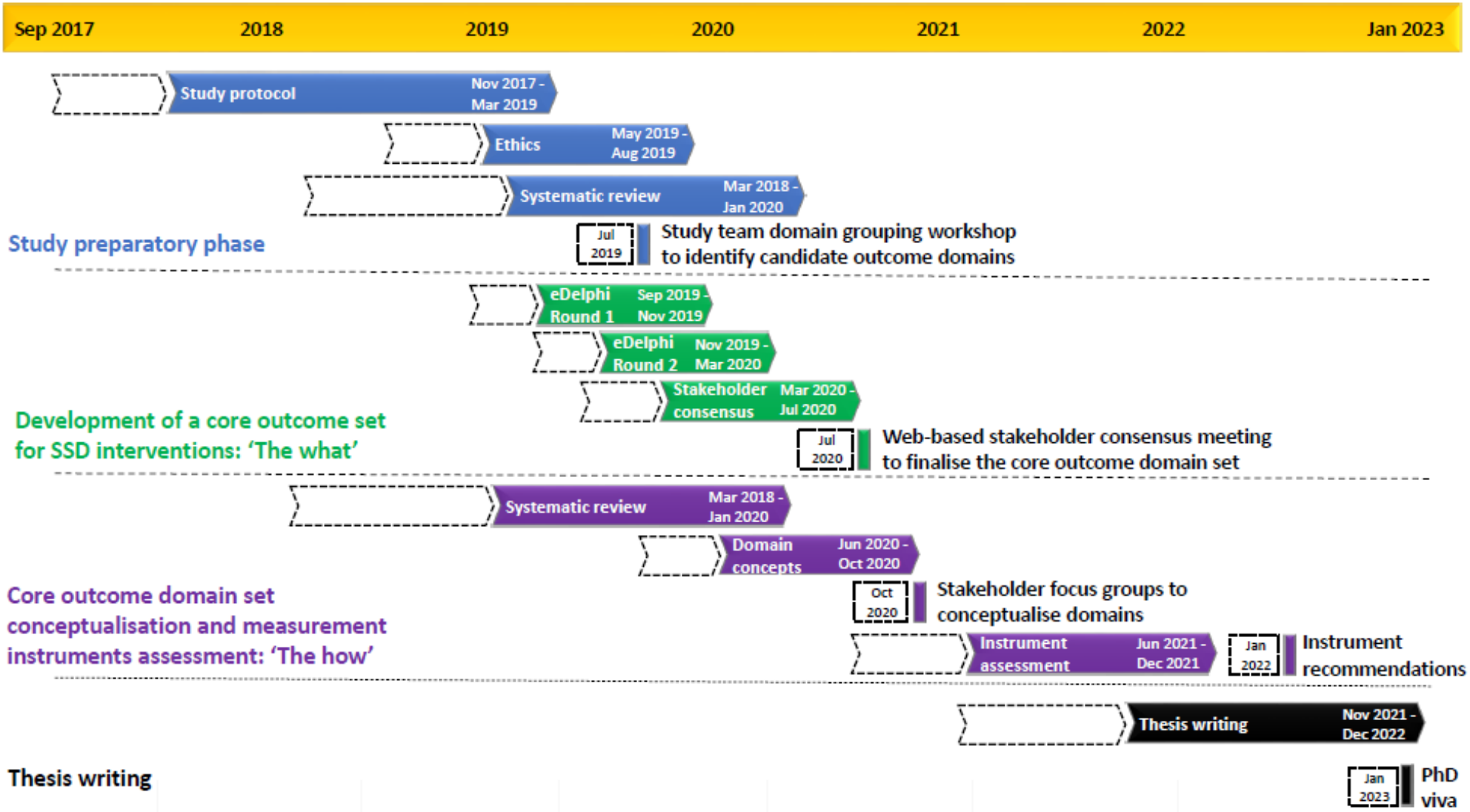

Figure 0-2. Gantt chart summarising the project schedule and time-lines.

1. Living life with one ear only

1.1 Single-sided deafness

Single-sided deafness (SSD) arises when there is normal or near-normal hearing in one ear and a severe-to-profound sensorineural (inner ear related) hearing impairment in the other ear (Van de Heyning et al., 2017). SSD is defined by a specific audiological classification: the mean pure tone average (PTA) at frequencies of 0.5, 1, 2 and 4 kHz should be ≥70 dB HL on the poorer ear, and ≤30 dB HL on the better ear, with an interaural threshold gap of ≥40 dB HL. This definition is in line with a previous definition published in a proceedings paper which aimed to differentiate between SSD and asymmetric hearing loss (AHL) (Vincent et al., 2015). With regards to terminology, SSD is sometimes used interchangeably with unilateral hearing loss (UHL) which may incorporate conductive (middle ear related) or mixed (both middle and inner ear related) hearing losses (BSA, 2018). Developing a consensus around the definition (Van de Heyning et al., 2017) allowed us to differentiate between SSD and AHL when comparing data.

1.1.1 Chapter aims and objectives

Chapter 1 aims to provide a narrative overview of SSD and its consequences on adults living with the condition, and available device-based interventions.

The chapter objectives were:

(i) To outline the aetilogies of SSD in adulthood

(ii) To outline the associated functional, psychological, social, and other related consequences of SSD

(iii) To list the available device-based interventions for SSD

(iv) To provide a brief overview of the measurement methods adopted by clinicians or researchers to date to define their benefits or harms of interventions

(v) To set the scene and provide a rationale for the thesis aims and objectives.

1.1.2 Aetiology

SSD can be congenital, of sudden onset, or progressive. The most common causes of SSD in adulthood are sudden and idiopathic.

The cause of SSD can be congenital (Everberg, 1960; Huttunen et al., 2019; Widen et al., 2000). Cochlear nerve deficiency is the most common cause of paediatric SSD (Usami et al., 2017), followed by sudden idiopathic sensorineural hearing loss, inner ear malformation, head trauma, central nervous system tumour(s), or in-utero or post-natal infections such as cytomegalovirus or meningitis (Dewyer et al., 2022; Ghogomu et al., 2014). The causes can also be genetic, secondary to family history, or syndromic (Fitzpatrick et al., 2017).

In adulthood, SSD can be of sudden causes secondary to conditions like Ménière's disease (an inner ear disorder leading to hearing loss and balance problems) (Wu et al., 2019), follow viral infections such as labyrinthitis, idiopathic (Chandrasekhar et al., 2019; Mirian and Ovesen, 2020; Simani et al., 2022), or due to autoimmune systemic diseases (Li et al., 2018; McCabe, 1979; Rossini et al., 2017). Sudden onset of SSD can be caused by temporal bone fracture(s) following head trauma , or iatrogenic following otological surgery (Bird and Bergin, 2018; Deep et al., 2021). More recently, case reports of sudden onset SSD following COrona VIrus Disease (COVID-19) (Asfour et al., 2021; Koumpa et al., 2020; Pokharel et al., 2021), or attributed to immunisation for COVID-19 with SARS-CoV-2 mRNA vaccines (Ekobena et al., 2022) have been documented.

SSD can also be progressive, for example, in cases of cholesteatoma (abnormal collection of skin cells around the eardrum and middle ear) (Usami et al., 2017), cerebellopontine angle tumour(s), neurofibromatosis (a genetic disorder that causes tumours to form on nerve tissue) (Jia et al., 2020), or vestibular schwannoma (a non-cancerous tumour that grows on the VIIIth vestibulocochlear cranial nerve) (Daniels et al., 2000; Douglas et al., 2007; Staecker et al., 2000). SSD can also follow surgical removal of vestibular schwannoma (Sanna et al., 2021; Staecker et al., 2000).

Other causes including ototoxicity, vascular conditions, demyelinating conditions, Lyme disease, otosyphilis, human immunodeficiency virus, and miscellaneous causes have been proposed (Chau et al., 2010; García-Berrocal et al., 2006;Lee and Baloh, 2005; Peltomaa et al., 2000; Schreiber et al., 2010; Timon and Walsh, 1989). Although the causal relationship between these causes and unilateral sensorineural hearing loss is difficult to verify, these causes should be out-ruled in cases of SSD in adulthood (Chandrasekhar et al., 2019;Lawrence and Thevasagayam, 2015; Twigg et al., 2020), and be treated with steroids if indicated (Herrera et al., 2019).

1.1.3 Associated otologic features

SSD can be associated with tinnitus, which is defined as 'the conscious awareness of a tonal or composite noise for which there is no identifiable corresponding external acoustic source' and/or tinnitus disorder, which arises when tinnitus is 'associated with emotional distress, cognitive dysfunction, and/or autonomic arousal, leading to behavioural changes and functional disability' (De Ridder et al., 2021). It is estimated that approximately 80% of patients with sudden idiopathic sensorineural loss have tinnitus (Levy et al., 2020; Nosrati-Zarenoe et al., 2007; Schreiber et al., 2010). It is hypothesised that this can be due to reduced or absent auditory input that can lead to changes in neural activity (Eggermont and Roberts, 2012). Studies that used the Tinnitus Handicap Inventory (THI) (Newman et al., 1996) and the Hearing Handicap Inventory for Adults (HHIA) (Newman et al., 1991) to investigate the prevalence of tinnitus in those with idiopathic SSD showed that two thirds of patients reported intrusive tinnitus as per THI scores (Chiossoine-Kerdel et al., 2000). Two 100-mm Visual Analogue Scales (VAS) indicating the loudness of the tinnitus, and distress evoked by the tinnitus showed correlations between tinnitus loudness, distress, and hearing handicap (Chiossoine-Kerdel et al., 2000). Of those diagnosed with SSD secondary to Ménière's disease 78.6% report tinnitus (Young et al., 2022). In a retrospective study including 22 individuals with a vestibular schwannoma, tinnitus burden was measured using the (THI) (West et al., 2022). The authors highlighted that the methods adopted to date for evaluation of tinnitus may be a limitation due to participants being inadequately instructed to distinguish between the ears or situations (e.g., when wearing the processor or not). Tinnitus is also experienced by those who sustain SSD

due to endolymphatic hydrops, labyrinthitis (an inner ear infection), trauma, iatrogenic causes, due to herpes zoster oticus, otosclerosis, cholesteatoma, or cerebrovascular accident (CVA) (Arndt, Aschendorff, et al., 2011; Buechner et al., 2010; Mertens et al., 2016; Ramos Macías et al., 2018; Van de Heyning et al., 2008).

Alongside the experience of tinnitus, some people with SSD also experience hyperacusis, which has been attributed to excessive gain increase in the central auditory pathway (Ramos Macías et al., 2018). Hyperacusis is a chronic disorder of loudness perception (Tyler et al., 2014) that involves reduced tolerance or increased sensitivity to regular noises (Adams et al., 2021; Baguley and Hoare, 2018; Fackrell et al., 2019). Hyperacusis is sometimes used interchangeably with loudness recruitment, which is a common symptom of peripheral hearing loss and is defined as an abnormally fast growth of loudness perception of sound intensity (Shi et al., 2022). Hyperacusis in SSD has been linked to reduced median scores on the attention, social, and emotional sub-scales of the Khalfa et al. (2002) hyperacusis questionnaire (Mertens et al., 2016). The hyperacusis questionnaire however focuses on the psychological and social aspects of hearing, rather than on hyperacusis itself (Mertens et al., 2016). The sound hypersensitivity questionnaire (Herráiz et al., 2006) was used in a Spanish multi-centre study (Ramos Macías et al., 2018) to measure the impact of loud sounds and noise on quality of life in patients with SSD. It has 15 questions reported in four grades (Grade I: mild 1-10, Grade II: moderate 11–17, Grade III: severe 18–25, and Grade IV: very severe: 26–45) for three subscales of behaviours, cognitive reactions, and emotional reactions. Patients with unilateral hearing loss score on average ‘severe’ degree (Grade III) of incapacity (Ramos Macías et al., 2018).

SSD due to sudden causes has been associated with aural fullness, which is described as ‘ear pressure’, ‘sense of fullness’, or ‘clogging sensation’ (Park et al., 2012; Sakata and Kato, 2006; Westerlaken et al., 2003). Aural fullness in sudden onset losses has no relationship to gender and age at the time of first assessment, or two months after hearing thresholds are stabilised; however it is more common in low-frequency hearing loss audiograms (Sakata et al., 2008). In those diagnosed with Ménière’s disease, 57.1% report unilateral aural fullness (Young et al., 2022), which is attributed

to pressure imbalances between the round and oval windows in the inner ear (Sakata et al., 2008).

The vestibular (balance) system can also be involved in 30-40% of cases with sudden unilateral loss (Nakashima and Yanagita, 1993; Schreiber et al., 2010; Shih et al., 2017). In Ménière's disease, individuals experience acute vestibular dysfunction (Thai-Van et al., 2001; Wu et al., 2019) due to decreased potassium levels in the endolymph sector and increased potassium levels in the perilymphatic sector of the inner ear balance system (Lawrence and McCabe, 1959). In cases of SSD due to VIIIth vestibulocochlear cranial nerve involvement individuals can experience instability while moving their head, imbalance, or vertigo (Greene and Al-Dhahir, 2022; Nicoucar et al., 2006).

1.1.4 Cortical changes in single-sided deafness

Studies have also reported central auditory system re-organisation in cases of unilateral deafness (Alzaher et al., 2021; Legris et al., 2018). These studies however, pool together data from individuals with various degrees of hearing loss that fall into the highly asymmetrical hearing loss category, as opposed to an SSD cohort explicitly. In adults, brain reorganisation is detectable 5 weeks after onset of SSD (Suzuki et al., 2002), and functional magnetic resonance imaging (fMRI) studies demonstrated that reorganisation plateaus after 1 year (Bilecen et al., 2000). Magnetoencephalography studies of brain activation during performance of auditory syllable sequence reproduction tasks demonstrate that in adult-onset SSD there is both functional and structural alterations to the dorsal temporal and frontal-parietal areas of the brain (Shang et al., 2018). SSD also leads to physiological lateralisation of auditory cortical activity, which has an impact on auditory spatial abilities (Karoui et al., 2022). Speech-evoked cortical auditory evoked potentials studies show that the side of deafness can have an effect (Cañete et al., 2019). In this study with 13 participants with unilateral hearing loss, Cañete et al. (2019) found that there was a greater effect of right ear than left ear hearing loss on N1 amplitude hemispheric asymmetry and N1 latencies evoked by speech syllables in noise. N1 amplitudes correlated with speech scores, larger N1 amplitudes were associated with better speech recognition in noise scores. N1 latencies were delayed (in the better ear) and amplitude hemisphere asymmetry

differed across unilateral hearing loss participants as a function of side of deafness, mainly for right-sided deafness. An asymmetry of neuronal activity of the inferior colliculus and primary auditory cortex (PAC) has been demonstrated using ^{18}F-FDG PET imaging studies (Speck et al., 2020, 2022). There is a significant reduction in regional metabolism of both the inferior colliculus and PAC contralateral to the most hearing-impaired ear, when compared with the ipsilateral side. Asymmetric hearing loss has a significant impact on glucose metabolism of the auditory pathway (Speck et al., 2020), which in turn can negatively influence audiological performance (e.g., speech recognition in noise) following cochlear implantation (Speck et al., 2022). Speck et al. (2022) enrolled nine participants with either asymmetric hearing loss, or SSD, with heterogeneous aetiology, disease onset, and duration of deafness, so they suggest larger longitudinal studies to be able to confirm their hypothesis.

1.1.5 Prevalence and incidence of single-sided deafness

Prevalence is a measure of the frequency of a disease or health condition in a population at a particular point in time (Department of Health, 2022). The prevalence of unilateral hearing loss is estimated to be 3.0 to 6.3% of the general population, depending on the audiometric criteria definition used (Ross et al., 2010). In the United States of America (USA), according to data collected by the National Health and Nutrition Examination Survey (NHANES) it is estimated that 1.5% of the population have moderate or worse hearing loss in one ear (Golub et al., 2018). The prevalence of SSD in newborns is estimated to be 0.5 per 1,000 (Watkin and Baldwin, 2012), and prevalence increases with age (Shargorodsky et al., 2010). It has been suggested that SSD affects between 12 and 27 individuals in every 100,000 of the general population (Kitterick et al., 2014). More recently, it has been estimated that 10.4 to 25.4 individuals per 100,000 are at risk for SSD (Sprinzl and Wolf-Magele, 2016); with 5 to 20 per 100,000 due to sudden sensorineural hearing loss (SSNHL) (Plaza et al., 2011); although a later study that used data from a medical and pharmaceutical claims database containing information for more than 60 million unique patients estimated the prevalence of SSNHL in the US to be 27 per 100,000 (Alexander and Harris, 2013); 1.1 per 100,000 due to acoustic neuroma removal (Gal et al., 2010); and 4.3 per 100,000 due to Ménière's disease (Kotimaki, 2003). The NHANES epidemiologic study

in the USA estimated the prevalence of SSD in adults to be 0.14% (Kay-Rivest et al., 2021); and to be higher in females (0.17%) versus males (0.11%). The NHANES data also demonstrated that the prevalence of SSD was higher in individuals aged 60-79 years (prevalence of 0.25%) compared to younger individuals (0.11% in ages 20-39 years, and 0.11% in ages 40-59 years).

Incidence is a measure of the number of newly diagnosed cases within a particular time period (Department of Health, 2022). In children, it is estimated that the incidence of unilateral hearing loss is 0.6 to 0.7 per 1,000 live births in the USA (Hunter et al., 2022). In 2006, it was estimated that the incidence of SSD in the UK was 7500 new adult cases per year (Baguley et al., 2006). Extrapolating to the current population in the UK of approximately 67 million, as per the Office for National Statistics[4], the incidence is estimated to be approximately 9000 new cases per year. Baguley et al. (2006) calculated that the highest incidence of SSD per 100,000 of the adult population per year was due to SSNHL, followed by Ménière's disease, and vestibular schwannoma being the lowest.

1.2 Impact of single-sided deafness

The disabling effects of SSD (speech, spatial, qualities domains), and impact of these effects on the degree of handicap experienced by the hearing impaired individual, vary considerably (Gatehouse and Noble, 2004; Noble and Gatehouse, 2004). Evidence stemming back to qualitative research studies published in the 1960s refers to the significant degree of communication impairment caused by SSD in everyday life (Giolas and Wark, 1967; Harford and Barry, 1965; Harford and Dodds, 1966).

1.2.1 Why we need two ears

Good hearing in both ears (binaural hearing) helps us deal with everyday listening tasks (Dwyer et al., 2014; Snapp and Ausili, 2020). Processing speech in complex environments gives listeners with binaural hearing a benefit of 4-10 dB in processing

[4] www.ons.gov.uk

speech (Hawley et al., 2004) in comparison to monaural (hearing with one ear only). Benefits of binaural hearing include understanding speech in noisy or reverberant environments and locating where sounds such as the telephone or car traffic are coming from (Gallun, 2021; Hawley et al., 2004; Levitt and Rabiner, 1967; Snapp, 2019; Snapp and Ausili, 2020).

Sound localisation in the horizontal (azimuth) plane relies mainly on interaural time differences (ITDs) and interaural level differences (ILDs) (Agterberg et al., 2012; Pedley and Kitterick, 2017; Rothpletz et al., 2012). In other words, the auditory system helps us judge our positioning in space by dynamically calculating our interaction with signals that are constantly changing in terms of pitch (frequency spectrum), level (intensity), and time (latency) (Akeroyd, 2006; Arndt, Aschendorff, et al., 2011; Snapp and Ausili, 2020).

The integration of acoustic information from both ears is essential for spatial awareness (Güldner et al., 2013; Karoui et al., 2022), for example, determining where sounds are coming from (Douglas et al., 2007; Pedley and Kitterick, 2017; Snapp, 2019). ITD is the difference in arrival time (latency) for a stimulus to reach both ears, and ILD is the difference in the intensity (level) of a stimulus reaching both ears; and serves to provide critical information for speech processing, localisation, the segregation of auditory streams and the perception of fused sounds (Akeroyd, 2006; Snapp and Ausili, 2020).

Although there can be a degree of adaptation in certain monaural listeners (Rothpletz et al., 2012; Slattery and Middlebrooks, 1994) and possible long-term compensation for loss of binaural cues (Alzaher et al., 2021; Liu et al., 2018); localisation abilities can be severely impaired in those hearing monaurally (Agterberg et al., 2012; Hoth et al., 2016; Pedley and Kitterick, 2017; Snapp, 2019; Wazen et al., 2005). A further complication for monaural listeners is introduced by the head shadow effect, where the head acts as an acoustic barrier to signals that travel from one side of the head to the other, which can lead to significantly impaired speech understanding (Akeroyd, 2006; Pedley and Kitterick, 2017; Snapp, 2019). In cases of SSD, speech originating

from the poor-hearing side of the head is reduced in intensity by 6.4 dB by the time it reaches the normal-hearing ear, therefore it arrives distorted due to loss of high-frequency information from the speech spectrum (McLeod et al., 2008).

1.2.2 Functional difficulties experienced by adults with single-sided deafness

Due to the challenges arising from monaural access to sound, individuals with SSD have difficulties dealing with everyday tasks such as speech recognition (Dwyer et al., 2014; Lieu et al., 2010) and impaired ability to understand speech in the presence of background noise (Akeroyd, 2006; Douglas et al., 2007; Firszt et al., 2017; Kitoh et al., 2022; McLeod et al., 2008; Peters et al., 2021; Rothpletz et al., 2012; Vannson et al., 2017; Welsh et al., 2004; Wie et al., 2010). It is estimated that there is a reduction in speech understanding by approximately 3 dB in signal-to-noise ratio (SNR) in cases of SSD (McLeod et al., 2008). SNR is a measure that compares the level of a signal (e.g., a speech sound) to the level of background noise. A ratio greater than 0 dB indicates more signal than noise, which would make speech understanding easier. In cases of SSD, speech understanding is reduced due to reduced signal loudness detected by the hearing impaired individual.

Different features of the conversation context, for example the complexity of the acoustic environment, the type or loudness of the background noise, or the number of people in a group can influence speech perception and impact on individuals' need to modify their communication strategies (Hadley et al., 2021). Adults with unilateral hearing loss are more likely to report a higher level of communication difficulties in comparison to normal-hearing adults (Choi et al., 2021; Dwyer et al., 2014). SSD also imposes difficulties localising where sounds are coming from (Grossmann et al., 2016), and poor spatial awareness (Pedley and Kitterick, 2017; Snapp and Ausili, 2020; Welsh et al., 2004). SSD can also have an impact on music appreciation. Music can sound unnatural, unpleasant and indistinct, lack perceptual qualities such as stereo sound, and be confounded by distortion effects and tinnitus (Meehan et al., 2017).

Moreover, SSD is associated to increased listening effort when compared to normally hearing individuals (Dwyer et al., 2014; Lopez et al., 2021). Listening effort is defined as

the mental exertion required to attend to and understand an auditory message (McGarrigle et al., 2014). Hearing impaired listeners may experience increased listening effort in challenging listening situations in comparison to normally hearing individuals, even if they use hearing aids (Alhanbali et al., 2017). The constant effort applied by a listener with SSD to adjust to their listening environment is fatiguing, and can be unsustainable for many (Snapp, 2019). The real-world impact of increased fatigue is dependent on personal factors and lifestyle (Holman et al., 2019), and can influence social activity level (Holman, Drummond, et al., 2021). Fatigue could arise due to decreased audibility of sounds, and in part, increased requirement for listening effort (McGarrigle et al., 2014). Other factors such as related challenges in auditory processing, and increased listening effort required in demanding listening environments have been proposed (Hornsby et al., 2016; Ohlenforst et al., 2017; Peelle, 2018). Associations to work, social, or physical activity levels, and well-being are also relevant and have implications on daily-life fatigue in people with hearing loss (Holman, Hornsby, et al., 2021). Objective measures of pupil dilation as an indicator of listening effort during listening tasks demonstrate that the individual's motivation is a factor that can influence objective measures of fatigue (Wang et al., 2018). Qualitative studies interviewing people with hearing loss identified factors such as lifestyle, personality, situational control, the relationship with those in conversation and the attribution of blame are key to individual emotional experiences (Holman et al., 2022). For example, Holman et al. (2022) identified that situations with high levels of control (e.g., passive listening) were associated with more enjoyment for people with hearing loss; whereas negative emotions like resentment and anger can be experienced by both conversation partners and those with hearing loss in cases of conversation breakdown (if the individuals are blamed instead of the hearing loss). Future studies with adult listeners with SSD need to investigate the aforementioned factors more closely for this population specifically.

Although non-specific to the SSD population, since the onset of the COVID-19 pandemic and the introduction of face coverings several studies reported on the detrimental effects on communication for those with hearing impairments due to reduced access to facial expressions and lip-reading (Chodosh et al., 2020; Perea Pérez

et al., 2022). Different types of face masks (Goldin et al., 2020) and different signal-to-noise (SNR) conditions have variable effects on speech perception and hearing-related quality of life (Alkharabsheh et al., 2022; Tofanelli et al., 2022). One blog post on communicating through a face mask by someone with SSD supports these reports (Sygrove, 2020a).

1.2.3 Psychological impact of single-sided deafness

The psychological impact of SSD in adulthood has been well-documented in the literature, including worry about losing the hearing in the other ear, embarrassment related to the social stigma attached to hearing loss, and reduced confidence and belief in one's own abilities to participate (Choi et al., 2021; Lucas et al., 2018; Sano, Okamoto, Ohhashi, Iwasaki, et al., 2013). Individuals with unilateral hearing loss are at a disadvantage in social and emotional situations. They report being upset, anxious, frustrated and isolated due to their hearing handicap secondary to monaural listening (Araújo et al., 2010; Lucas et al., 2018; Sano, Okamoto, Ohhashi, Ino, et al., 2013). It has also been reported that SSNHL is associated with anxiety and depression (Arslan et al., 2018). Furthermore, increased stress levels related to the need to find an optimal position in social settings, that will help with speech perception and participation, have been reported in interview studies (Lucas et al., 2018). Those who acquired SSD secondary to a vestibular disorder (e.g., labyrinthitis, Ménière's disease) could be at risk of chronic anxiety which could precede depressive states (Hilber, 2022). Analysis from the 2008 National Health Interview Survey, which included approximately 18 million people with vestibular vertigo in the USA, suggested that cognitive impairment (memory loss, difficulty concentrating, confusion) and psychiatric diagnoses (depression, anxiety, panic disorder) are comorbidities in those with vestibular deficiencies (Bigelow et al., 2016), which can also be linked to difficulties remembering in 32% of individuals. In addition, individuals diagnosed with SSD report decreased self-esteem when in places with lots of background noise that can leave them feeling frustrated and isolated (Lucas et al., 2018). They also report increased stress levels and exhaustion related to their constant attempts to maximise their abilities to hear and participate in complex social situations (Kuppler et al., 2013; Wie et al., 2010). Associated feelings of frustration, annoyance, helplessness, embarrassment, and

depressive symptoms have been reported by multiple studies (Choi et al., 2021; Gatehouse and Noble, 2004; Giolas and Wark, 1967; Lucas et al., 2018; Sano, Okamoto, Ohhashi, Iwasaki, et al., 2013; Wie et al., 2010).

1.2.4 Impact of single-sided deafness on well-being and quality of life

Well-being is defined as 'a state of health, happiness and prosperity, which is affected by various factors, including: a balanced diet, regular exercise, supportive relationships, adequate financial resources, stimulating work, education and leisure activity, health monitoring, preventive services (e.g., screening and vaccination), and risk management to protect individuals and promote personal safety' (Segen's Medical Dictionary, 2011). Population-based studies indicate significant associations between hearing impairment and well-being (Dawes et al., 2014; Pierzycki et al., 2020). For example, Pierzycki et al. (2020) evaluated the risks of adverse hearing and well-being outcomes (including self-reports on depression, health rating, satisfaction with health, happiness and loneliness), in 113,804 UK Biobank participants aged 40-69 years who self-reported unilateral hearing loss. Participants with unilateral hearing impairment were significantly more likely to report poor health, dissatisfaction with health, and loneliness than those with normal hearing. Although not specifically tailored to the SSD population, a recent review of the literature on hearing loss, associated listening-related fatigue, hearing device use, and activity levels; demonstrated that there is an association between these factors and an individual's well-being (Holman, Hornsby, et al., 2021).

Quality of life (QoL) is defined as 'a patient's general well-being, including mental status, stress levels, sexual function, and self-perceived health status' (Farlex Partner Medical Dictionary, 2012). The multi-dimensional burden of SSD on overall health is indicated by reductions in health-related QoL in individuals with a diagnosis of SSD, despite use of hearing-assistive devices for SSD (Arndt, Aschendorff, et al., 2011; Kitterick et al., 2015; Pierzycki et al., 2020; Vannson et al., 2015; Wie et al., 2010). One study reports that the impact of SSD on QoL can exceed that reported by listeners with bilateral hearing loss (Sano, Okamoto, Ohhashi, Iwasaki, et al., 2013). This Japanese study included 167 adult participants with idiopathic SSNHL and 134 participants with

bilateral hearing loss to act as controls. They measured health-related QoL with the Japanese version of the Short-Form Health Survey (SF-36) (Fukuhara et al., 1998). The term 'health-related quality of life' (HRQoL) narrows quality of life to aspects relevant to health (de Wit and Hajos, 2013). This study concluded that there was reduced mental functioning in those with idiopathic SSNHL, compared to averages in the Japanese population, which was similar to their participants with bilateral hearing loss. The psychosocial impact has also been documented, with annoying tinnitus and remaining vertigo after SSNHL to be the strongest predictors of negative effects on QoL (Baguley et al., 2006; Carlsson et al., 2011). Quality of life can be affected in those who have vestibular schwannomas surgically removed, as indicated by lower scores yielded on the 36-Item Short Form (SF-36) survey instrument (Ware and Sherbourne, 1992), in all categories, but more significantly in physical ability, social functioning, emotional status and vitality (Nicoucar et al., 2006).

1.2.5 Social consequences of single-sided deafness

All the aforementioned functional difficulties experienced by adults with SSD, the psychological impact, and impact on well-being and quality of life; can in turn have an effect on social aspects, including decreased levels of confidence, reduced self-esteem, increased stress levels, and a possible consequence is higher level of social isolation (Chang et al., 2020; Wie et al., 2010). The Chang et al. (2020) qualitative study explored what communication and social challenges individuals face post their diagnosis of SSD. They interviewed 52 internationally recruited participants aged 18 to 69 years old. They derived key themes around factors that individuals with SSD identified as communication and social challenges regarding their family and medical team networks. Their findings showed that family members are a critical component to the quality of healthcare received during and after SSD diagnosis. For example, individuals with SSD increase their reliance on family members, which decreases their sense of autonomy, and the communication quality, dynamics, and family members' emotions change following a diagnosis of SSD. Individuals with SSD report feeling that their medical professional team being disparate, disconnected, and hard to reach. For example, they often have to interact with multiple professionals, and there is a lack of knowledge in what to anticipate post diagnosis. The Chang et al. (2020) study also

concluded that participants experienced stress from seeking multiple health professionals' opinions, anxiety from different specialists with conflicting views, and frustration from information uncertainty.

Similarly, Wie et al. (2010) conducted semi-structured interviews with Norwegian individuals with unilateral hearing loss and normally-hearing individuals from the same family or social circle, that were induced with temporary hearing loss in one ear with insertion of an ear plug. The study concluded that individuals with unilateral deafness reported feeling excluded in conversations with multiple speakers, have reduced well-being in social settings, and a preference to avoid social gatherings in which they thought significant background noise would be present. This finding is in line with other qualitative studies that indicate that coping strategies of individuals with SSD include withdrawal from within a situation and in some cases, from the social situation completely (Lucas et al., 2018). The impact of SSD on communication can also affect intimate relationships (Hétu et al., 1993; Lucas et al., 2018). SSD can have an impact on individual's vocational activities such as business negotiations, customer service, and meetings, contribute to absences or days away from work, and early retirement (Härkönen et al., 2015; Marx et al., 2019; McLeod et al., 2008; Snapp, 2019). These studies' findings disagree with the Colleti et al. (1988) who found no difference between monaurally and binaurally hearing individuals on educational, social and employment achievement. Their participants however were aged 30 to 55 years, and had suffered unilateral hearing loss since childhood (Colletti et al., 1988), as opposed to hearing loss in adulthood like the other studies. However, longitudinal studies with older adults with age-related hearing loss in the United States (US) report that hearing loss may be associated with reduced engagement in physical and mental activities (Goman et al., 2021; Kuo et al., 2021) and have higher odds of reporting loneliness compared with those reporting excellent hearing after adjusting for comorbidity index, functional and cognitive ability, self-reported health, and demographic characteristics (Huang et al., 2021). It is well documented in the recent literature that hearing impairment can impair social engagement, can alter social roles, and impede the formation and maintenance of relationships (Barker et al., 2017; Heffernan et al.,

2022; Vas et al., 2017). The societal costs of bilateral severe-to-profound hearing loss have been primarily attributed to reduced work productivity (Mohr et al., 2000).

1.3 Treatment options for single-sided deafness

The impact on hearing abilities and consequences for communication for individuals with SSD, and the need to intervene has been recognised and documented in the literature since the 1960s (Harford and Barry, 1965; Harford and Dodds, 1966). The aim of SSD device-based treatments is to address the functional difficulties imposed and in turn improve everyday listening and communication abilities (Dwyer et al., 2014; McLeod et al., 2008; Snapp and Ausili, 2020).

1.3.1 Rerouting devices for single-sided deafness

The most commonly used treatment options for SSD enable access to sounds on both sides of the head (bilateral hearing) by rerouting sounds from the impaired ear to the hearing ear (Harford and Barry, 1965; Harford and Dodds, 1966; Peters et al., 2015; Snapp, 2019; Snapp, Hoffer, et al., 2017; Snapp and Ausili, 2020; Valente et al., 1995). Rerouting interventions include the Contralateral Routing of Signals (CROS) hearing aid (Choi et al., 2019; Harford and Dodds, 1966; Leterme et al., 2015; Lin et al., 2006; Ryu et al., 2015; Snapp, 2019; Snapp, Holt, et al., 2017). The CROS system (Figure 1-1) is made of two parts: a wireless microphone which is mounted onto the poor-hearing ear and is paired wirelessly to a hearing aid that is worn on the better-hearing ear. The Snapp (2019) review lists several advantages of the CROS device including sound awareness on the poor-hearing side, improvement of the signal-to-noise ratio for sounds directed to the poor-hearing ear in noisy environments, and ease of use. Limitations of this technology include that binaural input is still impaired, poor sound localisation in the horizontal plane due to disruption of the available monaural level and spectral cues (Pedley and Kitterick, 2017), and impairments related to hearing in noise, especially if the interfering noise is amplified in the better-hearing ear (Snapp, 2019).

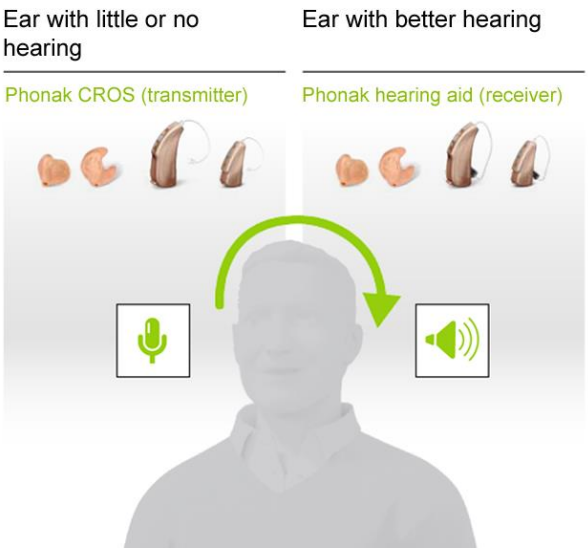

Figure 1-1. Schematic representation of the Phonak Contralateral Routing of Signals (CROS) hearing aid.
*Retrieved from www.phonakpro.com and used with permission © 2022 Sonova AG.

An alternative widely used rerouting intervention for SSD is the Bone Anchored Hearing Aid (BAHA) which can be implanted on the poor-hearing side. BAHAs were first implanted in the 1970s (Tjellström and Granström, 1994) and since then many variations have been developed (Håkansson et al., 2019; Iwasaki, 2022; Maier et al., 2022). A BAHA fitting requires surgical implantation of a transcutaneous abutment (Figure 1-2) or a subcutaneous magnet (Figure 1-3) into the skull bone behind the ear. It delivers sounds into the skull by means of sound vibrations, which transfer sound transcranially from the poor-hearing side to the contralateral side. In 2002 the Food and Drug Administration (FDA) approved BAHA implantations for management of SSD (Linstrom et al., 2009).

Advantages of the BAHA for SSD include overcoming the negative consequences of the head-shadow effect (Niparko et al., 2003; Snik et al., 2004), improvement in hearing speech in noise, when noise is presented on the better hearing ear side (Hol et al., 2005), and improvement in quality of life (Leterme et al., 2015). A study that recruited nine individuals with SSD reported improvement in word discrimination and sound localisation in noise, when the stimulus and noise were presented on the same side as the implanted ear, when using a percutaneous BAHA compared to no intervention (Monini et al., 2015).

A review of four controlled trials that attempted to determine the benefit of BAHA vs CROS vs the unaided condition concluded that there is a paucity of evidence to support the efficacy of BAHA in the treatment of acquired SSD; however they suggested that speech discrimination in noise and subjective questionnaire measures of auditory abilities showed an advantage for BAHA over CROS and the unaided condition (Baguley et al., 2006). A systematic review comparing the clinical outcomes of the CROS and BAHA devices concluded that there is no difference between the two treatment options regarding speech perception in noise and localisation, and a moderate improvement in subjective speech communication when using either a CROS or a BAHA (Peters et al., 2015). Other studies also concluded that the BAHA does not improve nor deteriorate the localisation abilities of individuals with SSD (Agterberg et al., 2019; Lin et al., 2006; Wazen et al., 2005).

A study that included 44 individuals with SSD assessed the subjective benefits of BAHA with four questionnaires, with a median of 50 months follow-up period (Desmet et al., 2014). Their findings suggest that the majority of individuals (86%) use their processors, and report an overall improvement, however device use reduces at long-term follow-up, especially in noisy situations.

Figure 1-2. Schematic representation of the Oticon Medical™ percutaneous Bone Anchored Hearing Aid (BAHA).
*Retrieved from www.oticonmedical.com and used with permission from Oticon Medical™.

The subcutaneous magnet version of the BAHA system (Figure 1-3) was compared to the percutaneous (Figure 1-2) on a prospective study evaluating the long-term audiological and clinical outcomes (Kruyt et al., 2020). The findings suggested that the percutaneous system provided statistically significant or near-significant improvement compared with the unaided condition in all audiometric tests throughout the 24-month follow-up, except for speech recognition in noise at the 24-month visit. However, the statistically significant clinical improvements recorded with questionnaires at 6 months were no longer present at 24 months. Another study that included five individuals with SSD and compared the percutaneous vs subcutaneous devices during the first six months post implantation found an improvement in sound, speech understanding, and quality of life in those implanted with the percutaneous device, but limited improvement in localisation abilities, and there were no adverse effects noted (Kong et al., 2021).

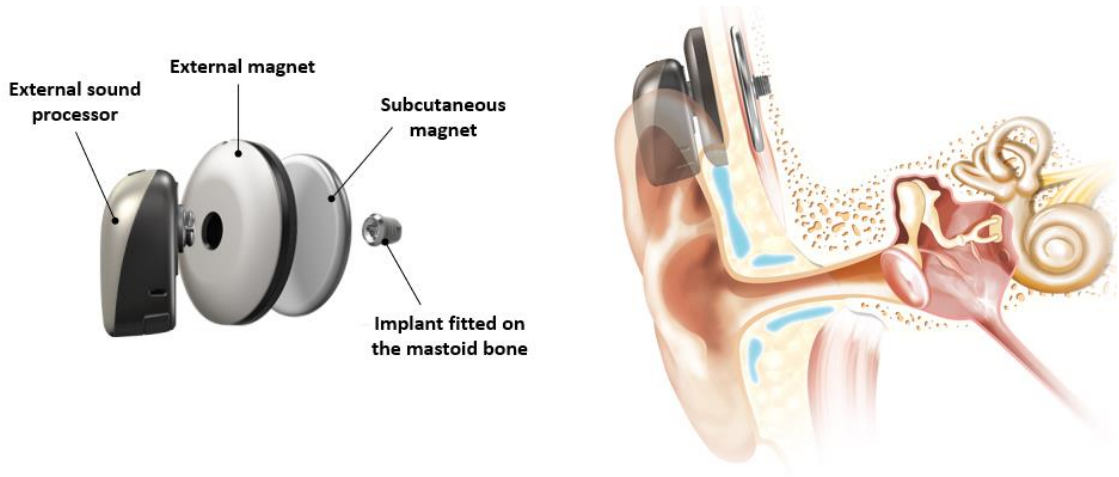

Figure 1-3. Schematic representation of the Cochlear™ Baha® 6 Max Attract system, a subcutaneous Bone Anchored Hearing Aid (BAHA).
*Images courtesy of Cochlear Bone Anchored Solutions AB, © 2022.

Active bone conduction implant systems, like the MED-EL BoneBridge™ (Figure 1-4) have been used to alleviate the impact of SSD in adults (Bianchin et al., 2015; Ratuszniak et al., 2022; Schmerber et al., 2017; Sprinzl and Wolf-Magele, 2016; Zernotti and Sarasty, 2015). This transcutaneous device was first implanted in 2011 as part of a clinical trial (Magele et al., 2019). The BoneBridge™ consists of an external audio processor and an implantable bone conduction implant which lies completely under the skin on the poor-hearing side. The bone conduction implant is composed of

an active electromagnetic bone conduction floating mass transducer, an electrical demodulator, and a receiver coil. Sound vibrations delivered through the skull are transmitted directly to the inner ear.

A longitudinal, 5-year follow-up economic analysis of the BoneBridge™ compared to the percutaneous BAHA (Figure 1-2) demonstrated that the BoneBridge™ is a good alternative option with reduced skin complications reported due to the lack of a percutaneous abutment, however, a drawback of this device is the attenuation of high frequency auditory output by the skin (Amin et al., 2021). Another study that evaluated the post-operative pain following BoneBridge™ implantation concluded that pain scores were similar to those experienced by individuals with other transcutaneous auditory implants (Lassaletta et al., 2016). Structured interviews conducted with 20 adult participants with SSD by Ratuszniak et al. (2022) demonstrated that the BoneBridge™ device provided less subjective satisfaction in those with SSD vs other types of loss (conductive or mixed hearing loss). Their interviews included questions on (i) satisfaction of the effect achieved, (ii) sound quality of the device, and (iii) change in hearing (improvement or deterioration).

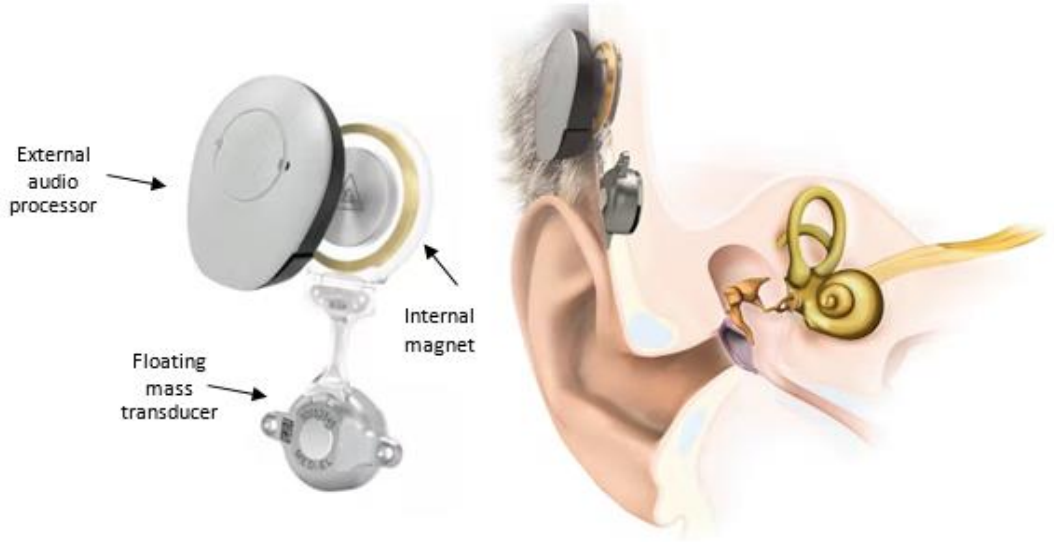

Figure 1-4. Schematic representation of the MED-EL BoneBridge™ bone conduction implant. *Retrieved from www.medel.com and used with permission from MED-EL.

An adhesive bone conduction device, the ADHEAR (Figure 1-5) by MED-EL, has also been used to alleviate the functional effects of SSD (Mertens et al., 2018; Moteki et al.,

2020). The device comprises a removable, single use adhesive adapter and an audio processor that are worn behind the poor-hearing ear. The adhesive adapter secures the audio processor and provides sufficient contact force to provide good physical contact between the vibrating portion of the hearing aid and the user's skull (Mertens et al., 2018). A study aiming to obtain preliminary results regarding the use of ADHEAR in individuals with various types of hearing loss found no improvement in speech perception or sound localisation, despite functional hearing gains in their three participants with SSD (Moteki et al., 2020). The speech perception findings mirror the Mertens et al. (2018) conclusions, although they did observe slight improvement in sound localisation when wearing the ADHEAR with the omnidirectional microphone programme enabled, when compared to the CROS device in 17 participants with SSD. However, due to the large variation in outcomes and limited statistical power no firm conclusions could be made.

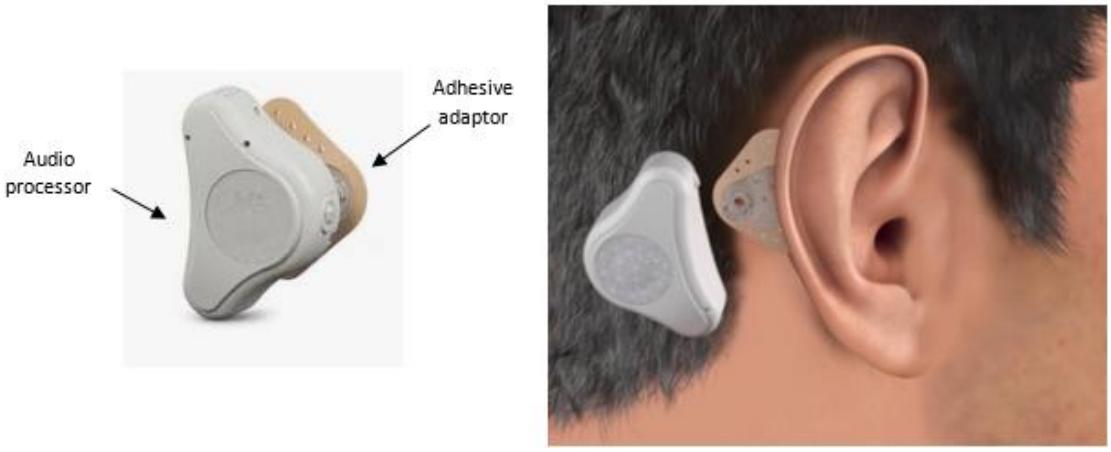

Figure 1-5. Schematic representation of the ADHEAR by MED-EL bone conduction device. *Retrieved from www.medel.com and used with permission from MED-EL.

Another rerouting device, the SoundBite™ dental implant (Figure 1-6) by Sonitus Medical, has been tested in the past but is currently not used (Gurgel and Shelton, 2013; Luo et al., 2020; Miller et al., 2011; Moore and Popelka, 2013; Murray et al., 2011; Popelka et al., 2010).

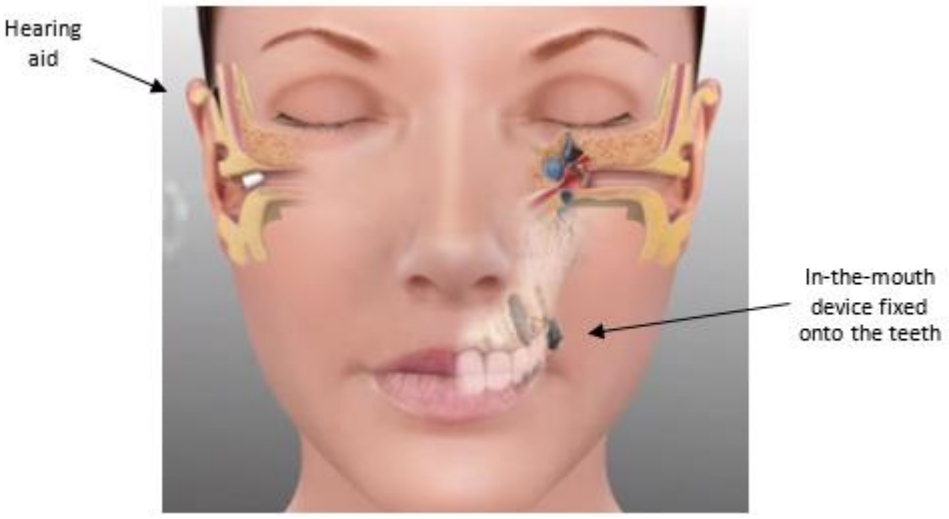

Figure 1-6. Schematic representation of the SoundBite™ dental implant.
*Retrieved from SoundBite hearing (SoundBite Hearing, 2013).

The SoundBite™ is a removable in-the-mouth device that is fixed onto the teeth, and directly coupled to the skull. The device is directly fixed onto the dental bones, and it generates vibration that passes through the skull to the cochlea. A study that recruited nine Chinese individuals with SSD aged 24 to 61 years assessed speech recognition in quiet and noise, and quality of life when using the SoundBite™ compared to no intervention (Luo et al., 2020). The findings suggest a significant improvement in speech perception benefits in quiet and noise (when noise was presented on the better-hearing ear), and improvement in quality of life.

1.3.2 Restoring devices for single-sided deafness

Auditory input to the poor-hearing ear can be restored (binaural hearing) by delivering information about sounds directly to the auditory pathway on the side of the impaired ear. Binaural hearing can be achieved using auditory prostheses like a middle ear implant (MEI), such as the MED-EL Vibrant SoundBridge™ (Figure 1-7).

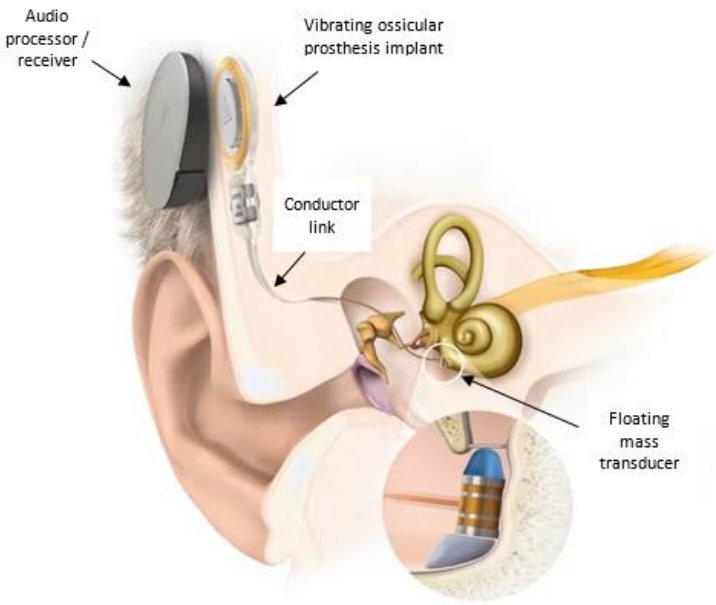

Figure 1-7. Schematic representation of the MED-EL Vibrant SoundBridge™ middle ear implant.
*Retrieved from www.medel.com and used with permission from MED-EL.

The device consists of an externally worn audio processor and an implant that is surgically positioned under the skin. The audio processor is held onto the implant by magnetic attraction. The microphones of the audio processor pick up sound waves and the audio processor converts sounds into electrical signals, which get transmitted through the skin to the implant. A small part of the device, the floating mass transducer, converts the signals into mechanical vibrations which in turn stimulates the inner ear (Gerdes et al., 2016; Laske et al., 2015; Schmerber et al., 2017). Schmerber et al. (2017) included 12 individuals with SSD in their study aiming to validate the safety and efficacy of MED-EL middle ear implant to find an improvement in speech-in-noise performance when the speech was presented on the poor-hearing side with the device on. The findings are in agreement with the Laske et al. (2015) study whom also found improvements when the speech signal was presented on the poor-hearing side with the device on.

More recently, the Cochlear™ Osia® system (Figure 1-8) has been used for SSD (Rauch et al., 2021; Willenborg et al., 2022). The Osia® system is an active bone conduction hearing implant system that has a transcutaneous connection between an external processor and an implant. The vibrator (actuator) is piezoelectricity based and is

connected directly to a titanium implant that is anchored and osseointegrated to the skull bone (Arndt et al., 2021; Hwa et al., 2022). Piezoelectric effect, or piezoelectricity is the ability of certain materials to generate an electric charge in response to applied mechanical stress (vibrations), or reversibly to generate mechanical stress (vibrations) in response to an external electric charge (Goycoolea et al., 2020). A multi-centre study including five individuals with SSD investigated the clinical performance, safety, and patient-reported outcomes of the Osia® system (Briggs et al., 2022). They demonstrated a statistically significant and clinically relevant improvement in speech recognition in quiet and noisy situations in comparison to the unaided situation, and a subjective improvement in hearing benefit when compared to pre-operative scores. The authors acknowledge that due to the limited number of participants with SSD recruited in this study, the results should be interpreted with caution. Another study reviewed the medical device reports associated with the MED-EL active transcutaneous device and the Osia® system (Crowder et al., 2021). Adverse effects of the Osia® system included malfunctions (9.8%), and patient injuries (91.2%). The authors concluded that the device malfunction rates are similar for the two devices.

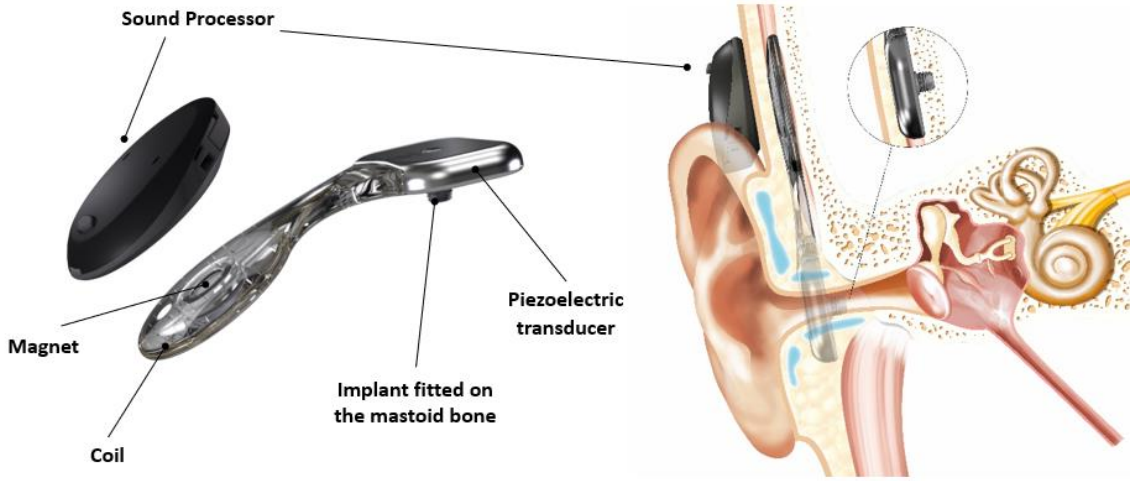

Figure 1-8. Schematic representation of the Cochlear™ Osia® system, an active bone conduction hearing implant.
*Images courtesy of Cochlear Bone Anchored Solutions AB, © 2022.

Cochlear implantation as an intervention for SSD was first piloted by Van de Heyning and colleagues, to assess the effect of electrical stimulation via a cochlear implant (CI) in individuals with SSD and intrusive ipsilateral tinnitus (Van de Heyning et al., 2008).

Since then cochlear implantation has been utilised by several teams, mainly in Europe, North America and Australia (Arndt et al., 2017; Härkönen et al., 2015; Marx et al., 2019; Poncet-Wallet et al., 2020; Távora-Vieira et al., 2015). A CI can deliver information about sounds directly to the auditory pathway, electrically stimulating the impaired ear (Figure 1-9), thus creating a sensation of binaural hearing (Arndt, Aschendorff, et al., 2011). Auditory cortical plasticity studies have suggested that cochlear implantation in asymmetrical hearing loss enables reconstruction of the cortical mechanisms of spatial selectivity needed for sound localisation (Karoui et al., 2022).

A systematic review of the literature up to 2015, analysed the influence of cochlear implantation in a total of 137 individuals with SSD with regards to sound localisation, speech perception, tinnitus, and quality of life (Cabral Junior et al., 2016). Despite the variation in participant characteristics, onset and duration of SSD, and the diversity of outcomes reported, the authors conclude that cochlear implantation enhances sound localisation, speech perception, and contributes to improvement in tinnitus. A more recent systematic review including 50 studies, which consisted of 674 individuals with SSD, aged 19 to 93 years, with an average duration of deafness ranging from 0.8 to 68 years aimed to analyse the impact of CI on speech perception in quiet and noise, tinnitus control, sound localisation, and quality of life (Oh et al., 2022). Similar to the Cabral Junior et al. (2016) review, the authors concluded that CI in individuals with SSD provides significant improvement in speech perception, tinnitus control, localisation and quality of life. Oh et al. (2022) also highlighted a large variability in the participant characteristics (e.g., aetiology, onset, duration), numbers recruited in studies (e.g., numbers ranged from 3 to 70 participants), choice and reporting of outcome measures (e.g., speech testing configurations, reporting parameters), follow-up time (e.g., range varied from 6 months to 3.5 years) across studies.

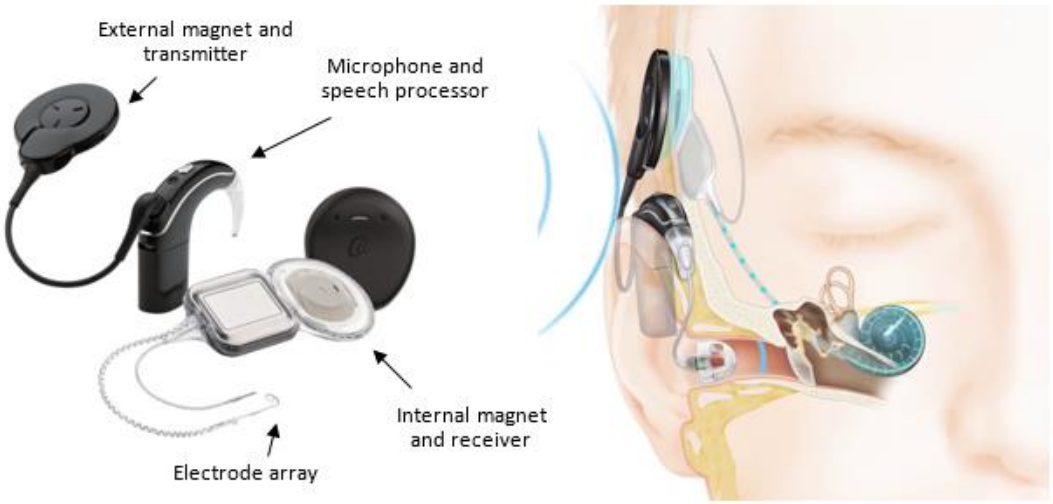

Figure 1-9. Schematic representation of a cochlear implant device.
*Images courtesy of Cochlear Limited, © 2022.

Of note, a recently reported retrospective case series with 66 adults with SSD that were implanted with a cochlear implant report that duration of deafness is not associated with significant differences in speech recognition performance (Lindquist et al., 2022). They measured speech recognition with the Consonant-Nucleus-Consonant (CNC) words and the AzBio sentences in quiet. A systematic review including 31 studies, which aimed to provide a comprehensive overview of the short- and long-term effects of cochlear implantation on disabling tinnitus in adults with SSD, report an improvement in tinnitus suppression scores despite variability in patient characteristics (Idriss et al., 2022).

Cochlear implantation as an intervention for SSD in the UK has been examined in longitudinal trials comparing CI to the CROS aid (Kitterick, 2015). The outcomes of this clinical trial are not yet published. A French multi-centre prospective study rolled out in 2019 aiming to assess the efficiency of CI in SSD, compared to CROS and BAHA trials, using a cost-utility analysis (Marx et al., 2019). Initial findings indicate that approximately half of the participants opted for a CROS aid, but over one third of the 104 participating individuals with SSD were dissatisfied with the CROS and BAHA devices, and those that opted for CI experienced more severe handicap and had a poorer quality of life than the other groups (Marx, Mosnier, Vincent, et al., 2021). There was no significant difference between the groups of participants that opted for

CROS vs BAHA vs CI vs no intervention in terms of aetiology, deafness duration, side of deafness, hearing thresholds in the better ear, or tinnitus severity. When the outcomes of the 51 participants that opted for a CI were considered with regards to generic and auditory-specific quality of life, there was significant improvements noted, especially in participants with SSD and associated severe tinnitus (Marx, Mosnier, Venail, et al., 2021). The authors acknowledge the small participant number and the short-term follow-up, restricted to 6 months post implantation. A recent study including 20 participants with SSD implanted with CI demonstrated that localisation abilities improve with long-term use, with more consistent responses in sound source localisation performance at their 5-year visit (Thompson et al., 2022).

The Kitterick et al. (2015) systematic review of the literature included 23 studies and examined the impact of hearing-assistive devices on the health-related quality of life (HRQoL) of adults with SSD as measured using generic and disease-specific instruments. The average effect of air conduction devices is small and bone conduction devices have a medium effect, whereas cochlear implantation has a large effect, with a caveat that it should be considered a medium effect because in the included studies it was derived from within-subject comparisons of HRQoL before and after implantation.

Finally, auditory brainstem implantation (ABI) has also been used as an intervention for SSD, but sporadically (Mueller et al., 2000). The ABI (Figure 1-10) was specifically designed to bypass both the cochlea and the cochlear nerve to directly stimulate the cochlear nucleus in the brainstem (van den Berge et al., 2019). Therefore, ABIs are suitable in cases of destruction of the cochlear nerve, rendering cochlear implantation ineffective (Schwartz et al., 2008). An example of such case is neurofibromatosis which is a genetic condition that causes benign tumours to grow along the nerves.

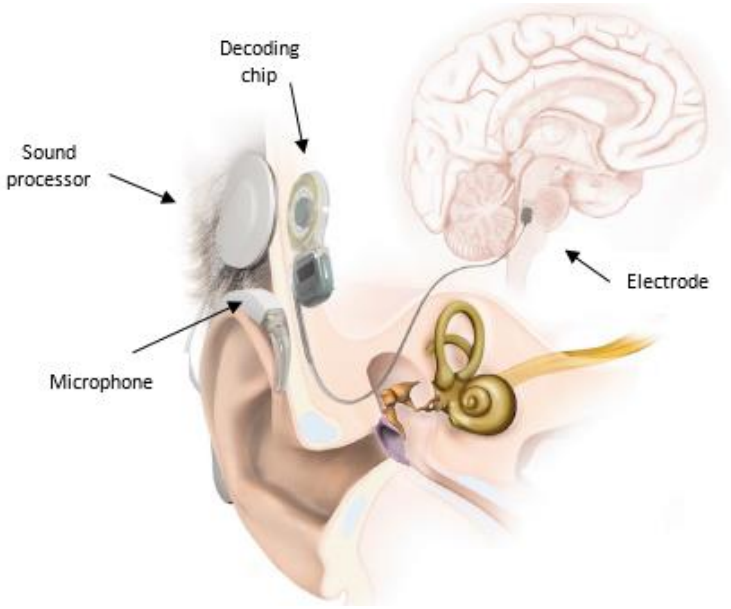

Figure 1-10. Schematic representation of an auditory brainstem implant.
*Retrieved from www.medel.com and used with permission from MED-EL.

1.3.3 Cost effectiveness of interventions

Hearing aid and auditory implant cost-effectiveness studies have become increasingly important (Caspers et al., 2022; Neve et al., 2021; Theriou et al., 2019). The device purchasing cost varies from a few hundred pounds for the rerouting hearing aid solutions to approximately £20,000 for the restoring implants. A formal cost-effectiveness analysis for BAHA devices via a prospective case-control study of 70 pathways was done by Monksfield et al. (2011); who found that there was limited data for cost effectiveness calculations for BAHA devices. They presented total costs from initial evaluation, surgery, ongoing annual evaluation and maintenance, and processor upgrades after five years to the newest model for an estimated life expectancy of the individual patient (Monksfield et al., 2011). The Health Utilities Index (HUI) questionnaire (Horsman et al., 2003) was used in conjunction with life expectancy estimations to derive Quality-Adjusted Life Year (QALY) and Incremental Cost-Effectiveness Ratio (ICER) ratios. There is limited quality of life data available for patients living with an osseointegrated implant. As a result, the cost-effectiveness of the osseointegrated implant, specifically the BAHA, compared to conventional hearing aid devices remains unclear (Crowson and Tucci, 2016).

A retrospective case series analysis with a longitudinal economic analysis was performed by Amin et al. (2020) using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) reporting guidance. They concluded that the mean total cost per patient of the MED-EL middle ear implant was significantly higher than percutaneous BAHA at 1-year post-implantation, however, by 5-years post-implantation this difference was no longer statistically significant. Unfortunately, cost-effectiveness evaluations are limited by the lack of usable data on quality of life and device usage (Caspers et al., 2022). Based on evidence of moderate quality, cochlear implantation and bone-conduction implants improve functional and patient-important outcomes in adults and children with SSD (Ontario Health, 2020).

1.4 Outcome measurement for single-sided deafness interventions

Existing literature has highlighted inconsistencies in what benefits and risks (side-effects) are assessed when evaluating hearing aid(s) and auditory implant interventions for SSD (Kitterick et al., 2016). The challenge of synthesising evidence for ENT and audiological interventions from trials, and the importance of utilising valid measurement instruments that effectively measure the intended audiological outcomes has been highlighted in the case of SSD (Hall, Kitterick, et al., 2019). Choosing the appropriate intervention for adults with SSD presents a clinical dilemma (Sin Wai and Chua Wei De, 2021; Underdown and Pryce, 2022).

Researchers investigating SSD intervention outcomes have measured a plethora of outcomes, such as speech understanding in quiet (Firszt et al., 2012; Niparko et al., 2003), or speech understanding in the presence of noise. When assessing speech outcomes in the presence of noise various configurations get adopted, for example Niparko et al. (2003) chose three conditions of (i) noise-front, (ii) noise-to-normal-ear, and (iii) noise-to-deaf-ear to compare BAHA vs CROS devices, using the Hearing in Noise Test (HINT) (Nilsson et al., 1994) that includes noise that is filtered to match the long-term average spectrum of the sentences. Arndt et al. (2017) compared speech outcomes in noise with the CROS, a demo BAHA device, and cochlear implantation in three conditions: (i) speech and noise from the front, (ii) speech from the hearing side

/ noise from the deaf side, and (iii) speech from the deaf side / noise from the hearing side, using the adaptive Oldenburger Sentence Test (OlSa) (Arndt, Aschendorff, et al., 2011; Arndt, Laszig, et al., 2011). Härkönen et al. (2017) compared cochlear implantation outcomes in SSD using a speech-in-noise test that included phonetically balanced bisyllabic Finnish words at a level of 65 dB SPL from the loudspeaker at 0° of azimuth, and unmodulated artificial noise presented from four loudspeakers (Härkönen et al., 2015). Finally, a study assessing the masked speech recognition in 16 participants with SSD and cochlear implant, suggest a revised test battery for this cohort of patients to ensure binaural hearing abilities are captured; suggesting presentation of the target from the front speaker and the masker co-located with the target, 90° toward the implanted-ear, or 90° toward the normally-hearing-ear (Anderson et al., 2022).

Other measures include the impact of BAHA vs middle ear implant device on the recipient's quality of life (Schmerber et al., 2017) using the Glasgow Benefit Inventory (GBI) (Robinson et al., 1996) and the International Outcome Inventory for Hearing Aids (IOI-HA) (Cox and Alexander, 2002). Finally, tinnitus effects in cochlear implantation studies have been measured (Holder et al., 2017) using Tinnitus Handicap Inventory (THI) (Newman et al., 1996), subjective tinnitus loudness measured using a Visual Analogue Scale (VAS) (Mertens et al., 2016), or tinnitus distress measured on a numeric rating scale with a maximum score of 10 (Song et al., 2018).

The question of what outcome domains are important and relevant to individuals with SSD when deciding whether an intervention works has yet to be fully addressed. One attempt to harmonise assessment of interventions across trials of SSD was made in 2017, but this was based on two discussions among professional experts in cochlear implantation at international conferences (Van de Heyning et al., 2017) and was intended for adoption in clinical practice. Recommendations for a minimum set of outcome measures were made, and these included daily device use, pure tone audiometry, free-field testing of speech perception in noise, and sound localisation; using the Speech, Spatial, and Qualities of hearing (SSQ) questionnaire (Noble et al., 2013), the Health Utilities Index (HUI) Mark 3 (Horsman et al., 2003) and, if applicable,

the Tinnitus Functional Index (TFI) (Meikle et al., 2012). This consensus work by Van de Heyning et al. (2017) was however only focussed on cochlear implantation as a treatment for SSD and so the expert panels comprised professionals from cochlear implantation centres. Furthermore the recommendations included measurement instruments that were readily available in the hearing clinic (e.g., pure tone audiometry, standard audiometric and validated sentence test, binaural effect measures), and there was lack of healthcare user involvement in the decision-making process. Therefore, it is unclear whether the recommended measures are assessing outcome domains that are most meaningful to healthcare users (e.g., impact on individual's well-being, social identity) (Lucas et al., 2018; Underdown and Pryce, 2022). There has been no rigorous scrutiny of outcome reporting for rerouting or restoring interventions, no systematic patient involvement, and no specific consideration of what should be recommended for clinical trials. Consequently, investigators adopt markedly different methods when assessing the clinical benefit of rerouting and restoring interventions for SSD.

A recent systematic review and meta-analysis on the use of hearing instruments for SSD in adults has demonstrated ambiguity in the absolute benefit and efficacy of the available SSD treatment options (Kitterick et al., 2016). For example, the meta-analysis showed that there was a statistically significant benefit (mean benefit: 2.5 dB) to speech perception in noise for devices that reroute speech signals from the poor-hearing ear to the better-hearing ear using either air or bone conduction. However, rerouting devices also degrade speech understanding significantly (mean deficit: 3.1 dB) when noise gets rerouted from the poor-hearing ear to the better-hearing ear. In relation to sound localisation, there was inconsistency in the assessment of outcomes chosen by clinical researchers, precluding the synthesis of evidence across studies. Finally, health-related quality of life was measure by two studies (out of 27 included in the review), and the findings were inconclusive. In summary, Kitterick et al. (2016) concluded that inconsistent measurement of outcomes and observational biases lead to reduced quality of evidence. Kitterick et al. (2016) also concluded that outcome selection has been somewhat biased towards assessing functional impairments for which measures are readily available and widely used, such as tests of speech

perception in noise; but limited focus on measuring hearing-related quality of life for example, which is meaningful to healthcare users (Lucas et al., 2018). Another systematic review of outcomes of cochlear implantation in patients with SSD focused on assessing (i) sound localisation, (ii) speech perception, (iii) tinnitus, and (iv) quality of life outcomes (Cabral Junior et al., 2016). The authors discovered a large variation in choice of outcomes in the included studies, and highlighted the need for high quality studies. Encouragingly, Mertens et al. (2022) have recently developed a consensus classification system for the reporting of sound localisation testing results in the field of cochlear implantation. This builds on the Van de Heyning et al. (2017) recommendations, and application of this classification system will allow multi-centre studies comparisons and improved meta-analysis in this field (Mertens et al., 2022).

Difficulties that SSD imposes can also affect the individual's psychological and social well-being (Carlsson et al., 2011; Lucas et al., 2018; Sano, Okamoto, Ohhashi, Iwasaki, et al., 2013), and therefore outcomes that assess the impact on an individual's overall health and well-being are also relevant and potentially as important (Kitterick et al., 2015). With respect to health-related quality of life, there is a known inconsistency in the choice of measurement instruments in trials assessing the benefits of SSD interventions (Kitterick et al., 2016). The authors highlight the need to utilise and consistently use patient-reported outcome measures that are sensitive to the impact of devices used by those with SSD, such as the Health Utilities Index (HUI) Mark 3 (Horsman et al., 2003), so that we can generalise study findings to everyday listening situations.

Often, it is unknown which aspects play a role in decision making and identifying better candidates for specific SSD interventions (Kosaner and Urban, 2014). Qualitative studies demonstrate that healthcare users express uncertainty about choice of treatment options for SSD mainly due to a lack of clarity about their benefit (Underdown and Pryce, 2022), and they seek clinical advice when they need to make a decision. However, due to the varied evidence for appropriate treatment options, clinicians may not know which treatment option is ideal and for whom (Hall, Kitterick, et al., 2019).

These inconsistencies in outcomes used in the field of SSD and the variety of methods used to measure them have been identified as a major barrier to synthesising evidence across trials (Kitterick et al., 2016). Therefore, comparison between studies and meaningful synthesis of results is challenging. Furthermore, it is unclear whether outcomes that have been measured in previous SSD intervention studies are outcomes that are of importance to all key stakeholders (i.e., the patient, the healthcare professionals involved, clinical researchers, commercial representatives, or the relevant funding bodies). Inconsistencies in outcome measurement also impact healthcare users' abilities to take informed decisions about the ideal intervention for them, and often rely on information provided by clinicians (Hampton et al., 2022; Kosaner and Urban, 2014; Munro et al., 2021; Underdown and Pryce, 2022; Williamson et al., 2017). Consequently, clinicians providing advice about available interventions adopt hugely diverse protocols when managing individuals presenting with SSD (Underdown and Pryce, 2022). The currently reported outcome measures are therefore clinician centred, lab centred, or tailored to healthcare systems. It is also unclear what outcome domains are relevant and important to individuals with SSD when it comes to deciding which intervention is ideal for them. This lack of consistency emphasises the need to define an agreed minimum standard for what is critically important to assess in all clinical trials evaluating SSD interventions. Without such consensus, it will remain challenging to make evidence-based decisions about the relative benefits of the different treatment options.

1.5 Wider problem of outcome measurement in clinical trials

It has been nearly two decades since the research community have been alerted to the problem of diverse outcome choice and research waste when conducting clinical trials, and how researchers should base the choice of outcome measures on what is important and of interest to people making decisions about healthcare (Clarke, 2007; Gandhi et al., 2008; Sinha et al., 2009), not on what measurement instruments are available or most commonly used (Gargon et al., 2014). In other words, it is recognised that the healthcare user perspective should also be incorporated, rather than choosing clinician-reported outcomes alone (Fitzpatrick et al., 1998; Harman et al., 2015;

Williamson, Altman, Blazeby, Clarke, Devane, et al., 2012). There is a growing general recognition that selection of appropriate outcomes is crucial when designing clinical trials in order to directly compare the effects of different interventions. If evidence is lacking for an important outcome, this should be acknowledged, rather than ignoring the outcome, and clinical trial results should be publicly available (Chan et al., 2004; Ghersi et al., 2008; Williamson et al., 2017).

The need for standardisation of reporting methods has also been discussed (Chan et al., 2013; Moher et al., 2010; Williamson and Clarke, 2012; Zwarenstein et al., 2008). Diversity in outcomes and measurement instrument selection hinders researchers in making decisions about the choice of outcome measures for health and social care trials of clinical efficacy and hinders comparison and meta-analysis across studies (Clarke and Williamson, 2016; Williamson and Clarke, 2012). For example, a case study in hearing sciences includes tinnitus, a perception of phantom sound (Hall, Haider, et al., 2015), which is a chronic condition that can be managed with various intervention approaches including sound devices, psychologically informed therapies, or pharmaceutical products (Hall et al., 2016). Hall et al. (2016), found a wide diversity in the outcomes (35 different primary outcome domains) assessed and reported in 228 studies of tinnitus interventions, with no single outcome being selected across all studies, and no common standards for assessing or reporting intervention efficacy.

With the aim to improve tinnitus research quality, enhance clinical decision-making, and facilitate meta-analysis in systematic reviews, they formed the Core Outcome Measures in Tinnitus (COMiT) initiative that successfully developed three core outcome domain sets for Sound-, Psychology-, and Pharmacology-based interventions trials for chronic subjective tinnitus in adults (Hall, Smith, Hibbert, et al., 2018). The authors went on to examine if it is important to tailor outcome domain selection to the three tinnitus intervention approaches (sound, psychology, pharmacology), and their stakeholder consensus confirmed their recommendation of three unique intervention-specific outcome domain sets (Hall, Hibbert, et al., 2019).

The evidence synthesis in systematic reviews for example would be enhanced if a core outcome set in a particular field is utilised, by reducing the risk of outcome-reporting bias, and ensuring that all trials contribute usable information (Williamson et al., 2017), and thereby avoiding duplication and reducing research waste (Gargon, Williamson, Altman, et al., 2017; Ioannidis et al., 2014). Ioannides et al. (2014) for example outline several problems and solutions to help reduce waste in the design, conduct, and analysis of research. Suggestions of solutions include: (i) advance public deposition of study protocols, (ii) choice of patient-centred outcomes that are important to end-users, (iii) consideration of all available existing evidence when designing new studies, and (iv) common language use among investigators for clinical definitions, laboratory measurements, and statistical analyses.

A core outcome set (COS) developed from the perspectives of healthcare users (Hsiao and Fraenkel, 2017; Kirwan et al., 2005; Serrano-Aguilar et al., 2009); healthcare professionals and other relevant stakeholders would overcome this problem of inconsistent and diverse choice of measures, if endorsed and adopted (Mease et al., 2008; Sinha et al., 2011, 2012; Williamson, Altman, Blazeby, Clarke, Devane, et al., 2012). A COS is defined by the Core Outcome Measures for Effectiveness Trials (COMET) as an agreed minimum set of outcomes (benefits or risks) or outcome measures (Williamson et al., 2017). A COS comprises a standardised collection of outcomes (also known as outcome domains), that should be measured and reported worldwide, as a minimum, in all controlled trials within a research area (Chan et al., 2013; Moher et al., 2010; Williamson and Clarke, 2012; Zwarenstein et al., 2008); and a recommended measurement instrument for each outcome domain.

There are different ways that healthcare users and the public can be involved in the process of designing, running and disseminating a study. For example, international discussion-based workshops with healthcare users identified unique challenges, such as (i) no straightforward steps to follow for seeking healthcare users' input, (ii) no training or support for clinical researchers regarding involvement of healthcare users, and (iii) difficulties ensuring international relevance to healthcare users (Young and Bagley, 2016).

There are solutions to help overcome these challenges. For example to ensure that healthcare users fully participate in the process of core outcome set development for a tinnitus study, Smith et al. (2018) involved healthcare users with lived experience of tinnitus in the design of their research study. This approach can improve the relevance and interest of the study to healthcare users (Smith et al., 2018), which can help avoid attrition bias too (Harman et al., 2015). Ways to embrace the perspectives of healthcare users with metastatic melanoma in a research process have been discussed by a Danish group (Skovlund et al., 2020) who identified challenges to be time, financial resources, and emotional and intellectual effort, not only to the research organisations and teams, but also to the healthcare users who get involved (Thompson et al., 2014). The healthcare users who participated in the study had considerations about discussing sensitive topics, offering themselves in discussions, and how their work had contributed to the trial.

COMET has established minimum standards to guide the COS development process, as well as to help users of core outcome domain sets to evaluate whether they have been developed using appropriate methodology (Kirkham, Davis, et al., 2017). Kirkham et al. (2017) set out to create a quality assessment recommendations for core outcome set development with the Core Outcome Set-STAndards for Development (COS-STAD) project. They brought together experienced COS developers, methodologists, journal editors, potential users of COS (clinical trialists, systematic reviewers, and clinical guideline developers), and patient representatives to form an international consensus on 11 minimum standards to be followed when COS developers plan their projects encompassing three main domains: (i) scope specification, (ii) stakeholder involvement, and (iii) consensus process followed. One limitation of the COS-STAD project was that there was limited participation from low- and middle-income countries.

The COMET initiative has also published a handbook to support the development of consensus-based recommendations for core outcome domains (Williamson et al., 2017). They recommended a four-step process to develop a COS: (i) define the scope of the COS, (ii) check whether a new COS is needed, and register it in the COMET

database, (iii) develop a COS development protocol, and (iv) determine 'the what' to measure by identifying existing knowledge, or incorporating new knowledge, and running a consensus process before reporting a final COS. Ongoing stakeholder awareness, dissemination, publicity and promotion of adoption and implementation is integral. Determining 'the how' to measure the COS is not comprehensively described in the COMET handbook, although the authors state that making recommendations on outcome measurement instruments is crucial for future uptake and realising the benefits of COS development (see Section 1.7 for details on measurement instrument recommendations). The authors clarify that an agreed minimum standard would not restrict trial investigators from assessing additional outcomes, but rather would aim to reduce diversity in reported outcomes and provide a basis for comparison between trials (Williamson et al., 2017).

Alternative ways of developing a COS have also been suggested by other initiatives. For example the HOME (Harmonising Outcome Measures for Eczema) initiative developed a methodological framework to develop core sets of outcome measurements in dermatology (Schmitt et al., 2015). The authors describe the process of COS development, starting with defining the scope and setting of the COS, determining the core domains to be measured such as symptoms or quality of life, the identification / development and assessment of the measurement properties of potential outcome measurement instruments for the core domains, recommending core measurement instruments, and finally dissemination and implementation. The HOME roadmap describes a detailed 5-stage process to identify, and recommend adequate measurement instrument(s) for each core outcome domain. They discuss the three important measurement properties that need to be assessed for measurement instrument(s) that include their: (i) validity (the degree to which an instrument measures the construct(s) it purports to measure), (ii) reliability (the degree to which the measurement is free from measurement error), and (iii) responsiveness to change (the ability of an instrument to detect change over time in the construct to be measured (Mokkink, Terwee, Patrick, et al., 2010b). An important aspect in determining if a measurement instrument meets the requirements for inclusion in a core set is feasibility, which aims to assess if the instrument be applied easily in its

intended setting, given constraints of time, money, and interpretability (Schmitt et al., 2015). For example, if a measurement instrument comprises 150 questions, its feasibility will be reduced because it is anticipated that it will take a long time to complete and analyse. Schmitt et al. (2015) also incorporate interpretability (the degree to which one can assign qualitative meaning to quantitative scores), a characteristic of measurement instruments to be assessed (Boers et al., 1998) in the HOME roadmap.

The Outcome Measures in Rheumatology (OMERACT) consensus initiative has been active since the early 1990s and have developed multiple core outcome sets for conditions including rheumatoid arthritis, osteoarthritis, osteoporosis, and psoriasis / psoriatic arthritis (Tugwell et al., 2007), by including and engaging multiple stakeholders and recognising the importance of meaningful healthcare users' input (Kirwan et al., 2003). The OMERACT framework encompasses the complete content of what is measureable in a trial, including both patient-centred and intervention-specific information in three core areas: (i) death, (ii) life Impact, and (iii) pathophysiologic manifestations; as well as a strongly recommended area (iv) resource use (Boers et al., 2014). The authors suggest identifying at least one core domain within each of the three core areas, to form the 'core domain set'; and at least one applicable measurement instrument that is valid, discriminative, and feasible for each of the core domains to form the 'core outcome measurement set'. OMERACT also flag the importance of reporting on and quantifying adverse effects as part of the core set to allow for transparent assessment of interventions.

Numerous other fields have adopted COS development to address inconsistency in choice of outcomes and potential reporting bias in trials. Early examples include the World Health Organisation (WHO) in the 1970s, relating to cancer trials (Miller et al., 1981), the IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) study for chronic pain (Dworkin et al., 2005, 2008). More recently, the CoRe Outcomes in Women's and Newborn health (CROWN) initiative have developed a core outcome set for studies evaluating the effectiveness of pre-pregnancy care for women with pre-gestational diabetes (Egan et al., 2017), the GASTROS (Standardising

Outcome Reporting in Gastric Cancer Surgery Research) study for reporting outcomes in gastric cancer surgery (Alkhaffaf et al., 2017), the COMiT'ID (Core Outcome Measures in Tinnitus International Delphi) for chronic subjective tinnitus (Hall, Smith, Hibbert, et al., 2018), and the newly COVID-19 (Evangelidis et al., 2020; Tong et al., 2020).

1.6 Need for development of a core outcome domain set for single-sided deafness

The audiology and ENT community have been alerted to the importance of choice of relevant outcomes which are clinically meaningful to the patient to (i) comprehensively assess a patient with a specific clinical diagnosis, for example, SSD versus bilateral hearing loss; and (ii) for the purpose of measuring the therapeutic benefit for determining clinical efficacy (Hall, 2018). Understanding which intervention approaches are optimal for patients with SSD should be based on robust evidence from well-designed trials (Chalmers and Glasziou, 2009; Gargon et al., 2014). To standardise the reporting methods for SSD interventions and to be able to select suitable measurement instruments; an agreed minimum set of outcome domains relevant to both patients and professionals should be measured and reported in all future trials examining SSD interventions. The commonly agreed minimum set of outcome domains should be adopted, regardless of whether the intervention restores two-sided (bilateral) access to sound via the better ear or delivers sound information directly to the impaired ear (binaural hearing).

1.7 Identification of suitable instruments for measurement in single-sided deafness intervention trials

Once an agreement has been reached regarding the outcomes in the COS, the next step entails determining how these outcomes should be measured (Prinsen et al., 2014). It is important to choose measurement instruments that are comprehensive and sensitive to treatment-related change (Prinsen et al., 2016) as well as inclusive and

equitable to ensure they incorporate the diversity of all patients being assessed with the condition of interest (Calvert et al., 2022).

The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) initiative aims to improve instrument selection in research and clinical practice. COSMIN proposes standardised, consensus-level agreed, methodological guidelines and tools for selecting the most appropriate measurement instruments (Mokkink et al., 2016), including a guideline for systematic reviews of Patient Reported Outcome Measures (PROMs) (Prinsen et al., 2018). Briefly, the process entails (i) clearly defining each of the outcome domains in the COS in detail, (ii) a systematic review of measurement instruments to identify all relevant outcome measurement instruments, and (iii) evaluation of the reliability, validity and responsiveness of available measurement instruments using like the recommended COSMIN taxonomy and definitions, and the COSMIN checklist (Mokkink et al., 2016). Through this process, a generic recommendation on the selection of outcome measurement instruments for outcomes included in a COS set can be made (Prinsen et al., 2016). The Prinsen et al. (2016b) guideline is based on the methodology derived from the COSMIN initiative and recommendations from OMERACT (Boers et al., 2014). Although the authors acknowledge the HOME and IMMPACT initiatives, they do not incorporate their recommendations. For example, HOME recommend that for an outcome measurement instrument to be included in the list of possible outcome measurements, the instrument's responsiveness to change (the ability of an instrument to detect change over time in the construct to be measured) should be assessed (Schmitt et al., 2015). However, the Prinsen et al. (2016b) consensus suggests only gathering high quality evidence for good content validity (the degree to which an instrument measures the construct(s) it purports to measure), and for good internal consistency (evidence for test-retest or interrater reliability). The HOME initiative also suggest that measurement instrument properties, such as feasibility, should be assessed prior to considering other aspects.

1.8 Study aims and objectives

The Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) study sought to examine and address problems with inconsistent outcome reporting in SSD intervention trials. To achieve this, CROSSSD set out to develop a core outcome set through a rigorous evidence-based process and by actively involving all relevant stakeholders in decision making (Chapter 2).

The overall aim of the CROSSSD study was to develop an agreed minimum set of outcome domains relevant to both healthcare users and professionals that should be measured and reported in all future trials examining SSD interventions, irrespective of whether the intervention restores two-sided (bilateral) access to sound via the better ear or delivers sound information directly to the impaired ear. The overall aim was achieved via these key objectives:

(i) to develop an international consensus on a core outcome domain set for SSD interventions using a long-list list of candidate outcomes identified in a systematic review (Chapter 3) and available qualitative data, a two-round modified electronic Delphi survey, and a final consensus meeting with relevant stakeholder representatives (Chapter 4),

(ii) to conceptualise and operationalise the outcome domains in the core outcome domain set using qualitative data collected at focus groups with stakeholder representatives (Chapter 5),

(iii) to assess available measurement instruments for suitability in measuring the domains in the core outcome domain set (i.e., the content validity) by synthesising evidence on available outcome measurement instruments for measuring the construct outcomes (Chapter 5), and

(iv) to develop recommendations for future measurement instrument developers in the field (Chapter 5).

Stakeholder awareness, dissemination, publicity, and promotion of the study findings were incorporated as an integral part of the CROSSSD study throughout.

2. Methods

This chapter is adapted from these peer reviewed publications:
Katiri, R., Hall, D. A., Buggy, N., Hogan, N., Horobin, A., Van de Heyning, P., Firszt, J. B., Bruce, I. A., & Kitterick, P. T. (2020). Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) study: protocol for an international consensus on outcome measures for single sided deafness interventions using a modified Delphi survey. *Trials*, 21(1), 238. doi: 10.1186/s13063-020-04240-2.

Katiri, R., Hall, D. A., Hoare, D. J., Fackrell, K., Horobin, A., Buggy, N., Hogan, N., & Kitterick, P. T. (2021). Redesigning a web-based stakeholder consensus meeting about core outcomes for clinical trials: formative feedback study. *JMIR Form Res*, 5(8), e28878. doi: 10.2196/28878.

COMET initiative registration

The study is registered on the COMET (Core Outcome Measures in Effectiveness Trials) initiative database: Registration number 1084. Registered on 09 January 2018, last updated on 13 June 2022.

2.1 Background

This chapter aims to map the methodology utilised to develop the COS for SSD interventions, and the rationale behind the steps taken. We adopted recommendations by the COMET initiative (Brookes et al., 2016; Kirkham et al., 2016; Kirkham, Davis, et al., 2017; Sinha et al., 2011; Williamson and Clarke, 2012), and the COMET Handbook version 1.0 (Williamson et al., 2017) for the core outcome domain set development. We used a modified e-Delphi process (a series of online survey rounds) followed by a consensus meeting to achieve a consensus of opinion from broadly representative and international expert stakeholder groups (Keeley et al., 2016). A prospective study protocol was registered on the COMET database in January 2018. For the measurement instruments assessment process we adopted COMET and

COSMIN methodological guidelines (Mokkink, Terwee, Patrick, et al., 2010a; Prinsen et al., 2014, 2016).

2.1.1 Chapter aims and objectives

Chapter 2 aims to describe the methods adopted, the theoretical background, and detailed rationale for adopting the chosen methodology.

This chapter objectives were:

(i) To describe the development of the Core Outcome Set for Single-Sided Deafness (CROSSSD) initiative

(ii) To describe the design of an international consensus process to develop a core outcome set for SSD interventions, comprising an agreed minimum set of outcome domains relevant to both patients and professionals.

2.2 Core outcome set development process

The core outcome domain set development roadmap adopted is summarised in Figure 2-1 and described in detail below.

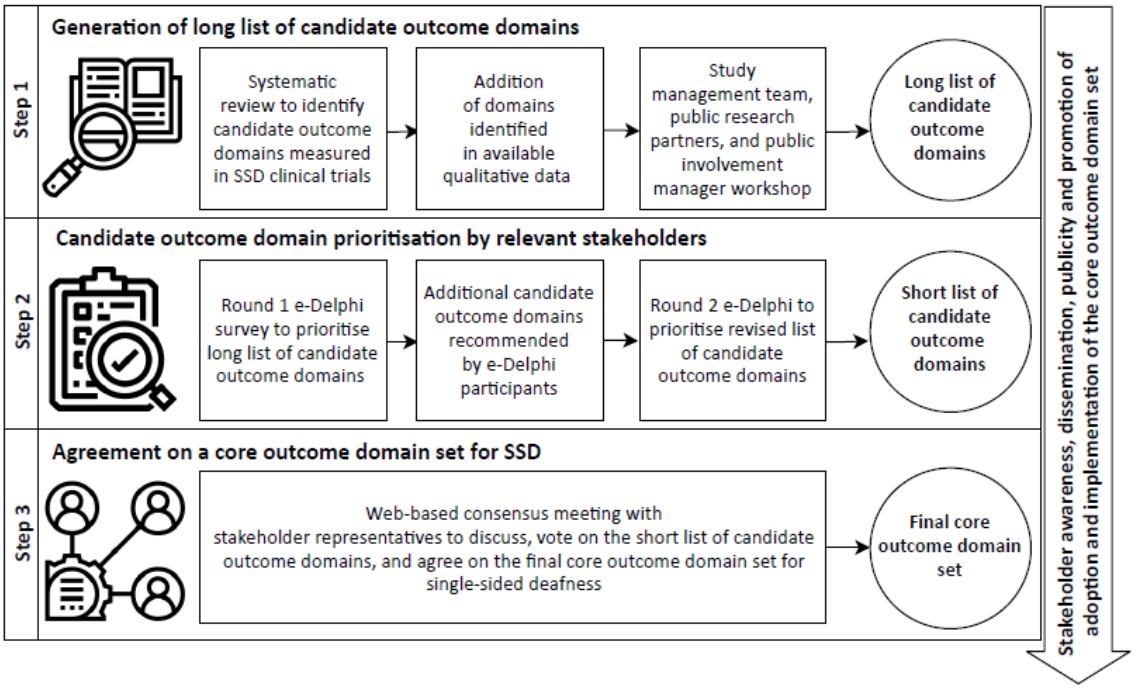

Figure 2-1. Overview of the process used to develop a core outcome domain set for clinical trials investigating single-sided deafness interventions in adults.

In summary, the study comprised of three main steps:

Step 1: Generating a long list of candidate outcome domains utilised to date in clinical trials assessing rerouting and restoring interventions for adults with SSD.

Step 2: Prioritising which of these outcome domains are critically important to measure when assessing whether an SSD intervention has worked, or not, by involving a large representative set of SSD stakeholders (healthcare users and professionals, i.e., healthcare practitioners, clinical researchers, commercial representatives, and funders working in the field of SSD).

Step 3: Reaching a final consensus decision with a subset of stakeholder representatives on which outcome domains are sufficiently critically important to constitute the core outcome domain set for SSD interventions in adults.

Ethical approval was sought for each aspect of the study where ethical approval was required. The Good Clinical Practice (GCP) guidelines and regulations were followed at all times by the study lead (RK) who attended the relevant courses and refreshers. The study protocol was compiled (Appendix 5) and once approved by the Sponsor, the University of Nottingham (UoN), ethical approval was authorised by the Nottingham 2 Research Ethics Committee (REC), Health Research Authority (HRA) and Health and Care Research Wales (HCRW), Reference: 19/EM/0222, Integrated Research Application System (IRAS project ID 239750) on 06 August 2019.

2.2.1 Generation of a long list of candidate outcome domains

Potentially important outcomes were first gathered from a systematic review of the literature (Chapter 3) which identified those outcome domains and measurement instruments reported in studies investigating interventions that sought to restore hearing in adults with SSD (Katiri, Hall, Killan, et al., 2021), and by considering published qualitative data from focus group interviews examining subjective psychological and social effects of highly asymmetric hearing loss (Lucas et al., 2018).

A two-day face-to-face workshop was organised in July 2019 with members of the study management team (see Section 2.4.1 for the composition of this team) and the research steering group (see Section 2.4.2 for the composition of this group). The

workshop short guide and agenda shared with the study management team and steering group attendees prior to the workshop can be found in Appendix 4. During the workshop the long list of candidate outcome domains was reviewed, with the following objectives:

(i) exclude outcome domains that were deemed out of scope for this COS,
(ii) identify any missing outcome domains,
(iii) consider the choice of language used to label and define each outcome, and
(iv) generate plain language descriptions for each outcome domain.

First, the CROSSSD study management team collated all primary and secondary outcome domains that were identified by the systematic review (Katiri, Hall, Killan, et al., 2021). All individual outcome domains were first listed in an Excel spreadsheet (Microsoft Corporation, 2022), duplicates were removed, and the remaining were transferred onto PowerPoint slides, and then printed on cards in preparation for the workshop. During the workshop each member first performed an independent rapid review of the individual outcome domains and marked those that were thought to not fit in the scope of core outcome domain set for SSD interventions. It was agreed that an outcome domain would be excluded, as not fitting in the scope, if all six members unanimously agreed to exclude or there was no more than one dissenting opinion.

The workshop team next systematically reviewed and discussed the findings published by Lucas et al. (2018) to determine whether qualitative interviews might have identified any other candidate outcome domains. Using qualitative methods in the pre-Delphi stage can help to identify what outcomes are important to stakeholders and has the potential to increase the research community's confidence in the COS (Keeley et al., 2016). Alternatives to qualitative interviews, which are done in less than 5% of studies, with small samples of 5 to 15 patients have been proposed by Chevance et al. (2020). For example generating lists of candidate outcome domains by mapping the expectations toward treatment of a large number of stakeholders (1,000 to 3,000), internationally, by using an online survey with open-ended questions has been suggested to be more feasible (Chevance et al., 2020).

Once a shorter list of candidate outcome domains was finalised, theirs labels were reviewed, plain language descriptions were developed for each domain, and they were categorised as per recommendations (Williamson et al., 2017). Some of the outcome domains were the same as had been defined in previous work on tinnitus (Hall, Smith, Hibbert, et al., 2018) or hearing loss (Vas et al., 2017); and so we used the same plain language definitions where appropriate. Others required plain language descriptors to be developed through interactive discussion during the workshop. The discussions allowed us to understand the items from the perspective of participants, and refine them where indicated (Harman et al., 2015; Wilson and Cleary, 1995). Input from healthcare users with lived experience of SSD in naming the outcome domains and modifying the plain language descriptions was important to ensure they were unambiguous, understandable and relevant (Harman et al., 2015; Smith et al., 2018). Healthcare users have an important role in developing clear explanations of a COS and associated concepts, and help minimise the risk of using concepts that are not accessible by the general public (Young and Bagley, 2016).

An example of a study where the concepts used were off-putting and had a negative impact on accessibility was the management of Otitis Media with Effusion in children with cleft palate (mOMEnt) feasibility study, where low levels of recruitment were observed as a consequence (Bruce et al., 2015; Harman et al., 2015). One example where healthcare user input helped refine the domain descriptors in our study was for Listening effort and Physical tiredness outcome domains. In the original descriptors, both domains included the concepts of feeling tired and fatigued. Therefore, a clarification had to be included to ensure the two outcome domains could be distinguished. The long list of candidate outcome domains, labels and plain language descriptors were subsequently circulated electronically to the CROSSSD study steering group (see Section 2.4.2 for the composition of this group) for feedback. The steering group were asked to comment on the clarity of the plain language descriptors. This was done to ensure that the outcome domain concepts were explained in ways that were understandable and meaningful to an international audience, especially to those whose first language was not English. The study steering group was also prompted to suggest any missing candidate outcome domains. The study management group

utilised this feedback and following further revisions to the long-list prepared a final list of candidate outcome domains that were incorporated into the e-Delphi.

2.2.2 Candidate outcome domain prioritisation by relevant stakeholders

A common technique to elicit stakeholder views and develop consensus about important outcomes is using Delphi surveys (Turoff, 1970). The technique provides anonymity so opinions are not influenced by dominant individuals, and can be shared with stakeholders internationally, either by post or electronically. Indeed, it was first reported on in the 1960s, where it was used to establish opinions anonymously, on issues related to sensitive military operations (Dalkey and Helmer, 1963). It is now common for sequential surveys to be shared with relevant stakeholders online, responses are analysed and subsequently shared back anonymously within the context of another survey. Participating stakeholders can consider the views of others globally (e.g., other healthcare users, or professionals) before anonymously re-rating items in the subsequent survey, to eventually achieve a final level of agreement and where agreement reaches a pre-defined level, consensus. Delivering this study online allowed us to capture the opinions of a diverse population of stakeholders with an interest in shaping outcome measures for SSD interventions. If any healthcare users did not have home access to a computer or a tablet, they were offered the option of visiting the NIHR Nottingham BRC to complete the two online rounds using one of the centre's computers.

The e-Delphi technique can minimise response bias as individual feedback is anonymised and not affected by views of influential individuals (Keeney et al., 2001), and it has several advantages over other methods such as forums or discussion meetings to reach consensus (Sinha et al., 2011). Advantages include maintaining participant anonymity (Thiebes et al., 2018), and avoiding dominance of more assertive participants. Delphi studies can therefore be used to gather expertise on essential outcomes for a particular disease or condition, from a variety of stakeholders to establish consensus (Williamson et al., 2017). Researchers have expressed concerns about the lengthy process of multiple Delphi rounds, which can lead to dissatisfaction

and loss of interest among participants; which in turn can have a detrimental effect on recruitment and retention of participants (Hall, Smith, Heffernan, et al., 2018).

Alternative methods have been proposed, such as the 'real-time Delphi' methods (Gordon and Pease, 2006). In the real-time Delphi participants are encouraged to revisit the Delphi and amend their ratings throughout the period the Delphi is live, which has been found to be cost-effective and have a positive impact on attrition (Geist, 2010). A recent COS development study for interventions for the treatment of neonatal encephalopathy aimed to identify whether different outcomes are prioritised when using a multi-round compared with a real-time Delphi method (Quirke et al., 2021), but the results are not yet published.

Surveys can also be perceived as intimidating for members of the public as a result of the long number of outcomes that have to be scored at every round (Keeney et al., 2001). However methodological features highlighted by Smith et al. (2018), such as refining the long list of outcome domains and using plain language definitions as enabling user participation were adhered to where possible (Smith et al., 2018). The COMET handbook highlights the benefit of qualitative research findings from healthcare user focus groups for ensuring that the outcome domain names and definitions are understandable to healthcare users, but Williamson et al. (2017) do not specifically mention the role of research partner involvement in the process. Smith et al. (2018) however provide recommendations on helpful principles when involving healthcare users including: (i) planning what patient involvement steps are likely to be most beneficial in the COS development process and incorporate into the ethical approval processes, (ii) appoint eager and engaged research partners who are willing to share their opinions generously, and (iii) careful reviewing focusing on discussions on the names of the candidate outcome domains, underlying theoretical constructs and plain language definitions.

Evaluations discussed by Hall et al. (2018), were considered to ensure robust recruitment and retention of healthcare users (Hall, Smith, Heffernan, et al., 2018).

These included (i) a dedicated study webpage[5], (ii) personalised email invitations and reminder emails, (iii) development of information sheets with input from the research partners, (iv) naming and developing outcome domain descriptions with input from the research partners, (v) creation of demonstration videos to promote usability of the online survey tool (CROSSSD initiative, 2019), and (vi) minimum wait between rounds to promote retention. Recent studies investigated the topic of outcome domain translation and cross-cultural adaptation in the context of developing Delphi surveys for COS, using a multi-language international Delphi survey (Alkhaffaf et al., 2017). The authors translated their survey into seven languages. Although the English language survey was offered to all participants, most preferred to complete the Delphi in their native language; and their resulting number of participants from non-English-speaking nations was significantly higher than those recruited from English-speaking countries (Alkhaffaf, Blazeby, et al., 2021). However, although the number of participants increased with this approach, it was not clear in this study whether these additional participants brought a different perspective that has not already been captured through the English-language version of the survey. Indeed, a follow-up study by the same group indicated that there was little variation in opinion within stakeholder groups when participant region and other characteristics are considered (Alkhaffaf, Metryka, Blazeby, Glenny, Williamson, et al., 2021).

The modified international e-Delphi survey used for the CROSSSD study comprised two sequential questionnaires or 'rounds' aiming to obtain a consensus of opinion from professional and healthcare users stakeholder groups. The modified e-Delphi surveys presented participants with a long list of candidate outcome domains, each accompanied by a plain language definition. Each Delphi survey was managed using a bespoke online e-management system, the DelphiManager software, version 4.0 maintained by the COMET initiative (COMET initiative, 2019). Each panellist received a unique identification code and an e-link to the webpage. A video explanation (CROSSSD initiative, 2019) was developed to illustrate how to complete the online tool (e-Delphi), with input from the research partners.

[5] www.nottingham.ac.uk/go/CROSSSD

The randomisation feature of the DelphiManager software was utilised to avoid potential weighting (Blackwood et al., 2015; Brookes et al., 2018), i.e., outcome domain items were presented in a random order to reduce the potential for systematic contextual effects on scoring (Gargon, Crew, et al., 2019; Williamson et al., 2017). Gargon et al. (2019) reviewed 31 COS studies, and refer to the importance of maximising response rates to a Delphi study and minimising attrition rates and potential attrition bias (Gargon, Williamson, & Young, 2017). The authors highlight that outcome domain presentation order matters, and derived two further characteristics that led to reduced response rate: (i) larger size of panels, and (ii) studies with more items included in the second round. Brookes et al. (2018) completed a randomised controlled trial to explore the impact of question order within a Delphi survey used in the development of a COS for oesophageal cancer surgery. The study focused on the impact of question order on Round 1 responses. Outcome domains presented at the beginning of a survey may motivate or demotivate an individual to respond, and in this study, healthcare professionals were less motivated to respond if clinical outcome domains appeared first (Brookes et al., 2018). In addition, in the Brookes et al. (2018) patients inflated the importance of patient-reported outcomes when rating them last in the survey, whereas professionals inflated the importance of clinical items when they appeared last. The authors concluded that question order within the Delphi survey should be randomised in terms of presentation of patient-reported and clinical outcomes to avoid contextual effects on scoring, which will ultimately influence the final COS.

Both survey rounds contained a questionnaire that included the final long list of categorised outcome domains developed in Step 1 (Figure 2-1). Eligible international healthcare users and professionals with experience in receiving or managing SSD interventions were identified and invited to take part. They were asked questions that confirmed their stakeholder group, and that they met the eligibility criteria for their stakeholder group. See Table 2.1 for eligibility criteria for participation for each of the stakeholder groups.

Table 2.1. Eligibility criteria for participation for each of the stakeholder groups.

Stakeholder group	Eligibility criteria (as listed on the participant information leaflets)
Healthcare users	✓ Are aged 18 years or over, ✓ Have been diagnosed with SSD 12 months ago, or more ✓ Are able to read, understand and complete questionnaires in English ✓ You have received or considered trying treatment for your SSD
Healthcare practitioners	✓ Have a clinical qualification ✓ Are currently employed by a public or private institution that provides SSD interventions to patients ✓ Experience of assessing, diagnosing or managing SSD in adults
Clinical researchers	✓ Have an academic qualification ✓ Are currently employed by a research organisation ✓ Have current or 'recent past' experience with studies that focus on questions of clinical efficacy (benefit) of SSD interventions in humans ✓ Evidence of 'recent past' experience in clinical research will be defined as having been a co-author on a relevant peer-reviewed journal publication in the past 3 years
Commercial representatives	✓ Are currently employed by a company that develops, manufactures or sells product(s) that may be used an SSD intervention
Funders	✓ Are currently employed by an organisation that funds SSD research ✓ Experience of reviewing funding applications for SSD interventions research in the last 3 years

* Participants could complete the surveys if they: (i) were able to read, understand and complete questionnaires in English, and (ii) fulfilled any of the roles and criteria specified in the table.

Professional stakeholder groups included individuals involved in the management or research in the field of SSD. These were healthcare professionals, clinical researchers and commercial representatives, funders and journal editors. These groups had been identified as those representing the main professional categories in SSD research and clinical trials.

The study was adopted by the National Institute for Health Research (NIHR) Clinical Research Network (CRN) portfolio, Central Portfolio Management System, CPMS record 42260. Informed consent was obtained from all study participants as per approved final study protocol version 2.0, dated 06 July 2019.

Upon entering the online survey webpage, an introductory page reiterated key information previously provided in the participant information sheets (see Appendix 6 for the healthcare users information sheet), including an embedded link to a video explanation on how to complete the survey (CROSSSD initiative, 2019). The video explanations guided participants through the round. Participants were then asked to give informed consent using an online consent form (Appendix 7) and a unique identification code was generated to allow for tracking of individual responses in Round 2.

Following this, participants were asked to complete a checklist of relevant personal characteristics. These included personal and/or professional experience with the interventions, treatments trialled for SSD (e.g., BAHA, CROS), the group they primarily identified with (e.g., healthcare users, healthcare practitioners, clinical researchers, commercial representatives, funders), age range, gender, country of residence, primary language for communication, professional role (if applicable), time since SSD diagnosis, treatments primarily used (for healthcare users, in case they had two devices e.g., a CROS and a BAHA), and email address.

The draft survey was piloted by the study management team and public research partners (see Section 2.4.2 for description of the public research partners) for face validity, understanding, and acceptability. The aim of piloting the survey was to try to overcome limitations identified by previous teams whose e-Delphi participants had reported that the language used was somewhat difficult to understand (Hall, Smith, Heffernan, et al., 2018). An example finding was that, once reviewed a comment was added to highlight that hovering the computer mouse over the name of the outcome domain allows users to view the outcome domain definition, which was not immediately obvious in the initial draft survey. Following this, if needed, modifications were made before finalising and launching the questionnaire. When the first round of the e-Delphi was launched, participant recruitment commenced immediately. Participant response rates were monitored throughout, and the study management team kept clearly defined records of the number of participants that completed the rounds and those who did not.

2.2.2.1 e-Delphi Round 1

For each of the outcome domains, participants were asked to think about the importance of each and indicate how important it is to measure when deciding if an intervention is working. Participants were asked to assign a score to each of the candidate outcome domains. A 9-point Likert scoring system was utilised with a score of 1 to 3 signifying an outcome domain is of *limited importance*, 4 to 6 *important but not critical*, and 7 to 9 *critical and important* (Guyatt et al., 2011). Participants were made aware that an outcome domain would only be considered for inclusion in the core outcome domain set if 70% or more of the participants in each of the stakeholder groups selected scores 7-9 on the scale. If a participant felt that they did not understand a particular outcome, they were able to select '*unable to score*'.

A 9-point scale is commonly used in COS development studies (Diamond et al., 2014; Schmitt et al., 2011; Williamson, Altman, Blazeby, Clarke, Devane, et al., 2012), however one study involving total knee arthroplasty participants compared three different rating scales (3-point, 5-point, 9-point) in reaching consensus (Lange et al., 2020). The healthcare users that participated in the Lange et al. (2020) study, 36% preferred the 5-point scale, 23% the 3-point scale, and 16% the 9-point scale, whereas one quarter of participants had no preference. The use of different ratings scales lead to different consensus in this study. However the authors were unable to comment on the 'best' scale to use due to test-retest reliability and stability of the consensus results. One limitation of this study was that participants saw and rated the treatment goals on all three scales simultaneously, which might have introduced bias.

Following each outcome and at the end of the questionnaire, participants were offered an open-text box to add any comments about particular outcome domains. This was optional but participants were encouraged to provide a reason for their scores on individual outcomes, as recommended by the COMET handbook (Williamson et al., 2017). These comments were summarised as part of the feedback to participants after Round 1. Participants were also able to propose additional outcome domains. These additional outcome domains were reviewed and coded by the study management team members (see Section 2.4.1 for description of the study management team), with

appropriate plain language descriptions, to ensure that they represented new items for inclusion in Round 2. Where uncertainty existed, the study steering group was consulted, and all new outcome domain terms, concept definitions and category labels were reviewed. Adhering to current recommendations, reporting of the e-Delphi surveys described any new outcomes introduced into the consensus process at the end of Round 1, with reasons (Kirkham et al., 2016).

2.2.2.2 e-Delphi Round 2

The purpose of Round 2 was to enable participants to reflect on their scores considering the viewpoint of their stakeholder group, and the other stakeholder groups who participated in Round 1. Participants were presented with the score they personally gave each outcome domain during Round 1 together with numerical and graphical feedback on histograms (Appendix 8) on the distribution of scores across the key stakeholder groups (healthcare users, healthcare professionals, clinical researchers, or commercial representatives).

Feedback enabled participants to reflect on their scores considering the distribution of scores from their own and the rest of the stakeholder groups and re-score each outcome domain if they choose to do so. The importance of providing high-quality feedback on group responses as a way of ensuring validity of consensus-based Delphi processes has been highlighted in qualitative studies (Khodyakov and Chen, 2020). Participants were asked to re-score the same list of outcome domains, considering this new information. To help give meaning to the 9-point Likert scoring system scale (Guyatt et al., 2011), participants were reminded that individual outcome domains would only be considered for inclusion in the core outcome domain set if 70% of all participants selected points 7-9 on the scale. The distribution of the new scores for each outcome domain were calculated for each stakeholder group. Other aspects of design and analysis were the same as for Round 1.

The impact of different feedback strategies on subsequent agreement and variability in Delphi studies was explored in the context of a prostate cancer COS (MacLennan et al., 2018). They randomised participants in Round 2 to receive Round 1 feedback from (i)

peers only, or (ii) multiple stakeholders separately, or (iii) multiple stakeholders combined. There was no evidence of a difference between different feedback strategies. Similarly, Brookes et al. (2016) randomised participants to receive Round 1 feedback from (i) peers only, or (ii) multiple stakeholder group feedback. They found that feedback did not impact on the percentage of items for which a participant subsequently changed their rating, however it did impact on items retained at the end of Round 2. Furthermore, differences in Round 2 scores were smaller between stakeholder groups receiving multiple feedback than between those receiving peer group feedback only. Therefore, they concluded that providing feedback within Delphi questionnaires from all stakeholder groups separately may influence the final core outcome set and improve consensus between the groups (Brookes et al., 2016). Other multi-panel studies indicate that healthcare users are more likely to change their responses and to do so meaningfully in mixed panels, whereas professionals are more likely to do so in homogeneous panels, but response change varies according to topic (e.g., level of outcome seriousness) (Khodyakov et al., 2022).

Participants were eligible to continue to Round 2 if they had scored at least 50% of the outcome domains in Round 1. Corresponding data from those participants who responded to less than this were removed. Consensus was defined as at least 70% of the participants in all three stakeholder groups scoring 7-9 (*critical to measure* in all trials) and fewer than 15% in any stakeholder group scoring 1-3 (*not important* in deciding whether an SSD intervention is effective).

The protocol set out to consider commercial representatives and funders collectively as one stakeholder group due to similar stakeholder opinions expected and the anticipated small number of participants (Katiri, Hall, Buggy, et al., 2020). Similar to the methods utilised by the mOMEnt (management of Otitis Media with Effusion in children with cleft palate) team if a reduced number of responders (n<10) was observed for one or more stakeholder groups then Round 2 Delphi data would be reviewed and revised (Harman et al., 2013). For example, we would consider amalgamating stakeholder groups if the number of participants in individual groups was too low. No funders participated in Round 2, so the last group comprised

commercial representative participants only. All participants received the same list of outcome domains with feedback tailored according to their key group allocation (healthcare users, healthcare professionals, clinical researchers). Participants who identified themselves as commercial representatives when they registered were considered collectively, and feedback on their scores was reported separately from the three stakeholder groups. However the commercial representatives were eventually amalgamated with clinical researchers to compensate for the small number in their group, and all candidate domains 'voted in' as per the pre-determined '70 / 15%' consensus approach were progressed to the consensus meeting prioritisation exercise.

Compliance in the e-Delphi survey was defined according to the number of participants completing Rounds 1 and 2. Participation within each stakeholder group was assessed including (i) numbers who were directly contacted, (ii) numbers who registered in the e-Delphi software, (iii) numbers enrolled; and (iv) numbers who completed each e-Delphi round. Other analysis incorporated participant characteristics, such as gender, country, region, native English language speaker (or not). We analysed the shifts in scores between Round 1 and 2 for each outcome domain and stakeholder group, after they considered the anonymised feedback from other participants.

Attrition, referring to the percentage of participants who withdrew or dropped out between rounds was analysed and reported using similar methods used by the mOMEnt team (Harman et al., 2013) and the COMiT'ID team (Hall, Smith, Hibbert, et al., 2018). For example, attrition bias which might occur if participants who do not respond in Round 2 have different views from their stakeholder group peers who participate at both rounds (Williamson et al., 2017) was considered and analysed. Methods used by other COS developers were adopted, such as drawing response distributions of withdrawn and completing participants (Bruce et al., 2015), or drawing graphical representations by stakeholder group (healthcare users, healthcare professionals, clinical researchers) to indicate whether attrition bias is likely to have affected the outcome domain recommendations (Hall, Hibbert, et al., 2019).

2.2.3 Consensus meeting

A face-to-face consensus meeting was organised as per protocol (Katiri, Hall, Buggy, et al., 2020) to take place in London, UK, on 19 March 2020, at the Action on Hearing Loss headquarters (now known as the Royal National Institute for the Deaf). Twenty-two participants were invited (six healthcare users, eight healthcare professionals, two public research partners, who have first-hand, or lived experience of SSD; a patient involvement manager, two facilitators, two members of the study management team, and one observer). Fifteen participants were travelling from within the UK and seven from Europe.

To comply with the travel and physical distancing restrictions imposed by the UK government in response to the COVID-19 pandemic, a modification to a web-based meeting in place of a face-to-face consensus meeting was introduced. On cancellation of the face-to-face meeting, we invited participants to continue their participation. The web-based meeting was scheduled to take place on 07 July 2020. A non-substantial category C amendment to the ethical approval was obtained to accommodate the change to a web-based consensus meeting and follow-up focus groups (Sponsor reference: 19032, minor amendment reference number: NSA01). Informed consent using an online form (Appendix 9) was obtained prior to participation at the consensus meeting and follow-up focus groups. Participants were reminded that they could withdraw from the study at any point without needing to give a reason. All participants were volunteers and no reimbursement was given for their contribution.

2.2.4 Agreement on a core outcome domain set for single-sided deafness interventions

The aim of the third and final step (Figure 2-1), which included the web-based stakeholder consensus meeting, was to integrate healthcare users' and professionals' perspectives on outcome domains and provide final recommendations on an agreed core outcome domain set for SSD interventions. Round 2 score distributions for each outcome domain was considered at the final consensus meeting using a nominal group technique (Van de Ven and Delbecq, 1972) to evaluate individual perspectives. For example, like Harman et al. (2013) adopted methods, the results of the stakeholder

group responses were compared with the whole group response and percentage agreement was considered to plan the focus of the consensus meeting (Hall, Smith, Hibbert, et al., 2018).

Participants who had completed the two rounds of the e-Delphi survey, responded to at least 90% of the outcome domains in Round 2, and registered an interest in participating in the consensus meeting were eligible to participate. Some COS developers run consensus meetings separately for healthcare users and professionals (Potter et al., 2015). Their rationale for separating the groups was to allow healthcare users' views to be heard without contamination from other stakeholder groups. Other COS developers brought healthcare users and professionals together to discuss their views, but attendance at the consensus meeting was lower than expected (Harman et al., 2015). More recently, the COS for surgical trials in gastric cancer (GASTROS study) team introduced a hybrid method of participating in their consensus meeting (Alkhaffaf, Metryka, Blazeby, Glenny, Adeyeye, et al., 2021). Participants could take part by attending the meeting venue in person (n=18), or through an online platform (n=25). The authors have not discussed the benefits or limitations of this approach in their published paper (Alkhaffaf, Metryka, Blazeby, Glenny, Adeyeye, et al., 2021).

Places were allocated on a first come, first served basis. In the absence of firm recommendations on this aspect of the consensus process (Williamson et al., 2017), recruitment was guided by a previous hearing research COS development study, the COMiT'ID study (Fackrell et al., 2017). Allocated places maintained a 50:50 balance across healthcare users and professionals; and aimed to include non-UK, non-native English language speakers.

As far as possible, the COMET guidance for designing an accessible face-to-face consensus meeting was followed (Williamson et al., 2017). The conventional final step of the consensus process recommends a smaller scale consensus meeting to discuss the outcomes of the e-Delphi surveys and agree a final COS (Williamson et al., 2017). The consensus meeting is typically face-to-face, consistent with other applications of

the nominal group technique in the context of healthcare research (Gladman et al., 2020; Harvey and Holmes, 2012).

There was limited information about web-based qualitative data gathering from groups in healthcare (Dodds and Hess, 2021; Flynn et al., 2018; Imlach, 2020; Olsen, 2019), and its evaluation from the participant perspective appeared somewhat minimal (Daniels et al., 2019). Given that CROSSSD is about people with SSD, the web-based methods adopted had to be accessible to people with possible communication difficulties (Choi et al., 2021; Dwyer et al., 2014; Snapp and Ausili, 2020), as well as suitable for data gathering, adding an extra layer of considerations.

Methodological changes required only notification of a non-substantial category C amendment to the study sponsor, the University of Nottingham. Examples of these changes included: (i) amendment of the participant information leaflet to say 'web-based consensus meeting', (ii) recording individual consent online, and (iii) extending the study end date. Participants consented to take part in the consensus meeting by completing an online form (Appendix 9). Voting during the consensus meeting was conducted using hyperlinks to Jisc surveys[6].

After confirming their attendance to the consensus meeting, participants were sent an email with information on how to attend the web-based meeting. The aims of the meeting were stated, and the participant information sheet (see Appendix 6 for the healthcare users information sheet) was shared again as a reminder, ensuring that all participants understood the purpose and could ask questions before consenting. Experienced independent moderators were recruited to facilitate the consensus meeting discussions to agree a final COS. Participants were also given materials summarising the anonymised Round 2 results, to support the discussions during the day. Finally, the 12 voting participants were also emailed a link to a Jisc survey asking them to choose their 'top three outcomes' out of the 17 short-listed domains. This

[6] https://www.onlinesurveys.ac.uk/

survey was introduced following modification from a face-to-face consensus meeting to a web-based meeting to help fast-tract the process on the day.

Microsoft Office Teams was used for online discussions because (i) it was supported by the study sponsor (University of Nottingham), (ii) download was freely available, and (iii) it had desirable features including gallery view of all participants, a chat function, live caption ability, and audio recording. Optional one-to-one practical software tutorials were offered to all participants prior to the meeting to ensure all necessary functionality was accessible and understood by participants. To enable participants to test the technology and meet each other socially, a discretionary virtual coffee morning was held the week prior to the meeting.

The public research partners, patient involvement manager, and facilitators with experience in conducting COS face-to-face consensus meetings and qualitative research contributed to the planning of the web-based meeting including its structure, timing, preparatory activities, communication strategies, discussion points, and voting techniques. The public research partners helped to enhance accessibility for those with hearing difficulties, drawing upon their own lived experience, as per recommendations when designing COS studies (Williamson et al., 2017; Young and Bagley, 2016). These enhancements included meeting etiquette (e.g., use the 'raise hand' function and wait your turn), chairing (e.g., making the facilitators aware of their role, ways to resolve conflict, adhering to the agenda), accessibility (e.g., enabling the automatic captions) and troubleshooting (e.g., use the chat function, or exit and re-enter the software).

In line with the approach advocated by COMET (Williamson et al., 2017), and to obtain qualitative information from our participant group in a structured manner (Azzari and Baker, 2020), a nominal group technique approach (Van de Ven and Delbecq, 1972) was adopted. Nominal group technique allows groups to explore and thoroughly discuss issues in hand, identify, rank, and rate various problem dimensions with limited researcher influence or interference (Gladman et al., 2020; Olsen, 2019).

Conventionally, the nominal group technique comprises the following steps:

(i) a chairperson introduces the group, sets ground rules, and explains the purpose of the meeting and procedures for the day,
(ii) the chairperson states the question and encourages each participant to individually reflect and brainstorm,
(iii) with the help of a facilitator, participants have an opportunity to discuss and clarify ideas; and
(iv) participants evaluate the ideas and vote anonymously for the 'best ideas'.

In CROSSSD, steps (iii) and (iv) were conducted in three parallel sub-groups. Each facilitator presented the main discussion points using pre-determined guidance (Appendix 10) before voting. When consensus was required, an additional step (v) shared the voting results with the group and provided the opportunity to discuss and vote again. In the present study, results were presented using histograms embedded in PowerPoint slides. If consensus was not reached after two rounds of voting, a 'majority rules' approach was to be applied. Because time for discussion would be limited, there was no discussion about outcomes whereby the Round 2 data met the criteria for exclusion based on the pre-defined consensus definition.

Consensus recommendations were guided by Round 2 results. The '70 / 15%' consensus approach as described by the COMET Handbook and other COS developers (Hall, Smith, Hibbert, et al., 2018; Harman et al., 2015; Williamson et al., 2017; Williamson, Altman, Blazeby, Clarke, Devane, et al., 2012) was utilised:

- For outcomes recommended to be included based on the Round 2 analysis (70% scored 7-9), the moderator would establish whether anyone has a major reason to want any to be excluded. The moderator would focus the discussion and voting on these outcomes. Domains would be included if at least 70% of participants vote *'In'*. All other outcomes recommended for inclusion would be *'In'*, without further discussion.
- For outcomes where at least 50% of more than one stakeholder group scored 7-9 on the Round 2 analysis, the moderator would focus the discussion and voting. Domains would be included if at least 70% of participants vote *'In'*.

- For outcomes where less than 50% of the participants in all stakeholder groups scored 7-9 in Round 2, the moderator would establish whether anyone had a major reason to want any to be included. Domains were only included if at least 70% of participants voted them *'In'*.

During the consensus meeting, which was 7 hours long with three 30-minute breaks, a series of discussion and voting steps reduced the pool of candidate outcomes to a final COS. The first step was to present the results from the 'top three outcomes' survey conducted prior to the meeting and asked whether whether participants agreed to exclude those outcomes that had not been selected by anyone to be in their top three. Voting options were *Agree*, *Disagree*, or *Unsure*.

Next, participants were asked to consider the remaining outcomes and to identify five that they considered critical to be measured in every clinical trial of interventions for SSD. During sub-group discussions, the facilitators moved the outcomes around on a shared visual display to reflect discussions (Figure 2-2). The green zone included outcomes considered 'always critical', the grey zone included outcomes considered 'not critical' and the intermediate zone was for those with mixed opinions or not yet discussed.

When participants returned to the full group, they were asked to vote whether they would exclude those outcomes considered 'not critical' (i.e., in the grey zone). This process was repeated after whole group and sub-group discussions to reduce the list of candidate outcomes. Finally, participants considered the remaining outcomes that had not yet been voted 'in' or 'out' and voted on whether the 'always critical' set should form the COS for SSD interventions. Applying the criterion of 70% agreement as per protocol (Katiri, Hall, Buggy, et al., 2020), at least nine out of the 12 participants had to agree for any decision to be carried.

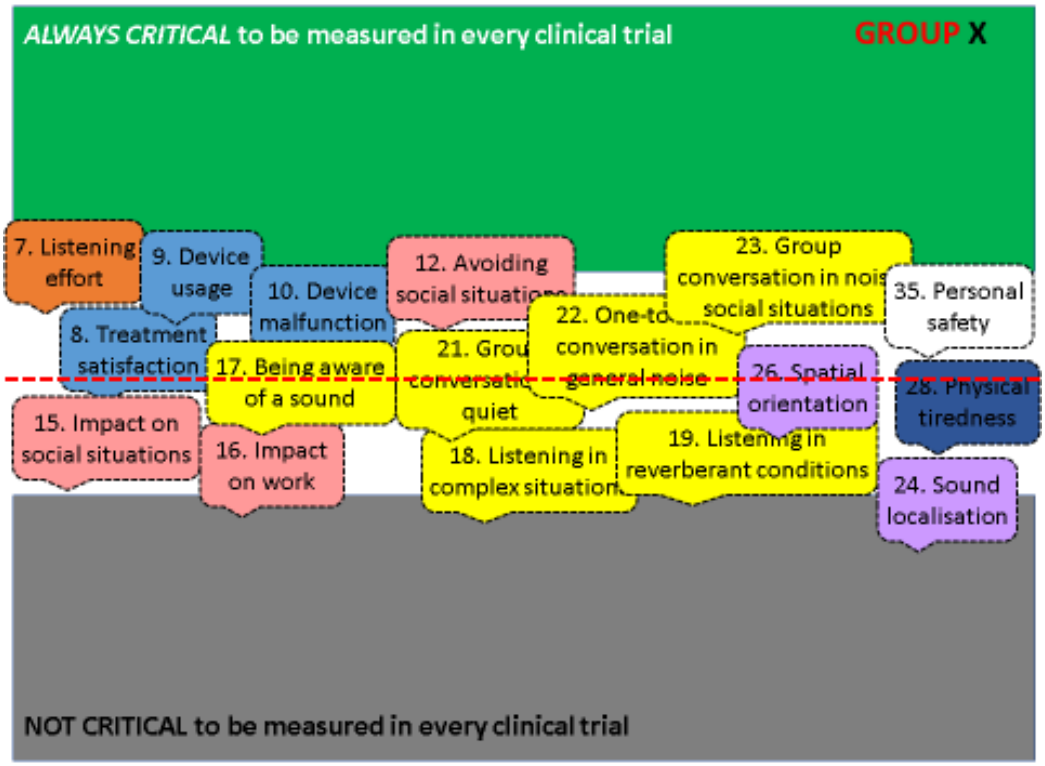

Figure 2-2. The PowerPoint slide used to provide a visual display of the outcome domains for consideration during the group discussions.
*The various colours represent the domain categories, which the outcome domains were arranged into for the Delphi surveys (Orange: *Other effects*, Light blue: *Factors related to the treatment being tested*, Salmon pink: *Health-related quality of life*, Yellow: *Hearing disability*, Purple: *Spatial hearing,* Dark blue: *Physical effects*, White: *Self*). The number the outcome domains are labelled with is consistent with the numbering that was used in the Delphi surveys.

The consensus meeting was recorded and transcribed to facilitate reporting. Recordings were classed as source data and were retained in the study archives. For formative feedback, all voting participants were asked to complete an online consensus meeting evaluation form (Appendix 11). This was adapted and modified from the recommended template developed by the COMET initiative (COMET initiative, 2022) and was distributed to participants online using Microsoft Forms as opposed to printed out as originally planned for the face-to-face consensus meeting. Data from the Delphi feedback questionnaire and consensus meeting evaluation form comprised open-text responses and these were analysed using a thematic analysis approach. This approach was adopted because it is a flexible way to analyse qualitative data (Braun and Clarke, 2006).

2.2.5 Web-based consensus meeting stakeholder feedback

The amendment of the consensus meeting format from face-to-face to web-based was evaluated by collating stakeholder experiences. For formative feedback, participants responded to six statements (Table 2.2) on the pre-meeting information they were issued, their experience of the consensus meeting, and fairness of the outcome using a 5-point Likert scale (Strongly agree / Agree / Neither / Disagree / Strongly disagree) and open-text boxes for further comments. It was estimated that completion of the form took approximately 10 minutes and completion was entirely voluntary.

Table 2.2. Statements consensus meeting participants were asked to give feedback on using a 5-point Likert scale.

	Statement scored using a 5-point Likert scale
1	The information that the organisers provided me with in advance of the meeting was helpful
2	I was satisfied with the process used to agree the core outcomes set on the meeting day
3	I was satisfied with the way the meeting was facilitated
4	I felt able to contribute to the meeting
5	I felt comfortable in communicating my views
6	The workshop produced a fair result

The two further open-text boxes sought feedback on the practical arrangements for the meeting and suggestions for improvement. All other meeting participants (facilitators and observers) were invited to respond to a modified version of the evaluation involving the open-text comments only.

2.2.6 Dissemination and engagement strategy

Barriers to dissemination and uptake of core outcome sets include lack of involvement of relevant stakeholders in developing the set, lack of buy-in from relevant stakeholders, and disagreement among researchers, clinicians and policymakers (Tunis et al., 2016; Williamson, Altman, Blazeby, Clarke, and Gargon, 2012). A case study on dissemination of core outcome sets and associated core outcome measurement sets,

including 70 respondents summarised helpful dissemination ideas in seven categories: (i) dissemination and circulation through professional associations and research groups, (ii) provide online COS resources, (iii) publication of results and implementation in clinical practice guidelines, (iv) promotion on social media, (v) contribution to educational training programmes / webinars, (iv) advocacy for the COS to be incorporated in funding bodies applications, and (vii) follow-up with a study examining the rate of use of the COS (Akinremi et al., 2019).

According to the COMET handbook, regular communication with participants in COS studies may be important in maintaining participant engagement, for example by providing regular updates on the study progress (Williamson et al., 2017). Engagement is defined as information and knowledge sharing with the public, with some interactions and listening to the public (University of Oxford, 2016). This guide put together to support researchers in the University of Oxford's Nuffield Department of Primary Care Health Sciences suggest monitoring performance and track engagement using Google analytics to monitor the study website, or count the amount of shares, or mentions on Twitter. Measuring engagement was not part of the study aims, so no plan was put in place to measure it.

The project proposal was registered on the COMET initiative database (registration number 1084) at the inception of the study. A dynamic dissemination strategy was developed. Data from the final analysis of the e-Delphi, consensus meeting, and follow-up focus groups was presented at relevant national and international conferences; e.g., British Society of Audiology e-conference (December 2019), Implantable Acoustic Devices meeting in Oxford (September 2021). A comprehensive list of all dissemination activities (poster and conference presentations, dissemination activities) can be found in the introductory part of the thesis, and examples of relevant articles published in Appendix 12, presentation slides used in Appendix 13, and posters presented at conferences in Appendix 14. Peer-reviewed publications resulting from the research were also planned throughout the project delivery. An animated infographic describing the CROSSSD study aims, methods, and study outcomes was also developed to help with dissemination (ScienceSplained, 2022a). Constant

engagement was maintained via the study's social media channel, with scheduled soft publications, blog posts (Sygrove, 2020b) and presentations at team meetings. In the absence of formal recommendations on how to measure the impact of engagement and dissemination activities, the aim was to engage with relevant stakeholders are widely as possible, disseminate outcomes in print, online, via other media and through live events as appropriate.

NHS England have recently developed a guidance for integrated care boards, NHS trusts, foundation trusts and NHS England. It aims to support effectively partnership working with people and communities to improve services and meet the public involvement legal duties (NHS England, 2022). The guidance discusses processes and suggestions reinforced with case studies on informing, consulting, engaging, co-designing and co-producing with people with communities. Long-term partnerships to ensure sustainability for CROSSSD have been initiated, for example with contributions to charity websites such as the Sudden Hearing Loss Support website[7] (April 2021), the Ménière's Society hearing loss support page[8] (May 2021), and by joining the British Society of Audiology (BSA) Bone Conduction and Middle Ear Devices Special Interest Group[9] (February 2022) which is currently compiling a new practice guidance on unilateral hearing loss interventions. With these activities multiple principles for working with people and communities stated in the NHS England guidance (2022) are addressed, for example (i) involve people and communities at every stage and feed back to them about how it has influenced activities and decisions, (ii) work with voluntary, and community sectors, (iii) provide clear and accessible public information, and (iv) use community-centred approaches to empower people and communities, making connections to what works already.

[7] https://suddenhearingloss.support/2021/03/21/what-if-your-hearing-does-not-recover/
[8] https://www.menieres.org.uk/information-and-support/treatment-and-management/other-non-surgical-treatments#heading2
[9] https://www.thebsa.org.uk/bsa-groups/group-abc-me/

2.2.7 Outcome domain conceptualisation

Conceptualisation is the process of developing a description of the concept that the main domain represents. Each concept is then defined in detail, by describing one or more conceptual elements. Following conceptualisation the outcome domain needs to be operationalised (Prinsen et al., 2016). Operationalisation involves identifying the variables that act as indicators for the conceptual elements that a measurement tool should measure to adequately assess the concept (Figure 2-3).

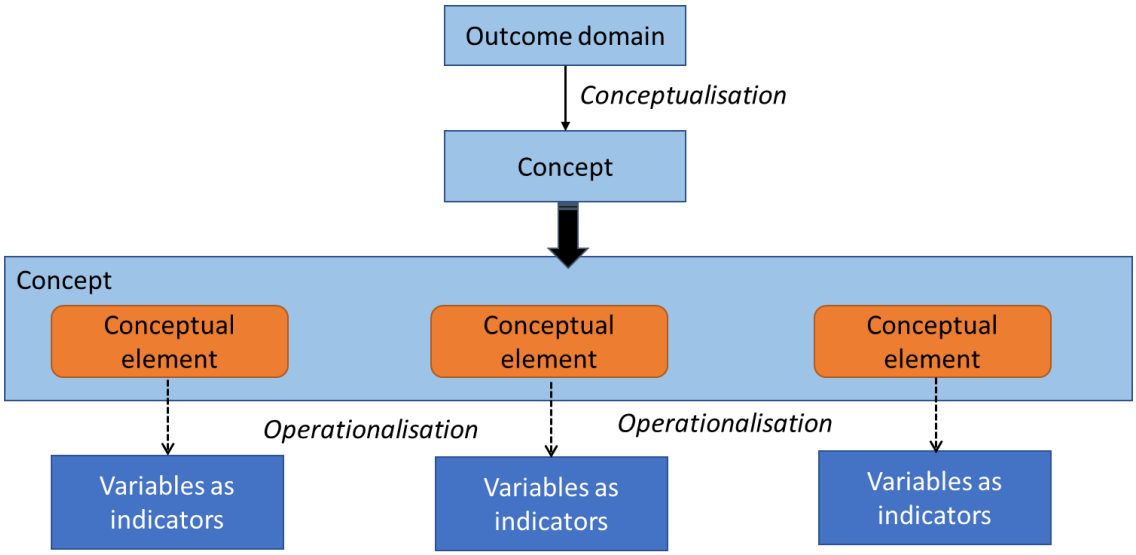

Figure 2-3. Schematic summary of the outcome domain conceptualisation and operationalisation stages.

The stages on Figure 2-3 are necessary to progress to the follow-up step of measurement instrument selection for the outcome domains in the COS (Prinsen et al., 2014). The COSMIN and COMET initiatives collaborated to develop a guideline on how to select outcome measurement instruments for outcomes included in a COS (Prinsen et al., 2016; Terwee, Prinsen, Chiarotto, Westerman, et al., 2018). This guideline focuses on Patient Reported Outcome Measures (PROMs). The COSMIN initiative subsequently developed a risk of bias checklist for use in systematic reviews of PROMs (Mokkink et al., 2018). The Harmonizing Outcome Measures for Eczema (HOME) initiative have also developed and published a methodological framework on the definition of a core set of outcome domains, followed by the identification or

development and validation of appropriate outcome measurement instruments to measure these core domains (Schmitt et al., 2015).

Investigators in several fields have adopted the Mokkink et al. (2018) methodology. Recently published examples include patient-reported measurement in dysphagia in head and neck cancer (Manduchi et al., 2022), measurements for health-related quality of life in people living with human immunodeficiency virus (HIV) (Wen et al., 2022), assessments of the stigma related to visible skin diseases (Luck-Sikorski et al., 2022), evaluation of measures of quality of life in adult scoliosis (Archer et al., 2021), child maltreatment (Yoon et al., 2021), and in hearing sciences in the context of measurement in the fields of tinnitus (Hall, 2017).

A challenge of adopting the Mokkink et al. (2018) method to assess PROMs is that many studies might not have followed the COSMIN criteria for psychometric properties, therefore data extraction and evaluation of methodological quality can be difficult, or that outcomes of a specific condition might not align with the constructs assigned by authors of included PROMs (Manduchi et al., 2022). Wen et al. (2022) did however successfully utilise the COSMIN criteria to summarise, and rate the psychometric properties of 30 measurement instruments identified in a systematic review of health-related quality of life (HRQoL) in people living with HIV. Luck-Sikorski et al. (2022) also effectively used COSMIN guidelines to report measures of stigmatisation in patients with visible skin diseases, however, they did not include authors' self-constructed instruments, just validated instruments in their assessment.

The rationale behind the items included in the COSMIN checklist were discussed in a follow-up paper in 2010 in which the authors elaborate on relevant aspects such as (i) internal consistency (relevance for reflective and formative models, and distinction with unidimensionality), (ii) content validity (judging relevance and comprehensiveness), (iii) hypotheses testing as an aspect of construct validity (specificity of hypotheses), (iv) criterion validity (relevance for PROMs), and (v) responsiveness (concept and relation to validity, and (in) appropriate measures) (Mokkink, Terwee, Knol, et al., 2010). A manual was compiled in 2018 by the COSMIN

steering committee (Terwee, Prinsen, Chiarotto, Vet, et al., 2018), on the basis of a Delphi study that had 159 experts from 21 countries participating in an online 4-round Delphi study (Terwee, Prinsen, Chiarotto, Westerman, et al., 2018). Ten criteria for good content validity were defined by participating experts regarding (i) item relevance, (ii) appropriateness of response options and recall period, (iii) comprehensiveness, and (iv) comprehensibility of the PROM being assessed, to ensure high-quality PROMs are used in research and clinical practice.

In brief, as per the Prinsen et al. (2016) consensus-based guideline to define how to measure core outcomes for any disease or condition in health and social care, the following steps should be adopted:

(i) outcome domain conceptual considerations,
(ii) systematic literature search for existing outcome measurement instruments (Scholtes et al., 2011)
(iii) quality assessment of outcome measurement instruments (i.e., evaluation of the measurement properties and feasibility aspects) (Mokkink et al., 2018), and
(iv) develop recommendations on the selection of outcome measurement instruments for outcomes included in a COS.

To follow the above steps effectively, to operationalise how to measure the outcome domains that were identified as critical to assess in every SSD interventional trial; it is important to have an in-depth understanding of the concept of each domain. Although, plain language descriptions were derived for each of these domains with input from the CROSSSD public research partners and steering group (see Section 2.4.2) during the COS development process; for the measurement instrument assessment step of the process there is a need for detailed operational definitions. Conceptualisation for the CROSSSD study was achieved with two follow-up focus groups, aiming to discuss in more detail the outcome domains that were voted into the core outcome domain set. The objective was to develop an understanding of all the important facets of each outcome domain before seeking to identify suitable measurement instruments for each of the outcome domains in the COS. All participants had previous interactions and an established relationship with the

facilitators and each other, having met in a previous stage of this work (COS consensus meeting that took place in July 2020); and a social coffee morning held shortly before the focus groups (Katiri, Hall, Hoare, et al., 2021).

Upon completion of all aforementioned studies, the study sponsor (University of Nottingham) and the REC were informed of the study completion with a declaration of the end of study form dated 13 March 2022 and a final report on the research.

2.3 Methodological considerations

During the planning stage of the CROSSSD study, a dilemma arose regarding amalgamation of the rerouting (bilateral) SSD interventions (CROS / BAHA / SoundBite™, ADHEAR) and restoring (binaural) interventions (MEI / CI) into one Delphi survey that would identify a single common minimum reporting standard for the two intervention approaches. When considering the scope of the study, issues like attrition, participant numbers, methodological execution, and clinical aspects were considered. Available literature was reviewed, and evidence was collected for the pros and cons of proceeding with one vs two Delphi survey(s) and stakeholder consensus meeting(s); and the dilemma was discussed with the CROSSSD study steering group (see Section 2.4.1). The CROSSSD study research steering group was asked to consider the advantages and disadvantages and to help decide.

Advantages of considering both intervention approaches together were:

- A single COS would set a standard for outcomes that are critical and important for any of the common intervention strategies. This would facilitate comparisons across intervention methods.
- A single minimum reporting standard may encourage uptake, minimise the cost and time resources required, and reflect the fact that SSD is a relatively small field in otology with a limited number of clinical trials whose designs and methodological quality are highly variable (Hall, Kitterick, et al., 2019).

- A single Delphi would improve our confidence with regards to adequate numbers of stakeholders recruited internationally to ensure the decision-making represents the wider view.

Disadvantages of considering both intervention approaches together were:

- Outcomes common to both intervention approaches might be less specific to the unique benefits of either intervention. The chosen outcomes might not be optimally sensitive to detecting treatment-related change.
- Seeking a single COS might reduce the potential for reaching our consensus criteria on individual outcome domains because the different intervention approaches can be very different in their intended effects.
- Few participants were likely to have expertise in both intervention approaches.
- Two separate Delphi surveys would potentially deliver a stronger message because they would be tailored to individual approaches: rerouting and restoring interventions.

Following thorough consideration of the arguments put forward, it was agreed to proceed with a single consensus process to develop one COS that would be applicable to both intervention approaches. A similar predicament has previously been considered by the IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) group (Turk and Dworkin, 2004) leading to the same decision. The IMMPACT team proposed that development of a single core set of domains and measurement procedures would facilitate the comparison and pooling of data, while leaving investigators free to augment the core domains with other outcomes of their choice. Therefore, it was decided here to run one decision-making process (2-round e-Delphi survey and consensus meeting) that considered any treatment approach. One set of minimum reporting standards would highlight all outcomes important for and common to the main SSD treatment strategies and this will facilitate comparisons across intervention methods.

2.4 Study team roles

2.4.1 Study management team

The COMET handbook (Williamson et al., 2017) suggests formation of a multi-disciplinary study management group, to be responsible for the day-to-day management of the project. For the CROSSSD study, Deborah A. Hall (DAH) whom had extensive expertise on outcome measurement and development of core outcome domain sets for tinnitus, and Pádraig T. Kitterick (PTK) who had expertise in severe-to-profound hearing impairment first proposed the study idea, and general approach to adopt for COS development. They also successfully secured funding for the PhD project, and recruited the PhD student, Roulla Katiri (RK), who is also a clinical audiologist. During the course of the study both DAH and PTK had changed job roles and moved to other institutions, therefore Derek J. Hoare (DJH) and Kathryn Fackrell (KF) both of whom had long-standing expertise in hearing research and stakeholder consensus processes replaced them. The study management team, or at least two members, met regularly, usually weekly, throughout the course of the project. During the initial stages of the project, the meetings concentrated on creating a detailed study protocol and obtaining the necessary ethical approvals. The meetings also helped plan and conduct the systematic review, recruit research partners, plan and deliver the core outcome domain set development study, and eventually the measurement instrument assessment methods study. Another important role of the group throughout the study included maintaining engagement with stakeholders, spread awareness of the study and help with recruitment, and disseminate findings in soft and peer reviewed publications. Overall, all important decisions concerning the course of the CROSSSD study were brainstormed, discussed, agreed, and implemented by the study management team.

2.4.2 Study steering group

A study steering group was appointed in December 2017 to guide the protocol development and oversee the CROSSSD study, as per COMET handbook (2017) recommendations. The group comprised international colleagues who were experts in SSD research methodologies and intervention approaches Paul Van de Heyning (PVH), Department of Otorhinolaryngology, Head and Neck Surgery, Antwerp University

Hospital, Antwerp, Belgium, Jill B. Firszt (JBF), School of Medicine, Washington University in St. Louis, St. Louis, Missouri, USA, and Iain A. Bruce (IAB), Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK. These colleagues were approached to be part of the steering group due to their extensive clinical experience, expertise in COS development in the hearing field, experience in running clinical trials for SSD, and experience in consensus methods.

PVH was the first ENT surgeon to implant a cochlear implant to a patient with SSD and intrusive tinnitus (Van de Heyning et al., 2008), and he led the professionals' consensus discussions on clinical measurement for SSD interventions (Van de Heyning et al., 2017). PVH and his team also led several SSD-related intervention studies reporting on various outcomes including functional, psychological, and social aspects; and has published widely in this field (Andries et al., 2022; Landsberger et al., 2020; Mertens et al., 2015; Vermeire and Van de Heyning, 2009). PVH is also actively involved in the HEARRING group[10] which is a global network of world leading centres and experts dealing with all aspects of hearing disorders aiming to improve worldwide quality standards, and provide high quality training in the field of auditory science.

JBF leads a team of researchers closely affiliated to a clinical setting at the University of Washington in St Louis, therefore has an understanding of both the research landscape in the US and the clinical service delivery. She has led multiple studies and longitudinal clinical trials focusing on asymmetrical hearing loss and SSD interventions, measuring multiple effects such as localisation, speech recognition, and other auditory abilities (Firszt et al., 2012, 2017, 2018; Vincent et al., 2015). JBF is also actively involved in the American Cochlear Implant Alliance (ACIA) as a member of the board of directors. JBF has worked with other leaders in the field of SSD in the USA, to develop professional guidelines for clinical assessments and management of adult cochlear implantation for SSD (Dillon et al., 2022).

[10] https://www.hearring.com/

IAB is a UK-based ENT surgeon who worked in COS development on both hearing-related studies such as the PONCHO study (Bruce et al., 2017), ENT-related studies like the mOMEnt study (Bruce et al., 2015; Harman et al., 2013; Liu et al., 2020), and has supervised a study on development of a core outcome domain set for gastric cancer, the GASTROS study (Alkhaffaf et al., 2017; Alkhaffaf, Metryka, Blazeby, Glenny, Adeyeye, et al., 2021). IAB has also served as a council member at several professional bodies in the UK, and is as a journal editor.

A Patient and Public Involvement (PPI) and engagement manager, Adele Horobin (AH), affiliated to Hearing Sciences at the University of Nottingham, two healthcare users with lived experience of SSD, referred to as public research partners, Nóra Buggy (NB) and Nicholas Hogan (NH), and the study management team (RK, DAH, PTK, DJH, KF) were also part of the steering group. A recently-published study by Dawes et al. (2022) presented several case studies from the Manchester Centre for Audiology and Deafness, reflecting on the benefits and challenges of PPI in translational research according to their experiences. They advocate for co-production at all stages of hearing research, and to routinely report PPI impacts so the benefits can be fully realised and monitored in the hearing field (Dawes et al., 2022).

The COMET handbook suggests obtaining input from the study steering group at critical points during the study where multi-disciplinary input is warranted (Williamson et al., 2017). Examples of tasks for the steering group, or study advisory group, include (i) review of the categorisation and description of outcomes, (ii) decisions regarding the structure and content of the list of items to be considered in a consensus process, and (iii) review of the final report following the consensus meeting.

There is no established guidance on the number of experts to include in a steering group. A recently published COS development study reported that their steering committee comprised 46 members from 13 countries (Munblit et al., 2022). They included health-care professionals, researchers representing a range of medical fields, methodologists, World Health Organisation (WHO) representatives, and people with post-COVID-19 condition and their carers, whom were actively involved in the design

and conduct of their study. Their steering group roles included (i) helping them generate candidate outcomes for Round 1, (ii) classify outcomes into categories using the Dodd et al. (2018) taxonomy, and (iii) decide which outcomes to automatically include in the final COS. Discussions with their steering group incorporated communication via email and Zoom meetings. On the basis of experience reported by the COMiT'ID initiative (Fackrell et al., 2017), whom found that their steering group assisted in improving the appeal of the study to health care users, reduced attrition, as well as helped them reduced the long list of candidate outcome domains and utilise appropriate language for use during the Delphi surveys a steering group was created.

The role of the CROSSSD study steering group was predetermined and agreed with all members to include:

- Support the development of the study protocol, specifically commenting on the feasibility of the modified Delphi process and considering any necessary revisions to the protocol which may inadvertently arise whist the study was underway.
- Review study documentation (e.g., advertisements, information leaflets, supporting video explanations of the survey, website content), and participate in a pilot of Round 1 of the e-Delphi survey.
- Review the initial list of outcome domains and associated descriptions, specifically commenting on the readability of the outcome descriptions, the appropriateness of the grouping of outcomes into categories, and providing any additional outcomes that they believed should be included in Round 1 of the e-Delphi survey.
- Assist with participant recruitment and to engage in dissemination activities, such as contributing to publications.

Contribution of the steering group members to the study was voluntary. The research partners (NB, NH) were reimbursed for their time as per UK standards for public involvement in research (NIHR, 2022b). Please refer to the introductory Funding statement section (pages 5-6) for a detailed breakdown of the PPI reimbursements.

The steering group contributions were invaluable to the development and fine tuning of the CROSSSD study methods, participant recruitment, dissemination of the study findings, and when taking important decisions about the future directions of the study. All steering group meeting scheduled throughout the course of the study and their outputs are listed on Table 2.3.

Table 2.3. Steering group meetings organised during the course of the study and output of each meeting.

Date	Meeting topic	Output
23/01/2018	Inaugural meeting introductions and general study methodology	CROSSSD study draft protocol
30/11/2018	Systematic review outcome domains: 'Split the Delphi?' discussion	Finalisation of the Delphi protocol
18/04/2020	COVID-19: transition to a web-based consensus meeting?	Amendment of consensus meeting to web-based delivery
09/07/2020	Outcomes of the consensus meeting	Update on agreed core outcome domain set
14/09/2021	Measurement Instruments assessment: methods and preliminary data	Suggestions for next steps and dissemination of outcomes
01/03/2022	Outcomes of PROM assessment: where next?	Finalisation future plans / end point for the CROSSSD study

The 5th annual update to a systematic review of COS for research which aimed to review if core outcome sets are being developed and reported to a higher standard (Gargon, Gorst, et al., 2019) assessed a total of 12 criteria representing the 11 minimum standards. Two of these standards, (i) the initial list of outcomes considered both healthcare professionals' and patients' views, and (ii) care taken to avoid ambiguity of language used in the list of outcomes were achieved for CROSSSD with the help of the steering group. The steering group members co-authored the CROSSSD study protocol paper (Katiri, Hall, Buggy, et al., 2020), the redesigning of a face-to-face stakeholder consensus meeting to a web-based meeting paper (Katiri, Hall, Hoare, et al., 2021), and the core outcome set development paper (Katiri et al., 2022).

2.5 The CROSSSD study logo and identity

Upon inception of the project and agreement amongst the study management team on the study methodology to be adopted, the need for a study logo was identified. A logo is a visual or textual mark used to identify a brand and their product (Luffarelli et al., 2019b). There is no research data available tailored around logos for COS development studies, but artistic effects and logo creating, although time-consuming, when designed accurately can help with visualisation without language barriers (Zheng, 2022). Luffarelli et al. (2019) conducted a series of studies on logo designs which demonstrated that that descriptive logos that can be easily processed and display authenticity can positively influence brand evaluations, purchase intentions, and brand performance. Three studies in the business world by Mahmood et al. (2019) that included a survey, a field study, and an experiment aimed to ascertain how low validity visual cues can impact the behaviour of backers. They concluded that logo complexity in their studies was interpreted by backers as a signal of venture innovativeness because more complex logos are more difficult to process, and thus, feel less familiar, more unique, original, and novel to a backer (Mahmood et al., 2019). In summary, a study of 597 logos suggested that a well-designed logo can offer substantial benefits to brands, such as (i) differentiate the brand, (ii) facilitate brand recognition, (iii) influence investors' decisions, and (iv) convey what a brand is all about (Luffarelli et al., 2019a).

The rationale behind creating a logo for the CROSSSD study was to have a visual reminder of the project that would serve as a tool to catch the relevant stakeholders' attention. The logo could also be used to promote the study material, to engage with colleagues internationally, and the general public. It could act as an ubiquitous communication tool to appear on the study website, grant applications, and as a promotional material to be shared with stakeholders and study participants.

Due to the nature of the study, aiming to engage with healthcare users with lived experience of SSD, healthcare professionals, manufacturers, researchers and other colleagues interested in the field of SSD, it was desired that the logo was engaging and noticeable to variable groups. A short CROSSSD study brief was composed and

submitted to the DesignHill[11] designers who subsequently developed several logos on the basis of the brief (Figure 2-4). The list of produced logos was reviewed by hearing researchers, ENT surgeons, audiologists, and other healthcare professionals from the NIHR Nottingham BRC, the Manchester Royal Infirmary, University College London Hospitals, colleagues at the Mater Misericordiae University Hospital in Dublin, and friends and family (to represent the general public), as well as two healthcare users. They were provided with a brief description of the study and the logo purpose and were asked to assess the list of submitted designer logos and to vote their top three choices. They were also encouraged to provide feedback on the logo designs and give suggestions for amendments if they had any.

Figure 2-4. Examples of logos produced by the DesignHill designers.

The final logo was selected based on the tallied votes from a total of 26 responses and weighting placed on healthcare users' and professionals' comments equally. For

[11] www.designhill.com

example, one healthcare user commented "t*wo key aspects of the designs really appealed to me. One was the legible wording of the logo. I think that this would be of particular importance, the other was the imagery used. I found the image of the ears and the cross to be the most relevant and accessible to an unfamiliar audience. It draws the person's attention to the topic of the research"*. A healthcare professional comment on a logo with a description was "*really like this, it looks professional and legible*". Figure 2-5 presents the final CROSSSD study logo.

Figure 2-5. The CROSSSD study logo.

The logo was then finalised by the designer and was saved in .jpeg, .tiff, .png, .ai, Power Point and Microsoft Word versions. Following financial settlement ($99US), a design transfer agreement was drawn that granted the CROSSSD study lead (RK) legal ownership to the designs. The logo could subsequently be used by the study management team as indicated: study documentation, information leaflets, newsletters, on the website, blog posts, the @CROSSSD_ Twitter account[12], at conference presentations, grant applications or as deemed otherwise necessary.

2.6 Participating stakeholders

2.6.1 Eligibility criteria

A range of expertise within the Delphi panel is an important quality criterion for development of a core outcome domain set (Williamson et al., 2017). Specific inclusion criteria have been defined for key stakeholder groups (healthcare users, healthcare

[12] https://twitter.com/CROSSSD

professionals, clinical researchers, commercial representatives, funders, journal editors). General eligibility for participation included men and women aged 18 years or older, who were computer literate, with sufficient command of English to read, understand and independently complete the questionnaires and can give informed consent.

All enrolled e-Delphi panellists were eligible to register their interest to attend the consensus meeting, and/or a follow-up focus groups. However, allocation of places was limited to those respondents who completed both rounds of the e-Delphi survey. None of the steering group members were allowed to participate or vote on outcome domains in the consensus meeting because this risked inadvertently introducing a power differential across participants, but they could participate in the e-Delphi surveys.

2.6.2 Survey participants sample size

There is no agreed method to statistically calculate a sample size for e-Delphi surveys or for consensus meetings, panel members can range from 10 to 1,000 (typically between 10 to 100) in published studies (Nasa et al., 2021). Generally 30 to 50 is considered optimum, and sample sizes over 1,000 are unusual (Diamond et al., 2014). A systematic review including 80 studies conducted between 1978-2009 calculated the median number of panel members to be 17 (Boulkedid et al., 2011), but highlighted that the composition of the panel (e.g., including multiple specialities stakeholder representatives) was an important parameter to consider. One of the key deciding factors is that the participant panel membership should adequately represent their corresponding stakeholder group (Williamson et al., 2017). A review of 31 COS studies indicated that studies with larger panel sizes have significantly lower response rates (Gargon, Crew, et al., 2019).

Since adult SSD is a relatively rare hearing disorder and SSD interventions is also a relatively new field; the number of professionals and members of the public with knowledge and experience of these interventions is small. The aim was therefore to recruit enough participants so that a minimum of 20 participants complete the two

rounds of the e-Delphi survey in each of the key stakeholder groups (healthcare users, healthcare professionals, clinical researchers). The consensus meeting and follow-up focus groups required in-depth discussions and therefore it was estimated that up to 20 participants would be recruited for each.

2.6.3 Recruitment of healthcare users

In the context of clinical trials, adopting a business model approach and marketing techniques for recruitment and retention has proven successful (McDonald et al., 2011). The importance of recruiting a heterogeneous participant sample in the context of COS development, with variation in characteristics has been highlighted (Keeley et al., 2016). For example, diversity of age and development in the mOMEnt (management of Otitis Media with Effusion in children with cleft palate) study influenced the outcomes their participants perceived as important (Bruce et al., 2015). Effective recruitment methods, like the ones described by the COMiT'ID initiative were utilised; for example, adopting an explicit marketing plan and engaging with charities or participants to act as 'champions' were successful strategies that helped recruitment for healthcare users (Hall, Smith, Heffernan, et al., 2018). Young and Bagley (2016) who run a series of workshops with COS developers regarding healthcare user input in their projects recommended gaining a diversity of perspectives such as by promoting the study in the healthcare setting (e.g., health clinics) patient organisations (e.g., charities), and via social media (e.g., Twitter). In terms of healthcare user participant retention over the study's timeframe, recommendations to maintain interest included (i) managing expectations about time-scales from the outset, (ii) keeping participants informed of the study progress, (iii) building rapport and showing appreciation for healthcare users' contributions, (iv) creating a sense of curiosity and excitement about the COS development process and (v) create a sense of ownership (Hall, Smith, Heffernan, et al., 2018).

An application was submitted for adoption of the CROSSSD study into the NIHR Clinical Research Network (CRN) portfolio through which other NHS sites can express their interest to support the study by being a Participant Identification Centre (PIC). The PICs that committed to support recruitment were (in alphabetical order): Aintree University

Hospital Liverpool, Bwrdd Iechyd Prifysgol Hywel Dda University Health Board, Cambridge University Hospitals NHS Foundation Trust, Charing Cross Hospital Imperial College Healthcare NHS Trust, Gartnavel General Hospital NHS Greater Glasgow and Clyde, Guy's and St Thomas' NHS Foundation Trust, Kingston Hospital NHS Foundation Trust, Manchester Royal Infirmary Manchester University NHS Foundation Trust, Mater Misericordiae University Hospital Dublin, New Victoria Hospital NHS Greater Glasgow and Clyde, Newcastle Hospitals NHS Foundation Trust, NIHR Manchester Biomedical Research Centre, Norfolk and Norwich University Hospitals NHS Foundation Trust, Nottingham University Hospitals NHS Trust, Royal Victoria Hospital Belfast Health and Social Care Trust, Salford Royal NHS Foundation Trust, Sherwood Forest Hospitals NHS Foundation Trust, South Warwickshire NHS Foundation Trust, St George's University Hospitals NHS Foundation Trust, Trafford Healthcare NHS Trust, University Hospital Ayr NHS Ayrshire and Arran, University Hospitals Birmingham NHS Foundation Trust, and Withington Community Hospital Manchester University NHS Foundation Trust. A further seven sites subsequently approached the study management team and enrolled as PICs. These were East Kent Hospitals University NHS Foundation Trust, Gloucestershire Hospitals NHS Foundation Trust, Greater Manchester, South East: Kent, Surrey and Sussex, West Midlands: Birmingham, West of England: Bristol, and Yorkshire and Humber.

Small information posters (Figure 2-6) and advertising A4 size posters (Appendix 15) were designed, printed, laminated, and posted to all PICs. PICs were asked to display study posters in the audiology and ENT clinic waiting rooms, share information posters and distribute participant information sheets (see Appendix 6 for the healthcare users information sheet) to individual patients who might be interested in the study. Where feasible, participant invitation letters (Appendix 16) were posted by local PICs clinicians to their database of patients diagnosed with SSD.

Specific e-promotion routes included several organisations that agreed to support the project by publishing newsletter articles and announcements to their members (e.g., Manchester Hearing BRC volunteers, Ménière's disease society). A healthcare user-led blog post (Sygrove, 2019) was also developed to raise awareness on the purpose and

importance of the CROSSSD study and give insights to healthcare users how to participate, and how their contribution would help the study outcomes and future research studies. The blog, My Hearing Loss Story, reaches approximately 15 to 20,000 people per year, across 96 countries. Finally, the lead study site, the NIHR Nottingham Hearing BRC, has a participant database containing email contacts for approximately 70 healthcare users who have been diagnosed with SSD, and all were invited to participate.

Figure 2-6. Recruitment mini poster used to distribute information on the study via the participant identification sites.

2.6.4 Recruitment of healthcare professionals

For healthcare professionals' recruitment, engaging with a number of professional networks and organisations via direct communication, conferences, contribution to society member magazines, social media posts are engagement strategies that proved effective in other studies (Fackrell et al., 2017). We aimed to recruit experts who would maximise the international relevance of the study findings (Keeley et al., 2016). A number of professional networks and organisations were approached to circulate invitations to their membership (e.g., British Society of Audiology (BSA) Adult Rehabilitation Interest Group (ARIG), HEARRING network, Hearing Australia, and American Cochlear Implant Alliance (ACIA)). Several soft publications (see page 10 for a list) were compiled to spread awareness of the study and recruitment criteria (e.g.,

Research round-up at the BSA Audacity magazine (Appendix 12), Hearing Journal article (Katiri, Hall, & Kitterick, 2020)). The CROSSSD steering group members were asked to approach their networks to make the approach more personal. Suggestions to promote engagement, retention of participants, and adherence to study deadlines for completion of surveys include (i) sending personalised emails from a distinguished researchers in the field, (ii) seeking endorsement from influential individuals in the field, and (iii) personalising correspondence and reminders sent to participants (Hall, Smith, Heffernan, et al., 2018). Parallel routes for recruiting healthcare professionals also involved personal invitation via email or face-to-face contact (e.g., see page 11 for conference presentations, pages 14-19 for meetings attended,and Appendix 13 for an example presentation slides content) at teams' monthly journal clubs or research meetings). Engagement with professionals was sought at local, national and international conferences, using poster presentations (Appendix 14) and networking at exhibition spaces (e.g., Ci1018.org, BAA conferences). The study management team had created a long list of potential participants with relevant expertise via exiting connections with the NIHR Nottingham BRC, manual searches of relevant hearing-related organisations (e.g., UHealth Ear Institute at the University of Miami), corresponding authors from the relevant research publications identified by the systematic review (Katiri, Hall, Killan, et al., 2021), manual searches of relevant conference proceedings in the last 3 years (e.g., Implantable Devices Meeting, Cochlear Implants International Meeting Ci2018.org, OSSEO International Congress on Bone Conduction Hearing and Related Technologies), and email queries sent to representatives from each additional stakeholder organisations from commercial sectors (e.g., clinical research managers for relevant device companies) and funding bodies asking for recipients to nominate any colleagues with expertise in SSD interventions.

2.6.5 Stakeholder engagement and recruitment

The CROSSSD study recruitment plan included e-promotion routes via a study webpage and regular updates on the study progress via social media platforms (e.g., Twitter @CROSSSD_, @hearingnihr). The INVOLVE guidance on the use of social media to actively involve people in research was adopted as appropriate (INVOLVE, 2014). A

video advertisement (ScienceSplained, 2019) promoting the study was developed alongside patient and public involvement collaborators. The primary aim of video was to promote the CROSSSD study, enhance participant recruitment, and to advertise on social media. The objective of the video was to explain what a COS is, and why it is important in the field of SSD. It was distributed via the NIHR YouTube channel, the CROSSSD study website, NIHR Hearing Theme website, Twitter social media platform, CROSSSD related conference presentations, and during presentations to clinical audiology and ENT teams (Appendix 13).

2.7 Summary of Chapter 2

This chapter describes the design of an international consensus process to develop a core outcome set for SSD interventions, comprising of an agreed *minimum* set of outcome domains relevant to both patients and professionals. This COS will be applicable to all future trials examining SSD interventions, irrespective of whether the intervention is rerouting sounds to the better hearing ear or restoring function of the impaired ear.

The systematic review will be discussed in Chapter 3, the development of an internationally agreed core outcome domain set in Chapter 4, and the measurement instrument(s) assessment process in Chapter 5.

3. Systematic review

This chapter is adapted from this peer reviewed publication:
Katiri, R., Hall, D. A., Killan, C. F., Smith, S., Prayuenyong, P., & Kitterick, P. T. (2021). Systematic review of outcome domains and instruments used in designs of clinical trials for interventions that seek to restore bilateral and binaural hearing in adults with unilateral severe to profound sensorineural hearing loss ('single-sided deafness'). *Trials*, 22(1), 220. doi: 10.1186/s13063-021-05160-5.

PROSPERO registration

The systematic review protocol is registered on PROSPERO (International Prospective Register of Systematic Reviews): Registration number CRD42018084274. Registered on 13 March 2018, last updated on 23 March 2021.

Acknowledgements for this chapter

We would like to acknowledge contributions from Nicholas Hogan and Nóra Buggy, collaborators with lived experience of SSD and Adele Horobin, Patient and Public Involvement and engagement manager whose viewpoints during workshop discussions have guided outcome domains categorisation. Many thanks to Henryk Faas, Assistant Professor in Neuroimaging, Sir Peter Mansfield Imaging Centre, School of Medicine, University of Nottingham who has assisted with the systematic review qualitative synthesis of publications in German.

3.1 Background and objectives

3.1.1 Background

The first step recommended for the development of a COS is to identify existing knowledge about outcomes in the area of interest by performing a systematic review of outcomes in published studies (Williamson et al., 2017). The identified outcomes can be subsequently used for consensus development to agree with the wider stakeholder group what outcomes should be included in the COS. Our published

protocol (Katiri, Hall, Buggy, et al., 2020) describes the roadmap adopted by the CROSSSSD initiative and this systematic review formed one of the first steps.

3.1.2 Objectives

The primary objective of the systematic review was to identify outcome domains and measurement instruments reported in published clinical studies evaluating rerouting and/or restoring interventions in adults with SSD. This information was used to subsequently generate a 'long list' of candidate outcomes to be rated by SSD stakeholders according to whether each is important and critical to determine if an intervention works in this clinical population as part of the development of a core outcome domain set (Katiri, Hall, Buggy, et al., 2020).

There were two secondary objectives.

1. To compare and contrast outcome domains and measurement instruments reported for interventions that aim to re-establish (i) bilateral hearing (i.e., CROS aid, BAHA, ADHEAR, SoundBite^{TM}), and (ii) binaural hearing (i.e., MEI, CI).
2. To examine what outcome domains had been assessed and measurement instruments used as a function of time-point after intervention. This information was used to distinguish short- and long-term treatment-related changes.

A separate, exploratory objective, was also added. The objective was to examine if studies that recruited participants with unilateral hearing loss, that did not fit the SSD audiometric criteria stated in the Van de Heyning et al. (2017) consensus paper, chose different outcome domains.

3.2 Methods

3.2.1 Searches

Details of the specific review questions, search strategy, study eligibility criteria, information sources, selection and data collection processes, quality assessment, as well as data synthesis methods were published on the PROSPERO international

prospective register of systematic reviews in advance of data extraction (Hall, Kitterick, et al., 2018). There were no modifications to this PROSPERO protocol, but the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009) was modified for reporting purposes in this study.

3.2.2 Study inclusion and exclusion criteria

The eligibility was defined according to PICOS (Participant, Intervention(s), Comparator(s), Outcome, Setting) criteria (Table 3.1). All included records assessed adults (male or female), aged 18 years or older, with a diagnosis of congenital or acquired SSD. For the primary objective, diagnoses had to meet an audiometric profile independently defined through consensus (Van de Heyning et al., 2017).

Eligible interventions comprised hearing aids and/or auditory implants designed specifically to restore bilateral (two-sided) or binaural (both ears) hearing. Any comparators in the study design were allowed, but studies exclusively evaluating other audiological interventions such as conventional hearing aids, assistive listening devices, audiological counselling, communication strategies, or providing no intervention (unaided or placebo) were excluded. These comparators were excluded because the focus of the systematic review was to identify outcome domains and measurement instruments reported in published clinical studies evaluating rerouting and/or restoring interventions in adults with SSD. Conventional hearing aids are not a suitable rehabilitation option for those with no aidable hearing in one ear only (Harford and Barry, 1965). It is common practice to deliver audiological counselling, discuss communication strategies, and if applicable, issue assistive devices during hearing aid(s) and/or auditory implant clinical rehabilitation sessions (BSA, 2016), as opposed to be delivered in isolation. There were no restrictions on outcomes or research settings.

The systematic review included records reporting randomised controlled trials, quasi-randomised controlled trials, non-randomised controlled trials, before and after studies, cross-over studies, trial registrations and published protocols of such ongoing studies. Relevant systematic reviews were not subjected to the data collection process

itself but were reviewed to ensure all eligible records had been captured. Case control studies, cohort studies, non-systematic literature reviews (e.g., scoping reviews), practice guidelines, expert opinions, case series, case reports, book chapters, conference papers, manufacturers' articles (e.g., white papers), animal studies, and studies that use predictive modelling (e.g., prognostic factors established by acoustic test box measurements or studies performed with cadavers) were excluded.

Table 3.1. PICOS (Population, Intervention, Comparator / Control, Outcomes, Setting) inclusion and exclusion criteria.

PICO *inclusions* in detail	
P -Inclusions	Adult male and female participants with SSD, of minimum age 18 years. Participants with a diagnosis of congenital or acquired SNHL of threshold severity worse than 70 dB HL at audiometric frequencies ranging from 1-4 kHz on the worse-hearing ear and normal hearing thresholds on the better-hearing ear, defined as pure tone average of ≤30 dB HL.
I -Inclusions	Bilateral (rerouting Interventions): (1) Contralateral Routing of Signals (CROS) hearing aid devices and (2) Bone Anchored Hearing Aids (BAHA). Binaural (direct stimulation of impaired ear): (1) Middle Ear Implants (MEI) and (2) cochlear implants (CI). We also include studies that evaluate accessories for the above devices e.g., Roger pen, controlled studies that compare for example different types of cochlear implants, studies comparing different algorithms or fitting strategies or insertion depth. Auditory brainstem implants and the SoundBite™ are included.
C -Inclusions	Hearing impaired group.
Design type -Inclusions	Randomised controlled trials, quasi-randomised controlled trials, before and after studies, non-randomised controlled trials, cross-over studies. trial registrations of such ongoing studies, systematic reviews (for record checking).
PICO *exclusions* in detail	
P -Exclusions	Participants younger than 18 years of age. Participants with a diagnosis of mild-moderate asymmetrical hearing losses who are candidates for hearing aid amplification in the poor-hearing ear, or have 'near-normal' better hearing ear. Participants with a diagnosis of mild-moderate conductive or mixed hearing loss.
I -Exclusions	Conventional hearing aids.
C -Exclusions	Normal hearing group only.
Design type -Exclusions	Case control studies, cohort studies, literature reviews, practice guidelines, expert opinions, case series, case reports, book chapters, conference papers (including peer reviewed conference papers), manufacturers' articles, animal studies. Also exclude studies that use predictive modelling (prognostic factors). Also exclude editorials and letters to the editor. Also exclude retrospective studies of clinical cases.

Original searches were performed from 1946, which is the earliest entry on databases (Gusenbauer and Haddaway, 2020); or the start date of databases, whichever was earlier, up to March-April 2018 inclusive. The searches were updated to 18 March 2020. There were no restrictions on language of the publication.

During the data collection process, a few records were identified where information about age-related eligibility, audiometric thresholds, or type of hearing loss in either the better or poorer hearing ear were missing. The corresponding author was contacted for more details by email, and a decision was made regarding inclusion considering the new information provided. In cases where the author did not respond, a decision was taken to (i) include, (ii) exclude or (iii) use for sensitivity analysis; following discussion with one of the two senior members of the study management team (PTK or DAH). Cases in the sensitivity analysis were those trials or studies in which: (i) participants' audiometric profiles were close to our adopted SSD definition but differed from those criteria by up to 20 dB in individual frequencies either in the better or worse ear; (ii) the corresponding author was asked to clarify the audiometric profiles of participants but did not respond; and (iii) ongoing studies recruiting a mixture of participants (including children aged less than 18 years of age) and where it was not clear if results would be reported separately for the adults (aged 18 years or over).

3.2.3 Information sources

Published, unpublished and ongoing studies were identified by electronically searching the following databases from their inception: EMBASE, MEDLINE, PubMed, CINAHL, ClinicalTrials.gov, ISRCTN, CENTRAL, ICTRP and the NIHR UK Clinical Trials Gateway (Table 3.2). Electronic searchers were run by RK and PTK on 18 March 2018 and 01 April 2018 and then updated on 18 March 2020. In addition, a hand-search was conducted when reviewing the 76 published articles that had met the eligibility criteria at the abstract and full-text screening stages. Two potential articles were identified (Bovo et al., 2011; Harford and Dodds, 1966), but following closer scrutiny neither met eligibility.

Table 3.2. Table summarising the electronic information sources used and the number of records identified.

Type of electronic search	*Database*	*Date range*	*Number of items (n)*
Academic databases	Excerpta Medica dataBASE (EMBASE) via OvidSP	1974 to 18 March 2020	1463
	Medical Literature Analysis and Retrieval System Online (MEDLINE) via OvidSP	1974 to 18 March 2020	1144
	PubMed National Centre for Biotechnology Information	1946 to 18 March 2020	1223
	Cumulative Index of Nursing and Allied Health Literature (CINAHL) via EBSCO	1982 to 18 March 2020	384
		Searched on	
Clinical trial registers and/or other sources	ClinicalTrials.gov (www.clinicaltrials.gov)	18 March 2020	193
	International Standard Randomised Controlled Trials Number (ISRCTN) Registry (www.isrctn.com)	18 March 2020	48
	Cochrane Central Register of Controlled Trials (CENTRAL)	18 March 2020	962
	World Health Organisation (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp)	18 March 2020	270
	NIHR UK Clinical Trials Gateway (www.ukctg.nihr.ac.uk)	18 March 2020	67

3.2.4 Search strategy

The search strategy used in this systematic review was registered on PROSPERO (Hall, Kitterick, and Katiri, 2018). Search terms for the PubMed, EMBASE and MEDLINE databases were informed by the PICOS criteria and comprised a set of terms to identify the population combined with a set of terms to identify relevant interventions. Where possible using the database interface, the scope of the search was limited to humans (not animals), and adults (not paediatric). The search strategy was discussed and submitted for review to an information specialist that is employed by the library at RK's workplace (Mater Misericordiae University Hospital, Dublin). An example of the search syntax for MEDLINE and EMBASE via OvidSP can be found in Table 3.3.

Table 3.3. Example of the search syntax for MEDLINE and EMBASE via OvidSP.

	Term Type	Search term	Field restrictions
Condition and causes			
1.	MeSH	unilateral hearing loss	
2.	MeSH	acoustic neuroma	
3.	MeSH	sudden hearing loss	
4.	MeSH	meniere disease	
5.	Text	unilateral adj3 hearing loss	title, abstract
6.	Text	unilateral adj3 deafness	title, abstract
7.	Text	single sided adj3 deafness	title, abstract
8.	Text	asymmetric adj3 hearing	title, abstract
9.	Boolean	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	
Interventions			
10.	MeSH	bone conduction hearing aid	
11.	MeSH	bone conduction	
12.	MeSH	middle ear implant	
13.	MeSH	cochlear implant	
14.	Text	bone anchored adj2 implant*	title, abstract
15.	Text	bone anchored adj2 aid*	title, abstract
16.	Text	bone conduction adj2 device*	title, abstract
17.	Text	BAHA*	title, abstract
18.	Text	BCD*	title, abstract
19.	Text	contralateral routing adj2 sound*	title, abstract
20.	Text	contralateral routing adj2 signal*	title, abstract
21.	Text	contralateral rerouting adj2 sound*	title, abstract
22.	Text	contralateral rerouting adj2 signal*	title, abstract
23.	Text	contralateral re-routing adj2 sound*	title, abstract
24.	Text	contralateral re-routing adj2 signal*	title, abstract
25.	Text	CROS	title, abstract
26.	Text	BiCROS	title, abstract
27.	Text	middle ear implant*	title, abstract
28.	Text	MEI	title, abstract
29.	Text	auditory implant*	title, abstract
30.	Text	cochlear implant*	title, abstract
31.	Text	transcranial	title, abstract
32.	Text	percutaneous adj2 device	title, abstract
33.	Text	percutaneous adj2 implant	title, abstract
34.	Text	subcutaneous adj2 device	title, abstract
35.	Text	subcutaneous adj2 implant	title, abstract
36.	Boolean	10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35	
Composition			
37.	Boolean	9 AND 36	
Commands specific to OvidSP interface: * = truncated match			

MeSH = Medical Subject Headings Boolean = Operators used to retrieve search terms adj2 = Adjacency / Proximity, words have to appear within 2 words of each other

The search strategy for the other databases was modelled on this search strategy and adapted where necessary to ensure the strategies were highly sensitive across each of the database interfaces. As an example, the syntax for search of the CENTRAL trials registry of the Cochrane Collaboration can be found in Table 3.4.

Table 3.4. Search syntax for CENTRAL (Cochrane Central Register of Controlled Trials).

Keyword search: (PICO**)** – Title, Abstract, keywords search
#1 single sided deafness:ti,ab,kw (Word variations have been searched) **#2** unilateral hearing loss:ti,ab,kw (Word variations have been searched) **#3** unilateral deafness:ti,ab,kw (Word variations have been searched) **#4** asymmetric hearing:ti,ab,kw (Word variations have been searched) **#5** 'acoustic neuroma':ti,ab,kw (Word variations have been searched) **#6** 'sudden hearing loss':ti,ab,kw (Word variations have been searched) **#7** meniere disease:ti,ab,kw (Word variations have been searched) **#8** (unilateral next/3 hearing loss):ti,ab,kw (Word variations have been searched) **#9** (unilateral next/3 deafness):ti,ab,kw (Word variations have been searched) **#10** (single sided next/3 deafness):ti,ab,kw (Word variations have been searched) **#11** (asymmetric next/3 hearing) .:ti,ab,kw (Word variations have been searched)
MeSH terms: (PICO**)**
#12 MeSH descriptor: [Hearing Loss, Unilateral] explode all trees **#13** MeSH descriptor: [Neuroma, Acoustic] explode all trees **#14** MeSH descriptor: [Hearing Loss, Sudden] explode all trees **#15** MeSH descriptor: [Meniere Disease] explode all trees
(PICO**) Combinations**
#16: #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
Keyword search: (PICO**)** – Title, Abstract, Keywords search
#17 Bone Anchored Hearing Aid:ti,ab,kw (Word variations have been searched) **#18** Middle Ear Implant:ti,ab,kw (Word variations have been searched) **#19** Contralateral Routing:ti,ab,kw (Word variations have been searched) **#20** Cochlear Implant:ti,ab,kw (Word variations have been searched) **#21** bone conduction device:ti,ab,kw (Word variations have been searched)
MeSH terms: (PICO**)**
#22 MeSH descriptor: [Hearing Aids] explode all trees **#23** MeSH descriptor: [Bone Conduction] explode all trees **#24** MeSH descriptor: [Ossicular Prosthesis] explode all trees **#25** MeSH descriptor: [Cochlear Implants] explode all trees **#26** MeSH descriptor: [Cochlear Implantation] explode all trees
(PICO**) Combinations**
#27: #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26
Both searches P and I (PICO**) combined for final yield**

3.2.5 Data management

The study management team (RK, DAH and PTK) were responsible for data management and maintained editorial rights. All identified records were saved into an Excel spreadsheet (Microsoft Corporation, 2022) masterfile where records were tracked through the screening and data collection process by a unique study identification code.

3.2.6 Selection process

All identified records were uploaded into the EndNote™ software (version X7) (Clarivate, 2022) which was used to remove duplicates using the records' title, list of authors, year of publication, and journal of publication. In a few isolated cases, the abstract was also used to double-check if there was duplication, mainly for records that were published in a different language and the translated title or name of journal were different. The resulting number of records were subjected to eligibility screening.

Eligibility screening was carried out by RK, DAH, CFK, SS, PP and PTK, according to the PROSPERO record (Hall, Kitterick, and Katiri, 2018). For each record, the title and abstract screening decision was captured using a simple set of descriptors (Table 3.5).

Two co-authors (RK and DAH, or PTK) independently performed and/or reviewed each step (i.e., title and abstract screening, full text screening, data extraction, risk of bias assessment). Records that were included to conduct the sensitivity analysis only were extracted by RK alone. On rare occasions where agreement could not be reached between co-authors, disagreements were resolved by a third reviewer (DAH or PTK). The risk of bias assessment did not affect which findings were included in the analyses.

Table 3.5. The numbering system adopted to screen articles on the basis of Title and Abstract only in the initial screening phase.

No	Title and Abstract screening criteria	
1	**Relevant-Include**	It definitely fits all the CROSSSD PICO criteria. Even if the outcomes measured e.g., speech testing / questionnaires are not explicitly mentioned or clearly listed in the Title / Abstract please code as n=1; i.e., do not exclude if unsure of outcomes employed specifically.
2	**Unsure / Possibly relevant**	Not entirely clear if it definitely fits all the CROSSSD PICO criteria. Most commonly the Title and Abstract describe 'implanted participants' but do not explicitly state they have bilateral or unilateral deafness. Even if it seems like they probably have bilateral deafness, please code as n=2 so that we can be confident at ruling out at the full-text screening stage.
3	**Irrelevant-Out of scope**	Does not fit the CROSSSD PICO criteria e.g., middle ear surgery is used as an intervention. If this reason is given by one screener, but a more specific reason is given by the other screener, then go with the more specific reason. If a study is an animal study exclude using code n=3. If a study is purely a cost utility / effectiveness study exclude using code n=3.
4	**Irrelevant-P, not SSD, not SNHL**	Participants do not fit the SSD definition e.g., have mixed loss, or moderate severity. If the Title / Abstract are not explicit about whether patients have SSD or bilateral deafness, then pass the article to full text screening by coding n=2. If the study is referring to NF2 (Neurofibromatosis type 2) patients; these are known to have either unilateral and/or bilateral deafness, so if not clear of the participants audiometric characteristics in Title / Abstract please code n=2 so the full text can be retrieved to clarify. 'Aural atresia' describes a conductive or mixed hearing loss, not SNHL, thus can also be excluded with code n=4.
5	**Irrelevant-P, not adults**	All participants groups who are under the age of 18 years. If the Title / Abstract indicate that both children and adults are included, then code the article as n=1 to pass to full text screening.
6	**Irrelevant-Intervention**	Intervention is not any technological intervention designed to restore bilateral (two-sided) or binaural (both ears) hearing in order to address the impact of SSD in adults. Auditory Brainstem Implants (ABI) and the SoundBite™ studies should be coded as n=1 if they fit the rest of the PICO criteria.
7	**Irrelevant-Design type**	Study cannot be included because it is e.g., a case study or a literature review. Retrospective case series-exclude by coding n=7. Systematic reviews should be coded as n=1 if they fit the rest of the PICO criteria.
8	**Incomplete reference**	The Title and/or Abstract were not pulled through to EndNote and cannot be found online.
9	**Abstract not accessible**	Title is available but no abstract is available e.g., it's a book chapter, it's a correspondence with no abstract, or from a dated publication that did not include abstracts.
	Coding strategy	Please number according to the first applicable reason identified (moving hierarchically from code 1 to code 9 in that order). e.g., Conductive hearing loss and cranial osseous dysplasia secondary to Neurofibromatosis type 1 (NF1): A case report and literature review. Should be coded n=4 because the population is not SNHL (not n=7, as per design type being a case review). The only exception to this has been for some articles that could potentially be coded as n=3 (out of scope). If the article is completely out of scope, then code as n=3. If a more specific code can be given e.g., n=4, 5, 6; then use the lowest number on the list (n=4), hierarchically. i.e., The most specific code and the one earlier on the hierarchy of codes should be used.

3.2.7 Risk of bias assessment

Given that the primary objective of this systematic review concerned methodology (not therapeutic effects), we limited the assessment of risk of bias to the data collection methods for consolidated records rather than any analysis of the intervention-related changes. The consolidated record data (e.g., outcome descriptors, published primary / secondary findings) was critically analysed for consistency of outcome reporting by two independent reviewers (RK and DAH). Risk of bias was assessed by analysing the reporting of outcomes both within and across manuscripts reporting study findings. Bias was determined by whether outcomes were reported prospectively through trial registration or published protocol, and whether outcomes were reported consistently between the protocol and/or registration, and study report. If consensus could not be reached on whether outcomes had been reported consistently then disagreements were resolved by discussion with a third reviewer (PTK). No contact was made with corresponding authors to investigate the rationale of altered reporting. This is because it would not influence the outcome inclusion for the purpose of this study, all outcomes were included. The quality of a record did not affect its inclusion in the synthesis of outcomes. The purpose of a quality assessment in systematic reviews is to examine the confidence of review findings (Seo and Kim, 2012). The data extracted for the purpose of this systematic review aimed to provide a meticulous catalogue of investigators' chosen outcome domains and measurement instruments, for SSD studies investigating both rerouting and restoring interventions. Although not part of the systematic review objectives, compiling quality assessment data would be a valuable contribution to the SSD field, so researchers can judge the overall strength of evidence, and methodological quality of SSD intervention studies.

To enhance our data quality, data collection was guided by a data extraction protocol (Appendix 17), which informed the headings of the data masterfile. A calibration exercise was conducted for 10 included records, reviewed for consistency across two coders, and the data extraction protocol was revised according to the lessons learned. Reviewers were excluded from coding records that they had been involved in as an author.

3.2.8 Data items

Data items included PICOS fields as described by the PROSPERO record (Hall, Kitterick, et al., 2018) and summarised on Table 3.6.

Table 3.6. Collected data items as per PICOS (Population, Intervention, Comparator / Control, Outcomes, Setting) fields.

Data items	Inclusion criteria
Participants	**1.** SSD cause / aetiology **2.** age range **3.** mean age **4.** age standard deviation **5.** time since SSD diagnosis
Intervention	**6.** type of intervention device used **7.** time of implementation of intervention (how long after the onset of SSD the intervention was implemented) **8.** the comparator device (if applicable)
Trial design	**9.** the type of trial design **10.** the time duration for which each intervention or comparator device were used
Outcome(s)	**11.** the outcome domain(s) specified by the investigators **12.** measurement instruments specified by the investigators **13.** measurement time frame *Information relating to these three data items was recorded separately for all primary and secondary outcomes
Supplementary information	**1.** countries where the study was conducted **2.** corresponding author contact details **3.** source title (e.g., journal) **4.** date of publication (printed copy) **5.** primary and/or secondary objective(s) **6.** sample size (estimated sample for ongoing trials) **7.** description of any modifications to the study, particularly any discrepancies between the trial protocol and the subsequent report of the findings **8.** any conflicts of interest identified by the authors

Where authors were not explicit about the distinction between primary and secondary outcomes, the Methods and Results sections of each article were examined to identify any relevant information related to this distinction. If the study investigators did not explicitly distinguish multiple outcome domains as primary or secondary, they were all classified as primary. Supplementary information was also extracted from each individual record (Table 3.6). If any information was not reported, then 'not stated' was recorded in the corresponding field. Where trial records had been consolidated into a single study, the data items reported in the synthesis related to the most recent

study publication. For those records in which several pieces of information were consolidated for a single study, any inconsistencies between the protocol and the final reported study findings were noted (e.g., if the intended participant sample size was different in the published clinical trial record in comparison to the final study findings publication).

For the purpose of collating the data, and to allow for consistent categorisation across studies, some outcome domain names had to be recoded. For example, outcome domains labelled by study authors as: 'speech recognition in noise', 'speech perception in noise', 'speech reception in noise', 'speech understanding in noise', 'speech comprehension in noise', were all recoded to 'speech in noise'. Another recoding example is 'spatial hearing', which used for the outcome domain labels 'spatial domain', 'ability to judge direction of sound', and 'spatial abilities'. This task was conducted in pairs by RK and/or PTK / DAH; to reduce the impact of individual opinions. Both the authors' original description, and the recoded outcome domain names were saved on the systematic review data masterfile (Additional file 7 in the published manuscript Katiri et al. (2021)) for transparency.

3.2.9 Outcomes and prioritisation

The primary research question was to identify outcome domains and measurement instruments reported in studies investigating interventions that seek to restore hearing in adults with SSD. There are no validated taxonomies specific to the hearing field. Although not part of our published protocol (Katiri, Hall, Buggy, et al., 2020), for our classification of outcome domains we felt that it was sufficiently important to implement a standard taxonomy for this systematic review. We chose to use the Dodd taxonomy (Dodd et al., 2018). Strengths of this taxonomy are that it has been developed specifically for trial outcomes, it is comprehensive, not disease specific, not limited to patient-centred outcomes, and is applicable to trials irrespective of the field being studied. It comprises 38 categories across five core areas: death, physiological or clinical, life impact, resource use, and adverse events. The study management team determined it insufficient to delineate the different outcome domains in the ear and labyrinth category, therefore this category was expanded using our own subcategories.

Classification of the review findings with respect to this taxonomy was conducted by RK and PTK. Finer breakdown of outcomes with the category 'ear and labyrinth outcomes' was informed by the two-day outcome domain grouping workshop that took place in July 2019 with members of the research steering group and the two public research partners (Chapter 4). Details on the individual outcome domains review, consolidation and categorisation during the workshop can be found in Chapter 2 and the CROSSSD study protocol (Katiri, Hall, Buggy, et al., 2020).

3.3 Results

3.3.1 Search results

Figure 3-1 displays the results of the search strategy used to identify the relevant articles as recommended by the PRISMA statement (Moher et al., 2009). The search strategy yielded 5754 records from which 2554 were excluded as duplicates. This resulted in a total of 3200 unique records being subjected to eligibility screening.

Most exclusions during title and abstract eligibility screening were because the study was out of scope (e.g., examined surgical methods, assistive hearing devices, or hearing therapy techniques), the wrong trial design (e.g., case series, scoping reviews), not recruiting SSD participants, or not recruiting adults. This left 564 records (Figure 3-1) for which full texts were obtained, and where necessary, translated to the English language. Full text eligibility screening enabled a further 446 records to be excluded, with most exclusions due to participants not meeting the working definition of SSD (Van de Heyning et al., 2017), (n=281) or using an ineligible trial design (n=111). These exclusions left 118 records for data extraction.

Full text screening confirmed that 76 records reported trials in which the diagnosis of SSD fully met our criteria according to the Van de Heyning et al. (2017) definition, whilst 30 records reported participant criteria that narrowly missed the inclusion criteria (see study inclusion and exclusion criteria in Section 3.2.6) but were sufficiently close to the criteria for inclusion in the sensitivity analysis.

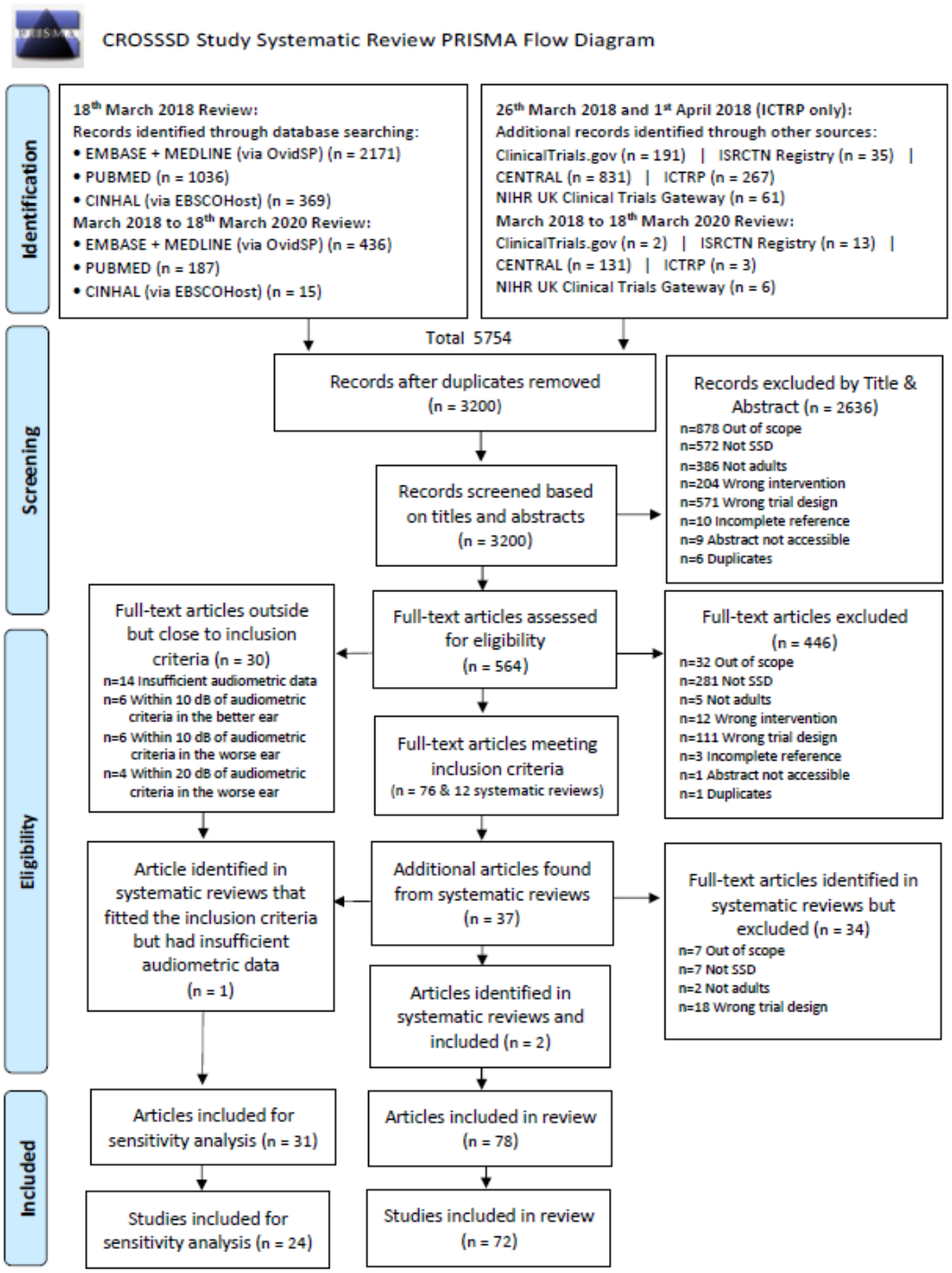

Figure 3-1. Reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram.

During eligibility screening, corresponding authors for 17 records (Table 3.7) were contacted to ask for more detail on the participant audiometric eligibility criteria or the definition of SSD adopted. Six authors responded with new information that allowed the screeners to come to a decision to: (i) include for data extraction and synthesis (n=1) (Song et al., 2013); (ii) exclude from data extraction (n=2) (Brendel and

Hamacher, 2018; Willeboer, 2005); or (iii) include for sensitivity analysis (n=3) (Doobe et al., 2015; Gnansia and Frachet, 2016; Smith and Knappett, 2015). Three emails were undeliverable, for these, so we decided to exclude two records (Hill et al., 2006; Kubo et al., 2001); but include one record (Syms and Galow, 2013) which was a clinical trial intending to recruit participants with SSD. Six authors did not respond, and so we decided to include all six for sensitivity analysis (Table 3.7). Two authors responded but their responses did not adequately clarify the query; one record (Sladen et al., 2017) was included for sensitivity analysis and one (Dumon et al., 2016) was excluded from data extraction.

The remaining 12 recorded were systematic review articles (Blasco and Redleaf, 2014; Cabral Junior et al., 2016; Cohen and Svirsky, 2019; Kim et al., 2017; Kitterick et al., 2015, 2016; Magele et al., 2019; Peter, Liyanage, et al., 2019; Peters et al., 2015; Sprinzl and Wolf-Magele, 2016; van Zon et al., 2015; Wendrich et al., 2017) which were reviewed to check for any missed trials or studies for inclusion, and 37 potentially eligible articles were identified by this approach. Of these, 35 were excluded, two met the inclusion criteria (Ahmed and Khater, 2017; Kitoh et al., 2016), and one was included in the sensitivity analysis (Lin et al., 2006). Please refer to the published systematic review manuscript (Katiri, Hall, Killan, et al., 2021) for a comprehensive reference list of all records included in the review (Additional file 6), as well as the data masterfile (Additional file 7).

Table 3.7. Table of records containing missing data that was queried to the corresponding author by email, and outcome.

Study record	Query	Outcome	Decision
(Buechner et al., 2010)	Exact audiometric thresholds	No response	Included for sensitivity analysis
(Cabral Junior et al., 2016)	SSD definition not explicitly defined	No response	Included for sensitivity analysis
(Brendel and Hamacher, 2018)	Unsure if inclusion criteria allow SSD participant recruitment	Response from authors: no SSD participants included	Excluded from data extraction
(Syms and Galow, 2013)	SSD not explicitly defined	Email to authors undeliverable	Included for data extraction as intention is to recruit SSD participants
(Smith and Knappett, 2015)	SSD criteria not explicitly defined	Response from authors: some participants had asymmetric hearing loss	Included for sensitivity analysis
(Gnansia and Frachet, 2016)	Audiometric criteria for 'normal or near normal' ear not explicitly stated	Response from authors: 'no exact criteria set for normal ear'	Included for sensitivity analysis
(Willeboer, 2005)	Audiometric criteria not listed	Response from authors: study include participants with bilateral hearing loss	Excluded from data extraction
(Dillon, Buss, Anderson, et al., 2017)	Audiometric thresholds listed for up to 2 kHz, no information on 4 kHz	No response	Included for sensitivity analysis
(Dillon, Buss, Rooth, et al., 2017)	Not all participants meet SSD definition	No response	Included for sensitivity analysis
(Doobe et al., 2015)	Hearing thresholds for non-Ménière's disease ear not explicitly listed	First author responded; team were to follow up, no subsequent response	Included for sensitivity analysis
(Dumon et al., 2016)	Insufficient details given to check if participants met PICO. Just states "…candidacy based on clinical parameters" without stating what these were	Response from authors: still unclear, asked for further clarification, no response	Excluded from data extraction
(Hill et al., 2006)	Exact audiometric thresholds for 'asymmetric hearing loss' not stated	Email to authors undeliverable	Excluded from data extraction
(Hol et al., 2010)	Audiometric thresholds of poor ear not explicitly listed	No response	Included for sensitivity analysis
(Kubo et al., 2001)	Audiometric criteria not listed	Email to authors undeliverable	Excluded from data extraction
(Louza et al., 2017)	Audiometric thresholds for poor ear not explicitly listed	No response	Included for sensitivity analysis
(Sladen et al., 2017)	Audiometric criteria for 'unilaterally deaf' not explicitly stated	Response from authors: a few participants do not fit the SSD definition in worse ear	Included for sensitivity analysis
(Song et al., 2013)	SSD criteria not explicitly defined	Response from authors: all participants fit SSD definition	Included for data extraction and synthesis

3.3.2 Consolidated records

Several records were consolidated for the purpose of reporting because they described the same trial or study. Two records reported different measures obtained from the same group of participants (Härkönen et al., 2015, 2017). Two records reporting on a United Sates of America (USA) multi-centre study were also consolidated as they reported on the same subset of participants (Niparko et al., 2003; Wazen et al., 2003). Four records reported on the same USA trial and participants, but presented different outcomes at different time-scales so they were grouped (Kleinjung, 2012; R. Miller et al., 2011; Murray et al., 2011; Popelka et al., 2010). A French clinical trial registration (NCT02204618) was consolidated with the study findings records (Marx, 2014; Marx et al., 2019). Similarly a Swiss clinical trial registration (NCT01749592) was consolidated with the published study findings records (Kleinjung, 2012; Peter, Kleinjung, et al., 2019). A USA clinical trial (NCT02259192) was consolidated with the equivalent published records (Galvin et al., 2019; Shannon, 2014). Another French clinical trial (NCT02966366) was consolidated with the published records (Gnansia and Frachet, 2016; Poncet-Wallet et al., 2020). Two records reported on the same 11 participants but presented outcomes at 6 months and at 12 months, so they were consolidated (Arndt, Aschendorff, et al., 2011; Arndt, Laszig, et al., 2011).

One composite article reported the methods and results of five separate trials (Weber et al., 1992). Data from this article were extracted as five distinct studies. This re-classification led to a final dataset of 78 records reporting 72 studies that met full eligibility, and 31 records reporting 24 studies for the sensitivity analysis (Figure 3-1). Of the 72 studies included, 37 assessed rerouting interventions, 29 studies assessed restoring interventions, and just 6 studies directly evaluated both types of interventions.

3.3.3 Study characteristics

The most common SSD diagnoses were sudden idiopathic or unknown cause (n=218, 41%) and vestibular schwannoma (n=134, 25%). Most rerouting intervention studies were conducted in the USA (n=25, 66%). Restoring intervention studies were conducted in the USA (n=8, 36%), Belgium and Germany (n=4, 19%). Studies recruited

a median of 10.5 participants (mean=25.3, range 3-160). Most multi-centre studies (n=7) were conducted to evaluate restoring interventions rather than rerouting interventions.

3.3.4 Outcome domains

To address our first objective, we examined the outcome domain data from the 72 included studies and classified them for reporting using the Dodd et al. (2018) taxonomy. Overall, 350 primary and 170 secondary data items were categorised across 19 of the 38 taxonomy categories (Table 3.8). Just over half (55%) of the reported outcome domains were physiological or clinical outcomes in the ear and labyrinth category (194 primary, and 90 secondary outcome domain data items). Within this category, the most common items were from speech-related domains (e.g., speech in noise, and speech in quiet), spatial-related domains (e.g., localisation and spatial hearing), hearing thresholds, and tinnitus loudness. Life impact was the next most frequently reported core area (33%; 120 primary and 50 secondary outcome domain data items). The most commonly reported categories within life impact were delivery of care, and quality of life. We observed that investigators sometimes reported multiple assessments of the same outcome domain within a study, and so the caveat to these findings is that these frequencies do somewhat over-estimate the proportion of included studies reporting the outcome domain. A total of 22 outcome domain data items (4%) could not be coded because they were not clearly defined by the authors. Overall, 73 unique outcome domains were reported across the 72 included studies: 55 primary and 18 secondary outcome domains (Table 3.8). A complete list of all reported outcome domains can be found in Table 3.9.

Table 3.8. Summary of primary and secondary outcome domains and data items across all 72 included studies.

Taxonomy core area	Taxonomy categories	Number of data items (primary outcome domains)	% of total number of primary outcome domains	Number of data items (secondary outcome domains)	% of total number of secondary outcome domains	Number of unique outcome domains reported as primary	Number of unique outcome domains reported as secondary only
Death	1: Mortality / survival	0	-	0	-	0	0
Physiological or clinical	6: Ear and labyrinth outcomes	194	55.4%	90	52.9%	15	3
	7: Eye outcomes	0	-	1	-	1	0
	9: General outcomes	9	2.6%	1	-	2	0
	17: Nervous system outcomes	3	-	3	1.8%	2	0
	21: Psychiatric outcomes	3	-	0	-	1	0
	23: Skin and subcutaneous tissue outcomes	2	-	0	-	1	0
Life impact	25: Physical functioning	2	-	5	3.3%	2	3
	26: Social functioning	1	-	3	2.9%	1	2
	27: Role functioning	1	-	1	-	1	0
	28: Emotional functioning / well-being	7	2.0%	5	3.3%	5	3
	29: Cognitive functioning	2	-	3	2.9%	1	2
	30: Global quality of life	55	15.7%	16	9.4%	7	0
	31: Perceived health status	1	-	-	-	1	0
	32a: Delivery of care - Satisfaction / patient preference	51	14.6%	17	10.0%	10	2
	32b: Delivery of care - Acceptability and availability	0	-	1	-	0	1
Resource use	34: Economic	2	-	2	1.2%	2	0
	35: Hospital	1	-	0	-	1	0
	37: Societal / carer burden	0	-	1	-	0	1
Adverse events	38: Adverse events / effects	11	3.1%	5	2.9%	3	0
Cannot code	0: Cannot code	5	1.4%	17	10.0%	N/A	N/A
	Total	**350**		**170**		**55**	18

*Data in the table is classified according to core areas and categories defined by Dodd et al. (2018). Percentage values less than 1% are not reported.

Table 3.9. A comprehensive list of all reported primary and secondary outcome domains.

Taxonomy core area	**Taxonomy categories** (number of reports as primary outcome, number of reports as secondary outcome)	**Outcome domain**	**Number of times primary outcome domain reported** (number of studies reporting as primary outcome)	**Number of times reported: rerouting / restoring**	**Number of times (n) secondary outcome domain reported** (number of studies reporting as secondary outcome)	**Number of times reported: rerouting / restoring**
Physiological or Clinical	6: Ear and labyrinth outcomes (194,90)	Speech in noise	64 (45)	33/23	15 (14)	9/1
		Localisation	36 (29)	19/14	5 (4)	1/1
		Speech in quiet	21 (17)	7/11	2 (2)	0/2
		Hearing thresholds	20 (13)	5/11	-	-
		Speech hearing	13 (12)	8/5	21 (16)	10/7
		Tinnitus loudness	9 (7)	0/9	4 (2)	0/4
		Spatial hearing	6 (6)	4/2	16 (8)	10/4
		Quality of hearing	5 (2)	2/2	9 (7)	1/6
		Reverberation	5 (5)	0/0	10 (10)	9/1
		Binaural hearing	5 (2)	3/2	-	-
		Psychoacoustic performance	5 (3)	2/3	-	-
		Motion perception	2 (1)	0/2	-	-
		Hyperacusis	1 (1)	0/1	3 (1)	0/3
		Loudness of sound	-	-	1 (1)	1/0
		Middle ear	1 (1)	1/0	-	-
		Softness of sound	-	-	1 (1)	1/0
		Tinnitus perception	1 (1)	0/1	2 (1)	0/2
		Tinnitus-related hearing	-	-	1 (1)	0/1
	7: Eye outcomes (0,1)	Vision	-	-	1 (1)	0/0
	9: General outcomes (9,1)	Dental	8 (1)	8/0	-	-
		Pain	1 (1)	1/0	1 (1)	0/0
	17: Nervous system outcomes (3,3)	Brain activity	2 (2)	0/2	3 (3)	0/3
		Brain activity (tinnitus related)	1 (1)	0/1	-	-
	21: Psychiatric outcomes (3,0)	Mental health	3 (2)	1/2	-	-

	23: Skin and subcutaneous tissue outcomes (2,0)	Skin safety	2 (1)	0/0	-	-
Life Impact	25: Physical functioning (2,5)	Ambulation Dexterity Physical health Tinnitus-related physical problems Vitality	- - 1 (1) - 1 (1)	- - 1/0 - 1/0	1 (1) 1 (1) 2 (2) 1 (1) -	0/1 0/0 1/1 0/1 -
	26: Social functioning (1,3)	Participation restrictions Social support Social impact	- - 1 (1)	- - 1/0	1 (1) 2 (2) -	0/0 1/1 -
	27: Role functioning (1,1)	Activity limitations	1 (1)	1/0	1 (1)	0/0
	28. Emotional functioning (7,5)	Tinnitus annoyance Tinnitus-related distress Coping Stress Work-related stress Emotion Tinnitus intrusiveness Tinnitus-related sleep problems	2 (1) 2 (1) 1 (1) 1 (1) 1 (1) - - -	0/2 0/1 0/1 0/1 0/1 - - -	- 2 (2) - - - 1 (1) 1 (1) 1 (1)	- 0/1 - - - 0/0 0/1 0/1
	29: Cognitive functioning (2,3)	Listening effort Cognition Tinnitus-related cognition	2 (2) - -	1/1 - -	1 (1) 1 (1) 1 (1)	0/1 0/0 0/1
	30: Global quality of life (55,16)	Tinnitus symptom severity Hearing disability Disease-specific quality of life Health-related quality of life Dizziness Hearing handicap Pre-intervention disability	22 (15) 14 (14) 9 (9) 4 (4) 3 (1) 2 (2) 1 (1)	1/20 5/6 5/3 2/0 0/3 2/0 1/0	2 (2) 2 (2) 8 (6) 2 (1) - 1 (1) 1 (1)	0/2 0/0 2/2 0/0 - 1/0 1/0
	31: Perceived health status (1,0)	General health	1 (1)	1/0	-	-
	32a: Delivery of care - Satisfaction / patient preference (51,17)	Device benefit Device use Satisfaction	19 (16) 11 (11) 8 (6)	13/4 5/5 8/0	1 (1) 1 (1) 3 (2)	0/0 0/0 2/0

		Aversiveness	5 (5)	5/0	6 (6)	5/1
		Residual (aided) disability	2 (2)	2/0	1 (1)	1/0
		Clarity of sound	1 (1)	1/0	1 (1)	1/0
		Device performance	1 (1)	1/0	-	-
		Device preference	2 (2)	2/0	-	-
		Likelihood of recommending	1 (1)	1/0	-	-
		Work-related performance	1 (1)	0/1	-	-
		Brightness of sound	-	-	1 (1)	1/0
		Fullness of sound	-	-	1 (1)	1/0
		Hearing benefit	-	-	1 (1)	1/0
	32b: Delivery of care -Acceptability and availability (0,1)	Self-image and stigma	-	-	1 (1)	1/0
Resource Use	34: Economic (2,2)	Cost	1 (1)	0/0	2 (2)	1/0
		Productivity loss	1 (1)	0/0	-	-
	35: Hospital (1,0)	In-patient stay	1 (1)	0/0	-	-
	37: Societal / carer burden (0,1)	Impact on others	-	-	1 (1)	0/0
Adverse Events	38: Adverse events / effects (11,5)	Adverse effects	7 (6)	5/2	5 (4)	3/2
		Safety	3 (1)	3/0	-	-
		Device failure	1 (1)	1/0	-	-
	0: Cannot code (5,17)	Not stated	5	N/A	17	N/A

*Data in the table is classified according to the Dodd et al. (2018) taxonomy. Categories within each core area are arranged by the most frequently used first. The number of individual studies that reported each primary and secondary domain is also listed. - = none reported.

3.3.5 Measurement instruments

Our first objective also asked about the measurement instruments used to measure the domains. For reporting purposes, measurement instruments are summarised according to whether they were, (i) investigator administered, (ii) Patient Reported Outcome Measures (PROMs), and (iii) unclear or unknown (Table 3.10). Within each of these categories, a finer breakdown was performed that was relevant to the instrument category (e.g., PROMs could be a numerical rating scale, multi-item questionnaire or diary record).

Collating information about the measurement instruments reported in the 72 studies revealed many ways to measure the domains of interest and that no single instrument was used by all studies. We observed that reporting was strongly biased towards reporting benefits and not reporting harms. Counting the exact number of measurement instruments is not straightforward because some of the instruments were reported both as global scores and subscale scores across different studies and different authors administered the same instrument to assess different outcome domains. For example, the Glasgow Hearing Aid Benefit Profile (GHABP) (Gatehouse, 1999) was reported in various forms under hearing handicap, pre-intervention disability, device benefit, device use, satisfaction, and residual (aided) disability. Regarding the Abbreviated Profile of Hearing Aid Benefit (APHAB) (Cox and Alexander, 1995) performance was most often reported as a subscale rather than the global score including all three speech communication subscales (Ease of communication, Reverberation, and Background noise subscales). For the purposes of reporting here, the different forms reported by the authors all contribute to the data item counts and so the numbers may over-estimate the number of measurement instruments *per se*. For that reason, we refer to these data as measurement 'methods' not 'instruments'. A summary of the number of methods used to measure the outcomes across the most frequently reported Dodd's taxonomy categories is given in Table 3.10. Comprehensive listing of all methods can be found in a spreadsheet, labelled Additional file 10 in the peer reviewed publication (Katiri, Hall, Killan, et al., 2021). The spreadsheet is organised according to the domains within the Dodd's taxonomy categories.

Table 3.10. Summary of the number of most frequently reported measurement methods used to assess treatment outcomes in each domain category in the Dodd et al. (2018) taxonomy.

Outcome domains	Investigator administered				Patient Reported Outcome Measures (PROMs)			Unclear
	Psycho-physical instruments	Objective instruments	Technical and lab measures	Investigator observation / judgement	Numerical Rating Scale	Multi-item question-naire	Diary	Unclear
Physiological or clinical core area, 6: Ear and labyrinth outcomes								
Hearing thresholds	8	1	-	-	-	-	-	-
Speech in noise	47	-	-	-	-	2	-	-
Speech in quiet	18	-	-	-	-	2	-	-
Speech hearing	6	-	-	-	-	3	-	-
Tinnitus loudness	1	-	-	-	2	-	-	-
Spatial hearing	1	-	-	-	-	3	-	-
Localisation	33	-	-	-	-	1	-	-
Quality of hearing	-	-	-	-	2	1	-	2
Rever-beration	-	-	-	-	1	1	-	-
Life impact core area, 30: Global quality of life								
Tinnitus-symptom severity	-	-	-	-	-	9	-	-
Hearing disabilities	-	-	-	-	-	9	-	-
Disease-specific quality of life	-	-	-	-	-	6	-	-
Life impact core area, 32a: Delivery of care - Satisfaction / patient preference								
Device benefit	-	-	-	-	2	8	-	-
Device use	-	-	3	-	1	2	1	1
Satisfaction	-	-	-	-	2	5	1	-

Aversiveness	-	-	-	-	-	1	-	
Adverse events core area, 38: Adverse events / effects								
Adverse effects	-	-	-	1	-	2	-	6

*Only items where there were more than 10 reports of the outcome domain (Table 3.9) and only those methods reported more than once across the 72 included studies are selected for reporting in this table.

Considering the ear and labyrinth outcome domains, the 18 outcome domains were assessed by 133 different measurement methods. A description of the most frequently reported methods is given in Table 3.11. The most common approach was an investigator administered psychophysical instrument. This was true for all speech-related domains (i.e., speech in noise, speech in quiet, and speech hearing), spatial localisation, and hearing thresholds. Speech performance was most often measured by a speech reception threshold, although there were many different testing methods. There was no clear preferred method for measuring speech in quiet, while speech in noise was most often assessed using the Hearing in Noise Test (HINT) (Nilsson et al., 1994). However, even here the choice of background noise was not consistent across studies. Localisation performance was most often measured by localisation accuracy using a horizontal circular or semi-circular array of loudspeakers. However, again the number of loudspeakers and angular separation between sound sources varied across studies. Perhaps unsurprisingly, hearing thresholds were most often assessed using pure-tone audiometry which tends to have a more standardised testing method. Tinnitus loudness was commonly measured using a Visual Analogue Scale (VAS), which is a form of PROM.

The seven global quality of life outcome domains were assessed by 36 different measurement methods. A description of the more popular methods is given in Table 3.12. The most common method of assessment was a PROM, in the form of a multi-item questionnaire. Most frequently reported were the Speech, Spatial and Qualities of Hearing (SSQ) (Gatehouse and Noble, 2004), Glasgow Benefit Inventory (GBI) (Robinson et al., 1996), Single Sided Deafness (SSD) questionnaire (Wazen et al., 2003), and the Tinnitus Handicap Inventory (THI) (Newman et al., 1996).

Table 3.11. Listing of all unique measurement methods used to assess the most frequently reported outcomes in the Dodd et al. (2018) taxonomy physiological or clinical #6, ear and labyrinth category.

Measurement methods (n>1) split by outcome domains and type of method		Primary outcomes	Secondary outcomes
Hearing thresholds, investigator administered			
Psycho-physical	Pure-tone audiometry	10	-
	Pure-tone audiometry (bone-conduction only)	2	-
	Soundfield audiometry	2	-
Speech in noise, investigator administered			
Psycho-physical	Bamford–Kowal–Bench Speech in Noise test (BKB-SiN) in four-talker babble, Speech Reception Thresholds (SRT)	3	-
	Bamford-Kowal-Bench Speech in Noise test (BKB-SiN) in multi-talker babble, Speech Reception Thresholds (SRT)	2	-
	Hearing In Noise Test (HINT) in multi-talker babble, Speech Reception Thresholds (SRT)	2	-
	Hearing in Noise Test (HINT) in R-space restaurant noise, Speech Reception Thresholds (SRT)	2	-
	Hearing in Noise Test (HINT) noise not specified, Speech Reception Thresholds (SRT)	2	-
	Hochmair-Schulz-Moser sentence test in speech-shaped noise, Speech Reception Thresholds (SRT)	3	-
	Leuven Intelligibility Sentences Test (LIST) noise not specified, Speech Reception Thresholds (SRT)	2	-
	Oldenburg Sentence Test (OlSa) noise not specified, Speech Reception Thresholds (SRT)	5	-
	Quick Speech-In-Noise (QuickSIN) test in multi-talker babble, Speech Reception Thresholds (SRT)	2	-
	Speech Intelligibility In Noise (SPIN) test in multi-talker babble, percent correct	3	-
	Speech-in-noise test in speech (not specified), Speech Reception Thresholds (SRT)	2	-
Speech in noise, PROM			
Multi-item questionnaire	APHAB background noise subscale	5	9
Speech in quiet, investigator administered			
Psycho-physical	Consonant-Nucleus-Consonant (CNC) word list	3	-
	Freiburger monosyllabic word discrimination in quiet, Speech Reception Thresholds (SRT)	2	-
	Monosyllable test (67S test), Japanese version	2	
Speech hearing, PROM			
Multi-item questionnaire	Abbreviated Profile of Hearing Aid Benefit (APHAB) ease of communication subscale	5	9
	Speech, Spatial and Qualities of Hearing (SSQ) speech subscale	4	9
Tinnitus loudness, investigator administered			
Psycho-physical	Tinnitus Loudness Matching	1	3
Tinnitus loudness, PROM			

Numerical rating scale	Numerical Rating Scale (not specified)	2	1
	Visual Analogue Scale (not specified)	6	-
Spatial hearing, PROM			
Multi-item questionnaire	Speech, Spatial and Qualities of Hearing (SSQ) spatial subscale	3	8
	Spatial Hearing Questionnaire (SHQ)	2	-
	Spatial Hearing Questionnaire (SHQ), various subscales	-	8
Localisation, investigator administered			
Psycho-physical	Horizontal semi-circular array of 7 loudspeakers, angular separation 30°, localisation accuracy	2	1
	Horizontal circular array of 5 loudspeakers, angular separation 45°, localisation accuracy	2	-
	horizontal circular array of 9 out of 33 loudspeakers, angular separation 5.6°, localisation accuracy	1	1
	Horizontal circular array of 19 loudspeakers, angular separation 10°, localisation accuracy	2	-
	Localisation from one or multiple loudspeakers (not specified)	1	2

*Only those domains where there was more than one report of the outcome measurement method are selected for reporting here. See Additional file 10 in the published manuscript Katiri et al. (2021) for full details.

Table 3.12. Listing of all unique measurement methods used to assess the most common outcomes in the Dodd et al. (2021) taxonomy Life impact #30, global quality of life category.

Measurement methods (n>1) split by outcome domains and type of method		**Primary outcomes**	**Secondary outcomes**
Tinnitus-symptom severity, PROM			
Multi-item questionnaire	Tinnitus Handicap Inventory (THI)	7	1
	Tinnitus Questionnaire (TQ)	2	1
	Tinnitus Questionnaire (TQ), German version	3	-
	Tinnitus Reaction Questionnaire (TRQ)	3	-
Hearing disabilities, PROM			
Multi-item questionnaire	Speech, Spatial and Qualities of Hearing (SSQ)	8	-
Disease-specific quality of life, PROM			
Multi-item questionnaire	Bern Benefit in Single Sided Deafness (BBSS) questionnaire	1	1
	Glasgow Benefit Inventory (GBI)	3	2
	Nijmegen Cochlear Implant Questionnaire (NCIQ)	1	2
	Single Sided Deafness (SSD) questionnaire	4	-
	Multi-item, multi-domain questionnaire (author's own)	-	2

*Only those domains where there was more than 1 report of the outcome measurement instrument are selected for reporting here. See Additional file 10 in the published manuscript Katiri et al. (2021) for full details.

The 12 delivery of care (satisfaction / patient preference) outcome domains were assessed by 37 different measurement methods. A description of the most commonly reported methods is given in Table 3.13. Once again, the most common method of assessment was a PROM, in the form of a multi-item questionnaire. The most frequently reported were the Abbreviated Profile of Hearing Aid Benefit (APHAB) (Cox and Alexander, 1995), and the Glasgow Hearing Aid Benefit Profile (GHABP) (Gatehouse, 1999).

Table 3.13. Listing of all unique measurement methods used to assess the most commonly reported outcomes in the Dodd et al. (2018) taxonomy; life impact #32a, delivery of care (satisfaction / patient preference) category.

Measurement methods (n>1) split by outcome domains and type of method		**Primary outcomes**	**Secondary outcomes**
Device benefit, PROM			
Multi-item questionnaire	Abbreviated Profile of Hearing Aid Benefit (APHAB)	6	-
	Glasgow Hearing Aid Benefit Profile (GHABP)	4	-
	Multi-item, multi-domain Questionnaire (author's own)	3	-
Numerical rating scale	International Outcome Inventory for Hearing Aids (IOI-HA), single item on benefit	1	1
	Visual Analogue Scale (not specified)	1	-
Device use, investigator administered			
Technical and lab measures	Device log (not specified)	2	-
	Device log average usage (hrs / day)	3	-
Device use, PROM			
Multi-item questionnaire	Glasgow Hearing Aid Benefit Profile (GHABP), hearing aid use subscale	2	-
Satisfaction, PROM			
Multi-item questionnaire	Glasgow Hearing Aid Benefit Profile (GHABP), various subscales	1	2
	Multi-item, multi-domain questionnaire (author's own)	2	-
Aversiveness, PROM			
Multi-item questionnaire	Abbreviated Profile of Hearing Aid Benefit (APHAB) aversiveness subscale	5	6

*Only those domains where there was more than one report of the outcome measurement instrument are selected for reporting here. See Additional file 10 in the published manuscript Katiri et al. (2021) for full details.

3.3.6 Comparison of outcome domains and measurement instruments across interventions

One of our secondary objectives was to compare and contrast outcome domains and measurement instruments reported for interventions that aim to re-establish (i) bilateral hearing (i.e., CROS aid, BAHA, ADHEAR, SoundBite^{TM}) through rerouting, and (ii) binaural hearing (i.e., MEI, CI) through restoring.

Across the 72 included studies, 37 assessed rerouting interventions only and 29 assessed restoring interventions only. The remainder assessed both interventions in the same study design and so are not included in this comparison. The two intervention approaches assessed the same outcome domains. But there were several notable exceptions. Tinnitus-related outcomes were almost exclusively limited to studies evaluating restoring interventions (reported 43 times) rather than rerouting interventions (reported once). The same was true for brain-related assessments of neural activity (restoring studies reported three times; rerouting studies none). In contrast, rerouting studies were also much more concerned about aversiveness (reported 10 times) than were restoring studies (reported once). Furthermore, all dental outcomes were limited to rerouting studies. Indeed, all eight reports came from a single study evaluating the SoundBite^{TM} intraoral device (Miller et al., 2011; Murray et al., 2011; Popelka, 2010; Popelka et al., 2010). The primary and secondary outcome domains reported for rerouting / restoring interventions are listed in Table 3.9.

Overall, restoring intervention studies reported a greater proportion of investigator administered tests than PROMs, while rerouting intervention studies reported more of a balance of these two measurement instrument types. It was not possible to determine the effect of intervention on the choice of measurement methods because the number of times each method used was generally very small. Perhaps the most striking effect observed was that speech hearing was assessed using the APHAB (Cox and Alexander, 1995) ease of communication subscale in rerouting studies (reported 13 times) much more often than in restoring studies (reported just once).

3.3.7 Use of measures over time frame

For both primary and secondary outcomes, there was significant variability in the duration of follow-up period, ranging from acute (baseline) testing to 10 years post-intervention. There was notable inconsistency in the number of testing sessions, from a single session to ongoing daily records (Schmerber et al., 2017), and when they were conducted after device fitting or surgery. For reporting, time frames were grouped into measures taken in a single session only, at a time point less than 3 months after baseline ('acute'), at a time point from 3 months to less than 1 year after intervention ('early' acclimatisation), and at 1 year or more after intervention ('long'). Eighteen of the 72 included studies were designed as a single session (12 rerouting, five restoring, one both), 26 had at least one acute follow-up (16 rerouting, nine restoring, one both) mostly at 1 month after baseline, 31 had at least one early follow-up (11 rerouting, 16 restoring, 4 both) mostly at 6 months after baseline, and 26 had at least one long follow-up (6 rerouting, 16 restoring, four both).

We evaluated whether there was any change over time in the choice of primary and secondary outcome domains and measurement methods by classifying the data according to the three major Dodd's taxonomy categories (Dodd et al., 2018) (#6 ear and labyrinth, #30 global quality of life and #32a delivery of care), and according to whether they were investigator administered tests or PROMs (Figure 3-2).

Single session studies almost exclusively focused on hearing-related outcome domains, but ear and labyrinth accounted for about 50% of the outcomes assessed, even at the longest time frame. Similarly, single session studies almost exclusively used investigator administered testing methods, but over time a more 50/50 balance was observed between these and PROMs. This pattern was true for the primary outcomes. However, secondary outcomes almost always used PROMs, irrespective of the time frame.

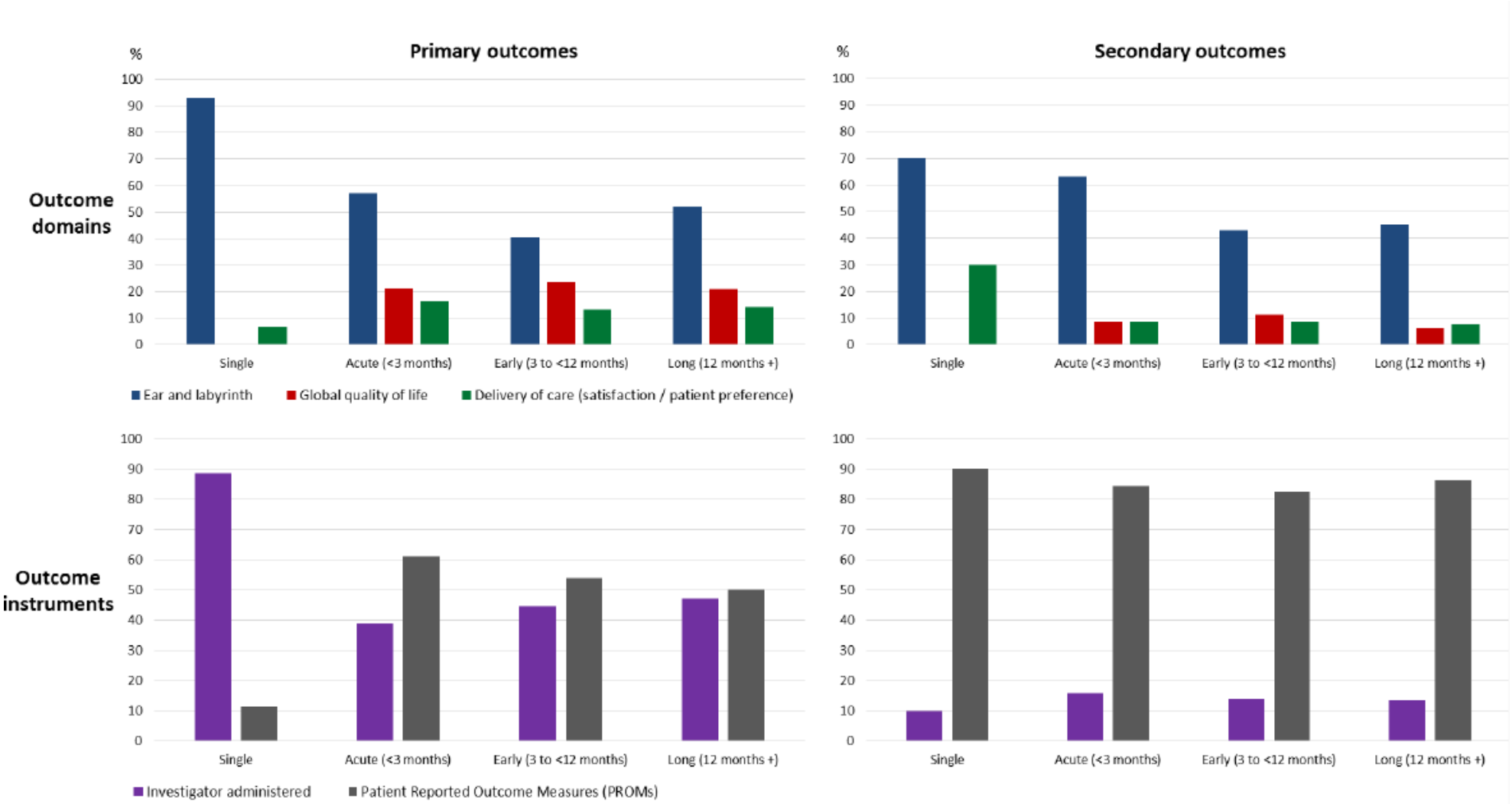

Figure 3-2. Change over time in the choice of primary and secondary outcome domains and measurement methods.
*Top panels illustrate reporting of the three major outcome domain taxonomy categories over the successive follow-up time points. Bottom panels illustrate reporting of the two major measurement methods over time. All data are reported as a percentage, normalised to the total number of outcome data items assessed at that time point, and calculated separately for primary and secondary outcomes.

3.3.8 Sensitivity analysis

The final exploratory objective examined whether we would identify any additional outcomes if we included studies where the audiometric eligibility criteria were more lenient than our working definition adopted from the Van de Heyning et al. (2017) consensus paper. The outcome domains reported by the 24 studies included for sensitivity analysis (Figure 3-1) were coded in the same way as described previously. Overall, 205 primary and 80 secondary data items were categorised. None of these reported outcomes had not already been captured by the 72 included studies.

3.3.9 Risk of bias

Assessment of the 72 included studies focused on (a) whether the outcomes were reported prospectively, and if yes, (b) whether there was consistency between the prospective registration and the published study. Notes on conflicts of interest and study design were also taken.

Although there were 11 clinical trial registrations, only four studies with reported findings had been pre-registered. One assessed the SoundBite™ (Miller et al., 2011), and three assessed cochlear implantation (Kleinjung, 2012; Marx, 2014; Syms and Galow, 2013). The SoundBite™ study (Syms and Galow, 2013) had two discrepancies: adverse effects were not reported in the protocol (NCT01933386) but were reported in the published record discussion, and the Pure Tone Audiometry (PTA) thresholds range were planned up to 4kHz in the protocol but reported up to 2 kHz in the study report. All three cochlear implant studies had discrepancies between the measures planned in the registered protocol and those reported in the study findings. Other discrepancies included lack of clarity in the report on whether adverse events were assessed at 1 month post-implantation, as per registration (NCT02259192) (Shannon, 2014), and differences between the planned and reported measurement time-frames (NCT01749592) (Kleinjung, 2012).

3.4 Discussion

There is a growing general recognition that insufficient attention has been paid to the outcomes measured and reported in clinical trials. The CROSSSD study group has established the need for a core outcome set for SSD interventions and we are the first to identify existing knowledge about outcomes and measurement instruments using a systematic review methodology.

3.4.1 Principal findings

Most studies included in the review evaluated rerouting interventions rather than restoring interventions. There was a large variation in the reported outcome domains, with most studies concentrating on physiological or clinical outcomes, followed by life impact outcomes. Only a minority of studies reported on resource use and adverse events. To improve reporting, the specialised Consolidated Standards of Reporting Trials (CONSORT) guidelines for reporting harms-related issues in a randomised controlled trials (Moher et al., 2010) can be utilised. Investigators did not always report what their intended outcome domain was, suggesting that their chosen measurement instruments were not actively matched to an outcome domain.

With regards to measurement instruments chosen by investigators, a large inconsistency was observed with investigator administered tests mostly adopted, focusing mainly on speech in noise and spatial-related testing. A diversity within these categories of measurement instruments was also observed with a plethora of signal and noise configurations that do not always fit existing recommendations that aim to reveal both the benefits and drawbacks of hearing devices. Similarly, multi-item questionnaires are frequently utilised but there is no consensus in their selection, nor the intended outcome domains to be measured. Although the range of functional difficulties imposed by SSD, as well as the impact on individual's social and psychological well-being, are well documented (Lucas et al., 2018); similar to other interventions in the hearing field, they are not always assessed in a systematic manner (Danermark et al., 2013; Hall et al., 2019; Hall et al., 2016).

The time-frame when interventions were assessed also varied, so it is challenging to compare the short- and long-term treatment-related changes for rerouting and restoring interventions.

3.4.2 Comparison with other studies

Our review identifies limitations in the range of reported outcomes in clinical trials that are reflected more broadly across clinical practice in ENT and audiology. In 2016, Van de Heyning led a several expert panel discussions to reach a consensus on a clinical protocol for SSD including a minimum set of outcome measures (Van de Heyning et al., 2017). This group recommended a core set of three ear and labyrinth and two life impact measures, tested using investigator administered tests and PROMs, respectively. Their ear and labyrinth measures were: (i) hearing thresholds using pure-tone audiometry, (ii) speech in noise perception using a standard audiometric and validated sentence test and a free-field setup in a sound-treated room, and (iii) sound localisation using a free-field system with at least seven loudspeakers horizontally distributed with equal angular separation, again in a sound-treated room.

In our review, we observed that these were some of the most popular domains reported across the 72 included studies. Common speech in noise materials included the Hearing in Noise Test (HINT) sentences, Oldenburg sentence test (OlSa), and the Speech Intelligibility In Noise (SPIN) test. Measurements for sound localisation perhaps diverged the most from this expert panel recommendation, with numerous studies either using fewer speakers or testing front and back localisation in a circular array. Recommended life impact measures were: (i) quality of life using both disease-specific (speech, spatial, and qualities of hearing (SSQ)) and generic health-related (Health Utilities Index (HUI) Mark 3) questionnaires, and (ii) delivery of care using a measure of device use (data logging or patient report). In our review, we coded the SSQ questionnaire as an ear and labyrinth assessment (not life impact) because it was most often reported as separate subscale scores for speech hearing, spatial hearing, and quality of hearing. We also observed that HUI-3 (Horsman et al., 2003) was rarely reported across the 72 included studies. Others were EuroQol-5D-3L (EuroQol Group,

1990), WHOQOL-BREF (Skevington et al., 2004), and SF-36 (Ware and Sherbourne, 1992).

Van de Heyning et al. (2017) also recommended tinnitus assessment if applicable; namely tinnitus loudness (using a Visual Analogue Scale (VAS)) and tinnitus symptom severity (using the Tinnitus Functional Index (TFI)). Our review confirmed that these domains were often limited to restoring interventions (cochlear implant) studies and therefore were perhaps considered less relevant to rerouting interventions for SSD by investigators. It is possible that this recommendation reached consensus because the panel(s) comprised cochlear implant experts attending a cochlear implant conference (s).

In terms of time frame for outcome measurement, Van de Heyning et al. (2017) recommended that outcomes should be collected at baseline, and at 1, 3, 6, and 12 months after intervention. This would mean that all studies should span the acute, early, and long-term time points coded in our review. Nevertheless, less than half of the included studies assessed outcomes at these time points.

3.4.3 Strengths and limitations of the review

Our review was guided by good practice as set out in the Core Outcome Measures in Effectiveness Trials (COMET) handbook (Williamson et al., 2017). In terms of outcome extraction from the academic literature, Williamson et al. state “it is recommended that all are extracted verbatim from the source manuscript” (page 10). This posed some challenges when it came to coding the outcome domains because different investigators used different terminology even when they were likely referring to the same construct. To collate the data, our team had to recode some of the domain names, conducting this task in pairs to reduce the impact of individual opinion (refer to Section 3.2.8 for details). For transparency, both the authors’ original description and the recoding were saved in the data masterfile (Additional file 7 in the published manuscript Katiri et al. (2021)). This allows external critical review of the CROSSSD core outcome domain set, whose development will be informed by this review, right back to its inception.

There is currently no consensus on how clinical trial outcomes should be classified (Gorst, Gargon, Clarke, Smith, et al., 2016). COS researchers often simply agree 'themes' in discussion with advisory groups (Alkhaffaf et al., 2017). However, it is recognised that this lack of a standardised outcome classification system results in inconsistencies due to ambiguity and variation in how outcomes are described across different studies. Recently a new taxonomy for outcome classification has been developed to promote efficient searching, reporting, and classification of trial outcomes (Dodd et al., 2018). Strengths are that it focuses on general outcomes, is comprehensive, is not disease specific, and is applicable to trials for any disease or health condition. For the purpose of this systematic review, the need arose to sub-categorise the ear and labyrinth category, which was done following discussion with the study management team and research partners at a workshop (Chapter 4). For transparency, full details of the customised sub-categorisation can be found in Additional file 10 of the published systematic review manuscript (Katiri, Hall, Killan, et al., 2021).

Also recommended in the COMET handbook (Williamson et al., 2017) is to perform the systematic review in stages to check whether outcome saturation is reached. In this sense, our sensitivity analysis can be considered such a check. We had identified 24 additional studies that just missed the eligibility criteria for inclusion, but none of these studies reported any novel outcome domains that had not already been captured in the first stage. As Williamson et al. (2017) state "if there are no further outcomes of importance then the systematic review may be considered complete" (page 10).

3.5 Conclusion

This review highlights outcome domains and measurement instruments reported by studies that have evaluated rerouting and/or restoring interventions for SSD in adults. The extracted data provides a meticulous catalogue of investigators' chosen outcome domains of which the majority were successfully categorised using the Dodd et al. (2018) taxonomy outcome classification system. Our findings emphasise the need to improve clinical trial design and reporting in this area of health research. We hope that

guidelines that have been developed explicitly with both rerouting and restoring interventions in mind will have broader take up across the ENT, audiology and hearing sciences communities.

The longer-term intention of this work was to develop a COS that identifies by consensus a minimum standard for reporting in clinical trials of SSD in adults. This review made a specific contribution to this endeavour by identifying outcome domains and measurement instruments that have been defined in relevant clinical trial designs to date.

We recognise that systematic reviews of outcomes simply aggregate the opinions of previous researchers on what outcomes they deemed important to measure. The outcome domains collated in this review will be put forward as potential candidates; as outcome domains in a long list that will be considered by a range of stakeholders using a Delphi consensus method (Williamson et al., 2017). For that long list of candidate outcome domains to be truly comprehensive, it is important to also give participants the option to nominate any new domains that they might consider missing. The patient perspective was incorporated and their contributions are described in detail in Chapter 4.

4. Development of a core outcome domain set for single-sided deafness

This chapter is adapted from these peer reviewed publications:
Katiri, R., Hall, D. A., Hoare, D. J., Fackrell, K., Horobin, A., Buggy, N., Hogan, N., & Kitterick, P. T. (2021). Redesigning a web-based stakeholder consensus meeting about core outcomes for clinical trials: formative feedback study. *JMIR Form Res*, 5(8), e28878. doi: 10.2196/28878.

Katiri, R., Hall, D. A., Hoare, D. J., Fackrell, K., Horobin, A., Hogan, N., Buggy, N., Van de Heyning, P., Firszt, J. B., Bruce, I. A., & Kitterick, P. T. (2022). The Core Rehabilitation Outcome Set for Single-Sided Deafness (CROSSSD) study: international consensus on outcome measures for trials of interventions for adults with single-sided deafness. *Trials*. 23(1), 764. doi: 10.1186/s13063-022-06702-1.

and this recommendation document:
Gorst, S.L., Barrington, H., Brookes, S.T., Chalmers, J.R., Devane, D., Fledderus, A.C., Grosskleg, S., Hall, D.A., Harman, N.L., Hoffmann, C., Katiri, R., Maeso, R., Saldanha, I.J., Tong, A., & Williamson, P.R. (2021). Online consensus meetings for COS development: issues to consider. https://www.comet-initiative.org/Resources.

Acknowledgements for this chapter
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4.1 Introduction

The need for harmonisation of assessment methods across trials of SSD interventions has already been acknowledged by professional panels at two international conferences (10th Asia-Pacific symposium on cochlear implants and related sciences, Beijing, China, in 2015; and the 14th International conference on cochlear implants and other implantable technologies, Toronto, Canada, in 2016); and recommendations for a minimum set of clinical outcome measures and readily available measurement instruments have been made (Van de Heyning et al., 2017).

The present harmonisation study addressed limitations of this previous work (i.e., consensus derived by professionals mainly working the clinical field of cochlear implantation, and using pre-existing measurement instruments), by considering all SSD interventions and all professional experts; by deliberately focusing first on establishing *what* is important to measure, and by giving the healthcare users' input equal weighting to that of the professionals (Williamson et al., 2017). It advocates consistent choice of outcomes to ensure high-quality, easily comparable trials that are concentrating on important outcomes relevant to all stakeholders involved.

The purpose of the study was to define an agreed minimum standard for what is critically important to assess in all clinical trials evaluating SSD interventions. The expected impact would be to increase the potential for evidence synthesis (i.e., meta-analysis) of published results to generate the required evidence base for commissioning of clinical services and for informed decision making between healthcare user and professional.

4.1.1 Chapter aims and objectives:

Chapter 4 aims to describe the development of the core outcome domain set for SSD device-based interventions.

The chapter objectives were:

(i) To describe the generation of the long list of candidate outcome domains

(ii) To discuss participant recruitment methods

(iii) To describe the Round 1 and Round 2 eDelphi surveys outcomes

(iv) To describe the stakeholder consensus meeting outcomes

(v) To provide feedback obtained from the wider group of participants on the finalised core outcome domain set.

4.2 Methods

The methodological process adopted to establish consensus on a core outcome domain set is described in detail in Chapter 2 and a summary of the process is outlined in Figure 2.1. The specific detail related to this dataset is described below.

In brief, CROSSSD extended the nominal group technique by requesting participants to engage in some activities in advance, namely:

(i) inviting them to meet the group at the discretionary coffee-morning,

(ii) introducing the meeting purpose, procedures and Delphi survey results via an information pack (Appendix 18), PowerPoint slides (Appendix 19) and a pre-recorded presentation (Additional file 2 in Katiri et al. (2022)).

(iii) asking them to vote for three outcomes they considered crucial to include in the COS before the day of the consensus meeting. Further modifications were

(iv) introducing a structured 'ice-breaker' activity,

(v) providing sub-group support from a public research partner or patient involvement manager and facilitator. Sub-group composition was pre-determined to achieve a balance of stakeholder perspectives and to facilitate the efficient organisation of sub-group discussions on the day of the meeting.

The protocol for prioritising the CROSSSD outcome domains has been published (Katiri, Hall, Buggy, et al., 2020), in addition to the methodology for conducting the consensus meeting online (Katiri, Hall, Hoare, et al., 2021). The core outcome domain set development process was informed by the COMET Handbook version 1.0 (Williamson et al., 2017) and the Core Outcome Set-STAndards for Development (COS-STAD) (Kirkham, Davis, et al., 2017). Ethical approval was granted from the Nottingham 2 Research Ethics Committee (Research Ethics Committee reference 19/EM/0222,

Integrated Research Application System Project ID 239750) on 06 August 2019. The study is reported according to the Standards for Reporting Qualitative Research (SRQR) (O'Brien et al., 2014).

4.3 Generation of a long list of candidate outcome domains

As described in Chapter 2, a list of candidate outcome domains was compiled using information derived from (i) a systematic review of the literature (Katiri, Hall, Killan, et al., 2021); (ii) available qualitative data (Lucas et al., 2018); and (iii) discussions during a workshop. The first step of the process of identifying and systematically refining the selection of candidate outcome domains is summarised in Figure 4-1. A total of 433 outcome domains were extracted from studies included in the systematic review (Katiri, Hall, Killan, et al., 2021). We removed 217 by excluding duplicates and grouping similar outcome domains.

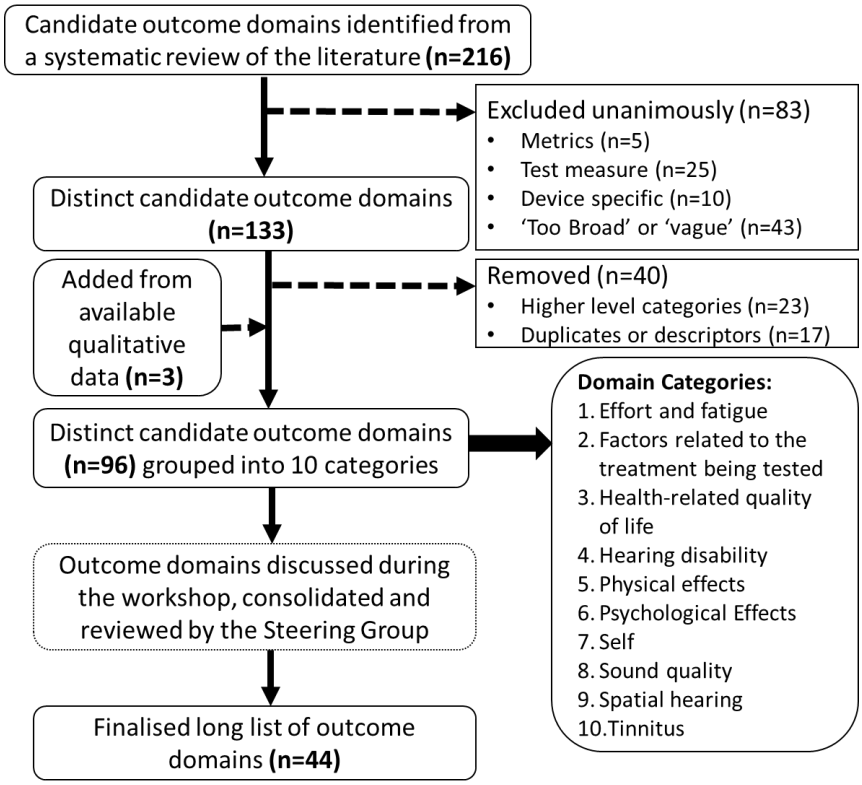

Figure 4-1. Summary diagram of Step 1: Generation of a long list of candidate outcome domains.

The remaining 216 were discussed at a study management team workshop. All individual outcome domains were printed on cards in preparation for the 2-day long workshop. Also in preparation for the workshop, the outcome domain cards were categorised into six preliminary groupings by RK: (i) adverse effects or harms, (ii) performance in a test situation, (iii) patient outcome, (iv) resource use, (v) satisfaction, and (vi) other / cannot code.

During the workshop 83 domains were excluded. Reasons for removing these included (i) the domain was a metric (e.g., Thresholds, Tonotopy) (n=17), (ii) the domain referred to the measuring instrument (e.g., Transcranial attenuation, Cortical change) (n=7), (iii) the domain was too generic or vaguely defined (e.g., Handicap, Cognition) (n=51), and (iv) the domain was device specific (e.g., Periodontal, Dental measures) (n=8). Examples of those domains excluded were phrases describing 'how' to measure such as Thresholds, Audiologic, Tonotopy, Informational masking, Cortical changes, and Brain activity; or outcome domains that were deemed too broad, generic, or ill-defined such as Qualities, Hearing, Therapy, Background noise, Mental health, and Cognitive distress.

Further group discussion during the workshop led to consolidation of an additional 23 outcome domain terms into a smaller number of outcome domain labels. For example, Hearing disability was considered synonymous with Residual disability, Perceived hearing disability, Hearing disability at everyday life, and Auditory disability. Another 17 outcome domain terms were deemed as duplicates or descriptions of already included outcome domains (e.g., Subjective assessment of handicap, Disability, Use, Benefit, and Satisfaction). This left 93 outcome domains for the long list.

The workshop team next systematically reviewed and discussed the findings published by Lucas et al. (2018) to determine whether qualitative interviews might have identified any other candidate outcome domains. This process added three new outcome domains which had not been assessed explicitly in previous quantitative studies: Personal safety (e.g., Road safety, Independent living), Motivation (e.g., to

engage in challenging listening situations), and Mood (e.g., general sense of well-being).

The resulting 96 outcome domains were consolidated further by grouping domains together that were considered by the group to be describing the same domain. For example, the outcome domains Sound localisation, Localisation, Localisation performance, Azimuthal sound localisation, Auditory localisation, Localisation ability, Source localisation, Localisation testing, and Ability to judge direction of sound, were consolidated into an outcome domain labelled 'Sound localisation' (telling where a sound is coming from).

The high-level categorisation, further re-grouping and consolidation resulted in a final list of 44 outcome domains. For ease of presentation to survey participants, these outcome domains were subsequently organised thematically into 10 categories (Figure 4-1): (i) Psychological effects, (ii) Factors related to the treatment being tested, (iii) Health-related quality of life, (iv) Hearing disability, (v) Spatial hearing, (vi) Physical effects, (vii) Self, (viii) Sound quality, (ix) Tinnitus, and (x) Other effects. A summary diagram of the domain grouping process adopted can be found in Figure 4-1. Each outcome domain had a plain language definition explaining in more detail the unique construct it encapsulated (see Table 4-1 for a list, categories, and definitions of initial outcome domains). Most outcome domains described benefits to healthcare users. A category encapsulated any bad or unexpected thing that might happen during the time an SSD treatment is being tested in a clinical trial, i.e., an adverse event.

Table 4.1. Table of domain categories, single-sided deafness (SSD) intervention-related outcome domains and concept definitions for all 44 outcome domains co-produced with collaborators with lived experience of SSD at the pre-Delphi stage.

	Category	SSD-related outcome domain	Concept definition	Source
1	Psychological effects	Aversion to loud sounds	Feeling uncomfortable when listening to loud sounds	CROSSSD workshop
2		Discomfort in listening situations	Finding yourself in listening situations that you feel you can't adequately control (for example, when you can't choose a favourable listening position); or situations in which you don't feel comfortable (for example when interacting with people who don't know you have a hearing loss)	CROSSSD workshop
3		Emotional distress	A negative unpleasant emotional reaction which may include fear, anger, frustration, anxiety, and suffering	COMiT'ID + added 'frustration'
4		Mood	General sense of well-being, ranging from feeling very low or negative to very positive	COMiT'ID
5		Motivation	A willingness to engage in challenging listening situations	Post-CROSSSD workshop discussion
6		Dissatisfaction with life	Being unhappy because you feel you should be achieving or should have achieved more in your life	Cambridge dictionary + discussion with PPIs
7	Other effects	Listening effort	Exerting greater effort to listen and follow a conversation. This might consequently lead to feelings of tiredness and fatigue, but those feelings would be a separate outcome domain	Post-CROSSSD workshop discussion
8	Factors related to the treatment being tested	Treatment satisfaction	How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment	COMiT'ID + added 'recommend'
9		Device usage	How you use the device (for example, in what situations, for how long)	COMiT'ID + removed 'how much'
10		Device malfunction	The device does not work as it should or it stops working	CROSSSD workshop
11		Adverse events	Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial	COMiT'ID

12	Health-related quality of life	Avoiding social situations	Choosing not to go to particular social situations because of your hearing loss	CROSSSD workshop
13		Impact on individual activities	Effect of your hearing loss or your device on your choice to engage in individual activities (for example, travelling alone, swimming or watching TV / films / movies)	COMiT'ID + modified post-CROSSSD workshop discussion
14		Impact on relationships	Effect of your hearing loss or your device on making new relationships and maintaining relationships with a spouse or partner, family, friends and colleagues	COMiT'ID
15		Impact on social situations	Your hearing loss or device limiting your ability to fully participate in the social world, especially in challenging situations or where a lot of effort is needed to follow the conversation (for example, at a restaurant, at the park, in a bar or at a party)	CROSSSD workshop
16		Impact on work	Effect of your hearing loss or device on your ability to carry out work tasks or job roles, or advancing your career	COMiT'ID
17	Hearing disability	Being aware of a sound	Being aware of a sound and recognising what that sound is (for example, being aware that someone has started to speak)	CROSSSD workshop
18		Listening in complex conditions	The difficulty experienced when listening to a sound while separating it out from a background of other sounds	CROSSSD workshop
19		Listening in reverberant conditions	The difficulty experienced when listening in places where the sound reflects off the walls, floor or ceiling (echoes); creating a blurred sound. For example, understanding announcements in train stations or airports	CROSSSD workshop
20		One-to-one conversation in quiet	Listening and understanding one person, in a quiet environment	CROSSSD workshop
21		Group conversation in quiet	Listening and following a conversation between a group of people, in a quiet environment	CROSSSD workshop

22		One-to-one conversation in general noise	Listening and understanding one person, in a noisy environment	CROSSSD workshop
23		Group conversations in noisy social situations	Listening and following a conversation between a group of people, when others are talking in the background	CROSSSD workshop
24	Spatial hearing	Sound localisation	Knowing where a sound is coming from	CROSSSD workshop
25		Sound distance	Knowing if a sound is close by or far away	CROSSSD workshop
26		Spatial orientation	Knowing where you are in relation to the position of a sound source	CROSSSD workshop
27		Enjoyment of listening to music	Appreciating 'stereo', '3-dimensional' or 'surround sound' quality of live or recorded music	Lucas et al. (2018) paper
28	Physical effects	Physical tiredness	Tiredness or fatigue from the effort of listening or when you need to turn your head repeatedly to listen in social situations	Lucas et al. (2018) paper
29		Balance problems	Feeling unbalanced and the effect it has on your ability to walk or move normally	CROSSSD workshop
30		Manual dexterity	Having the fine motor skills needed to use your device effectively (for example, putting the device on, changing the batteries)	CROSSSD workshop
31		Tinnitus-related brain changes	Changes in brain structure or function associated with tinnitus	CROSSSD workshop
32		Hearing-related brain changes	Changes in brain structure or function associated with hearing loss	CROSSSD Workshop
33	Self	Self-stigma	Negative perception of yourself due to your hearing loss and feeling stigmatised for using a hearing aid	Vas et al. (2017) paper + post-workshop discussion
34		Self-image	Feeling incomplete or incapable because you are unable to do all the things that you want to do	Vas et al. (2017) paper + modified 'unable to do before' to incorporate congenital SSD

35		Personal safety	How your hearing loss effects your awareness of potential hazards and threats in your daily life (for example, moving traffic, hazards at the workplace) and those you may not be able to see or hear (for example, other people behind you)	CROSSSD workshop + post-workshop discussion
36		Protecting your hearing	Making a conscious decision to avoid loud sounds or other risks to your hearing, or taking steps to protect your hearing	CROSSSD workshop
37	Sound quality	Loudness	How 'loud' a sound seems to you	CROSSSD workshop
38		Fullness	How 'full' a sound seems to you. This can also be described as the 'richness', 'warmth' or 'depth' of a sound	CROSSSD workshop
39		Clarity	How 'clear' a sound seems to you	CROSSSD workshop
40	Tinnitus	Tinnitus awareness	Noticing the sound of tinnitus is there	COMiT'ID
41		Tinnitus intrusiveness	Being acutely aware of the sounds of tinnitus, feeling that it is invading your life or your personal space, changing your thoughts or actions and negatively impacting on your life	COMiT'ID, revised after online discussion forum
42		Tinnitus loudness	How loud your tinnitus sounds	COMiT'ID
43		Tinnitus pitch	Whether your tinnitus has a note-like quality, for example high pitch like whistling or low pitch like humming	COMiT'ID
44		Tinnitus quality	What type of sound is heard (for example, hissing, buzzing, ringing, whistling etc)	COMiT'ID

4.3.1 Participants

All relevant stakeholders were invited to participate if they met the following inclusion criteria: (i) healthcare users with lived experience of SSD for 12 months or more, who had received or considered an SSD intervention, (ii) healthcare professionals (e.g., audiologists, ENT surgeons, neuro-otologists) with experience of assessing, diagnosing or managing SSD in adults, (iii) clinical researchers with recent experience with SSD intervention studies, who have an academic qualification, are currently employed by a research organisation, have current or 'recent past' experience with studies that focus on questions of clinical efficacy (benefit) of SSD interventions in humans (i.e., co-author on a relevant peer-reviewed journal publication in the past three years), (iv) commercial representatives that worked for industry partners that developed, manufactured or sold hearing aids or auditory implants used as SSD interventions, and (v) those employed by organisations that fund research focusing on SSD interventions, and have experience of reviewing funding applications for SSD interventions research in the last 3 years.

The rationale for the criterion of healthcare users to have had lived experience of SSD for 12 months or more was to ensure that only those with permanent SSD adhering to the audiological classification of 70 dB HL or worse in the poor ear (Van de Heyning et al., 2017) took part. For example, those with idiopathic sudden onset hearing loss may experience hearing fluctuation, or may have steroidal treatments at the early stages of their SSD diagnosis that improve their hearing thresholds (Chandrasekhar et al., 2019; Twigg et al., 2020). Another example is those diagnosed with SSD due to Ménière's disease, whom may have a variable clinical course with progressive hearing loss, tinnitus and vestibular effects; and demonstrate improved auditory performance following restoring interventions (Manrique-Huarte et al., 2018) that is influenced by brain reorganisation and rehabilitation (Alzaher et al., 2021).

4.3.2 Recruitment

Recruitment used a purposive sampling method to engage with qualified experts who had a deep understanding of the topic. All participants were required to be at least 18 years old and able to read, understand and complete web-based surveys in English.

Advertisements were targeted at relevant international conferences, professional groups (e.g., British Society of Audiology), relevant professional societies and charities (e.g., British Acoustic Neuroma Association), personal contacts of the study steering group, UK-based National Health Service (NHS) hearing clinics, and advertised more generally through social media groups. Communications by charities and UK-based hearing clinics were the main routes for healthcare user recruitment. For details on recruitment please refer to the Recruitment methods section of the published protocol (Katiri, Hall, Buggy, et al., 2020), or see Section 2.6.3 for healthcare users' recruitment and Section 2.6.4 for healthcare professionals' recruitment.

The recruitment target was that at least 20 participants in each of the three major stakeholder groups (healthcare users, healthcare professionals, clinical researchers) would complete both rounds of the e-Delphi survey. To minimise attrition between the two survey rounds, the importance of completing both rounds of the survey was emphasised to participants in the information sheets, which also stated the anticipated time-line of the study rounds. At the end of Round 1 survey participants were thanked for taking part and were reminded that they will be contacted in a few weeks with Round 2 of the survey which would give them the opportunity to review their scores allocated to each of the outcome domains.

Our operational definition of completion of the Round 1 surveys was for at least 50% of the outcome domains to be scored, as per protocol (Katiri, Hall, Buggy, et al., 2020). This criterion was stricter than that set by Fackrell et al. (2017) who stated a 40% response rate but had three rounds in their study. In the absence of any empirical evidence to inform the optimum approach (Williamson et al., 2017), the study management team decided that if a participant engaged and completed at least half of the outcome domains ratings, they would have engaged in the process thoroughly enough and had sufficient expertise required for the decision making.

4.3.3 e-Delphi surveys

As described in Section 2.2.2, a Delphi method was adopted, presenting participants with the list of 44 candidate outcome domains (Table 4.1); over two Delphi rounds,

using the DelphiManager v4.0 software tool developed and maintained by the COMET initiative at the University of Liverpool (COMET initiative, 2019). For each outcome domain, participants were asked to score how important it was to measure when deciding whether an SSD intervention works on the GRADE scale of 1 to 9 (Guyatt et al., 2011). Consensus was defined as at least 70% of the participants in all three stakeholder groups scoring 7-9 (*critical to measure* in all trials) and fewer than 15% in any stakeholder group scoring 1-3 (*not important* in deciding whether an SSD intervention is effective) (Katiri, Hall, Buggy, et al., 2020).

Each round was open for only as short time as possible to minimise attrition (Round 1 for 10.2 weeks and Round 2 for 13.3 weeks). Round 1 was opened in September 2019, after the summer holidays and with commencement of the new academic year, and was left open through to November 2019. This time-period was chosen because there was relevant international conferences scheduled where active healthcare professional and healthcare user participant recruitment and study promotion could take place (e.g., MED-EL® Innsbruck Binaurality conference, Manchester BRC Hearing Health showcase, British Acoustic Neuroma Association (BANA) annual conference, Ménière's disease society annual conference, Cochlear® Buenos Aires workshop on asymmetric hearing loss and cochlear implantation, and the British Academy of Audiology (BAA) conference in Liverpool). Round 2 opened the day after the completion of Round 1, in November 2019, to address attrition variables such as healthcare professionals leaving their posts, or participants becoming disinterested (Williamson et al., 2017). Round 2 was left open for longer than Round 1, until February 2020 to incorporate possible annual leave healthcare professionals and clinical researchers might have had during the December holiday season, which may increase attrition (Williamson et al., 2017). During this period the British Society of Audiology (BSA) e-Conference, the 7th OSSEO International congress on bone conduction hearing and related technologies in Miami, and the Cochlear® Together Towards Tomorrow symposium in York were forums to promote the study and engage with possible participants. Response rates were monitored weekly, and both generic reminder emails and personalised email reminders were sent to late responders to minimise attrition. Adopting a personalised approach has been suggested to increase

odds of response for surveys more generally (Edwards et al., 2009), and in Delphi surveys in COS development (Gargon, Crew, et al., 2019). Attrition rates that vary between the particular stakeholder groups can influence the overall consensus (Williamson et al., 2017) but two ENT-field COS studies that evaluated such potential biases found that it was unlikely that attrition bias affected their outcome domain recommendations (Bruce et al., 2015; Hall, Hibbert, et al., 2019; Harman et al., 2015). Gargon et al. (2019) do however highlight that maximising response rates to Delphi studies by minimising attrition rates is important to minimise potential bias, because the validity of the results will ultimately be affected by response rates (Hasson et al., 2000). Qualitative interviews have indicated that response rates in Delphi studies is an area that needs further research and guidance (Gargon, Williamson, and Young, 2017).

4.3.4 Consensus meeting

Participants who completed scoring for at least 90% of outcome domains in both rounds of the e-Delphi survey were invited to express their interest to attend the consensus meeting. A balance of 50:50 healthcare users and healthcare professionals was maintained for recruitment. Participant characteristics such as aetiology of SSD, SSD intervention they had expertise in, age, gender, and country of residence, were considered when invited to the consensus meeting. However due to the small number of participants expressing an interest to contribute to the consensus exercise selection was limited. Of the original group of participants, one healthcare user could not attend the rescheduled date (07 July 2020) and two healthcare professionals did not respond to the invitation to the web-based meeting. A further healthcare user was recruited to maintain the balance across stakeholder groups. One additional facilitator was also recruited so that the online discussion groups were manageable (e.g., smaller groups would mean all participants could be clearly seen on Microsoft Teams screen, and be given equal opportunities to participate).

Some individuals who had an interest in the process, but did not fit the inclusion criteria to actively participate in the consensus process, joined as non-participating observers. They were a commercial representative based in Denmark, and a clinical researcher based in the USA. Therefore, the final group of participants comprised 23

individuals, of whom 12 were eligible to vote because they had completed both rounds of the e-Delphi surveys.

All participants were invited to attend the virtual pre-consensus meeting coffee morning. It was chaired by RK with six healthcare users (100%), two healthcare professionals (40%), one of the public research partners (50%), the patient involvement manager, two of the facilitators (67%), and one observer in attendance (33%). Three healthcare professionals, two observers, one facilitator, and a study team member could not attend due to work commitments.

The web-based consensus meeting was 7 hours in duration, with three 30 minute breaks, and was delivered using Microsoft Teams software. The meeting comprised semi-structured discussions led by three facilitators in three groups (Group A, Group B, Group C), together with discussions and voting involving all 12 participants (6 healthcare users, and 6 healthcare professionals). The voting participants' demographics and expertise can be found in Table 4.2. The two public research partners and the patient and public involvement expert were also present and could take part in the discussions but not vote. All participants were given equal opportunities to voice their opinions.

To minimise screen time during the web-based consensus meeting, participants were sent a pre-recorded introductory video presentation (see Additional file 2, Katiri et al. (2022)) in advance describing the aims of the day, and a guidance document (Appendix 18) outlining the day's activities. Participant consent was obtained online.

Anonymised voting was performed using online surveys in real time during the consensus meeting. Participants were asked to vote *agree*, *disagree*, or *unsure* in response to questions about the inclusion or exclusion of specific outcome domains in a core outcome domain set for SSD interventions. Only outcome domains voted *agree* by at least 70% of participants were included in the core outcome domain set. In cases where a majority vote was not achieved, outcome domains were set aside for re-discussion and re-voting. The results of voting were presented using histograms

embedded in PowerPoint slides shared with all participants using Microsoft Teams. All consensus meeting discussions were recorded.

Table 4.2. Consensus meeting voting participants demographics and expertise.

	Participant expertise	Gender	Age range (years)	Country	SSD expertise	SSD intervention experience
Group A	Healthcare user: sudden onset loss	Female	30-39	Spain	3 years	CROS aid
	Healthcare user: acoustic neuroma	Male	70-79	England	28 years	CROS aid
	Audiologist and clinical researcher	Male	60-69	Netherlands	32 years	CROS aids / BAHAs cochlear implants
	Audiologist and clinical researcher	Female	40-49	England	13 years	CROS aids / BAHAs / middle ear implants
Group B	Healthcare user: acoustic neuroma	Male	70-79	England	18 years, 10 months	CROS aid
	Healthcare user: sudden onset loss	Male	60-69	England	3 years, 9 months	CROS aid
	Audiologist	Male	50-59	England	35 years	CROS aids
	Clinical researcher and commercial representative	Female	30-39	England	10 years	BAHAs / middle ear implants / cochlear implants
Group C	Healthcare user: sudden onset loss	Male	18-29	England	1 year, 1 month	CROS aid / BAHA / cochlear implant
	Healthcare user: childhood loss	Male	70-79	England	73 years	CROS aid
	Clinical researcher and commercial representative	Male	50-59	England	35 years	Cochlear implants
	Audiologist	Male	40-49	Germany	25 years	CROS aids / BAHAs / cochlear implants

4.3.5 Pre-consensus meeting survey

In advance of the consensus meeting, voting participants were sent a link to a short survey asking them to consider the outcome domains that had reached the criteria for inclusion in the core outcome domain set after the two rounds of the e-Delphi survey and to vote whether they agreed to limit the scope of the consensus meeting to discussing only those outcomes. A summary of the process adopted for outcome domain prioritisation to agree a final core outcome domain set can be found in Figure 4-2.

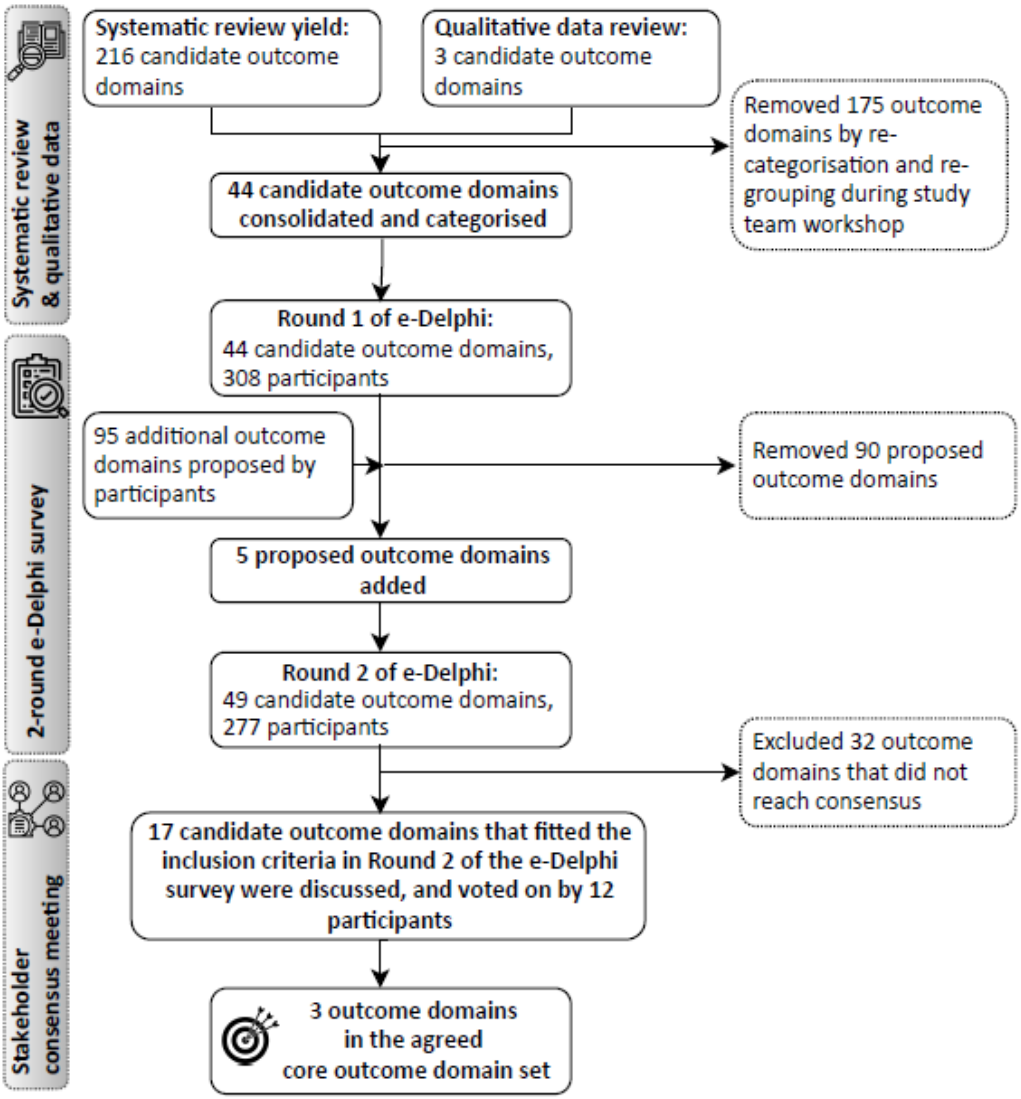

Figure 4-2. Summary of the steps taken in the outcome domain prioritisation process to agree a final core outcome domain set for clinical trials assessing single-sided deafness interventions in adults.

4.4 Results

4.4.1 Participants

Of the 308 participants who completed Round 1, 92 (29.9%) were healthcare users, 148 (48.1%) were healthcare professionals, and 59 (19.2%) were clinical researchers. Thirty-one participants (11 healthcare users, 13 healthcare professionals, 6 clinical researchers, 1 funder) rated fewer than 50% of outcome domains in Round 1 so were excluded from Round 2. Retention rate for all stakeholder groups exceeded 85%, except for clinical researchers (74%) and funders (0%) (Table 4.3).

Table 4.3. Number and percentage of participants in each e-Delphi survey.

Stakeholder group	Participated in Round 1 n (%)	Invited to Round 2 (completed >50% of Round 1)	Participated in Round 2 n (%)	Retention rate (%)
Healthcare users	92 (29.9)	81	71 (30.5)	87.7
Healthcare professionals	148 (48.1)	135	116 (49.8)	85.9
Clinical researchers	59 (19.2)	53	39 (16.7)	73.6
Commercial representatives	8 (2.6)	8	7 (3.0)	87.5
Funders	1 (0.3)	0	-	-
Total (n)	**308**	**277**	**233**	**75.6**

Most participants (n=98, 31.8%) were in the 30-49 age range, followed by the 40-49 years group (n=77, 25.0%). Only healthcare users (n=14, 15.2%) were aged above 69 years (Table 4.4).

Table 4.4. Age range of all 308 participants who consented to take part in the e-Delphi survey, arranged by stakeholder group.

Stakeholder group	18-29 years	30-39 years	40-49 years	50-59 years	60-69 years	70-79 years	80-89 years	Total
Healthcare users	7	15	18	17	21	12	2	92
Healthcare professionals	19	61	39	24	5	-	-	148
Clinical researchers	4	17	17	13	8	-	-	59
Commercial representatives	1	5	2	-	-	-	-	8
Funders	-	-	1	-	-	-	-	1
Total n (%)	**31 (10.1)**	**98 (31.8)**	**77 (25.0)**	**54 (17.5)**	**34 (11.0)**	**12 (3.9)**	**2 (0.6)**	**308 (100)**

Participants registered from 29 different countries. Figure 4-3 displays a world map illustrating the geographical distribution of all consenting participants. The majority of participants were from the UK (n=145, 47.1%), followed by Ireland and the USA (n=37, 12.0% from both). Table 4.5 lists a detailed breakdown of participant registrations in each stakeholder group per country.

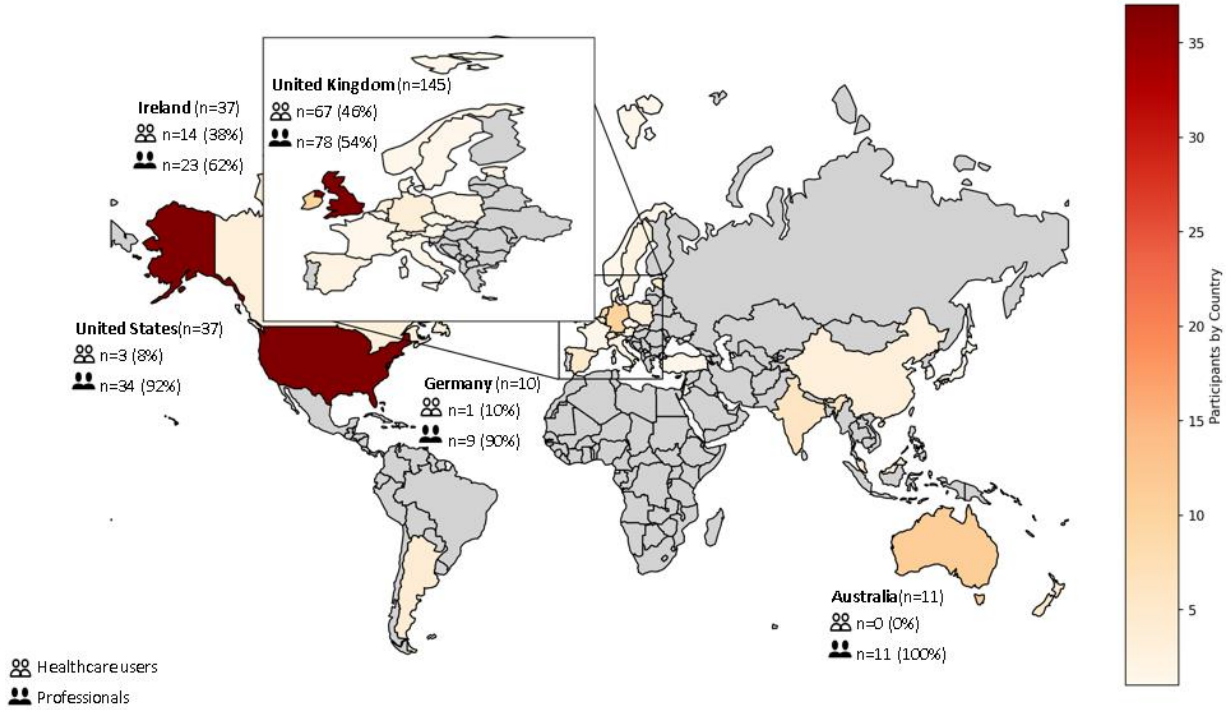

Figure 4-3. World map illustrating the geographical distribution of all consenting participants (n=308).
*The number of healthcare users and healthcare professionals for the five countries where most participants were recruited from are also listed.

Table 4.6 lists a detailed breakdown of the participant language for everyday communication. A variety of 25 different languages were listed. One healthcare professional did not disclose their primary language of communication.

Of the healthcare professionals that reported their roles (n=146), the majority were audiologists or clinical scientists in audiology (n=107, 73.3%), or otolaryngologists / ENT surgeons (n=11, 7.5%).

Table 4.5. Distribution of consenting participants (n=308), across countries (n=29), arranged per stakeholder group.

Country	Healthcare users	Healthcare professionals	Clinical researchers	Commercial representatives	Funders	Total per country n (%)
Argentina		2	2			4 (1.3)
Australia		9	2			11 (3.6)
Austria			2			2 (0.6)
Belgium		1	2			3 (1.0)
Canada	2		1			3 (1.0)
China		1	1	1		3 (1.0)
Cyprus		2				2 (0.6)
Czechia		1				1 (0.3)
Denmark			1	1		2 (0.6)
Estonia	1	3				4 (1.3)
France			1			1 (0.3)
Germany	1	4	5			10 (3.2)
India	1	4	1			6 (1.9)
Ireland	14	21	2			37 (12.0)
Italy			2			2 (0.6)
Japan		1				1 (0.3)
Jordan		1				1 (0.3)
Malaysia		4				4 (1.3)
Netherlands		4	4			8 (2.6)
New Zealand		5				5 (1.6)
Norway			1			1 (0.3)
Poland			3			3 (1.0)
South Korea			1			1 (0.3)
Spain	3	2				5 (1.6)
Sweden		1	1			2 (0.6)
Switzerland			3			3 (1.0)
Turkey			1			1 (0.3)
United Kingdom	67	63	8	6	1	145 (47.1)
United States of America	3	19	15			37 (12.0)
Total n (%)	**92 (29.9)**	**148 (48.0)**	**59 (19.1)**	**8 (2.6)**	**1 (0.3)**	**308 (100)**

Table 4.6. Primary language for everyday communication disclosed by consenting participants (n=308), across countries (n=29), arranged per stakeholder group.

Primary language	Healthcare users	Healthcare professionals	Clinical researchers	Commercial representatives	Funders	Total n of participants n (%)
English	88	117	31	6	1	243 (78.9)
German	1	4	10			15 (4.9)
Dutch		5	6			11 (3.6)
Spanish		4	2			6 (1.9)
Estonian	1	3				4 (1.3)
Polish			3			3 (1.0)
Swedish		1	2			3 (1.0)
French	1		1			2 (0.6)
Greek		2				2 (0.6)
Italian			2			2 (0.6)
Malay		2				2 (0.6)
Afrikaans		1				1 (0.3)
Arabic		1				1 (0.3)
Bahasa Melayu		1				1 (0.3)
Cantonese		1				1 (0.3)
Czech		1				1 (0.3)
Danish				1		1 (0.3)
Hindi	1					1 (0.3)
Japanese		1				1 (0.3)
Kannada		1				1 (0.3)
Korean			1			1 (0.3)
Mandarin				1		1 (0.3)
Marathi		1				1 (0.3)
Turkish			1			1 (0.3)
Welsh		1				1 (0.3)
Not stated		1				1 (0.3)
Total n (%)	**92 (29.9)**	**148 (48.0)**	**59 (19.1)**	**8 (2.6)**	**1 (0.3)**	**308 (100)**

*A variety of 25 different languages were listed. One healthcare professional did not disclose their primary language of communication.

Of those healthcare users (n=84, 91.3%) who disclosed the time since their diagnosis of SSD, most had a history of SSD for 2-5 years (n=18, 21.4%), followed by 5-10 years or 10-20 years (n=16, 19.0% in both cases). Figure 4-4 displays details of the time since SSD diagnosis as disclosed by participating healthcare users.

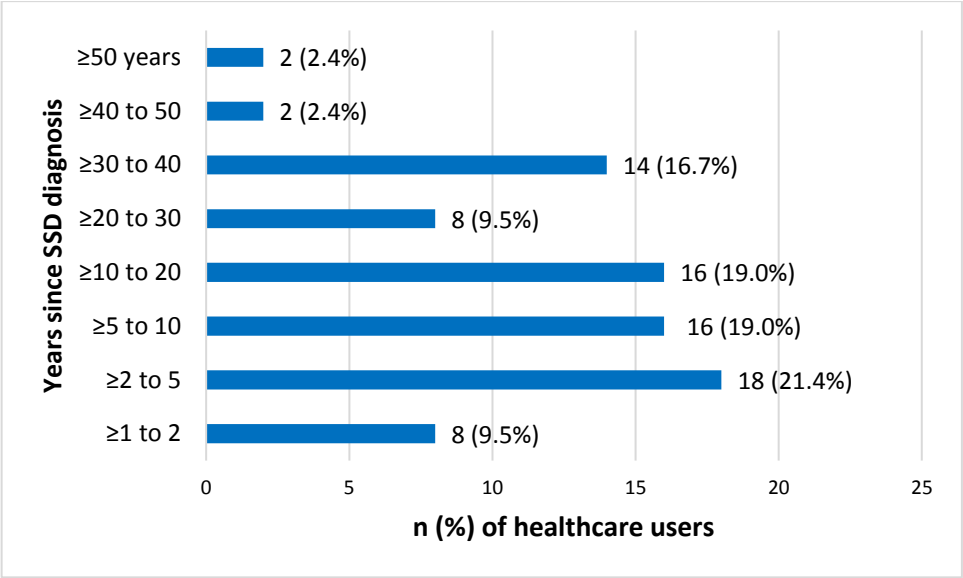

Figure 4-4. Time since SSD diagnosis as disclosed by healthcare users (n=84).
*For the majority, it had been 2-5 years since their diagnosis of SSD. Healthcare users needed to have lived experience of SSD for 12 months or more to be eligible to take part.

The majority of healthcare users (n=81, 88.0%) disclosed the devices they had trialled or were primarily using. The majority (n=47, 58.0%) had trialled or were using a CROS device, and a minority (n=9, 11.1%) trialled a BAHA. One participant (1.2%) had received a cochlear implant. Twelve participants (14.8%) had trialled two devices (CROS and BAHA). Three healthcare users (3.7%) reported that they had trialled three devices, including a combination of CROS, BAHA, remote microphone technology, middle ear, or cochlear implants.

When asked what interventions they considered trialling, 60 healthcare users (65.2%) provided a response. Twenty-three (38.3%) had considered a CROS aid, ten (16.7%) had considered a BAHA, one (1.7%) had considered the SoundBite™, three (5.0%) had considered cochlear implantation (n=3, 5.0%), and two (3.3%) had considered middle ear implants. The remaining 18 participants (30.0%) indicated that they considered trialling a combination of two or more re-routing and/or restoring interventions. Three (5.0%) participants commented that they were not aware of alternative options they could consider.

4.4.2 Round 1 e-Delphi survey

Three-hundred-and-eight participants completed e-Delphi Round 1. Histograms of the ratings for the 44 outcome domains can be found in Appendix 8. Fifty-four participants submitted 95 comments about potential additional outcome domains that they felt should be included in the list (Appendix 20). Most comments (n=43, 45.3%) were from healthcare users and healthcare professionals (n=35, 36.8%); followed by clinical researchers (n=16, 16.8%), and one commercial representative (1.0%).

Of the 95 comments, 24 were rejected because they were out of scope (e.g., concerned economic factors, auditory training, access to hearing loss support groups). Fifty-six suggested domains were already captured by one or more of the existing domains. Following discussion and feedback from the public research partners, and the study steering group; a further nine proposed additional outcome domains were rejected as less relevant. These included aspects of trial device usage, aetiology of the SSD, stigma, sound effects of the device, access to audiological services for timely device adjustment, family support, and availability of auditory implants in different healthcare systems. Three suggested domains (Ability to manage treatment option, Ease of use, Complexity of the device) were referring to the same concept, which was already captured by existing domains.

Hence, five additional outcome domains were included in Round 2. These were: Device usability, Impact on learning, Concern about your hearing, Vulnerability, and Independence. Two members of the study management team categorised and assigned plain language definitions to these five outcome domains prior to launching Round 2 of the e-Delphi survey. Table 4.7 shows the categories and plain language definitions assigned to the additional outcome domains. The definitions for the outcome domains included in Round 1 of the e-Delphi survey can be found in Table 4.1.

Table 4.7. Categories and plain language definitions for the five additional domains added in Round 2 of the e-Delphi surveys.

	Category	SSD-related outcome domain	Concept definition
45	Factors related to the treatment being tested	Device usability	How easy it is to learn; use; and maintain the device (for example, changing the batteries; cleaning)
46	Health-related quality of life	Impact on learning	Effect of your hearing loss or device on your ability to acquire new knowledge or skills; or further your education
47	Self	Independence	How your hearing loss affects how much you need to rely on other people in daily life
48	Psychological effects	Concern about your hearing	Feeling worried about the hearing in your better ear and the thought that it may decline
49	Self	Vulnerability	Feeling insecure because your hearing loss affects your awareness of potential hazards and threats in your daily life (for example, moving traffic; hazards at the workplace) and those you may not be able to see or hear (for example, other people behind you)

4.4.3 Round 2 e-Delphi survey

Two-hundred and thirty-three participants completed Round 2. See Appendix 21 for histograms displaying the ratings for the 49 outcome domains included in Round 2. A few scores changed between Rounds 1 and 2, such that the outcome domain reached consensus at Round 2 but not at Round 1. Most of these changes were made by the clinical researcher and commercial representative groups with many comments indicating that scores were changed after reviewing the healthcare user group responses. The outcome domain scores changed by two stakeholder groups for 6 outcome domains (Device usage, Discomfort in listening situations, Group conversation in quiet, Listening in reverberant conditions, Physical tiredness, and Spatial orientation). The outcome domain scores changed by one stakeholder group for 9 outcome domains (Adverse events, Being aware of a sound, Dissatisfaction with life, Emotional distress, Mood, Motivation, Personal safety, and Protecting your hearing). Two tinnitus-related outcome domains (Tinnitus loudness, and Tinnitus-related brain changes) which reached consensus within the commercial representatives at Round 1, did not reach consensus at Round 2 when ratings from the healthcare users were considered, as per protocol criteria for consensus (Katiri, Hall,

Buggy, et al., 2020). Finally, at Round 1, none of the four stakeholder groups reached consensus to include Device malfunction, but all four groups did so at Round 2.

Overall, from Round 2, stakeholder scoring for 17 outcome domains (Table 4.8) met the consensus criterion for inclusion. These were taken forward to the consensus meeting. The remaining 32 outcome domains did not reach consensus criteria for inclusion in the core outcome domain set. These included Adverse events which was the only harms outcome. Adverse events was scored 7-9 (critically important) by 51% of healthcare users, 59% of healthcare professionals, 81% of clinical researchers, and 100% of commercial representatives. For plain language definitions of the outcome domains see Table 4.1, and Table 4.6 for the five additional domains incorporated into Round 2 of the e-Delphi survey.

The 32 outcome domains were discussed by the study management group and the consensus meeting facilitators. Since they did not meet the pre-determined criteria for being important and critical for inclusion, they were not included in the consensus meeting discussions.

Table 4.8. Voting scores for the 17 outcome domains that met the criterion for inclusion.

Outcome domain name	**e-Delphi Round 2 scoring** (number and percentage of participants that scored 7-9 'critically important')				**Consensus meeting scoring**
	Healthcare users	Healthcare professionals	Clinical researchers	Commercial representatives	
Domain category: Factors related to the treatment being tested					
Treatment satisfaction	60 (87%)	105 (91%)	31 (79%)	7 (100%)	92.2% agreed to exclude
Device usage	48 (72%)	93 (81%)	28 (74%)	5 (71%)	25% agreed to include
Device malfunction	46 (72%)	83 (72%)	28 (74%)	5 (71%)	83.3% agreed to exclude
Domain category: Health-related quality of life					
Avoiding social situations	61 (85%)	108 (93%)	34 (89%)	7 (100%)	83.3% agreed to exclude
Impact on social situations	**63 (89%)**	**109 (96%)**	**32 (84%)**	**7 (100%)**	**100% agreed to include**
Impact on work	50 (76%)	110 (96%)	33 (87%)	7 (100%)	83.3% agreed to exclude
Domain category: Hearing disability					
Being aware of a sound	64 (89%)	101 (88%)	32 (80%)	7 (100%)	25% agreed to include
Listening in complex situations	72 (100%)	108 (94%)	37 (93%)	7 (100%)	58% agreed to include
Listening in reverberant conditions	70 (97%)	86 (75%)	29 (73%)	6 (86%)	83.3% agreed to exclude
Group conversation in quiet	55 (76%)	92 (80%)	32 (80%)	6 (86%)	83.3% agreed to exclude
One-to-one conversation in general noise	68 (96%)	103 (90%)	35 (88%)	7 (100%)	25% agreed to include
Group conversations in noisy social situations	**71 (100%)**	**105 (91%)**	**35 (88%)**	**6 (86%)**	**83.3% agreed to include**
Domain category: Other effects					
Listening effort	60 (83%)	107 (92%)	33 (85%)	7 (100%)	66.7% agreed to include
Domain category: Physical effects					
Physical tiredness	56 (79%)	94 (82%)	30 (77%)	7 (100%)	83.3% agreed to exclude
Domain category: Self					
Personal safety	56 (79%)	102 (89%)	31 (82%)	7 (100%)	83.3% agreed to exclude
Domain category: Spatial hearing					
Sound localisation	66 (92%)	94 (82%)	36 (92%)	7 (100%)	83.3% agreed to exclude
Spatial orientation	**62 (86%)**	**86 (75%)**	**33 (85%)**	**6 (86%)**	**100% agreed to include**

*Bold font denotes the three core outcome domains that were included in the final COS.

4.4.4 Pre-consensus meeting survey

All 12 consensus meeting participants completed this survey. The survey results were presented to all consensus meeting participants using a bar chart during a short introductory slide presentation. Ten (83.3%) participants agreed with the recommendation to discuss only the 17 outcome domains that met the consensus criterion for inclusion at the end of the e-Delphi survey process. Only one participant disagreed (8.3%). With regards to their personal choice of 'top 3' out of the 17 candidate outcome domains, the two most popular were Listening in complex situations and Impact on social situations, selected by five participants. Next were Sound localisation, Personal safety, Listening effort, and Group conversations in noisy social situations, selected by four participants. Physical tiredness, Impact on work, and Device malfunction were not chosen by any of the participants. The remaining eight outcome domains were selected by either one or two participants.

4.4.5 Consensus meeting

Participants first agreed (83.3% agreement) to set aside three outcome domains which were not in anyone's 'top 3' choices. These were Physical tiredness, Impact on work, and Device malfunction. The remaining 14 outcome domains were discussed during two small group discussions and subsequently voted on. Initial votes were around whether to exclude outcome domains where a lack of consensus to include them was apparent, and subsequent votes were whether to include remaining outcome domains for inclusion in the core outcome domain set (Figure 4-5).

Five outcome domains (Listening effort, Device usage, Being aware of a sound, Listening in complex situations, and One-to-one conversations in general noise) required more extensive discussion among the group to hear a variety of opinions. At voting none of these met the consensus criteria for inclusion (Figure 4-5).

Participants agreed that three outcome domains should form the minimum standard. These were *Impact on social situations* (100% agreement), *Group conversations in noisy social situations* (83.3% agreement), and *Spatial orientation* (100% agreement).

Supporting comments made during the consensus discussions can be found in Table 4.9 and there were no comments against their inclusion.

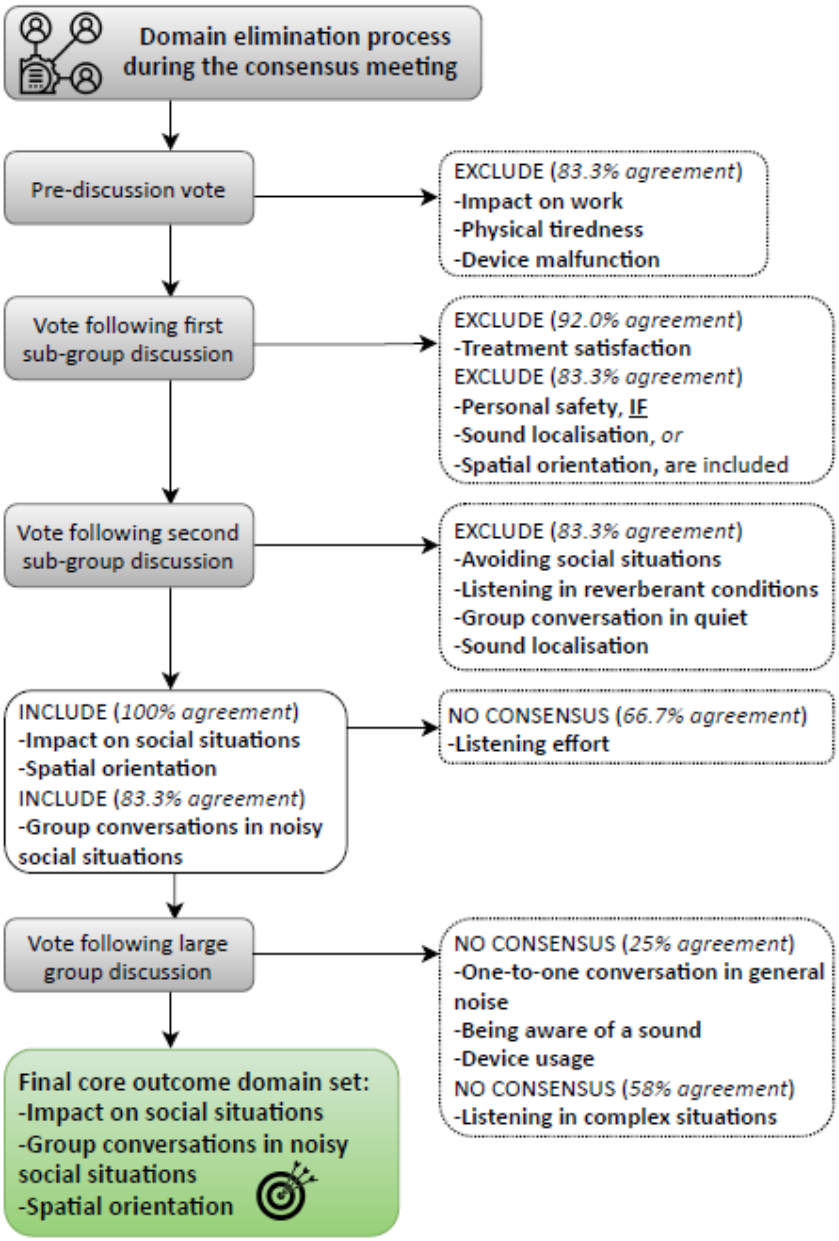

Figure 4-5. Outcome domain elimination process during the consensus meeting.
*Only outcome domains voted in by at least 70% of participants were included in the core outcome domain set.

Table 4.9. Comments in favour of inclusion of the three outcome domains, and other general discussion points.

Outcome domain	Participants comments
Impact on social situations	● "Thoroughly covers quite a few other outcome domains, it encapsulates social situations and captures the positives as well as negatives which is important according to the groups' discussions. Quite a few things can be captured with a single measure" ● "The social situations outcome domain covers whether someone knows when to stop talking and all of this is captured within this domain of social situations" ● "This outcome domain covers 'Listening effort' too" ● "Definition relates particularly to situations where a lot of effort is required, effort is a key part of the definition, there is an overlap between 'Listening effort' and 'Impact on social situations', therefore 'Listening effort' was not identified as a domain to be in [the core outcome domain set] on its own right" ● "For me it is about the social situations, it is about family, friends, relationships, when having a few pints down the pub, for me as someone with SSD is about the social side of things"
Group conversations in noisy social situations	● "Provides a good real world example of complex listening and where people with SSD generally have a challenge" ● "One of the hardest speech related tasks so it's an appropriate outcome measure, and in particular thinking about the devices, e.g., a cochlear implant has a speech processor, it promotes better speech comprehension" ● "This outcome domain captures 'Listening in complex listening situations' too"
Spatial orientation	● "Covers more than 'Sound localisation', more about the person, more valid: knowing which direction sounds is coming at you from. 'Sound localisation' is captured in orientation" ● "More valid for real world situations e.g., car in the street, walking across the road, and covers 'Sound localisation' as well" ● "Good fit because the definition includes a safety aspect to it, because it's about where you are in the world, that is an important aspect of spatial orientation" ● "Covers outcome domain 'Being aware of a sound'"

*As extracted from the consensus meeting discussions.

4.4.6 Participant feedback

The final core outcome domain set was shared with the 219 participants (64 healthcare users, 113 healthcare professionals, 36 clinical researchers, six commercial representatives) who completed both rounds of the e-Delphi survey but did not join the consensus meeting. Ninety-five (43.4%) participants responded of whom 32 (50.0%) were healthcare users, 48 (42.5%) were healthcare professionals, 14 (38.9%) were clinical researchers, and one (16.7%) was a commercial representative. Overall, 73 participants (76.8%) responded that they were very satisfied with the choice of included outcome domains, and 19 (20.0%) indicated that they were somewhat satisfied. One participant (healthcare professional) was neither satisfied nor

dissatisfied. Two participants (2.1%) responded that they were very dissatisfied, one was a healthcare user that commented that the batteries are too expensive, and the device was unsuitable for their ear, the other respondent was a healthcare professional that commented that '*the outcome domains chosen is what matters most to patients*'. None of the participants indicated that they were 'somewhat dissatisfied'. See Table 4.10 for a detailed breakdown of the participant feedback.

Table 4.10. Breakdown of responses received by 95 participants out of 219 who completed both rounds of the e-Delphi survey.

Stakeholder group	**Respondents n (%)**	***very satisfied* n (%)**	***somewhat satisfied* n (%)**	***neither satisfied or dissatisfied* n (%)**	***somewhat dissatisfied* n (%)**	***I am very dissatisfied* n (%)**
Healthcare users	32 (33.7)	25 (78.1)	6 (18.8)	-	-	1 (3.1%)
Healthcare professionals	48 (50.5)	38 (79.2)	8 (16.7)	1 (2.1)	-	1 (2.1%)
Clinical researchers	14 (14.7)	9 (64.3)	5 (35.7)	-	-	-
Commercial representatives	1 (1.0)	1 (100)	-	-	-	-
Total n (%)	**95 (100)**	**73 (76.8)**	**19 (20)**	**1 (1.1)**	**-**	**2 (2.1)**

*Participants were asked to rate on a 5-point rating scale how satisfied they were with the choice of outcome domains included in the core outcome domains set.

4.4.7 Web-based consensus meeting feedback

Formative feedback was received from nine (75%) voting participants (four healthcare users and five healthcare professionals) and four (40%) of the study team (two public research partners, patient involvement manager and one facilitator). To illustrate the key points, many of the comments from one healthcare user ('HU2') who was highly articulate with his feedback after the consensus meeting are shared below. These views were confirmed by the study team reflections.

Concerning whether the information provided in advance was helpful, all voting participants (n=9, 100%) agreed or strongly agreed. One said: '*Communication by the organisers with participants in advance of the meeting was absolutely first class with*

ample opportunity offered for consultation about any areas of concern and clarification when needed was always offered promptly and with considerable patience' (HU2).

One facilitator commented: '*The pre-meeting information was very thorough. The Teams meeting was extremely valuable -contrary to my expectations. I expected this to be a confirmatory meeting; instead, the facilitators highlighted aspects of the schedule which might not work so well, and everyone made contributive comments on how to make the online work. As a result, some fundamental changes were made but we all felt we input into this process'*. The patient involvement manager agreed: '*I had time at a prep-meeting to ask questions and to clarify the procedures for the day*'.

Regarding whether the process used to agree the COS was satisfactory, most participants (n=8, 89%) agreed or strongly agreed. One said: '*The process was particularly rigorous. The highest level of support was available from the leaders of the meeting but there was no heavy-handed intervention'* (HU2). One public research partner highlighted the benefit of preparation: '*The meeting had to be reconfigured to proceed remotely and this was handled exceptionally well […] a lot of thought went into it and it showed, […] technical support was provided promptly and without fuss or exasperation*'. Only one healthcare professional indicated that the process could have been improved by re-organising the sub-groups during the day: '*I think the discussion in each group was influenced by the members, so some mixing would have helped […] in the end there was a reasonably good outcome though*'.

All participants (100%) agreed or strongly agreed the meeting facilitation was satisfactory. Comments included: 'T*he leaders were superb facilitators and every participant was made to feel as if their voice was important'* (HU2)*,* and '*The facilitators were absolutely first class professionals and I felt privileged to have had the opportunity of working with them*' (HU2).

Again, all participants (100%) agreed or strongly agreed that they felt able to contribute to the meeting. One supporting comment was: '*Everyone without exception was encouraged to participate fully at the meeting and the facilitators displayed great*

sensitivity to the needs of each individual contributor. From a personal point of view, I was concerned that the technology used for the meeting might impede successful and effective communication, but it didn't, thanks to the watchful eye of the leaders of the meeting who actively encouraged free expression from every participant while at the same time subtly guiding the proceedings to ensure maintenance of a structure which would lead to fulfilment of the consensus meeting's objectives. I would also like to add that a very fine rapport between participants was quickly established' (HU2). A facilitator indicated that past experience was important: *'It had helped having been involved previously in facilitating three face-to-face COS consensus meetings. I drew heavily from that previous experience*'.

Similarly, all participants (100%) agreed or strongly agreed that they felt comfortable in communicating their views. For example: *'People taking part demonstrated great empathy for their fellows and there was a heart-warming sense of co-operation […] delegates had ample opportunity to share their 'story' […] I was made to feel like a person of value with something significant to contribute and I was particularly struck by the very high level of respect which people demonstrated for each other'* (HU2).

Finally, all participants (100%) agreed or strongly agreed the consensus meeting produced a fair result. One said: '*There was at times quite heated debate, but I believe that a consensus was finally reached which reflected the majority view*' *(*HU2).

One of the major recurring themes was the preference for social interaction over web-based meetings. Two healthcare professionals said: '*Given the circumstances, this was a perfect solution, nevertheless I missed the social interactions'* and '*I personally don't like remote meetings. I feel they stifle free speech and the normal interactions and debate cannot happen in the same way'*. HU2 said: '*Nothing could have been better other than the face-to-face interaction […] however, we enjoyed the benefits of the next best thing and there were also clearly some advantages in having a virtual workshop*'.

Another lesson concerned time management. At one point in the afternoon, there was some misunderstanding about the length of a break and when to reconvene, and this lost about 10 to 15 minutes of the schedule. Clear communication could avoid such matters. More generally, different stakeholders concurred that there was too little time for discussion. One healthcare professional said: '*I felt more time for each group to discuss the reasons behind their selected outcomes with the other groups, and to explain why they have selected one above another would have been useful... I enjoyed the in-group discussion, but felt the between-group discussions were a bit rushed / short*'. The patient involvement manager commented: '*We were a little rushed; not enough time for whole group discussions and voting*'.

With regards to improvements to the web-based meeting, one public research partner recommended more time at the end for discussion of the COS: '*I felt that maybe a safety net or reserve of one hour might have been added to the end*'. Taking fatigue into account, the patient involvement manager suggested a debriefing might be deferred to a later date and be organised in the same way as the discretionary coffee morning to '*allow participants to reflect with each other and to feel an appropriate 'closure', rather than a very intense day followed by a very quick 'goodbye''*.

4.5 Chapter summary

This study completes the first step in the development of a core outcome set for SSD interventions: reaching agreement on '*the what*' (Figure 0-1); i.e., the set of standardised outcomes to measure as a minimum in this clinical area (Clarke, 2007). An international group of stakeholder representatives came to a consensus about outcome domains that are important to measure in adults with SSD, and three outcome domains were identified by consensus as being critically important to measure in *all* clinical trials for hearing aids and auditory implants used as interventions in adults with SSD. The core outcome domain set recommends which are the most important outcome domains to measure to promote greater consistency across trials.

The core outcome domain set development process has also provided detailed information about the importance of a broader set of outcome domains from a diverse and international group of key stakeholders that can inform the selection of primary and secondary outcomes for future trials involving interventions for SSD.

The next steps will concentrate on determining '*the how*' (Figure 0-1) these outcomes should be operationalised and measured, i.e., the identification or development of robust measurement instruments that can measure the outcome domains. These steps are discussed in Chapter 5.

Consideration should also be placed on the measurement instruments' relevance to clinical practice from the perspective of healthcare users and professionals. Subsequent development of unified testing guidelines that incorporate the core outcome domain set, appropriate measurement instruments, and time-frame of measurement, will allow for elimination of the diversity and inconsistency of reported measures in the field of SSD.

5. 'The what' and 'the how'

This chapter is being prepared for a peer reviewed publication:
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5.1 Introduction

5.1.1 'The what'

To operationalise how to measure the three outcome domains that were identified as important to assess in every SSD clinical trial (Table 5.1), it is important to have an in-depth understanding of the concept of each domain. Although plain language descriptions were derived for each of these domains with input from the CROSSSD study public research partners and steering group (see Section 2.4.2 for the composition of this group) during the COS development process (Table 4.1 and Table 4.7); for the measurement instrument assessment step of the process there is a need for detailed operational definitions (Williamson et al., 2017). This is suggested in the COSMIN – COMET guidelines on how to inform the selection of the outcome measurement set for outcomes included in a core outcome domain set (Prinsen et al., 2014), because there is a wide variation in outcome definitions used by investigators

and it is often not clear as to what outcomes are measuring (Williamson et al., 2017). In the field of SSD interventions, systematic reviews of measurement instruments used in designs of clinical trials demonstrated that multi-item questionnaires are frequently utilised but there is no consensus in their selection, nor the intended outcome domains to be measured (Katiri, Hall, Killan, et al., 2021; Kitterick et al., 2016).

Table 5.1. The three outcome domains included in a core outcome domain set for single-sided deafness interventions and their plain language definition used in the core outcome domain set development.

Outcome domain name	Outcome domain plain language definition
Spatial orientation	Knowing where you are in relation to the position of a sound source
Group conversations in noisy social situations	Listening and following a conversation between a group of people, when others are talking in the background
Impact on social situations	Your hearing loss or device limiting your ability to fully participate in the social world; especially in challenging situations or where a lot of effort is needed to follow the conversation (for example, at a restaurant, at the park, in a bar or at a party)

A qualitative study was planned with the purpose to engage with relevant stakeholder representatives to understand what the COS outcome domains meant to the individual participants, and to identify any patterns of experience or understanding of the domains. The detailed descriptions are known as 'conceptual frameworks' (see Figure 2-3 for a schematic summary of the outcome domain conceptualisation and operationalisation stages.

Each conceptual framework includes (i) the main conceptual elements, (ii) detailed operational definitions, and (iii) other potentially related concepts that were deemed relevant but not core in describing the conceptual elements. Developing conceptual frameworks is important because an in-depth understanding of each concept indicates what sort of questions would need to be asked when assessing each outcome domain. In particular, it was emphasised that the recommended measurement instrument(s) for each outcome domain should have content validity (i.e., it is relevant to the

targeted construct and measures it as comprehensively as possible) (Mokkink et al., 2016; Prinsen et al., 2016).

5.1.2 'The how'

Once an in-depth understanding of each concept of each outcome domain is established, they can be operationalised and mapped onto candidate measurement instruments to ensure that any recommended instrument has good content validity (Hibbert et al., 2020; Prinsen et al., 2016; Williamson et al., 2017). Determining 'the how' to measure the outcome domains in a COS is an important enabler to achieve future uptake of a core outcome domain set (Hughes et al., 2021). The systematic review by Hughes et al. (2021) describes amongst other barriers to uptake of a COS the absence of validated measures, or no consensus on which measurement instruments should be used to assess the outcome domains. A qualitative study that aimed to describe the perspectives of clinicians and researchers on identifying, establishing and implementing core outcomes in haemodialysis and their expected impact, emphasised that core outcomes should be easily measured in a meaningful way, across multiple settings around the world with minimal bias (Tong et al., 2018).

Several measurement instruments may exist to measure a given outcome and in general the validity and reliability will vary across the instruments and populations (e.g., mild-moderate hearing loss patients, or those with conductive hearing loss). It is therefore essential to examine the evidence on the psychometric properties for potential measurement instruments to ensure they are of high quality and have robust psychometric properties (Karanicolas et al., 2009; Mokkink, Terwee, Knol, et al., 2010). Having confidence in clinical tools means that they measure what they are intended to measure (validity), they are stable over time (reliability) and can detect changes in a specific condition (responsiveness) (Mokkink et al., 2018; Prinsen et al., 2018). As aforementioned, the COMET and COSMIN initiatives have made recommendations on how to evaluate and select measurement instruments (Prinsen et al., 2014). As a first step it is important to assess the degree to which the instruments are measuring the concept.

The aim of this part of the study was to determine whether there are available measurement instruments which can potentially measure the three outcome domains in the CROSSSD core outcome domain set (Table 5.1). The method of assessment was developed using established guidelines proposed by the COMET and COSMIN initiatives to assess the quality of PROMs (Mokkink et al., 2018; Prinsen et al., 2018). The list of measurement instruments to be assessed was identified by available systematic reviews in the field (Katiri, Hall, Killan, et al., 2021; Kitterick et al., 2016). Measuring the psychometric properties of each measurement instrument was out of scope in this study.

5.1.3 Chapter aims and objectives

Chapter 5 aims to describe a qualitative study that concentrates on developing an in-depth understanding of each concept of each outcome domain in the core outcome domain set. The second study discussed in this chapter describes how the outcome domains were operationalised to help with the assessment of candidate measurement instruments. This chapter suggests 'the how' the core outcome domain set should be measured.

The chapter objectives were:

(i) To describe the domain conceptualisation process adopted using a qualitative focus group study

(ii) To describe the three outcome domains operationalisation process

(iii) To describe the measurement instrument assessment for the three outcome domains

(iv) To make recommendation on use of available patient reported outcome measures for the three outcome domains

(v) To make recommendation on development of future measurement instruments for the three outcome domains.

5.2 Methods

5.2.1 'The what': understanding the domains in the core outcome domain set

This study is reported according to the Standards for Reporting Qualitative Research (SRQR) reporting guidelines (O'Brien et al., 2014). There were two changes to the published protocol (Katiri, Hall, Buggy, et al., 2020). The first was a change from a face-to-face, 7-hour focus group to two 3-hour web-based meetings. This change was necessary because of travel and physical distancing restrictions imposed by the COVID-19 pandemic (Katiri et al., 2022). The second change from protocol was that the ratio of healthcare users to professional experts was 1:1 rather than the 4:1 stated in the protocol. All participants had previous interactions and an established relationship with the facilitators and each other, having met in a previous stage of this work (consensus meeting that took place in July 2020); and a social coffee morning held shortly before the focus groups (Katiri, Hall, Hoare, et al., 2021). Informed consent using an online form (Appendix 9) was obtained prior to participation at the focus group.

5.2.1.1 Qualitative approach and research paradigm

This study took a thematic approach using two focus groups to explore the personal patterns of experience and meaning of three core outcome domains for SSD interventions (Table 5.1). A thematic technique was adopted because the study was focusing on identifying, analysing and interpreting patterns of meaning within the generated qualitative data, which can vary depending on the stakeholder groups engaged with (Braun and Clarke, 2019; Malterud, 2001). Factors such as the frequency the generated themes were brought up by stakeholders was not delved into because frequency does not necessarily correspond to importance (Braun and Clarke, 2006). A thematic analysis approach was adopted because it offers a robust, systematic framework for coding qualitative data; and we could then use that coding to identify patterns across the generated dataset (Braun and Clarke, 2014). Participants were healthcare users and healthcare professionals. Facilitators took a position of appreciative inquiry, using active listening and being non-judgemental, and curious to explore and fully understand the participants' experience.

5.2.1.2 Researcher characteristics

Focus groups were co-facilitated by the lead for the CROSSSD study (RK) who is also a clinical audiologist with 14 years' clinical experience including working with patients diagnosed with SSD, and a researcher (PTK) who has previous qualitative research experience in the field of SSD (Lucas et al., 2018).

5.2.1.3 Reflexive statement by the lead author

I am a clinical audiologist interested in adult audio-vestibular diagnostics. I have been working at a large acute teaching hospital for the last decade. I am involved in SSD pathways, from diagnosis to prescription of interventions, and rehabilitation weekly. My role entails discussing SSD and its possible detrimental effects on hearing, communication, and social impact; for both congenital and acquired cases. I advise on the available interventions, I program and fit hearing devices and auditory implants, counsel on tinnitus management and communication strategies. I am also actively involved in teaching, contribute to clinical protocol development, design, implementation, and dissemination of clinical audits, and I assist in tenders for the supply of devices to the national Bone Anchored Hearing Aid (BAHA) programme in Ireland.

My existing understanding of the condition has been advantageous during this study: neither healthcare users, nor healthcare professionals who participated needed to explain in detail or expand on the 'basic concepts' around the outcome domains. I felt comfortable and confident facilitating the focus groups, the participants established trust and rapport quickly, which helped focus on the more intricate aspects during the discussions. However, my professional knowledge and experience have given me insights into the data collected, which I acknowledge could have influenced the analysis and interpretation. Adopting a thematic approach for data analysis, and involving the wider international CROSSSD study steering group (see Section 2.4.2 for the composition of this group) in the analysis, ensured a transparent method was utilised to eliminate possible biases and influences.

5.2.1.4 Sampling strategy

Participant selection inclusion criteria were: (i) adults ≥18 years of age that were healthcare users diagnosed with SSD at least a year ago, or professionals with experience in the field of SSD, and (ii) had already participated in the CROSSSD study consensus meeting. To maximise variation in expertise, and ensure the focus groups were representative of the consensus meeting experts, participants of a wide range of demographics (gender, age, country, cause of SSD), and who had experience in different SSD interventions were sought (Table 5.2). The lead researcher (RK) narrowed down the list of potential participants by reviewing their demographics and experience of SSD interventions, deliberately ensuring there was wide stakeholder representation (Braun and Clarke, 2019). One healthcare professional scheduled to participate in Focus group 1 withdrew the day before due to unprecedented family commitments (one of their children was unwell). It was not possible to find a replacement at short notice, therefore we proceeded with one healthcare professional instead of the planned two.

Table 5.2. Focus groups participant demographics.

	Participants	Gender	Age range (years)	Country	SSD expertise	SSD intervention experience
Focus group 1 Held on 22nd of October 2020	Healthcare user 1 (HU1)	Male	70-79	England	28 years	CROS aid
	Healthcare user 2 (HU2)	Male	60-69	England	3 years, 9 months	CROS aid
	Healthcare professional 1 (HP1)	Male	50-59	England	35 years	CROS aids
Focus group 2 Held on 27th of October 2020	Healthcare user 3 (HU3)	Male	18-29	England	1 year, 1 month	CROS aid / BAHA / CI
	Healthcare user 4 (HU4)	Female	30-39	Spain	3 years	CROS aid
	Healthcare professional 2 (HP2)	Male	40-49	Germany	25 years	CROS aids / BAHA / CI
	Healthcare professional 3 (HP3)	Male	60-69	Netherlands	32 years	CROS aids / BAHA / CI

*SSD expertise (for healthcare users (HU) this was the number of years since their diagnosis; for healthcare professionals (HP) this was the number of years since they started working in the field); and SSD intervention experience (CROS: Contralateral routing of signals aid; BAHA: Bone anchored hearing aid; CI: cochlear implant).

5.2.1.5 Ethical issues pertaining to human subjects

Ethical approval was granted from the Proportionate Review Nottingham 2 Research Ethics Committee (REC reference 19/EM/0222, IRAS project ID 239750) on 06 August 2019. Informed consent was taken prior to participation at the focus groups using an online consent form. Participants were reminded that they could withdraw from the study at any point without needing to give a reason. All participants were volunteers and no reimbursement was given for their contribution.

5.2.1.6 Data collection methods

Focus groups were conducted using the Microsoft Teams software in 1 week during October 2020. Participants received the plain language definition of each outcome domain (Table 5.1) the week prior to the meeting; and were asked in advance of the focus group to reflect on the outcome domains, and to think how each domain related to their own personal experiences.

During the focus groups, which were three hours long, the facilitators briefly reminded the participants of the meeting ground rules, the task in hand in the context of COS development for SSD interventions, and the plain language definition of each outcome domain. The plain language definition for each outcome domain was shared throughout the discussions using the screen sharing feature of Microsoft Teams software. Each outcome domain was allocated 45 minutes for discussion, with a short rest break between each discussion. The *Spatial orientation* domain was discussed first, followed by *Group conversations in noisy social situations*, and *Impact on social situations* last. Each participant was given a clear turn to voice their opinions and time was given prior to closing the discussion to comment on other participants' views or add further comments. Participants were given a choice when to take their turn, depending on how prepared they felt to discuss the particular outcome domain.

5.2.1.7 Data collection instruments and technologies

A topic guide with semi-structured discussion prompts was prepared by RK, PTK, and DAH. The guide outlined the areas of interest to be discussed but did not intend to dictate the exact course of the focus group. It encouraged free narrative responses to

collect raw data for analysis using a thematic method (Braun and Clarke, 2006, 2014, 2022).

The topic guide was prepared in advance of the meeting and was also reviewed by the CROSSSD study research partners (NH and NB) and Patient and Public Involvement (PPI) engagement manager (AH) for content, suitability and structure of the prompts, and clarity of the themes. See Figure 5-1 for the guide used to discuss *Group conversations in noisy social situations* outcome domain. It incorporated open-ended questions, designed to elicit detailed descriptions from participants, probed the experience of conversations, the nature of a group, the nature of the background noise, and what in their experience constituted 'noisy'. The topic guide was followed for each outcome domain, for both focus groups, to help the facilitator steer the discussions and ensure key areas were covered. All participants were given equal turns to voice their opinions, and the facilitators only closed the discussions after ensuring there was no further comments from any of the participants.

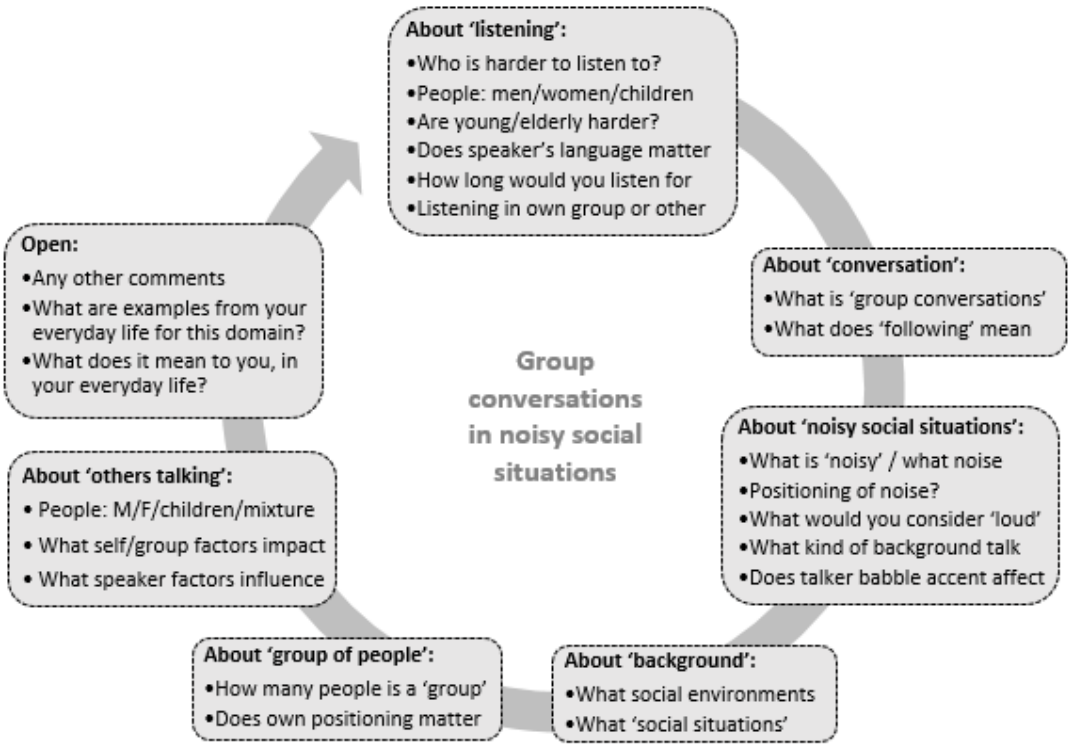

Figure 5-1. Example of the discussion prompts prepared for the *Group conversations in noisy social situations* outcome domain to facilitate discussions during the focus groups.

*_Group conversations in noisy social situations_ plain language definition was 'Listening and following a conversation between a group of people; when others are talking in the background'.

5.2.1.8 Data processing

Focus groups discussions were recorded using the Microsoft Teams recording feature. Recordings were later downloaded on University of Nottingham secure servers and were manually transcribed verbatim by RK. Transcripts and field notes were compiled and analysed in Excel (Microsoft Corporation, 2022). PTK made field notes during and after the meetings to reflect on the general themes and main discussion points relating to the data. RK also independently reflected on the main discussion themes following each focus group.

5.2.1.9 Data analysis

Thematic analysis was adopted to analyse the data (Braun and Clarke, 2006, 2014, 2022), as per rationale described in Section 5.2.1.1. First, data familiarisation included re-listening to the interview recordings and closely reading, and re-reading the transcripts. Then a long list of anonymised relevant keywords and short phrases was retrieved from the transcripts and compiled by RK for each of the outcome domains using Excel (Microsoft Corporation, 2022). Two distinct lists were maintained, to separate the healthcare users and professionals discussion themes. Following data re-familiarisation, RK coded the long lists of the key concepts for each of the outcome domains. Codes were generated by careful examination of the data and by referring to a framework from previous qualitative work on SSD (Lucas et al., 2018). PTK and DAH reviewed the coding against the transcripts to ensure data integrity was maintained.

The participants' interpretations and key concepts for each of the outcome domains were clustered and labelled. Concepts were discussed, revised, and refined by referring to the transcribed data and using participants' direct quotes. The labels formed the 'conceptual frameworks'. Each conceptual framework included: (i) the main conceptual elements, (ii) detailed description variables for each conceptual element, or 'operational definitions', and (iii) other potentially related concepts that were deemed relevant but not core in describing the conceptual elements.

5.2.1.10 Techniques to enhance trustworthiness

Continual analysis of the data helped the study team confirm the overarching ideas (i.e., conceptual frameworks, conceptual elements, and operational definitions) continued to fit the data. To ensure adequacy and transparency of data collection and analysis; and ensure trustworthiness the frameworks were reviewed by the rest of the study team (DAH, DJH) and the CROSSSD study research partners (NH, NB). They were also presented and discussed at an international CROSSSD study steering group meeting comprising of experts in the field based in Europe and the United States. The individual members of the steering group pre-reviewed the frameworks independently prior to the meeting. During the meeting they commented and provided feedback on the operational definitions and conceptual elements for each of the three outcome domains.

5.2.2 'The how': measurement instruments for the agreed core outcome domain set

Based on our conceptual definitions for the three outcome domains (Table 5.1), it was anticipated that all three would ideally be measured with patient reported outcome measures (PROMs) as opposed to investigator administered, or objective measures collected using clinical tests. Examples of other commonly used measurement methods employed to assess intervention outcomes in the field of SSD can be found on Table 3.10. PROMs are self-report tools (e.g., questionnaires, visual analogue scales (VAS)) that measure a healthcare user's perception of their health status or health-related quality of life, usually completed before and/or after introduction of a treatment (Mercieca-Bebber et al., 2018; Ousey and Cook, 2011). PROMs are increasingly accompanying the traditional clinical ways of measuring health and the effects of treatments on the healthcare user comprehensively (Mercieca-Bebber et al., 2018), both clinically and in the context of clinical trials (Meadows, 2011; Vodicka et al., 2015). For example, Vodicka et al. (2015) reviewed 96,736 clinical trials registered in the ClinicalTrials.gov database during the period of 2007-2013, to estimate the proportion of clinical trials using PROM(s). Their results suggested that for that time-period, there was an increase in the number of trials that use a PROM(s), particularly in oncology trials where use of PROM(s) increased from 27% to 33% from 2010 to 2013.

One type of PROM, the Measure Yourself Medical Outcome Profile (MYMOP) has been increasingly used for acute and/or chronic musculoskeletal or respiratory conditions, and gives an individualised approach and measures regarding a patient's symptoms and activities (Hermann et al., 2014; Paterson et al., 2000). The patient independently rates their symptom (e.g., right leg weakness) on a 0-6 rating scale (0=as good as it can be, 6=as bad as it could be), then they rate how this symptom has affected one of their activities (e.g., attending a social gathering); and they can also rate their well-being, but this is optional (Mirza et al., 2013; Polus et al., 2011). MYMOP2 has been validated, translated in other languages (Rosenberg et al., 2022), and been reported to be highly sensitive and responsive outcome measure (Hermann et al., 2014; Polus et al., 2011); although a recent appraisal suggests further validation (Ishaque et al., 2019). Nome of the studies in our systematic review (Chapter 3) for SSD interventions utilised MYMOP.

The information collected by a PROM can provide an indication on severity, symptoms and functioning, quality of life, well-being or a combination of these (Hutchings and Alrubaiy, 2017). The construct to be measured by the PROM (or subscale) should be clearly described by the PROM developers, to ensure content validity i.e., what the PROM actually measures and what it intends to measure (Mercieca-Bebber et al., 2018; Rothman et al., 2009).

There is a comprehensive recommended process for selecting PROMs to measure the outcome domains in a COS (Mokkink et al., 2018; Prinsen et al., 2018). Selection incorporates the steps described in Section 2.2.7. Briefly, the steps involve identification of measurement instruments by completion of a systematic review, and evaluation of methodological quality and psychometric properties. It is then possible to identify existing suitable measurement instruments, or to make recommendations to future instrument developers with regards to the necessary psychometric properties to be incorporated.

5.2.2.1 Patient reported outcome measures assessment

All identified PROMs were retrieved, numbered and saved in PDF format, in an alphabetical order.

Each of the three independent reviewers (or coders), was asked to code each section of PROMs using a coding key:

1: Irrelevant to the targeted construct

2: Somewhat relevant / possibly relevant

3: Explicitly / clearly relevant to the targeted construct.

To help the independent reviewers with their coding the first three columns of each assessment spreadsheet had a list of the individual outcome domains, conceptual elements, and operational definitions respectively. Please refer to Figure 5-2 for a snapshot of the assessment spreadsheet shared with each of the three coders for the *Spatial orientation* outcome domain.

	Coding key:						
1	Irrelevant to the targeted construct						
2	Somewhat relevant / possibly relevant						
3	Explicitly / clearly relevant to the targeted construct						
	Template						
	Outcome domain	**Conceptual elements**	**Operational definition**	**Qn 1**	**Qn 2**	**Qn 3**	**Qn 4**	**Qn 5**
	Spatial orientation: Knowing where you are in relation to the position of a sound source	Being aware that sounds are not in your visual field	Knowing that the sound is not where you are currently looking	3	1	1	1	1
			Being aware of threats or harms outside your visual field	1	1	1	2	1
			Not needing to rely on visual cues	1	1	1	1	1
		Knowing where sounds are in relation to you	Incorporates sound locations that are both in front and behind	1	2	1	1	1
			Incorporates sounds that are static, or moving	1	1	1	1	1
			Considers sounds that are both within and outside the visual field	1	1	1	1	2
		Attending to sounds in one location and not at other locations	Ability to attend to sounds in the correct location without a time delay: an active process	1	1	1	1	1
			Ability to attend to sounds in the presence of noise or other distracting sounds: a dynamic process	1	1	1	3	1

Figure 5-2. Example of the measurement instrument assessment spreadsheet used for the *Spatial orientation* outcome domain.

Individual assessment spreadsheets were created for all PROMs, with three sheets, one for each coder. Three additional sheets were compiled for each PROM to help the study management team with the comparison of codes and further analysis. Excel (Microsoft Corporation, 2022) formulae were developed to help compare the individual reviewer's codes and identify disagreements for discussion, and list the final decision taken by the coders (in case of disagreement). Finally, a summary sheet with calculations of the relevance and comprehensiveness of each conceptual element in capturing the outcome domain was created for each PROM assessed.

A pilot evaluation of five PROMs was run first by RK and PTK, to ensure the coding spreadsheets were accurate. DAH also piloted five PROMs independently and provided feedback prior to launching the assessment with the independent reviewers (coders). Once the coding for all measurement instruments was complete, the three coders met up to discuss their disagreements and mutually agree a final code for each of the questions of each PROMs.

5.3 Results

In total, four healthcare users and three healthcare professionals with relevant expertise participated. Their demographic data are summarised in Table 5.2. Three conceptual elements were identified for each of the outcome domains, which were described in more detail to form the operational definitions (Table 5.3).

Most themes derived from focus group 1 were comparable to the conversation in focus group 2, and parts of the discussions were repetitive. Therefore it is unlikely that additional focus groups would yield additional conceptual elements to majorly influence the following frameworks.

Table 5.3. The conceptual elements, operational definitions, and other related concepts derived for each of the three outcome domains.

Outcome domain and plain language definition	Conceptual elements	Operational definition	Other potentially related concepts
Spatial orientation: Knowing where you are in relation to the position of a sound source	Being aware that sounds are not in your visual field	Knowing that the sound is not where you are currently looking	○ Experiencing the world as 3-dimensional ○ Sense of ease or comfort ○ Sense of security ○ Personal safety aspect Feelings of: ○ Inadequacy ○ Frustration ○ Anxiety ○ Stress ○ Fear Constant challenge
		Being aware of threats or harms outside your visual field	
		Not needing to rely on visual cues	
	Knowing where sounds are in relation to you	Incorporates sound locations that are both in front and behind	
		Incorporates sounds that are static, or moving	
		Considers sounds that are both within and outside the visual field	
	Attending to sounds in one location and not at other locations	Ability to attend to sounds in the correct location without a time delay: an active process	
		Ability to attend to sounds in the presence of noise or other distracting sounds: a dynamic process	
Group conversations in noisy social situations: Listening and following a conversation between a group of people, when others are talking in the background	Dynamic involvement	Knowing when someone has started to talk	○ Being aware of all conversations taking place ○ Contributing appropriately at the right time ○ Having to rely on visual cues ○ Having to rely on help or hints provided by a partner ○ Being able to sustain attention for long enough Feelings of: ○ Being rude ○ Embarrassment ○ Being always on 'high alert' ○ Tiredness ○ Not being included Loneliness
		Being able to tell when someone new starts to contribute to the group conversation	
		Knowing who to listen to within the group	
		Following the thread of the conversation, when someone starts to contribute, and telling is it's a new conversation	
	Listening in the background of other conversations	Being able to know if the person talking is part of your conversation or another conversation	
		Being able to separate different streams of conversations	
		Maintain and sustain attention in the conversation	
	Conversations in other background noise	Being able to understand what is being said in a noisy environment	
		Being able to resist distracting sounds	
Impact on social situations: Your hearing loss or device limiting your ability to fully participate in the	Contributing to social interactions	Knowing when to take your turn	○ Demonstrate an understanding of what others are saying ○ Impact on relationships, work,
		Knowing what to do or say when it's your turn	
		Being able to take turns without relying on visual cues or prompts from others	

social world; especially in challenging situations or where a lot of effort is needed to follow the conversation	'Fitting in' socially	Feeling that you are contributing socially	education, community, society Feelings of: ○ Inability to contribute ○ 'Over-participation' ○ Loneliness Exhaustion
		Feeling that you are part of the social group	
		Not having to avail of help from others to participate	
	Ease of participation	Being able to participate without always having to concentrate intensely	
		Being able to sustain participation over time	
		Not having to avoid or withdraw from a situation	

5.3.1 Conceptual elements for the *Spatial orientation* outcome domain

The main conceptual elements derived for *Spatial orientation* were: (i) being aware that sounds are not in your visual field, (ii) knowing where sounds are in relation to you, and (iii) attending to sounds in one location and not at other locations.

The main discussion points revolved around the presence of visual cues, which people need to rely on, to help them orientate in their environment.

> [HU1] *"Where I always have a problem is basically where you can't use your eyes to identify where a particular sound is coming from"*
>
> [HP3] *"… have to turn their head all the time trying to oversee what's around them"*

If visual cues are not available people often have to rely on other hints, such as others' body language (e.g., where everyone else is looking) or assistance from others (e.g., a nudge from their partner).

> [HU2] *"If I am sitting around a circular table, and someone addresses me, am often unaware of it, unless I can actually see who is addressing me; unless I see their body language or their face"*
>
> [HP1] *"They say that they often get nudged or poked by the next person because they come in at the wrong time, or they miss something"*

Having an awareness that a sound (or a potential threat) is not in your visual field was also discussed, especially if it originates from behind.

[HP1] *"If you call for somebody or somebody talks to you or makes a sound and you don't have them in your vision, you have no idea where that is coming from – that gives safety implications"*

[HP2] *"It's not just about 'can I turn left or right' …, it's the safety aspect, and your place in the world, which also influences your balance … your own orientation within space"*

Whether the sound is static (e.g., a barman calling) or moving (e.g., a moving car or an airplane) is also important.

[HU1] *"The most crucial thing. If I go into a house and call the name of the person I'd like to talk to I don't know if they are upstairs or downstairs, I don't know what room they are in"*

[HP1] *"Many patients like to hear the birds singing and they'll say, 'I can hear the bird singing, but I don't even know which tree it's in, let alone which branch in which tree"*

Having an awareness that the sound is in a different space, and therefore does not require their attention or can be ignored helps people focus their attention accordingly and not get distracted.

[HU3] *"… it was a lot of people coming up behind me, it scared me because I didn't know they were there"*

[HP1] *"… just the awareness that you get, the dynamic awareness that you get, when you are just moving around in spaces, not necessarily listening to a thing, or listening out to a thing …"*

The ability to attend quickly and accurately to sounds in environments with other distracting sounds, like background noise, without a time delay, was another important concept discussed.

[HU2] *"The background noise is a problem, because the background noise seems to for some reason take precedence. I can hear what is going on around me, the things I don't need to hear I hear very clearly… It's quite difficult focusing onto*

the conversation that is going on in close proximity, because these other background sounds are very distracting"

[HP1] *"I've had people walk, you know, go out with their CROS aid, and marvel at the fact that they are now able to walk past the waiting room and find that they can hear that there's a noise there, even though they are not listening for it"*

Related to the main concepts, if people have a three-dimensional sense of their environment; they feel more comfortable, secure, and safe.

[HU4] *"… from behind in particular is quite scary because you don't even have that visual cue or clue"*

Otherwise, if their environment is always unpredictable, they feel that they 'miss out', 'stand out', appear 'vague', can experience feelings of anxiety, inadequacy, frustration, stress, fear and feel that they are constantly challenged, which can make them 'shy away' from situations.

5.3.2 Conceptual elements for the *Group conversations in noisy social situations* outcome domain

The main conceptual elements derived for *Group conversations in noisy social situations* were: (i) dynamic involvement, (ii) listening in the background of other conversations, and (iii) conversations in other background noise.

Being able to dynamically participate in a conversation (i.e., move their attention quickly from one contributor to another), when someone new starts a new conversation thread was considered an important element of this domain.

[HU2] *"In a group situation, its knowing when I can interject; and learn when I can't interject. Being aware of the fact that I have interjected when I shouldn't have done, because there was still a conversation going on around me, and I hadn't been aware of it, and that's quite embarrassing. It's very easy to retreat into a solitary existence; when it happens a couple of times, you feel you ought to, you know, step back and not get involved"*

It did not just include 'listening' and 'following' which are passive activities, but also 'actively participating' and contributing in conversations of groups constituting of three or more people.

> [HU1] *"If there's a group conversation with let's say 4 or more, you don't know when you can interject or something; and sometimes you might interject when someone is actually pausing, just to talk again. So I feel very, sort of, not very polite, actually talking over somebody"*
>
> [HP2] *"It's not just about 'following a conversation', because if you are following it you are always lagging behind, that would be being able to 'part-take' in a conversation"*

Maintaining attention for long enough can be influenced by the conversation partners. Family members can be more understanding and often choose more predictable topics, for example when around the dinner table.

> [HP1] *"Defining a group is something about how many sets of conversations are going on … if there's two conversations … and you get more of that as you get more people.*
>
> *So if you've got four people around the dinner table, often the conversation will be on one topic … if the conversations are too separate, that gets more challenging"*

However, it can be challenging to maintain conversations of a more unpredictable nature with new acquaintances or strangers who are unaware of the hearing impairment.

> [HU1] *"When there's 6 people having a conversation, there is a lot of cross-over conversations going. You know, one part if its talking about one subject, you can't differentiate too easily between the two different conversations … I sometimes get very rude and I say: 'can you just one person speak on one subject? And don't keep moving?' because I can't then follow"*
>
> [HP1] *"So it might be your wife and friend who have been in the conversation and suddenly they change topic and they are no longer in the conversation, they change from being conversation partners to 'others' in a second"*

The nature of background noise is also important: monotonous noise (e.g., a lawn mower) can be more easily ignored, speech sounds (e.g., children talking) are more difficult, and sudden unexpected sounds (e.g., a child starting to cry) present the greatest challenge.

> [HU4] *"Listening doesn't always mean the same as understanding. And following. So I can be listening to people in a restaurant and not really understanding anything they are saying because I am listening but only getting little bits of it"*
>
> [HU4] *"If there is any other sound in the room, it can 'short circuit' my concentration"*
>
> [HP2] *"Speech is the hardest, if you've got competing speech all around you, that's probably the hardest thing to filter out"*

When listening in the background of other conversations, it is hard knowing what information is coming from your conversation as opposed to a conversation elsewhere and focusing on the correct conversation are important elements to consider.

> [HU2] *"People address me from various directions and I could be standing there, having a conversation, with maybe 1-2 people almost simultaneously and then a third or a fourth is interjecting, I find this a very challenging situation indeed"*
>
> [HP1] *"There may be times when other people want to get your attention; and if you can't tell where that is coming from, you can't decide whether you are perfectly ok to ignore that interjection because it's irrelevant to that time, or whether it's important, or whether it's a safety issue like someone is calling you because something is about to fall on your head; or, you have no idea, so your brain is always on high alert I think, to all possible sources of information"*

The listening environment has an impact. Social environments (e.g., a pub, a restaurant), or environments with poor acoustics (e.g., a large cathedral, an airport) can be detrimental. In these settings, people often do not have complete awareness of all conversations taking place and rely on visual cues, or non-verbal hints from conversation partners to contribute meaningfully at the right time.

> [HU1] *"I won't go out to restaurants, I don't like noisy pubs"*

[HU3] *"It's quite funny that you said 'jokes' cause I remember I was just laughing at random times, and it was only because I was like, putting people's answers in their mouth for them. Because I was finding it funny and putting funny things in – I'd say 'ha, didn't you say that?', and they went –'no'. I was like 'aw'. And that was quite weird. It happened quite a lot to be actually a thing that was quite funny in the end but quite embarrassing for me"*

People often feel that they are 'being rude', they get embarrassed, they have to be constantly on 'high alert' which can be tiring, make them feel that they are not included in the group, feel lonely and 'retreat in solitary existence', or 'step back and not get involved'.

[HU3] *"I could have been surrounded by all my best friends in a pub. And I would feel so lonely, because I couldn't keep up. I didn't know what was happening. I wouldn't know where the conversation was going. I'd just be looking left and right. And it was quite sad*"

[HP2] *"You tend to withdraw, because it's frustrating and demoralising isn't it? And it is tiring"*

[HP3] *"Parties always are a problem, gatherings are a problem, and I think those who have problems with hearing in such situations they avoid those situations"*

5.3.3 Conceptual elements for the *Impact on social situations* outcome domain

The main conceptual elements derived for *Impact on social situations* were: (i) contributing to social interactions, (ii) 'fitting in' socially, and (iii) ease of participation.

The discussions concentrated on appropriate turn taking (i.e., knowing when it is appropriate to interject) and contributing to the social interaction with an appropriate interjection (e.g., comment on the correct topic). Accurate turn taking seems to be the key to 'full participation'.

[HU1] *"I'd be very careful when there's a group of people participating, to make sure I am fully aware of the subject they are discussing. Because I might miss some crucial points" ... "It'd be more effort to keep up …, to make sure you don't miss any particular subject. So you'd probably be using body language, eyes, a lot*

better … to actually try to ascertain what's happening" … "When someone is about to say something, you see them move. Or you see them move forward, with a group. So they are the sort of things you look for"

[HP1] *"Whether people would engage or withdraw from social situations and there's a lot of people who would say, 'I don't, I just don't go out any more, or if I do, I don't go out without my husband, or my wife, I have to make sure they always sit on my bad side because then I won't get a stranger on my bad side and they know me so they can nudge me and, so yea, it's those kind of things"*

The concepts discussed focused on the person with hearing loss being able to fully participate in a social situation, as opposed to just 'listening' and 'following' a conversation taking place with multiple people.

[HU4] *"I was not involved in the conversation. People at certain times were saying: 'aw what do you think, or … and I'd just be like: 'Can you tell me what you just said again please'? Because I had no idea what was happening in that conversation. So it's quite lonely and it's really sad when you have these situations"*

People often rely on conversation partners to inform them that the conversation has moved on to another topic (e.g., by repeating the last part of the conversation), or that someone else is still holding a turn. Inability to take correct turns (e.g., understanding and laughing at a joke at the right time) can make people feel that they are not an integral part of the social group.

[HP1] *"… about jokes and other new onsets of the conversation. You can follow a conversation maybe, but you don't get the tiny little asides, or the little, the 'hmhm', that people say that re-affirm if it's a positive or a negative or any of those things, or the new onsets, I forgot to mention earlier on, the 'new onsets' are the more challenging ones to get right. And maybe the more important ones to get right"*

Participating and being involved in social situations can be demanding and requires concentration and effort, therefore sustaining participation over a long period of time can be challenging.

> [HP1] *"Many people, probably more people than in the usual hearing aid population are working-age people. And they'd be at work. And there will be a different dynamic in work. And meetings. And the, ah all of the fear about participation at work, whether this is about to influence your income and your lifestyle, so your single-sided or other deafness would have more of a direct impact that can't really be got over by just your family members being kind to you"*

'Over-participating' (e.g., talking too much, or taking over the conversation) to compensate for the lack of awareness of correct turn-taking points, and because listening and following a conversation is too demanding, was a related concept discussed.

> [HP1] *"… your face, and your over-sharing, and over-participating. And if you don't absolutely fit in the norms of what that conversation is about, then you'd stand out. And people will either look at you funny or they will tell you, or they will ignore it. But either way, you probably don't feel that you have the same participation that other people might have"*
>
> [HU2] *"I may be guilty personally sometimes of over-participating or trying to compensate for the deficiency in one area, which is the hearing loss, and perhaps maybe sometimes in the social situation is; speculating a bit too wildly possibly even speaking a bit too loudly, and not being aware at all of the fact that my behaviour, my speech, the volume, so on, the amplitude, are exaggerated. And that might sort of, you know, cause me to sort of, stand out and seem a bit sort of odd in a way"*

Being able to successfully keep up with conversations, gaining acknowledgement from others, and successful interactions bring involvement in life situations and lead to feelings of contribution and happiness.

[HU1] *"When you are in a social situation, and you are intensely listening to a conversation, that must come across weird to other people; you are almost screwing your face up listening to it. Equally it might not be socially acceptable"*

[HU2] *"I'm probably not alone in the world in wanting to conform, in wanting to appear to be normal. And you know, enjoy the benefit of, you know, accepted by my peers, and so on. So, yes, any way which this might be difficult to fulfil, you know, it's kind of, it's challenging, and stressful"*

[HU3] *"The whole reason why we socialise as human beings, to get a lot of things, back and forth a lot of acknowledgement, a lot of happiness"*

[HP2] *"The impact on social situations, it is how can you, ... your ability to take part in life basically"*

Otherwise, it can have an impact on relationships, participation in family, community, or societal situations and be correlated to participation restriction.

[HU2] *"I think I do become tired, you know, I lose the ability to sort of concentrate so greatly, and I do, after a euphoric few minutes I then turn sort of to take a back seat. And sit there, almost incapable"*

[HU3] *"People are just moody, they are just not, they just withdraw, and push back, because they are fed up of trying. And it's, it can be quite traumatic … which I find quite, it's quite daunting to me"*

[HP2] *"To fully participate in the social world it is about inclusion … there is this danger, if you have a hearing loss you withdraw from society … it's got a massive impact"*

[HP3] *"The only thing you can do, is avoid these situations, or … be sure you are sitting on the right place on the table, close to the people you'd like to communicate with"*

Review of the finalised frameworks by the international CROSSSD study steering group led to the amendment of just one operational definition, that of the *Spatial orientation* domain, to include 'incorporates sounds that are static, or moving'.

5.3.4 Measurement instruments assessment

The systematic review reported in Chapter 3 identified the measurement instruments used to date (March 2020) to assess SSD interventions benefits and harms. A comprehensive list of all measurement instruments arranged according to our adopted taxonomy (Dodd et al., 2018), can be found in Additional file 10 of the published review (Katiri, Hall, Killan, et al., 2021). A total of 76 PROMs were identified for assessment. The PRISMA diagram in Figure 5-3 summarises the process.

Briefly, the systematic review identified 344 unique measurement instruments, and the sensitivity analysis of 24 studies identified 197 measurement instruments (Katiri, Hall, Killan, et al., 2021). When amalgamated, de-duplicated, and non-PROMs excluded, 281 measurement instruments were short-listed. Further de-duplication and amalgamation of subscales removed a further 154 PROMs from the list of measurement instruments for assessment. Nineteen non-English language PROMs were identified (n=5 Dutch, n=1 Finnish, n=4 French, n=5 German, n=3 Korean, and n=1 Mandarin). English-language versions were available for all but four measurement instruments: the RONDO® single-unit processor questionnaire was only available in Dutch (Mertens et al., 2015), the Occupational stress questionnaire from the Finnish institute of Occupational Health (Härkönen et al., 2015), the Oldenburg inventory in German (Häußler et al., 2020), and a Visual Analogue Scale (VAS) measuring quality of hearing were only available in German (Jacob et al., 2011). Further scrutiny identified 32 duplicates, and nine PROMs that were non-specific (e.g., cost diary, non-specified questionnaires or VAS, record of complications), mainly from clinical trial registration records (Dunn and Burke, 2019; Grolman, 2014; Kleinjung, 2012; D. J. Lee, 2015; Medtronic Surgical Technologies, 2017; Pelusso, 2019; Syms and Galow, 2013), and three PROMs that were not described in enough detail to be able to assess suitability for inclusion (e.g., 'interview with standard set of questions', 'multi-domain questionnaire', 'residual tinnitus inhibition after switch off') (Andersen et al., 2006; Gluth et al., 2010; Gurgel and Shelton, 2013; Mertens et al., 2016). From the Kitterick et al. (2016) systematic review of hearing instruments for unilateral severe-to-profound sensorineural hearing loss in adults, and hand-searching, 12 further PROMs were identified for assessment.

The final PROMs list compiled for assessment constituted of two diary records, 49 questionnaires, 17 rating scales, and eight other PROMs that did not fit into the categories (e.g., patient report, Yes/ No answers, single question). Appendix 22 lists the name of all PROMs included, the relevant reference or developer team, what type of PROM it is (e.g., questionnaire, visual analogue scale), the number of items it incorporates and if it is SSD specific. The measurement instrument assessment results for each outcome domain were summarised in order of relevance to the operational definitions. Please refer to Table 5.4 for *Spatial orientation* outcome domain, Table 5.5 for *Group conversations in noisy social situations* outcome domain and Table 5.6 for *Impact on social situations* outcome domain respectively.

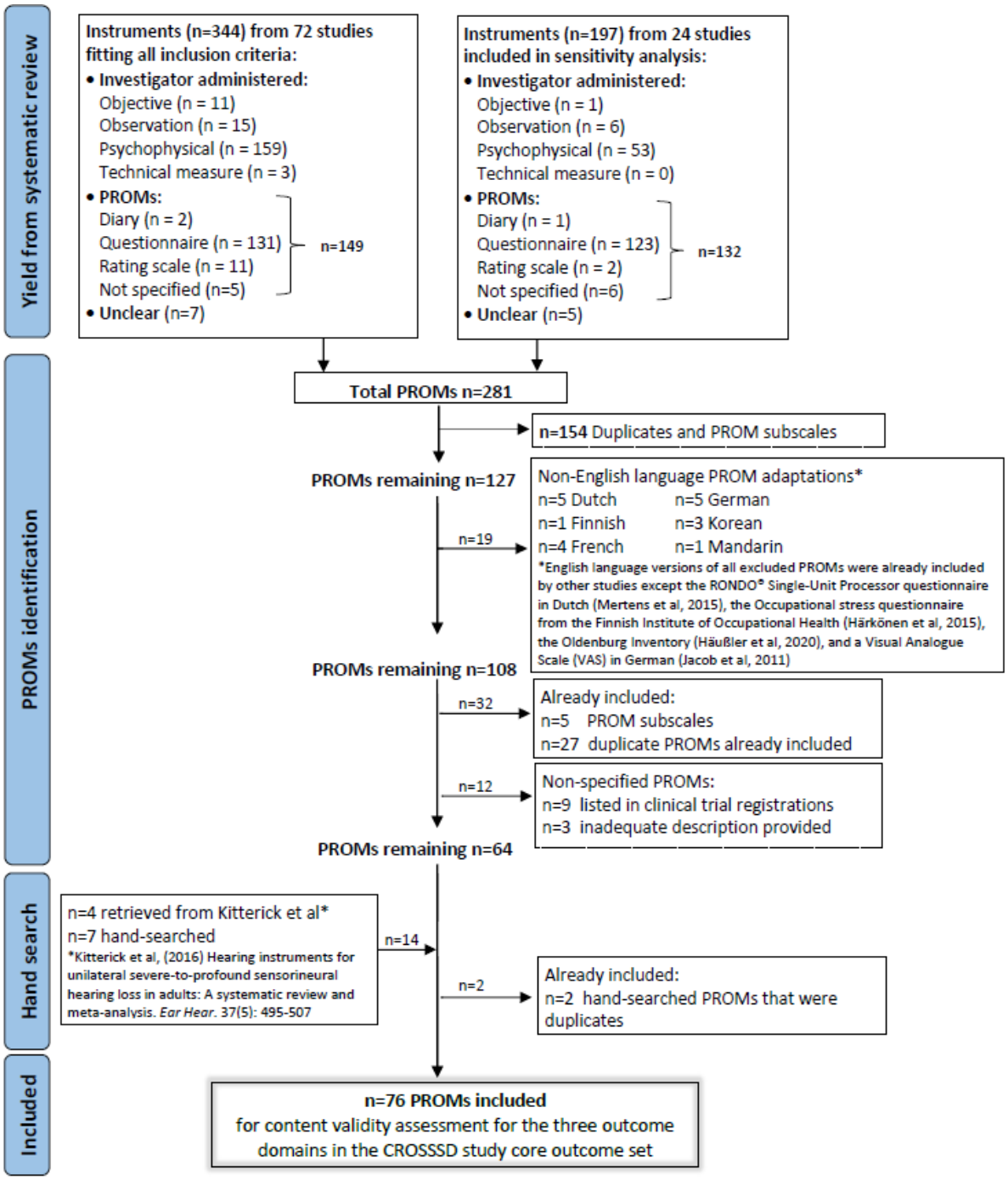

Figure 5-3. Measurement instruments reported in studies investigating interventions that seek to restore hearing in adults with single-sided deafness.
*PROM(s): Patient Reported Outcome Measure(s), VAS: Visual analogue scale, CROSSSD: Core Rehabilitation Outcome Set for Single-Sided Deafness, SSD: Single-sided deafness.

5.3.4.1 *Spatial orientation* outcome domain measurement instruments

For *Spatial orientation*, the short version of the Speech, Spatial and Qualities (SSQ-12) scale (Noble et al., 2013) and the Speech, Spatial and Qualities 18 Comparative (SSQ-18-C) questionnaire (Gatehouse and Noble, 2004) matched at least one aspect of every operational definition on Table 5.3. Five other PROMs matched between 5-7 operational definitions; these were the Spatial Hearing Questionnaire (SHQ) (Tyler et al., 2009), the Monaural auditory capacity assessment scale (MACAS) (McLeod et al., 2008), the Nijmegen Cochlear Implant Questionnaire (NCIQ) (Hinderink et al., 2000), the Communication profile for hearing impaired (CPHI) (Demorest and Erdman, 1987), the Speech, Spatial and Qualities 12 Comparative (SSQ-12-C), and the Speech, Spatial and Qualities 12 of Hearing Scale for Benefit Questionnaire (SSQ-12-B) pre and post (Gatehouse and Noble, 2004). The remainder PROMs matched less than four operational definitions (Table 5.4).

5.3.4.2 *Group conversations in noisy social situations* outcome domain measurement instruments

For *Group conversations in noisy social situations* there was one PROM, the Communication profile for hearing impaired (CPHI) questionnaire (Demorest and Erdman, 1987) that matched all operational definitions. Schafer et al. (2013) own questionnaire and the Speech, Spatial and Qualities 18 Comparative (SSQ-18-C) questionnaire (Gatehouse and Noble, 2004) matched eight of the total of nine operational definitions. Five other PROMs matched between seven and four operational definitions. These were the Hearing Implant Sound Quality Index (HISQUI-NL) (Amann and Anderson, 2014), the Monaural auditory capacity assessment scale (MACAS) (McLeod et al., 2008), the Abbreviated Hearing Aid Benefit Profile (APHAB) (Cox and Alexander, 1995), and three versions of the SSQ (SSQ-12, SSQ-12-C, SSQ-5) questionnaire (Gatehouse and Noble, 2004). The remainder PROMs matched less than two operation definitions (Table 5.5).

5.3.4.3 *Impact on social situations* outcome domain measurement instruments

For *Impact on social situations* there was only one PROM, the Communication profile for hearing impaired (CPHI) questionnaire (Demorest and Erdman, 1987) that matched

all operational definitions. The remainder PROMs matched less than three of the nine operational definitions (Table 5.6).

Table 5.4. Short list of measurement instruments that matched at least one of the operational definitions for the *Spatial orientation* outcome domain.

Measurement instrument name (n=14)	Relevance and comprehensiveness		Percentage (%) agreement of total number of PROM questions
	Number of relevant items (out of 8 operational definitions)	Comprehensiveness (all conceptual elements of the domain are covered)	
Short version of the Speech, Spatial and Qualities (SSQ-12) scale	8	Yes	25
Speech, Spatial and Qualities 18 Comparative (SSQ-18-C)	8	Yes	78
Spatial Hearing Questionnaire (SHQ)	7	Yes	50
Monaural Auditory Capacity Assessment Scale (MACAS)	6	Yes	22
Nijmegen Cochlear Implant Questionnaire (NCIQ)	6	Yes	5
Communication Profile for Hearing Impaired (CPHI)	5	Yes	1
Speech, Spatial and Qualities 12 Comparative (SSQ-12-C)	5	Yes	25
Speech, Spatial and Qualities 12 of Hearing Scale for Benefit Questionnaire (SSQ-12-B) pre and post	5	Yes	25
Speech, Spatial, and Qualities of Hearing Scale 5 Questions (SSQ-5)	4	No	20
Client Orientated Scale of Improvement (COSI)	3	No	19
Hearing Implant Sound Quality Index (HISQUI-NL)	2	No	0
Bern Benefit in Single-Sided Deafness (BBSS) questionnaire	1	No	10
Multi-item, multi-domain questionnaire (author's own) (Schafer et al., 2013)	1	No	2
Questionnaire (author's own) (Snapp et al., 2010)	1	No	50

*Relevance means all items in a PROM (Patient Reported Outcome Measure) are relevant to the construct of interest, for adults with SSD, in the context of clinical trials. Comprehensiveness (Yes) means no key aspects, or conceptual elements, of the outcome domain construct are missing. Percentage (%) agreement signifies the number of items in each PROM that matched the operational definitions.

Table 5.5. Short list of measurement instruments that matched at least one of the operational definitions for the *Group conversations in noisy social situations* outcome domain.

Measurement instrument name (n=15)	Relevance and comprehensiveness		Percentage (%) agreement of total number of PROM questions
	Number of relevant items (out of 9 operational definitions)	Comprehensiveness (all conceptual elements of the domain are covered)	
Communication Profile for Hearing Impaired (CPHI)	9	Yes	3
Multi-item, multi-domain questionnaire (author's own) (Schafer et al., 2013)	8	Yes	14
Speech, Spatial and Qualities 18 Comparative (SSQ-18-C)	8	Yes	22
Short version of the Speech, Spatial and Qualities (SSQ-12) scale	7	Yes	17
Hearing Implant Sound Quality Index (HISQUI-NL)	6	Yes	26
Monaural Auditory Capacity Assessment Scale (MACAS)	5	No	17
Speech, Spatial and Qualities 12 Comparative (SSQ-12-C)	5	Yes	17
Speech, Spatial and Qualities 12 of Hearing Scale for Benefit Questionnaire (SSQ-12-B) pre and post	5	Yes	17
Abbreviated Hearing Aid Benefit Profile (APHAB)	4	No	13
Speech, Spatial, and Qualities of Hearing Scale 5 Questions (SSQ-5)	4	No	40
Bone Anchored Cochlear Stimulator (BAHA) satisfaction questionnaire	2	No	7
Bern Benefit in Single-Sided Deafness (BBSS) questionnaire	1	No	10
Client Orientated Scale of Improvement (COSI)	1	No	13
Hyperacusis questionnaire (Khalfa et al., 2002)	1	No	7
Questionnaire (author's own) (Snapp et al., 2010)	1	No	25

*Relevance means all items in a PROM (Patient Reported Outcome Measure) are relevant to the construct of interest, for adults with SSD, in the context of clinical trials. Comprehensiveness (Yes) means no key aspects, or conceptual elements, of the outcome domain construct are missing. Percentage (%) agreement signifies the number of items in each PROM that matched the operational definitions.

Table 5.6. Short list of measurement instruments that matched at least one of the operational definitions for the *Impact on social situations* outcome domain.

Measurement instrument name (n=16)	Relevance and comprehensiveness		Percentage (%) agreement of total number of PROM questions
	Number of relevant items (out of 9 operational definitions)	Comprehensiveness (all conceptual elements of the domain are covered)	
Communication Profile for Hearing Impaired (CPHI)	9	Yes	20
Audio Processor Satisfaction Questionnaire (APSQ)	3	0	13
Hearing Handicap Inventory (HHIA)	3	0	16
Bone Anchored Cochlear Stimulator (BAHA) satisfaction questionnaire	2	0	10
Client Orientated Scale of Improvement (COSI)	2	0	13
Nijmegen Cochlear Implant Questionnaire (NCIQ)	2	0	5
Dizziness Handicap Inventory (DHI)	1	0	4
Expected Consequences of Hearing aid Ownership (ECHO)	1	0	6
Glasgow Benefit Inventory (GBI)	1	0	6
Glasgow Health Status Inventory (GHSI)	1	0	6
Multi-item, multi-domain questionnaire (author's own) (Schafer et al., 2013)	1	0	2
Short version of the Speech, Spatial and Qualities (SSQ-12) scale	1	0	8
Speech, Spatial and Qualities 12 Comparative (SSQ-12-C)	1	0	8
Speech, Spatial and Qualities 12 of Hearing Scale for Benefit Questionnaire (SSQ-12-B) pre and post	1	0	8
Speech, Spatial, and Qualities of Hearing Scale 5 Questions (SSQ-5)	1	0	20
Tinnitus Handicap Inventory (THI)	1	0	4

*Relevance means all items in a PROM (Patient Reported Outcome Measure) are relevant to the construct of interest, for adults with SSD, in the context of clinical trials. Comprehensiveness (Yes) means no key aspects, or conceptual elements, of the outcome domain construct are missing. Percentage (%) agreement signifies the number of items in each PROM that matched the operational definitions.

5.3.5 Patient Reported Outcome Measures (PROM) items percentage match

The percentage of items in each PROM that matched the operational definitions was also calculated (Tables 5.4-5.6). For example, in the *Spatial orientation* outcome domain, although the SSQ-12 scale (Gatehouse and Noble, 2004) matches all eight operational definitions, only 25% of its items (i.e., three out of 12) are relevant to this outcome domain (Table 5.4). On the contrary, although the Snapp et al. (2010) own questionnaire only addresses one operational definition, 50% of its items (i.e., two out of four) are relevant to this outcome domain (Table 5.4).

For the *Group conversations in noisy social situations* outcome domain the Communication profile for hearing impaired (CPHI) questionnaire (Demorest and Erdman, 1987) matched all operational definitions (Table 5.5). However it is composed of 145 items and only 3% of its items (i.e., three out of 145) are relevant to this domain. The Speech, Spatial, and Qualities of Hearing Scale 5 Questions (SSQ-5) questionnaire (Gatehouse and Noble, 2004) only matched four out of nine of the operational definitions, but 40% of its items are relevant.

For the third outcome domain, *Impact on social situations*, 20% of the items in both the Communication profile for hearing impaired (CPHI) questionnaire (Demorest and Erdman, 1987) and the Speech, Spatial, and Qualities of Hearing Scale 5 Questions (SSQ-5) questionnaire (Gatehouse and Noble, 2004) were relevant (Table 5.6).

5.3.6 Coder agreement

The three independent coders' disagreement was calculated from the number of items in each PROM they coded differently. For all 76 PROMs, coders agreed on their codes in 43 PROMs (57%) of the total, and therefore no discussion was needed. For 17 PROMs they had a 'minor disagreement' (less than ten items coded differently by at least two coders), therefore needed discussion to resolve the coding discrepancies. For the remaining 16 PROMs they had a 'major disagreement' (coded more than ten items per PROM differently), which needed further discussion to decide on a commonly agreed code.

5.3.7 Measurement instruments' comprehensiveness

Comprehensiveness means that no key aspects of the outcome domain construct are missing (Terwee, Prinsen, Chiarotto, Westerman, et al., 2018). When summarised in terms of comprehensiveness, eight PROMs covered all key aspects of the outcome domain construct for the *Spatial orientation* outcome domain, seven PROMs for the *Group conversations in noisy social situations* outcome domain and one PROM for the *Impact on social situations* outcome domain (Table 5.7). For a list of the 76 PROMs assessed, including their developer(s) and/or relevant publication, year developed, and details on their structure please refer to Appendix 22.

Table 5.7. List of Patient Reported Outcome measures (PROMs) that can comprehensively assess each of the three outcome domains in the core outcome domain set for single-sided deafness.

Spatial orientation	***Group conversations in noisy social situations***	***Impact on social situations***
1. Communication profile for hearing impaired (CPHI) **2.** Monaural auditory capacity assessment scale (MACAS) **3.** Nijmegen Cochlear Implant Questionnaire (NCIQ) **4.** Short version of the Speech, Spatial and Qualities (SSQ-12) scale **5.** Spatial Hearing Questionnaire (SHQ) **6.** Speech, Spatial and Qualities 12 Comparative (SSQ-12-C) **7.** Speech, Spatial and Qualities 12 of Hearing Scale for Benefit Questionnaire (SSQ-12-B) pre and post **8.** Speech, Spatial and Qualities 18 Comparative (SSQ-18-C)	**1.** Communication profile for hearing impaired (CPHI) **2.** Hearing Implant Sound Quality Index (HISQUI-NL) **3.** Multi-item, multi-domain questionnaire (author's own) (Schafer et al., 2013) **4.** Short version of the Speech, Spatial and Qualities (SSQ-12) scale **5.** Speech, Spatial and Qualities 12 Comparative (SSQ-12-C) **6.** Speech, Spatial and Qualities 12 of Hearing Scale for Benefit Questionnaire (SSQ-12-B) pre and post **7.** Speech, Spatial and Qualities 18 Comparative (SSQ-18-C)	**1.** Communication profile for hearing impaired (CPHI)

*Comprehensiveness means that no key aspects of the outcome domain construct are missing (Terwee et al., 2018).

5.4 Chapter summary

The qualitative study allowed us to explore and develop a deeper understanding of the three core outcome domains identified as critical by the CROSSSD initiative, through

the everyday experiences of healthcare users with SSD and professionals working in the field. These findings informed the identification of measurement instruments that putatively assess these concepts and for evaluating their content validity (Hibbert et al., 2020; Prinsen et al., 2016). The identified PROM(s) selection in this study was based on the relevance of the items they comprised of to the operational definitions of the outcome domains, rather than an assessment of the psychometric properties for potential measurement instruments.

The qualitative focus group study has revealed the complexity of SSD outcome domains from the point of view of healthcare users diagnosed with SSD and professionals working in the field. Prior to this study, there was little knowledge or consensus on how each of the outcome domains should be operationalised. The findings presented here formulate three primary conceptual elements for each of the outcome domains, indicating that appropriate measurement instruments will need to comprise multiple subscales or factors. The finalised operational definitions directly informed the process of available measurement instrument(s) assessment and selection for the outcome domains (Prinsen et al., 2016).

In the absence of a fully relevant and fully comprehensive measurement instrument for each of the outcome domains, the Speech, Spatial and Qualities (SSQ) scale (Gatehouse and Noble, 2004) is a PROM that matches several operational definitions in the *Spatial orientation* and *Group conversations in noisy social situations* outcome domains, therefore it would be a good choice of PROM in future clinical trials, until a tailored, more suitable measurement instrument is developed. Three other popular measurement instruments in the SSD field, the Nijmegen Cochlear Implant Questionnaire (NCIQ) (Hinderink et al., 2000), the Spatial Hearing Questionnaire (SHQ) (Tyler et al., 2009), and the Monaural auditory capacity assessment scale (MACAS) (McLeod et al., 2008) also matched a number of the operational definitions for the *Spatial orientation* outcome domain. The Hearing Implant Sound Quality Index (HISQUI-NL) (Amann and Anderson, 2014) and the Schafer et al. (2013) author's own questionnaire also match several of the operational definitions in the *Group conversations in noisy social situations* outcome domain. Only one measurement

instrument, the Communication profile for hearing impaired (CPHI) questionnaire (Demorest and Erdman, 1987), was identified as suitable for the *Impact on social situations* outcome domain It was developed in 1987 to assess the environmental, behavioural, emotional, and attitudinal factors that could contribute to communication problems in hearing-impaired adults. It comprises 145 items and provides 25 scores. The communication profile is organised into four areas: Communication performance, Communication environment, Communication strategies, and Personal adjustment. An additional three scores are reported for Communication importance in social, work, and home situations.

Going forward, adoption, implementation, evaluation and review of the measurement instrument(s) at pre-determined time-scales (e.g., every 5 years), will ensure a contemporary COS is being used in clinical trials (Hall, Szczepek, et al., 2015). Ongoing publications in leading journals, editorials, presentations at appropriate forums, as well as dissemination to manufacturers, charities and funding bodies, and the general public is highly recommended to promote the implementation of the COS to key stakeholders internationally (Schmitt et al., 2015; Williamson et al., 2017). The importance of implementation is highlighted, for example, by planned reviews aiming to assess the degree of concordance between outcomes recommended in COS for research, and in guidance provided by key regulators such as the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) are under way (Dodd et al., 2021).

6. General discussion and future directions

The overall aim of this thesis was to present the Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) study which sought to examine and address problems with inconsistent outcome reporting in single-sided deafness (SSD) intervention trials. This was addressed through (i) a systematic review of outcome domains and measurement instruments, (ii) development of a core outcome domain set, (iii) conceptualisation and operationalisation of the outcome domains in the core outcome domain set, and (iv) assessment of available measurement instruments for suitability in measuring the domains in the core outcome domain set. This chapter summarises how the research presented in this thesis addresses each of the key objectives listed in Section 1.8. The findings are considered in the context of previous and future research in the field of SSD interventions. The most important learning points, identified gaps, limitations and future directions are also discussed.

6.1 Summary of findings

6.1.1 Systematic review of outcome domains and measurement instruments

- Most studies included in the review evaluated rerouting interventions rather than restoring interventions.
- There was a large variation in previously reported outcome domains, with most studies favouring physiological or clinical domains, with fewer reporting life impact outcomes.
- Only a minority of previous studies reported on resource use and adverse events.
- Investigators did not always report what their intended outcome domain was, suggesting that their chosen measurement instruments were not necessarily matched to an outcome domain.
- Large variation was observed with regards to choice of measurement instruments, with investigator administered tests mostly adopted, focusing mainly on speech in noise and spatial-related testing. A diversity within these

categories of instruments was also observed with a plethora of signal and noise configurations that did not always fit existing recommendations that aim to reveal both the benefits and drawbacks of hearing devices.

- Multi-item questionnaires were frequently used but there was no consensus in their selection, nor the intended outcome domains to be measured.
- The time-frame when interventions were assessed varied, so it was challenging to compare the short- and long-term treatment-related changes for rerouting and restoring interventions.

6.1.2 Development of a core outcome domain set for single-sided deafness interventions

- 433 outcome domains were extracted from studies included in the systematic review, a list of 44 candidate outcome domains, organised thematically in 10 categories were included in a Delphi survey.
- 308 participants (92 healthcare users, 216 professionals) from 29 countries enrolled. Of those, 233 participants (71 healthcare users, 162 professionals) completed the survey.
- Discussions and voting involving 12 stakeholder representatives (6 healthcare users, 6 professionals) at a web-based consensus meeting identified three outcome domains for the core outcome domain set for SSD interventions: (i) *Spatial orientation* (100% agreement), (ii) *Impact on social situations* (100% agreement), and (iii) *Group conversations in noisy social situations* (83.3% agreement).
- Five other outcome domains (*Listening effort*, *One-to-one conversation in general noise*, *Being aware of a sound*, *Device usage*, and *Listening in complex situations)* reached the final stages of elimination and were considered highly important by stakeholders throughout the process despite not making it into the core outcome domain set.
- The core outcome domain set was shared with the 219 participants who completed both rounds of the e-Delphi survey but did not join the consensus meeting, of whom 73 responded that they were very satisfied with the choice

of included outcome domains, and 19 indicated that they were somewhat satisfied.

6.1.3 Conceptualisation and operationalisation of the outcome domains in the core outcome domain set

- Discussions at two focus groups with stakeholder representatives (4 healthcare users, 3 professionals) derived three conceptual elements and detailed definitions for each of the three outcome domains in the core outcome domain set.
- For *Spatial Orientation* outcome domain the conceptual elements were: (i) being aware that sounds are not in your visual field, (ii) knowing where sounds are in relation to you, and (iii) attending to sounds in one location and not at other locations.
- For *Group conversations in noisy social situations* outcome domain the conceptual elements were: (i) dynamic involvement, (ii) listening in the background of other conversations, and (iii) conversations in other background noise.
- For *Impact on social situations* outcome domain the conceptual elements were: (i) contributing to social interactions, (ii) 'fitting in' socially, and (iii) ease of participation.

6.1.4 Assessment of available measurement instruments for suitability in measuring the domains in the core outcome domain set

- 76 patient reported outcome measures (PROMs) were identified for assessment of relevance and comprehensiveness to the operational definitions of the outcome domains.
- The Speech, Spatial and Qualities (SSQ) scale (Gatehouse and Noble, 2004) is a PROM that matches several operational definitions in the *Spatial orientation* and *Group conversations in noisy social situations* outcome domains.
- The Nijmegen Cochlear Implant Questionnaire (NCIQ) (Hinderink et al., 2000), the Spatial Hearing Questionnaire (SHQ) (Tyler et al., 2009), and the Monaural

auditory capacity assessment scale (MACAS) (McLeod et al., 2008) match a number of the operational definitions for the *Spatial orientation* outcome domain.

- The Hearing Implant Sound Quality Index (HISQUI-NL) (Amann and Anderson, 2014) and the Schafer et al. (2013) author's own questionnaire match several of the operational definitions in the *Group conversations in noisy social situations* outcome domain.
- The Communication profile for hearing impaired (CPHI) questionnaire (Demorest and Erdman, 1987), was the only identified PROM suitable for assessing the *Impact on social situations* outcome domain.

6.2 Summary of the CROSSSD study roadmap

In the context of core outcome set development for SSD interventions roadmap (Figure 6-1), the CROSSSD study has examined and addressed multiple problems with inconsistent outcome reporting in SSD intervention trials.

Step 1 (Chapter 3 and Chapter 4) was completely achieved. Step 2 (Chapter 5) has also been achieved although a peer reviewed publication on the recommendations for future measurement instrument developers in the field is pending. Stakeholder awareness, dissemination, publicity, and promotion of the study findings were incorporated as an integral part of the CROSSSD study throughout.

Future steps (Step 3 and Step 4) include validation of candidate measurement instruments in the SSD field, assessment of feasibility, obtaining a stakeholder consensus on candidate measurement instruments; and a review to ascertain adoption and implementation at a specified time-frame (e.g., 5 years). The COSMIN initiative also recommend assessment of comprehensibility as well as relevance and comprehensiveness when assessing content validity. Completing these steps will establish an international standard for outcome assessment and reporting in clinical trials of device-based interventions for adults with SSD.

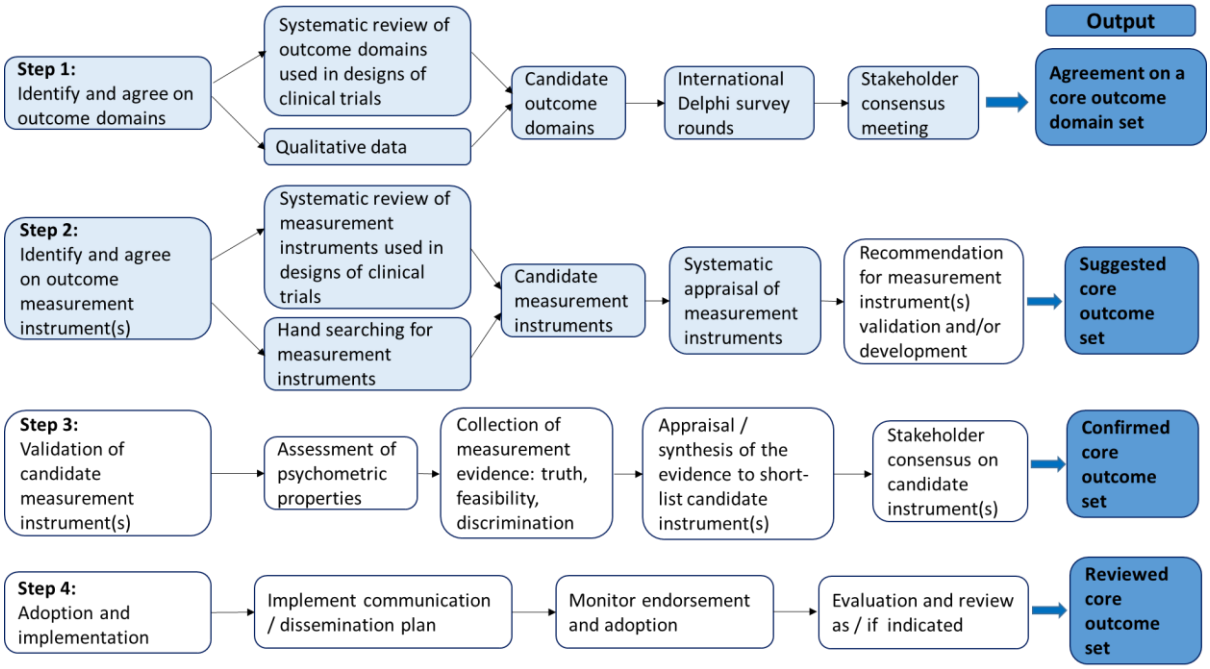

Figure 6-1. Summary of the CROSSSD study roadmap, steps achieved, and suggested future work.
*Sections highlighted in light blue have already been achieved by the work described in this thesis, to achieve the main output in the dark blue sections.

6.3 Outcome measurement in clinical trials

To be able to make well-informed decisions about healthcare, all relevant stakeholders must be able to compare and contrast research findings on the basis of the same outcomes (Chalmers and Glasziou, 2009). Choosing appropriate outcomes to measure and report on in clinical trials is an area of research with many challenges, highlighted extensively by clinicians and researchers in various fields (Gargon et al., 2014; Gargon, Gorst, et al., 2019). Inconsistent use of outcome measures from one research study to another, creates barriers to comparing, contrasting, and combining the findings when bringing evidence together in systematic reviews (Clarke and Williamson, 2016). Furthermore, the views and priorities of clinicians and researchers are not necessarily shared by healthcare users and/or their significant others (Young and Bagley, 2016). If researchers choose to measure outcomes that bear little relevance to healthcare users, their studies could be contributing to research waste (Chalmers et al., 2014).

The National Institute for Health and Care Research (NIHR) has recently awarded £800 million to 20 Biomedical Research Centres (BRCs) across England to support innovative research (NIHR, 2022a). To ensure appropriate use of funds, and to avoid research waste; future clinical triallists must consider their chosen reported outcomes carefully (Yordanov et al., 2018), and in terms of importance and relevance to all key stakeholders too (Gorst, Gargon, Clarke, Blazeby, et al., 2016).

An editorial in the field of dermatology discusses how choice of inappropriate outcomes can over-/under-estimate, or miss the benefits of an intervention, therefore triallists should choose valid and comparable endpoints when designing clinical trials. (Schmitt, 2015). There is therefore a need for ongoing review and evolution of the adopted core outcome sets. In the field of rheumatology, the OMERACT (Outcome Measures in Rheumatology) initiative have developed patient-centric, reliable, valid, and responsive outcome measures to accurately assess the domains in a core outcome set for myositis, a rare condition that causes weak, painful, or aching muscles (Regardt et al., 2019). However, further work done by an OMERACT myositis working group identified five additional core domains that can best reflect the life impact of adults living with myositis (Esfandiary et al., 2020). A subsequent review (Gregory and Saygin, 2022) identified and assessed the psychometric properties of available measures for the five additional domains suggested by the Esfandiary et al. (2020) working group. This is an example where collaborative work within the same field helped with the evolution of the core outcome set and choice of measurement instruments for myositis.

Monitoring and reporting of adverse events rigorously is crucial for evidence synthesis and for informing future decision making (Peryer et al., 2022). In the CROSSSD core outcome set the Adverse events outcome domain did not meet the criteria for inclusion. Every healthcare intervention is associated with a risk of harms that should be balanced against therapeutically beneficial outcomes. Despite this, a systematic review showed that reporting of harms data in randomised controlled trials across a range of clinical specialties failed to meet the Consolidated Standards of Reporting Trials (CONSORT) harms criteria (Hodkinson et al., 2013), and are rarely reported in

trials of SSD interventions (Kitterick et al., 2016). There may be several reasons for this, including the possibility of a mismatch between investigator-led assessment of harms and the experience of patients. Harms might be misreported because they are highly diverse, they might be documented in the trial yet under-reported by investigators or influenced by sponsors, and short-term follow-up might fail to identify long-term harms. In our study, we noted that most clinical researchers recognised the importance of reporting adverse events, but fewer healthcare users and healthcare professionals did so.

There is no standard way for handling adverse events during core outcome domain set development and different teams have taken different approaches. Some, like CROSSSD, are purely driven by the consensus process (Allin et al., 2019; Beuscart et al., 2018; Callis Duffin et al., 2018); whereas others are driven by panel discussions (Balakrishnan et al., 2019). Others agreed that adverse effects should be reported as per good clinical practice guidelines and are thus relevant to all clinical trials, so fall outside of the core outcome domain set concept (Haywood et al., 2018). A similar situation to the CROSSSD study arose in the development of multiple core outcome domain sets for tinnitus trials, in that all outcome domains related to intervention-related benefits rather than harms (Hall, Smith, Hibbert, et al., 2018). However, the authors were explicit in highlighting the importance of assessing and reporting harms regardless of their inclusion in the core outcome domain set or not. There is no apparent rationale for why an equal emphasis should not also be put on assessment and reporting of harms in trials of SSD interventions, both to promote patient safety, good clinical practice, and adherence to the CONSORT recommendations (Hodkinson et al., 2013). Although this approach is advocated, there are multiple challenges in implementing these recommendations including high diversity in the number and type of possible adverse effects, as well as variation in their definition, methods of ascertainment, incidence and time-course (Peryer et al., 2022).

The Cochrane Handbook for Systematic Reviews of Interventions also highlights that poor standardisation and usage of adverse effects terminology in published study reports is a hindrance (Peryer et al., 2022). In our systematic review (Katiri, Hall, Killan,

et al., 2021), the terminology used by triallists included adverse effects, adverse events, serious adverse event, and procedure or device-related adverse effects (see Additional file 7 in the published paper). The Cochrane Handbook for Systematic Reviews of Interventions, version 6.3 (Section 19.1.1) use the term adverse event for 'an unfavourable or harmful outcome that occurs during, or after, the use of a drug or other intervention, but is not necessarily caused by it', and an adverse effect (or harm) as 'an adverse event for which the causal relation between the intervention and the event is at least a reasonable possibility'. Primary and secondary adverse effect(s) should be pre-defined, as other outcome domains would, and be monitored and reported on throughout the duration of the study. They suggest ways forward for systematic reviewers including pre-specifying their approach of reviewing adverse effects in their protocol, and being mindful that adverse effect(s) data is often handled less rigorously than the primary outcomes, so to be aware of poor case definition, inadequate monitoring, and incomplete reporting when synthesising data. Adopting the Cochrane suggestions, such as pre-defining and including primary and secondary adverse effect(s) in systematic review protocols will improve monitoring and reporting in the hearing research field too.

The field of hearing research is no exception to diverse and inconsistent outcome reporting (Hall, 2018). Some fundamental concepts and challenges facing outcome measurement in healthcare practice and hearing research have been illustrated with three case studies in the areas of (i) mild-to-moderate hearing loss, (ii) tinnitus, and (iii) single-sided deafness (Hall, Kitterick, et al., 2019). Discussion of the three case studies demonstrated the considerable heterogeneity in outcome reporting in hearing research trials. The authors also highlight the importance of critical thinking about the choice of measures, rather than selecting measurement instruments based simply on their popularity or accessibility. The SSD case study focuses on the need to target specific health domains that are suitable for use as outcome domains in the context of clinical trials, and that are relevant and important to the health and wellbeing of the SSD patient group specifically.

According to ClinicalTrials.gov (Accessed 20/11/2022), there are 38 registered clinical trials worldwide, which are active and/or recruiting adult participants with SSD. Four are being delivered in North America and are currently actively recruiting participants (Crosson, 2022; Dunn et al., 2022; Sun, 2021; Young et al., 2020). Examples of the primary outcome measures they are capturing are: (i) speech recognition in quiet using the percent correct on Consonant-Noun-Consonant (CNC) words and phoneme (Crosson, 2022; Sun, 2021), (ii) speech recognition in noise assessed using the percent correct on AzBio with multi-talker babble at 8 dB signal-to-noise ratio (SNR) (Sun, 2021), (iii) speech in noise (noise not specified) with AzBio sentences when speech is presented to the front and noise is presented to the acoustic hearing (contralateral) ear (Dunn et al., 2022; Young et al., 2020), and (iv) sentence scores in noise with three speaker configurations using the Bamford-Kowal-Bench Sentence in Noise test (BKB-SIN), presented at 65 dBA with the level of noise varied stepwise at fixed signal-to-noise ratio to obtain a Speech Reception Threshold (SRT) where participants are able to repeat key words 50% of the time (Crosson, 2022). Examples of how patient reported outcomes are measured include the (i) Spatial Hearing Questionnaire, (ii) Tinnitus Handicap Inventory, (iii) Abbreviated Profile of Hearing Aid Benefit, (iv) Health Utility Index, and (v) Speech, Spatial, and Qualities of hearing scale. None of the four clinical trials are using the same outcome measures or measurement instruments. Only one trial stated that it is capturing procedure and device-related adverse effects (Crosson, 2022). The time scales of capturing outcomes vary from 6 to 36 months post introduction of the intervention. Lack of consistency in reported outcomes, and how they get measured, can make evidence synthesis difficult, therefore translating clinical trial outcomes to clinical practice becomes challenging. Clinical decision making by health providers relies on careful consideration of both benefits and harms, but they often face the problem of making decisions based on insufficient, or overload of often contradictory information. These challenges would be overcome if the CROSSSD initiative core outcome domain set and the available recommended measurement instruments for each outcome domain are adopted in the field of SSD.

Outcomes that assess an individual's well-being and overall health are also relevant but less often measured in SSD intervention trials (Kitterick et al., 2015). Kitterick et al.

(2016) reviewed studies evaluating the effectiveness of SSD interventions identified that outcome selection has been somewhat biased towards assessing functional impairments for which measures are readily available and widely used, (e.g., speech perception testing in noise, and localisation tests). However, there is a diversity in patient complaints, and the impact of hearing loss is individualised and is personal (Hall, Kitterick, et al., 2019). For example, qualitative work has highlighted that a healthcare user with SSD might be dealing with a variety of consequences that SSD imposes such as (i) knowing which direction traffic is approaching from (functional consequence), (ii) feeling guilty if they had missed what someone had said to them (psychological consequence), or (iii) reduced willingness to interact with others and participate in social situations since the onset of their SSD (social consequence) (Lucas et al., 2018). The core outcome domain set for SSD has incorporated all relevant stakeholder views during our consensus process, and our follow-up focus groups ensured that the core domains were conceptualised appropriately for the follow-up assessment of available measurement instruments. If future clinical triallists adopt the core outcome set for SSD, they will be ensuring that they capture all important consequences that can have an impact on the health and wellbeing of those diagnosed with SSD. Furthermore, when designing future SSD intervention clinical trials special consideration should be placed on outcome domains that nearly made it into the COS (Listening effort, One-to-one conversation in general noise, Being aware of a sound, Device usage, and Listening in complex situations). Particular attention should be paid to the Device usage outcome domain, which was deemed important by several stakeholders and was discussed elaborately during the consensus meeting.

A critical methodological feature that addresses risks and confounds biases in clinical trials is blinding. It is challenging to implement double-blinded (both participant and researcher are unaware of intervention allocation), or even single-blinded (participant is unaware of intervention allocation), in the field of device-based SSD interventions. This is because, for both rerouting and restoring interventions, the devices need to be individually fitted, therefore the healthcare professional is un-blinded and the healthcare user needs to consent to getting fitted with a device, of which a few require surgical implantation. Munro et al. (2021) provide an overview of the design, analysis,

and conduct of clinical trials for adults with hearing loss, with particular focus on improving the quality of such trials. Use of placebo hearing aids, where the characteristics of the devices are concealed to maintain blinding is a possible solution, although, they do discuss the challenges of introducing blinding in trials of medical devices and surgical interventions (Munro et al., 2021).

The use of both objectively and subjectively collected outcome measures in clinical trials, provide greater sensitivity and interpretability than a single measure (Munro et al., 2021). The three outcome domains included in the CROSSSD study COS, according to their definitions, can only be assessed subjectively. A randomised controlled trial aiming to compare the objective and the subjective assessments of hearing aid use in adults aged ≥60 years (Solheim & Hickson, 2017); demonstrated a significant inconsistency in datalogging records (mean = 6.12 hours, SD = 4.94), versus self-reports (mean = 8.39 hours, SD = 5.07). Persistent, long-term hearing aid use was also measured based on battery re-order data and compared to subjective data, although going forward, re-chargeable devices and use of devices alongside assistive devices or connected to mobile phone technology can have implications on battery re-order data measures (Zobay et al., 2021). Device usage, despite not making it into the COS, could be an outcome domain that can be measured objectively to consider in future SSD intervention trials. Listening effort is another outcome domain that nearly made it into the COS and could be measured objectively using pupillometry (Naylor et al., 2018), which has also been trialled recently in a cohort of bone conduction hearing aid users (Gawęcki et al., 2022).

In the field of hearing sciences, and otology, there is several COS developed or under-way (Fackrell et al., 2017; Heffernan et al., 2017; Smith et al., 2021). Collaboration and coordination between the various COS developers in the field would be advantageous, particularly when making recommendations to future clinical triallists for measurement instruments to adopt. For example, adopting strategies like the ones taken by the Red Hat Group (Gargon et al., 2018), can help with defining outcome domains and sharing knowledge that can increase efficiency. Learning from other fields, like dermatology (HOME) and rheumatology (OMERACT) who developed a

coherent strategy for COS development in their fields over the years has proven effective in developing, implementing, and reviewing their COS.

6.4 Translation of clinical trials findings to clinical practice

The need to present clear, useful and understandable information to healthcare users seeking interventions in the clinical setting has been highlighted in the context of surgical interventions (Main et al., 2017). The aforementioned challenges of outcome measurement and reporting (Section 6.3) hinder our ability to compare or synthesise evidence and make informed decisions about the optimal intervention for each individual with SSD (Hampton et al., 2022; Munro et al., 2021). When found in a position to choose an intervention for their SSD, patients find it very challenging to decide which one might be best for them, and rely on information provided by clinicians (Underdown and Pryce, 2022). But how do clinicians know which intervention is ideal, and for whom (Hall, Kitterick, et al., 2019)?

Adequate information sharing by clinicians was identified as an enabler for adoption of effective coping strategies and take-up of hearing aids and auditory implants (Lucas et al., 2018; Underdown and Pryce, 2022). Qualitative studies involving healthcare users in an oncology setting demonstrate that healthcare users show preference for basic information, and not all wanted further information at all stages of their journey (Leydon et al., 2000). Similar to the findings in Underdown and Pryce (2022), participants in oncology settings in Leydon et al. (2000) reported that 'faith' in their healthcare professional's expertise precluded them from seeking further information themselves. Underwood and Price (2022), discuss the complexity of decision making in the field of SSD and reiterate the importance of provision of simple, understandable information by clinicians, for example using a decision aid tool; to help healthcare users with SSD decide on uptake of SSD interventions.

Dodd et al. (2020) sought to determine the degree of overlap between outcomes within core outcome set for research and routine care in type 2 diabetes mellitus. They scrutinised relevant guidelines such as those from the European Medicines Agency

(EMA), Food and Drug Administration (FDA), and National Institute for Health and Care Excellence (NICE) to find that in this field, core outcome sets for research and core outcome sets for care were almost identical and largely concurred with the outcomes featured in drug regulators' guidelines (Dodd et al., 2020). They suggest that collection of routine clinical data used to monitor health provision should be guided by the priorities of healthcare users and clinicians, to ensure auditing of services is guided by the most important outcomes for all stakeholders involved. Another study is under way, aiming to assess the degree of concordance between outcomes recommended in COS for research undertaken during 2015-2019, and in guidance provided by the FDA and EMA (Dodd et al., 2021). Similar work in the field of audiology and/or ENT interventions would be beneficial. In fact, a success story in the field of paediatric audiology is the implementation of a minimum speech test battery developed by a working group comprised of clinicians, scientists, and industry representatives (Uhler et al., 2017) that was incorporated into the most recent guidelines for determining cochlear implant candidacy in children (Warner-Czyz et al., 2022). In the field of SSD interventions, future directions should include expanding on the work done by Van de Heyning et al. (2017) that proposed a unified clinical assessment protocol for cochlear implantation in SSD, to incorporate the CROSSSD initiative core outcome domain set for both rerouting and restoring SSD interventions.

To address the needs of individual healthcare users, and to ensure only critical information to inform understanding is shared in the clinical setting, a core information set has been developed in colorectal cancer surgery (McNair et al., 2019). This consensus study modified the Williamson et al. (2017) core outcome set development methods for the development of their core information set. In summary, their process included (i) compiling a long list of potential information of importance from existing systematic reviews and available qualitative data, and categorising it into domains, (ii) using Delphi methods to survey stakeholders' views on the importance of each domain, and (iii) hold a stakeholder consensus meeting to finalise the core information set. Recommendations could then be made about the points to always discuss in a healthcare user-clinician interaction in the healthcare setting, and to guide production of high-quality written information leaflets in the field of colorectal cancer

(McNair et al., 2019). A similar concept has been followed by a team that developed a core information set for healthcare users undergoing radiotherapy for rectal cancer (Kunneman et al., 2015) and for oesophageal cancer surgery (Blazeby et al., 2015). There is no core information sets developed in the field of hearing, and qualitative studies indicate that it could be beneficial for the SSD cohort (Underdown and Pryce, 2022).

6.5 Uptake of core outcome sets

The end user (healthcare user) of clinical trial results will only benefit from the core outcome set only if clinical triallists measure the agreed core outcomes in their trials. The COMET initiative advocates for uptake and implementation plans to be made during the development process of the COS (Williamson et al., 2017). The COMET handbook suggests (i) registration of intention to develop a COS on the COMET registry, (ii) dissemination through publications and conferences, (iii) liaison with funders of research, guideline producers, relevant commercial organisations, (iv) register relevant systematic reviews on PROSPERO (International prospective register of systematic reviews), and (v) compose editorials or commentaries about the COS in relevant journals. The Red Hat Group was formed at the COMET VII meeting in Amsterdam in 2018 and aims to work with other initiatives including OMERACT, CS-COUSIN, COSMIN and SONG on a project to share knowledge and understanding of mechanisms to promote uptake of COS in comparative effectiveness research (Gargon et al., 2018).

Engagement with triallists via interviews and surveys has demonstrated that the main facilitators of uptake relate to awareness and understanding of the COS (Bellucci et al., 2021; Hughes et al., 2022; Matvienko-Sikar et al., 2022). For example, the Bellucci et al. (2021) survey analysis including 62 clinical triallists identified barriers to using a COS to be (i) poor knowledge about the COS, (ii) difficulties identifying a relevant COS, and (iii) perceptions that a COS can be restrictive, often containing too many outcomes, whereas clear understanding of the COS and perceived importance were identified as enablers to use of the COS. Survey participants included two (3.2%) from the Ear,

Nose, Throat (ENT) research area. Hughes et al. (2022) performed semi-structured qualitative interviews with 13 UK-based NIHR-funded chief investigators from a variety of clinical areas and variable expertise, who had experience of issues that might affect COS uptake. Common enablers to the Bellucci et al. (2021) findings included awareness and understanding of the COS. They also identified recommendations to use COS from funders and journals as an enabler, whereas barriers included (i) the perceived characteristics of the COS (e.g., increasing patient burden, recommendations becoming outdated), and (ii) the COS development process (e.g., not including all specialties who will use the COS) (Hughes et al., 2022). There was no hearing research / ENT field investigators in the group recruited by Hughes et al. (2022).

The NIHR Health Technology Assessment (HTA) programme[13] funds healthcare research concerning clinical interventions and their cost-effectiveness. HTA funds a variety of studies including primary research, evidence synthesis, or feasibility and pilot studies, assessing the broader impact of interventions and tests, for those who plan, provide or receive care from the NHS, and social care services. Making HTA and other healthcare research funders aware of the importance of adoption of the CROSSSD core outcome set will ensure that all future HTA-funded SSD intervention studies incorporate the COS in their protocols.

A recent review suggests that COS uptake in new studies and systematic reviews needs improvement (Williamson et al., 2022). In the field of rheumatoid arthritis clinical triallists adopted a COS in 80% of recent drug trials. They attribute the 80% adoption to (i) working closely with trialists, regulators, and other stakeholders throughout the process, (ii) long-standing active outreach and engagement, and (iii) demonstrating what is possible with awareness, motivation, recognition by regulators, and deliberate dissemination (Kirkham, Clarke, et al., 2017). For CROSSSD we (i) engaged widely with all relevant stakeholders using multiple strategies (e.g., personal email communication, blogs, news pieces on healthcare users' support websites), (ii) have kept our stakeholders engaged throughout the process (e.g., peer reviewed publications,

[13] https://www.nihr.ac.uk/explore-nihr/funding-programmes/health-technology-assessment.htm

updates in professional magazines, a dedicated CROSSSD Twitter feed), (iii) deliberately engaged with multiple stakeholders internationally (e.g., created the CROSSSD recruitment and dissemination videos, linked in with manufacturers of devices and journal editors).

It has been suggested that identification of appropriate outcome measurement instruments for the outcome domains identified in the COS is important for adoption of the COS (Williamson et al., 2022). In cancer surgery core outcome sets for example, including gastric, oesophageal, colorectal, prostate, and oropharyngeal, no recommendations have been made on measurement instruments, which can be a barrier to adoption in future trials (Alkhaffaf and Kirkham, 2022). Despite published steps on identifying relevant PROMs for measurement by COSMIN (Prinsen et al., 2016) the road is less well-paved for identification of suitable clinical measures in the context of core outcome sets. The Cochrane Screening and Diagnostic Test Methods Group has developed resources that help summarise the evidence about test accuracy, which can be used (Cochrane, 2022). Clarifying the outcome domain concepts, and developing clear and elaborate definitions to be operationalised can be challenging, as demonstrated by the COMiT'ID follow-up study (Fackrell et al., 2017). Web-based discussion forums helped the COMiT'ID group operationalise the majority of their COS outcome domains (Hall, Smith, Hibbert, et al., 2018), but a complex concept of tinnitus intrusiveness proved challenging, were variability of viewpoints transpired (Hibbert et al., 2020). To date, there are no measurement instruments recommended by the COMiT'ID group. However, work is under way to identify existing measuring instruments assessing 'concentration' as a core outcome domain for sound-based interventions for chronic subjective tinnitus in adults (Shabbir et al., 2021). There is recognition that facilitators to moving this field forward include multi-disciplinary collaborations, and standardisation of research methods including tinnitus assessment (Simoes et al., 2021). These suggestions have been taken on board, for example UNITI (Unification of Treatments and Interventions for Tinnitus Patients), an EU-funded collaborative multi-center randomized clinical trial aims to systematically examine established tinnitus therapies and personalised treatment approaches both alone and in combination in a large sample of tinnitus patients (Schoisswohl et al., 2021).

The CROSSSD study has involved international stakeholders and engaged with influential clinicians and scientists in the field as members of the steering group since the inception of the study. Adoption of various methods of engagement and dissemination has been constant throughout the study. Domain conceptualisation and available measurement instrument assessment has been conducted to make recommendations on suitable available measurement instruments in the SSD field to use. The lead author (RK) is also involved in the development of practice guidelines for adults with SSD, as a member of the British Society of Audiology (BSA) bone conduction and middle ear devices special interest group.

6.6 Overall strengths and limitations

The CROSSSD study's approach to develop a core outcome domain set for SSD interventions in adults using COMET initiative recommendations (Williamson et al., 2017) proved effective. Effectiveness was demonstrated by low attrition rates at the e-Delphi surveys stage, as well as positive participant feedback; although a possible limitation is that only 43.4% (n=95) participants responded to the feedback questionnaire. The recommended outcome domains are deemed critically important to measure by all stakeholders. The methodological approaches used at all stages of the study ensured that all opinions were considered, and the resulting decisions were not biased towards clinical researchers or healthcare professionals' views.

Despite efforts to fully represent stakeholders internationally (e.g., recruitment strategies linking in ENT and audiology global ambassadors, professional bodies, charities, and the CROSSSD steering group representatives), recruitment for low- and middle-income countries was limited. This is an acknowledged challenge in core outcome domain set development, and previous studies have recommended that geographical and income-based differences should be considered in outcome prioritisation (Lee et al., 2020). In the current study, the use of a web-based e-Delphi approach aimed to eliminate barriers to participation and specific attention was given to recruiting stakeholders for the web-based consensus meeting from various backgrounds. Given that most published clinical trials of SSD interventions have been

conducted in North America, Australia, and Europe, and the CROSSSD study was focused on developing a core outcome domain set for clinical trials, the sample of participants involved in developing the core outcome domain set is representative of the geographical regions in which most future research on SSD interventions is likely to take place. Future reviews on the uptake of the COS should monitor this, to appraise whether for instance reduced contribution from certain geographical regions during the COS development is negatively correlated to uptake. Further work that includes identifying and appraising measurement instruments to assess the outcome domains in the core outcome domain set should ensure that accessibility is considered as part of that process (e.g., to assess comprehensibility of a PROM by various stakeholders from diverse geographical regions). The quality of care in maternity services in low- and middle-income countries has been assessed with the development of a maternity PROM (Dickinson et al., 2022). The steps included (i) conducting a systematic review of PROMs for use in pregnancy and childbirth (Dickinson et al., 2019), (ii) development of themes from data collected in Malawi and Kenya, (iii) construction of draft PROMs, and (iv) pre-testing the draft PROM in Malawi and Kenya before (v) finalising the proposed PROM (Dickinson et al., 2022).

Although the study recruitment strategy sought to engage a diversity of participants, there was a predominance of CROS aid healthcare users, audiology healthcare professionals, and female participants. These reflect real-world imbalances in current clinical practice. With respect to healthcare users, the greater numbers of CROS aid users is not surprising, since this device is the longest standing, non-surgical remediation solution for SSD (Harford and Barry, 1965; Snapp, 2019). With respect to healthcare professionals, in many of the participating countries, audiologists are the first point of call for SSD interventions because they assess, counsel, and rehabilitate hearing aid and auditory implant users (Underdown and Pryce, 2022). Nevertheless, the consensus meeting participants who discussed the short-listed outcome domains and voted on the final core outcome set were representative of the diversity of the stakeholder characteristics, so it is unlikely the final COS would have been different should all the e-Delphi groups were more balanced.

International and diverse health profiles are encouraged to ensure validity and generalisability of study findings (Redwood and Gill, 2013), but participants recruited for the conceptualisation study were predominantly white British living in England. Whilst a limitation, meaningful participation is also important, so recruiting engaged volunteers who had an in-depth understanding and awareness of the study, and were actively involved in the consensus meeting was deemed key, as per other COS developers suggestions (Chevance et al., 2020; Gargon, Williamson, and Young, 2017). No tangible difference was noted in the concepts discussed by the first focus group (all British, all male participants) and the second group (all non-UK European, predominately male participants). It is therefore unlikely that that sampling bias has had any implications for the conceptualisation data collected in the CROSSSD study.

Historically, studies have under-represented female participants and most research data have been collected from males and generalised to other genders (Liu and Mager, 2016). But this brings challenges, for example, females tend to wait longer than males for a diagnosis or pain relief (Chen et al., 2008), so being under-represented in pain studies has implications on the generalisability of the results. A recent Australian study identified that females are still under-represented in cardiology and nephrology studies, but over-represented in psychiatry, care of the elderly, and orthopaedic studies (Merone et al., 2022). It is well-recognised that there should be implementation of best practices for health care research across genders, and to establish gender specific evidence based guidance if applicable (Holdcroft, 2007; NIHR, 2020).

Participants commented on the clarity of definitions and choice of language used. Despite involving public research partners from the inception of the current study, as per recommended standards (Williamson et al., 2017), and having the outcome domain definitions reviewed by the study management team and steering group representatives, we observed there was still ambiguity detected by participants during both the e-Delphi surveys and consensus meeting. This challenge was also noted by others (Smith et al., 2018) who co-produced plain language descriptors and introduced additional examples to their definitions. Further work by Hibbert et al. (2020) in the

same area, the COMiT'ID study, demonstrated how concepts can be challenging to define, (e.g., tinnitus intrusiveness) although they run their study on web-based forums as opposed to face-to-face focus groups. Another example that demonstrates the challenge of defining outcomes is shown by a systematic review in the field of dermatology that found that concepts such as 'eczema flare' has been defined heterogeneously in the literature (Langan et al., 2014). A systematic review including 132 COS development studies demonstrated difficulties in defining unique outcomes in various other fields; where researchers reported different definitions for the same outcome across trials within the systematic review (Young et al., 2019). One suggestion to overcome this methodological challenge is to bring COS researchers together to undertake collaborative work to refine and validate a definition for a unique outcome. Future core outcome domain set developers could also seek feedback on the clarity of definitions from a larger number of stakeholder representatives internationally (e.g., via charities or professional bodies in various fields) to address any ambiguity, prior to distributing Delphi surveys to participants. A centralised outcome domain definition depository could be created for example, if the COMET initiative that holds a registry of all COS development projects could bring collaborators together.

Although authors have recommended offering participants a range of flexible times for consensus meetings, to allow for environment choice, for example, to fit around family timetables (Daniels et al., 2019; Dodds and Hess, 2021; Howells et al., 2017); this was not feasible in the CROSSSD study. The nominal group technique needed to be implemented during the web-based consensus meeting, and voting had to be conducted in real time. However, the modifications we have described contributed to ensuring participants felt at ease and promoted positive group dynamics (Katiri, Hall, Hoare, et al., 2021), as per other qualitative study recommendations (Daniels et al., 2019; Flynn et al., 2018). Examples of helpful approaches that were adopted include seeking input from public research partners during the meeting preparation, drawing in perspectives based on lived experience of SSD (Williamson et al., 2017; Young and Bagley, 2016); and providing detailed pre-meeting documentation informing participants about the process (Olsen, 2019), setting clear expectations (Smith et al., 2018) and explaining the minimum participant requirements (Daniels et al., 2019).

Gorst et al. (2021) have developed a list of issues to consider for web-based consensus meetings that suggest reducing the duration of the meeting between 2 to 4 hours, and perhaps repeating it if necessary. A shorter meeting might allow more flexibility for participants joining internationally. To achieve an effective shorter meeting Gorst et al. (2021) suggest sharing multiple participant resources, and resolving participant queries beforehand; or even asking participants to complete surveys in advance of the meeting to indicate the main points they would like to discuss. Agreed recommendations were directly relevant to many of the CROSSSD study participants' feedback findings including the need for careful pre-meeting preparation, setting expectations to achieve less than would be possible face-to-face, considering equity of engagement, ensuring the chairperson is strict with timings, and allowing time at the end for debriefing and reflection (Gorst et al., 2021).

6.7 Future directions

With regards to measurement instrument identification, one of the steps in the instrument assessment recommendation guideline (Prinsen et al., 2018) is a comprehensive literature search to identify all existing measurement instruments. Although we completed an SSD-related systematic review of measurement instruments (Katiri, Hall, Killan, et al., 2021), in the absence of a fully relevant and comprehensive measurement instrument for the *Impact on social situations* domain it would be worth expanding the literature search to instruments used in other fields of hearing research, and beyond, prior to developing a new measurement instrument. There is increasing evidence that hearing impairment in general is having an impact on social well-being, including social engagement, social roles, and can impede relationships and social well-being (Barker et al., 2017; Dawes et al., 2014; Heffernan et al., 2022; Pierzycki et al., 2020; Vas et al., 2017). This suggests that development of a tailored measurement instrument for the SSD interventions field, or all hearing-related interventions trials is warranted.

Further quality assessment of the identified or newly developed measurement instruments should be performed, to incorporate aspects such as sensitivity to change

in the context of clinical trial time-scales (Mokkink, Terwee, Patrick, et al., 2010b). Another aspect to assess is feasibility, i.e., can the measurement instrument be applied in future SSD clinical trials, given time and financial constraints, as well as interpretability (Schmitt et al., 2015). Feasibility captures pragmatic aspects beyond the classic psychometric properties of measurement instruments, for example, can the measure be applied easily, given time and financial constraints (Boers et al., 1998)? Interpretability is described as 'the degree to which one can assign qualitative meaning to quantitative scores' (Boers et al., 1998), but it also incorporates an assessment of floor and ceiling effects, and minimal important change (Schmitt et al., 2015). High quality validation of the chosen measurement instrument(s) for the COS is recommended with design of prospective studies if deemed necessary (Hall, Szczepek, et al., 2015).

Suggestions have been made for the most suitable PROMs to adopt (i.e., 'the how' to measure) to assess the recommended outcome domains, and which ones should be avoided. The SSQ-12 (Gatehouse and Noble, 2004) or the SSQ-18 (Noble et al., 2013) questionnaires proved to be a good interim choice of a PROM to utilise in future clinical trials, until a tailored, more suitable measurement instrument is developed for each of the individual outcome domains. One consideration for clinical trial developers is to collect data on reliability and validity for the SSQ questionnaires, and the other short-listed PROMs, as these steps will help inform whether they are measuring domains of interest for the SSD population.

The outcome domain conceptualisation process generated a list of conceptual elements for each of the outcome domains that should be considered by future measurement instrument developers when designing and validating PROMs for SSD intervention(s) clinical trials. Further assessment involving healthcare users, to ascertain whether they feel that all aspects of the outcome domains are covered with the short-listed PROMs, and that the items are clear, and not subject to significant misinterpretation, would be beneficial. For instance, cognitive interviews which are often used in questionnaire development might be applied (Willis and Artino, 2013). Cognitive interviewing entails engaging with individuals with lived experience of a

condition, administering the PROM to be assessed, and conducting interviews with them before, during, and after they complete the questionnaire. This process can provide quality assurance for the specific PROM, for comprehensibility of the PROM by those with SSD for example (Terwee, Prinsen, Chiarotto, Westerman, et al., 2018).

An ongoing challenge facing researchers, funders, clinicians and policy makers globally is adoption of translational research (Mosedale, Geelhoed, et al., 2022). A recent review suggests that COS uptake can be low in most research areas (Williamson et al., 2022), with most common barriers being not including all relevant stakeholder representatives in the COS development process and not making recommendations on measurement instruments for the domains in the COS. The CROSSSD study group endeavoured to break down these barriers using robust stakeholder engagement methods and making recommendations on measurement instruments. One suggestion going forward, is to adopt a realist evaluation to help understand how the research translation process contributes to health system sustainability and value-based healthcare (Mosedale, Hendrie, et al., 2022). Williamson et al. (2022) suggest a 'bottom up' approach to research translation, which can yield positive outcomes across impact domains in a COS, including advancing knowledge, collaboration and capacity building as well as contributing to changes in policy and practice. The work proposed by Dodd et al. (2021) to review the representation of published core outcome sets for research in regulatory guidance would help achieve the final step on the CROSSSD study roadmap (i.e., Step 4, Figure 6-1).

6.8 Final summary

The CROSSSD study, and the work reported on in this thesis, has contributed to the goal of bringing together relevant international stakeholder representatives in the field of SSD, to discuss outcome measurement for hearing interventions. We have adopted the COMET and COSMIN initiatives methodological recommendations to comprehensively review and assess outcome measurement in the SSD field. The CROSSSD study COS development process brought experts in SSD by experience and profession together for the first time, to develop an international consensus on

outcomes to measure in future clinical trials. The COVID-19 pandemic presented a need and opportunity to introduce and evaluate a web-based consensus method involving hearing-impaired participants. Our findings indicate that it is feasible to conduct successful web-based consensus exercises with multi-stakeholder groups using audio-visual virtual meeting technology. We anticipate that the methodological changes made, and the lessons learned are more widely applicable to other forms of research that require consensus-based decision making and are not necessarily limited to COS development studies. We have also developed recommendations on suitable measurement instruments to adopt, and what important concepts future measurement instrument developers should incorporate in tools developed specifically in the field of SSD. Finally, study awareness, results dissemination and publicity, promotion of adoption and implementation of the CROSSSD study COS for SSD interventions was an ongoing and integral part of our work. The work undertaken and shared as part of this study has made a valuable contribution to the field of SSD and future research studies.

Reflective statement

I am the eldest of a pair of twins, and have five siblings. I was born into a middle-class family in Cyprus, a decade after my dad's family was displaced to the outskirts of Nicosia due to the Turkish invasion in Cyprus in 1974.

None of my grandparents graduated secondary school, and neither of my parents were able to go to university. They were determined though that all six of us would have the opportunity to avail of higher education if we wanted to. So they worked tirelessly to give us access to good schooling, English language lessons, art, dance, and swimming classes, and private tuition for physics and maths when it was needed.

So when in September 2002, I found myself at the Gower Street entrance of University College London (UCL) for fresher's week I was in awe. I was always an average student with regards to academic achievement, and although I had graduated from a well-respected private secondary English school in Nicosia I was anxious about facing this vast new world.

Despite the ups and downs of being a BSc student, taking in all the cultures and ways of life in London, my BSc in Speech Sciences course was an excellent base for what was to come. I learnt about basic anatomy and physiology, neurophysiology, the complexity of linguistics, the importance of phonetics and psychoacoustics, that statistics are critical, and the role of hearing in our functioning, participation, and health.

Like most audiologists I know, I 'fell into' audiology when Professor Stuart Rosen who supervised my BSc research project on speech intelligibility in cochlear implant users suggested I applied for a funded MSc in Audiology degree at the University of Manchester. I had missed the deadline but he had a colleague he could speak to, if I could go up to Manchester to visit them. And so I did. Next thing I know, I was enrolled

at the University of Manchester for the MSc degree and a subsequent work placement year to earn a clinical competence certificate.

I was fortunate to be taught clinical audiology skills by experienced, knowledgeable, kind, generous, thoughtful, interested and interesting colleagues in clinics around Manchester. I realised the breadth and depth of audiology was vast, and how this work can interlink science and everyday people's lives perfectly!

I was excited and nervous in equal measures commencing my first basic audiologist job in London at the Royal National Throat Nose and Ear Hospital on Gray's Inn Road. Adult diagnostics team. I always had it in my mind that I would work in rehabilitation. That's what the educational advisor said to me when I completed a career aptitude and assessment test in my final year at school. So finding myself in a clinical environment where I was supposed to filter out 'what it is not' and 'what it is' that is causing a problem, and what to do next, was surreal. How did I enjoyed those years, soaking in all the knowledge and practical skills from my colleagues, learning how to be in a working environment, interacting with the general public, and realising how much more there's out there to learn. My audiological skills were cultivated and made friends for life.

When the opportunity arose four years later to go to Dublin for a year I was hesitant. I was happy in adult diagnostics. I belonged in a large supportive, progressive team. I was given access to all the professional learning opportunities I wished for, I progressed to a senior audiologist post. I had just gotten onto the property ladder. Yet, the idea of going to Dublin was intriguing and attractive.

I got a sabbatical from my NHS job and all parts aligned, so I found myself at Temple Street Children's Hospital in Dublin. The change was hard. The public system dissimilar to what I had known. The team smaller. The culture different. I did not enjoy working in paediatrics as much as I thought I would.

But when the time came to return to the UK and my current audiology job came up in adult diagnostics I decided to stay. One of the ENT consultants took the time to show me round the department before my job interview. It was in a new building, shiny, 'state of the art equipment and facilities' the job advertisement stated. There was no service, so even just rolling out the simplest of services would be progress a friend said. I was certainly apprehensive, but why not?!

A steep learning curve was ahead of me. I was the department. State of the art facilities, but no colleagues to rely on, and be guided by. I took one day at a time, I networked with UK colleagues, I asked for help when I needed it, and advice when I found myself in dead ends. I enrolled into a leadership and management development programme, and a Lean 6σ Green Belt for healthcare programme. Eventually I got an audiology colleague to join the department. I taught and learned, I succeeded and failed, I impressed and disappointed. I was learning, I was making a difference, I was finally getting the hang of it when the PhD opportunity came along.

I saw the advertisement on Twitter. Me doing a PhD? No way. I was not looking for a PhD. I have two cousins who completed PhDs but they went straight into academia after graduating from university. I was content going into work, participating in all those patient journeys, developing and shaping services, the hassle and bustle of the acute hospital floor, I was enjoying a healthy lifestyle in Dublin, and travelling the world when I could.

Pádraig and Deb said I could do it part-time from Dublin, my manager said I could change my ways of working to accommodate it. My family and friends said I could do it. It was funded, and it would be linked to my clinical interests. So, why not?!

If I knew in 2017 what I was signing up for, I would not do it! Yes it's rewarding, yes it's shaping the future of our field, yes I was privileged, and I have encountered wonderful, supportive, dedicated, kind, and generous colleagues throughout. But my god, what a challenge to balance clinical work, manage the department, change our ways of working to accommodate the pandemic, progress the PhD, and live life.

I do not know where the last five years have gone. I am not sure how I managed to complete a systematic review, write, re-write, review, re-review, publish, present, bring patients, clinicians and researchers together to develop a consensus, grow an understanding of this demanding, sometimes harsh, with slow return, nevertheless superb world of academia. I felt happy, excited, encouraged, content, motivated, committed, confident, successful, connected, courageous, and empowered; but also had moments of sadness, felt lost, unmotivated, demoralised, insecure, occasionally hopeless, and alone. I missed nights out, I missed family holidays, christenings, birthdays, and wedding celebrations, I sacrificed fun for study, I altered my ways of life, days rolled into weeks, weeks into months and years. Family and colleagues encouraged me, they stepped in to cover my clinics when I had to dedicate time to the PhD, some said a prayer and lit a candle for me, others became role models, dedicated time for weekly supervision meetings, neighbours brought me food, friends visited with flowers, others took me for a walk, some arrived with bottles of champagne to celebrate, or teabags when the times were hard. My skills improved, my confidence grew, my understanding widened.

What a privilege to have had the opportunity to bring the two worlds of clinics and research together. And how have I grown as a person, a clinician and a researcher! My existing understanding of the impact of hearing impairment and associated consequences on individuals and their communication partners was advantageous whilst setting us and delivering the PhD studies. Having a wide network of audiology colleagues both in the UK and internationally was also very beneficial; they supported me and the study, facilitated recruitment, and spread the study findings worldwide. The skills I developed whilst setting up, and shaping the departmental protocols in my clinical role were also valuable. These experiences, my diverse academic and clinical background, skills and knowledge, helped me evolve into a translational researcher. I had a deep understanding of the condition in question, and how the study findings can potentially improve the clinical outcomes in clinics around the world. Of course, there was biases too. The field of tinnitus has always been challenging for me, both academically and clinically. To ensure transparency and to eliminate personal biases I was careful to incorporate opinions and perspectives shared by the supervision team

and the CROSSSD study steering group when developing the study protocol and setting up the PhD studies. Overall, I feel that being a fairly experienced clinician at the inception of the project was beneficial in adopting a thorough, rigorous, comprehensive approach that focused on clinically relevant future end-points.

When I look back at the 18-year old Roulla at the gates of UCL, contemplating what was lying ahead, I would never have imagined that 20 years on I would be typing this. I am looking at the future with hope, confidence, excitement but also some anticipation. Will I be able to utilise all the skills and knowledge I have acquired effectively? Will there be a worthwhile return to the investment? Will I be able to do it justice? Will the right opportunities come along? I certainly hope so because I owe it to myself, my amazing supervisors and colleagues at Hearing Sciences, the audiology profession, and all those with hearing balance disorders whom I come across daily, who inspire and motivate me to do better!

I am finishing up with one of my favourite poems by Constantinos P. Cavafy (1863-1933), because the longer the journey got, the more marvellous it was, and the more privileged I felt for being part of it.

Ithaka

As you set out for Ithaka
hope your road is a long one,
full of adventure, full of discovery.
Laistrygonians, Cyclops,
angry Poseidon - don't be afraid of them:
you'll never find things like that on your way
as long as you keep your thoughts raised high,
as long as a rare excitement
stirs your spirit and your body.
Laistrygonians, Cyclops,
wild Poseidon - you won't encounter them
unless you bring them along inside your soul,
unless your soul sets them up in front of you.

Hope your road is a long one.
May there be many summer mornings when,

with what pleasure, what joy,
you enter harbours you're seeing for the first time;
may you stop at Phoenician trading stations
to buy fine things,
mother of pearl and coral, amber and ebony,
sensual perfume of every kind -
as many sensual perfumes as you can;
and may you visit many Egyptian cities
to learn and go on learning from their scholars.

Keep Ithaka always in your mind.
Arriving there is what you're destined for.
But don't hurry the journey at all.
Better if it lasts for years,
so you're old by the time you reach the island,
wealthy with all you've gained on the way,
not expecting Ithaka to make you rich.

Ithaka gave you the marvellous journey.
Without her you wouldn't have set out.
She has nothing left to give you now.

And if you find her poor, Ithaka won't have fooled you.
Wise as you will have become, so full of experience,
you'll have understood by then what these Ithakas mean.

C. P. Cavafy, "The City" from *C.P. Cavafy: Collected Poems.*

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Appendices

Appendix 1. Funding approval letter for DelphiManager software from Oticon Medical™.

oticon MEDICAL

CROSSSD Study Management Team,
FAO Dr Pádraig Kitterick and/or Roulla Katiri,
Research Theme Lead (Hearing) and/or PhD Student,
NIHR Nottingham Biomedical Research Centre,
Ropewalk House,
113 The Ropewalk,
Nottingham,
NG1 5DU.

Dear Dr Kitterick / Roulla,

Re: Funding Application for Delphi Manager Software for CROSSSD Study

I am pleased to inform you that your application through open competition for a grant of £850 + VAT to purchase the Delphi Manager Software has been successful.

To authorise payment by our accounting department we will require a copy of the Delphi Manager Software invoice to be sent to Maxine Oxford.

Upon completion of the Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) study we will require a short report on the benefit you have derived from Oticon Medical support.

Kind Regards

M Oxford

Maxine Oxford
Sales and Marketing Director UK
Oticon Medical

Oticon Medical UK
Cadzow Industrial Estate
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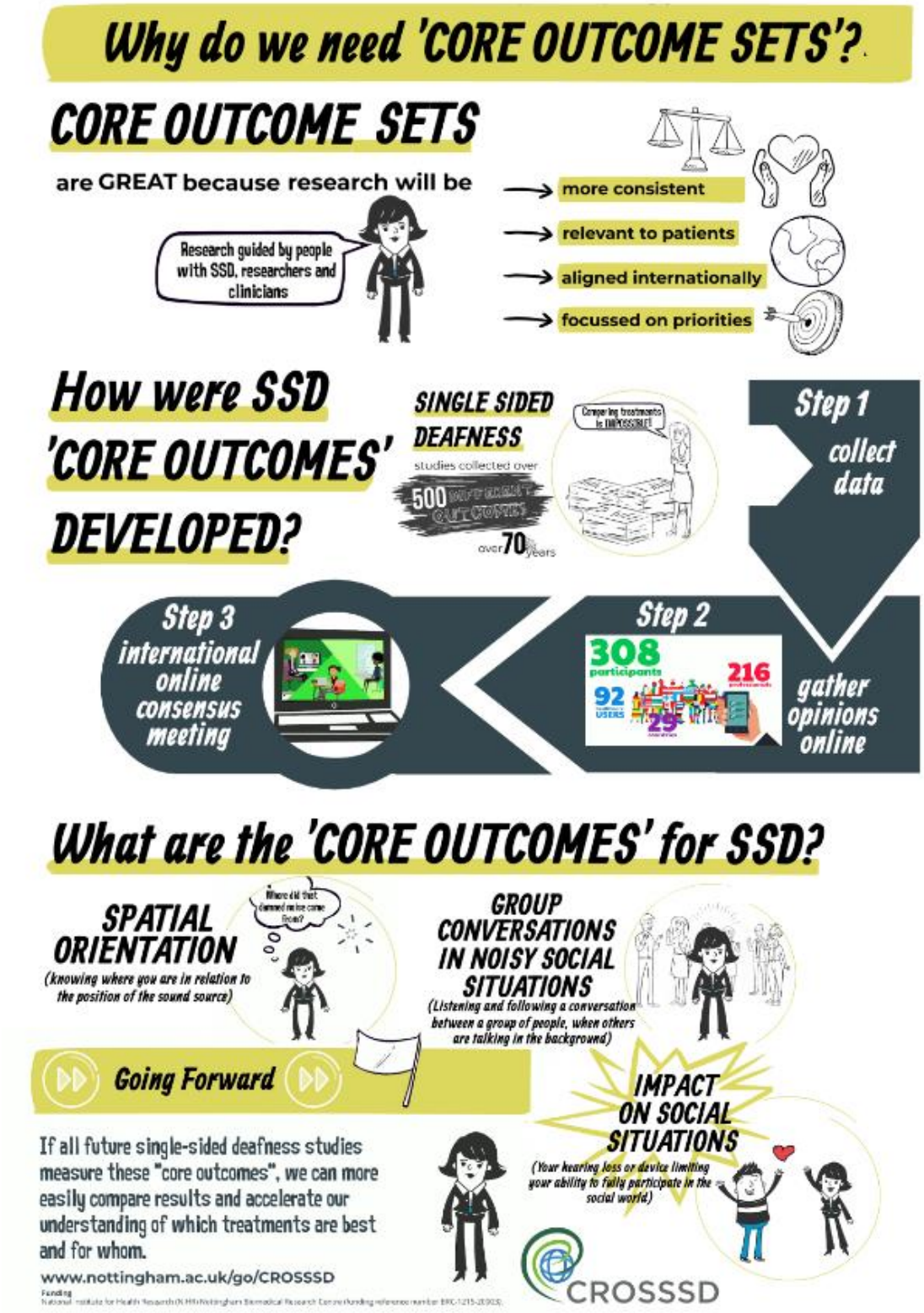
Appendix 2. The CROSSSD study infographic.



Appendix 3. NIHR Infrastructure SPARC (Short Placement Award for Research Collaboration) award letter.

NIHR | National Institute for Health Research

Dear Roulla,,

I am pleased to confirm that your application for SPARC funding, reference SPARC-05-18-08 has been successful and approved for funding by the Department of Health and Social Care.

Please can you now complete the attached award acceptance form and return it to academy@nihr.ac.uk by **28th February 2019.** I have also attached anonymised application assessment feedback, and I hope you find this constructive.

Providing the information requested will help us produce a 'Letter of Contract' for your home institution. As per the NIHR Infrastructure SPARC Round 5 Guidance notes, your salary or stipend will continue to be supported by your home institution, and research costs and supervisory fees will not be covered by this award.

I would also like to draw your attention to the following points:

1. Government procurement transparency regulations require publication of details of all contracts made with the Department of Health and Social Care on the Department of Health and Social Care website. Confidential information including research proposals, detailed finance information, bank details, and departmental staff names (other than the award holder's name) will be removed from the published versions.

2. Awards are granted to individuals on the condition that any part of work of the programme that requires NRES REC (National Research Ethics Service - Research Ethics Committee) approval cannot be undertaken prior to obtaining the necessary NRES ethical approval. You should begin immediately the process of obtaining any required NRES ethical approval if you have not done so already. If your local R+D office is unsure of whether your activities require NRES ethical approval, please contact NRES as soon as possible (http://www.hra.nhs.uk/about-the-hra/our-committees/research-ethics-committees-recs/ or HRA.Queries@nhs.net). In addition, if further ethical approvals (e.g. University specific ethical approval) are required, please also begin the process of obtaining these.

3. Individuals may be required to reconfirm the details of funding requested prior to starting the award, especially if the original finance section of the application is found to have errors or items that do not fit with the funding structure of this scheme. NIHR Academy reserves the right to reject any costs that it considers unreasonable or not fully justified.

A summary of the next steps are as follows:

1) The award acceptance form is completed by the awardee, and any queries or conditions are considered. Responses to queries or conditions and the completed

award acceptance form are returned to the NIHR Academy at academy@nihr.ac.uk by **28th February 2019**.

2) NIHR Academy reviews the award acceptance form and updates records accordingly.

3) NIHR Academy draws up a Letter of Contract, including the award amount, and sends an electronic copy to the awardee and 'authorised signatory' at the home institution (as named in the award acceptance form) for checking and approval.

4) The awardee and authorised signatory add their electronic signatures to the Letter of Contract and return it to the NIHR Academy at academy@nihr.ac.uk by the date specified.

5) NIHR Academy gains the appropriate signatory approval from DHSC, and emails the authorised signatory and applicant a copy for their records. *This needs to be done more than 2 weeks prior to the proposed award start date.*

Many congratulations again on being successful, and I look forward to hearing from you soon. If you have any queries at all, please do not hesitate to contact me or my colleague Gareth via academy@nihr.ac.uk.

Kind regards,

Dr Grania Fenton

Senior Programme Manager | NIHR Academy Infrastructure Team

21 Queen Street, Leeds, LS1 2TW

Appendix 4. Guide and agenda for the CROSSSD outcome domain grouping workshop.

A short guide to the CROSSSD Domain Grouping Workshop

Why are we meeting?
The aim of the workshop is to group the outcome domains yielded by the CROSSSD study systematic review. This is part of the preparatory phase for the e-Delphi survey.

When?
Monday 1st of July, 9:30am to 5pm
Tuesday 2nd of July, 9am to 4pm.

Venue?
Room 1. The Pillar Centre for Transformative Healthcare,
Level 3, Misericordiae Wing, Mater Hospital, Eccles Street. Dublin 7.
You need a visitor swipe card to access the Pillar Centre, Roulla will issue you with one on the morning of Monday 1st of July.

Who will be there?
Roulla Katiri, PhD student CROSSSD study.
Nora Buggy, PPI with CROS aid.
Nicky Hogan, PPI with BAHA implant.
Adele Horobin, PPI Manager NIHR Nottingham Hearing BRC.
Pádraig Kitterick, Chief Investigator CROSSSD study, expertise in SSD.
Deborah Hall, PhD supervisor, expertise in Outcome Measures.

Where do I go?
Roulla will be at Café Sol, Level 1, McGivney Wing, from 9am onwards on Monday to buy you coffee / breakfast if you like. Use the ***Eccles Street Entrance*** to the Mater Hospital. We'll move to the Pillar Centre at 9:25am sharp. See Mater Hospital Map below for more details.

What if I get lost?
Call Roulla 00 353 86 896 6461.

What about my suitcases?
Roulla can safely store your suitcases at the Audiology Department. Let her know if she can be of any help!

Can I use my laptop?
Yes, the Pillar Centre has excellent access to eduroam. There will also be access to a projector.

What about food?
There will be Elevenses followed by Lunch at 1pm. Fruit, snacks and drinks will be available throughout both days. Please let Roulla know if you have any dietary requirements.

How do I prepare?
You have been sent a long list of outcome domains. It will be helpful if you can read though this beforehand and decide if you can group any of those together according to your experiences. Make a note of your thoughts, you will not need to hand this in but it might be helpful to refer to your notes during the discussions.

Transfers:
Roulla will happily organise any transfers to and from town / airport for you, just drop her a line!
A taxi ride from the airport will cost you €25-30. Most taxis do not accept credit cards.
Dublin City (Yellow) Buses from Terminal 1 (where you'll be landing): **No 41** to Abbey Street (Faster, takes 20min or so) or **No 16** to Ballinteer (Takes 30min or so) can drop you off very close, 2min walk, from the Mater Hospital (Bus Stop Name: Upper Dorset Str / Temple Str).
The cost is €3, you need the exact fare, **coins only** to purchase this ticket on the bus, no change given. Most Dublin City Buses have free Wifi you can connect to very easily.

Monday Evening Social Plans (if you'd like to join):
6:30pm (Irish) Drinks at Dame Tavern, 18 Dame Ct, Dublin 2. https://dineindublin.ie/business/dame-tavern-2
7:30pm Dinner at Trocadero, 4 Andrew Street, Dublin 2. https://www.trocadero.ie/menu.html
If you'd like to bring friends, partners or family to dinner, they are very welcome! Please let Roulla know so she can alter the reservation accordingly.

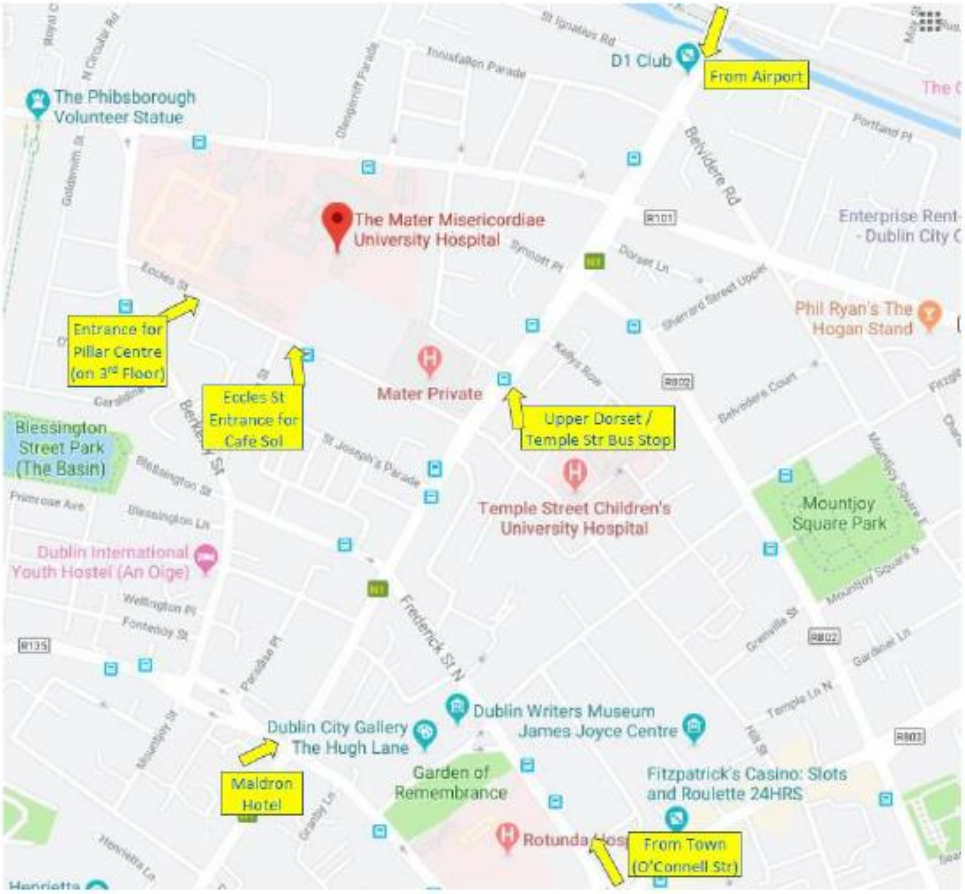
Social Media:
If you'd like to Tweet about the workshop you can use: @CROSSSD_ @hearingnihr @UoNHearSci @NottsSPHL @NIHRresearch @NIHRtakepart @RouKat @padraig_hearing @HorobinAdele @ThePillarDublin @MaterDublin
Please ***do not*** upload photos with the workshop members as not everyone has consented to use of their photo on social media.

Workshop Voice Recording:
It is advisable to sound-record the workshop discussions in case we need to revert back to it in the future. Please let Roulla know if you do not consent to your voice being recorded.

For the curious: What is the Pillar Centre?
The Pillar is a new centre for healthcare education, research and innovation launched in November 2018. For over 150 years, the Mater Hospital has been recognised as a leader in advancing healthcare in Ireland. Since 1852 the Mater Hospital have worked hand in hand with their education partner, University College Dublin (UCD); to deliver the very best clinical research and innovation as well as education and training. The fully refurbished centre focuses on supporting practical skills training, simulation training and team-based, interdisciplinary learning.

If you have time to kill in the proximity:
Cultured: High Lane Gallery - http://www.hughlane.ie/ (closed on Mondays)
A Breath of Fresh Air: Blessington Street Basin - https://bit.ly/2J5bYa0
Weather Permitting: The Botanic Gardens - http://botanicgardens.ie/
Next Door to the Botanic Gardens - https://www.glasnevinmuseum.ie/
Why Not: Henry Street Shopping - https://bit.ly/2WqzqkL
Proper Coffee I: Two Boys Brew - http://www.twoboysbrew.ie/
Proper Coffee II: Legit Coffee North Circular Road - https://www.legitcoffeeco.com/#legit-ncr

Mater Hospital Map:



Agenda for the CROSSSD Domain Grouping Workshop

Venue:
Room 1. The Pillar Centre for Transformative Healthcare,
Level 3, Misericordiae Wing, Mater Hospital, Eccles Street. Dublin 7.

Monday 1st of July 2019

9am-9:25am	Welcome: **Café Sol, Level 1, McGivney Wing,** Mater Hospital (via Eccles Street Entrance)
9:25-9:30am	Transfer from Café Sol to the Pillar Centre

9:30 -11am	Break	11:30am-1pm	Lunch	1:45-3pm	Break	3:30-5pm
CROSSSD Study Update & Domain Labelling Part A		Domain Labelling Part B		Domain Categorisation Part A		Domain Categorisation Part B

Tuesday 2nd of July 2019

9-11am	Break	11:30am-1pm	Lunch	1:45-3pm	Break	3:30-4pm
Domain Definitions Part A		Domain Definitions Part B		Domain Definitions Part C		What Next? CROSSSD Future Plans

Appendix 5. The CROSSSD study protocol.

University of Nottingham
UK | CHINA | MALAYSIA

Towards a Consensus on Outcome Measures for Interventions that Seek to Restore Bilateral and Binaural Hearing in Adults with Unilateral Severe-to-Profound Hearing Loss: The CROSSSD (Core Rehabilitation Outcome Set for Single Sided Deafness) Study

Final Version 2.0
06/07/2019

Short title:	Core Rehabilitation Outcome Set for Single Sided Deafness Study
Acronym:	CROSSSD
IRAS Project ID:	239750
Study Sponsor:	University of Nottingham
Sponsor reference:	19032
Funding Source:	National Institute Health Research (NIHR) Nottingham Hearing Biomedical Research Centre (BRC); The Graham Fraser Foundation; Oticon Medical.

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Study Coordinating Centre:	Hearing Sciences, National Institute for Health Research (NIHR) Nottingham Biomedical Research Centre (BRC) Ropewalk House 13 The Ropewalk Nottingham NG1 5DU

SYNOPSIS

Title	Towards a Consensus on Outcome Measures for Interventions that Seek to Restore Bilateral and Binaural Hearing in Adults with Unilateral Severe-to-Profound Hearing Loss: The CROSSSD (Core Rehabilitation Outcome Set for Single Sided Deafness) Study
Acronym	CROSSSD
Short title	Core Rehabilitation Outcome Set for Single Sided Deafness Study
Chief Investigator	Dr Pádraig T. Kitterick
Objectives	To advance standards for unilateral severe-to-profound hearing loss clinical trials by developing core rehabilitation outcome sets that should be measured and reported in every clinical trial measuring the efficacy of unilateral hearing loss interventions. More specifically the objective is to establish a Core Domain Set relevant to intervention strategies aiming to restore two-sided (bilateral) access to sounds and from both ears (binaural) access.
Study Configuration	Single-centre co-ordinating an international 2-Round Online Delphi (e-Delphi) Survey
Setting	Online
Sample size estimate	Not applicable
Number of participants	**e-Delphi Survey:** A minimum of 20 participants completing both rounds of the survey in each of 3 stakeholder groups (healthcare users, healthcare practitioners, clinical researchers). **Consensus Meeting:** up to 20 participants in a 1:1 allocation across the healthcare professionals and healthcare users stakeholder groups. **Follow-Up Workshop:** up to 10 participants (approximately 80% healthcare users and 20% healthcare professionals' allocation).
Eligibility criteria	All participants should be aged 18 years or over, be computer literate, and are required to have a sufficient command of English to read, understand and complete questionnaires independently. Additional inclusion criteria: **Healthcare users** with lived experience of Unilateral Severe-to-Profound Sensorineural Hearing Loss ('Single Sided Deafness', SSD) for 12 months or more; who have received or considered an SSD intervention. **Healthcare practitioners** with experience of SSD interventions, who have a clinical qualification, are currently employed by a public or private institution that provides hearing services to patients with SSD. **Clinical researchers** with an academic qualification, currently employed by a research organisation, have a current or 'recent

	past'* experience with studies that focus on the clinical benefit of SSD interventions in adults. (*Evidence of 'recent past' experience in clinical research will be defined as having been a co-author on a relevant peer-reviewed journal publication in the past three years). **Commercial representatives** who are currently employed by a company that develops, manufactures or sells hearing aids or auditory implants that may be used as an SSD intervention. **Funders** currently employed by an organisation that funds research focusing on SSD interventions, with experience of reviewing funding applications for SSD interventions research in the last three years.
Description of interventions	This is an observational study asking about personal perspectives on outcome measures. **e-Delphi Survey:** An e-Delphi survey will be delivered online using the e-Delphi Manager software. The survey is anticipated to consist of two rounds, with each round presenting the same list of outcomes. **Consensus Meeting:** Following completion of the final round, we will invite a subset of participants to take part in a face-to-face consensus meeting. The findings from the second round will be discussed with the aim to agree on the final set of outcome domains for SSD interventions. **Follow-Up Workshop:** To discuss the outcomes identified in the Consensus Meeting.
Duration of study	**Study Duration:** Up to 12 months. The first round of the e-Delphi will be launched in mid-2019 and the consensus meeting will take place in early 2020. **e-Delphi Survey Participant Duration:** Study participants will be participating in the study for two separate rounds of the e-Delphi survey (no more than 60 minutes per round) and the feedback questionnaire (10 minutes). **Consensus Meeting Participant Duration:** A one day face-to-face meeting (approximately 7 hours including lunch). **Follow-Up Workshop Duration:** A one day face-to-face meeting (approximately 7 hours including lunch).
Methods of analysis	Recommendations proposed in the Core Outcome Measures in Effectiveness Trials (COMET) Handbook version 1.0 (Williamson *et al.*, 2017) [1] will be adhered to. Descriptive statistics will be computed for scores on each domain (response distributions (%) of participants selecting each of the 1-9 Likert response options). Consensus is defined on the final round results according to Williamson *et al.* (2012) [2]: • Prioritise outcome domains in Core Domain Set: 70% or more of the participants in the group score 7-9 and fewer than 15% score 1-3. • Exclude outcome domains in Core Domain Set: 50% or less of the participants in each stakeholder groups score 1-7. Domains that achieve another score distribution, indicating a lack of consensus for inclusion in the Core Domain Set will be considered

	at the final consensus meeting using a nominal group technique to evaluate individual perspectives. At the Follow-Up Workshop each outcome will be scored anonymously and the results will be combined with the results of the Consensus Meeting for those outcomes.

ABBREVIATIONS

BRC	Biomedical Research Centre
CDS	Core Domain Set
CI	Chief Investigator overall
COMET	Core Outcome Measures in Effectiveness Trials
COS	Core Outcome Set
COS-STAR	Core Outcome Set–STAndards for Reporting
CRF	Case Report Form
CROSSSD	Core Rehabilitation Outcome Set in Single Sided Deafness
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
IMMPACT	Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials
mOMEnt	Management of Otitis Media with Effusion in childreN with cleft palate
NHS	National Health Service
NIHR	National Institute for Health Research
PI	Principal Investigator at a Local Centre
PIC	Participant Identification Centre
PIS	Participant Information Sheet
PPI	Patient and Public Involvement
PROSPERO	International Prospective Register of Systematic Reviews
R&D	Research and Development Department
REC	Research Ethics Committee
SPSS	Statistical Package for the Social Sciences
SSD	Single Sided Deafness
UoN	University of Nottingham

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STUDY BACKGROUND INFORMATION AND RATIONALE

What is known about Single Sided Deafness?
Single-sided deafness (SSD) is the term given to the condition where there is normal or near-normal hearing in one ear and a severe-to-profound hearing impairment in the other ear [3]. SSD can be congenital, sudden or progressive [4]. The most common causes of SSD in adulthood are sudden and idiopathic; including vestibular schwannoma [5] and associated surgery [6], Ménière's disease [7] and sudden onset sensorineural hearing loss [8]. The incidence of SSD in the United Kingdom is extrapolated to be approximately 9000 new cases per year as per data available from Baguley *et al.* (2009) [9].

Good hearing in both ears helps us deal with everyday listening tasks. These include understanding speech in noisy environments and locating where sounds, such as the telephone or car traffic, are coming from [10]. In adults with SSD both these abilities are compromised and can lead to functional, psychological and social consequences [11]. The multi-dimensional burden of SSD on overall health is not underestimated by neither SSD patients nor the general public that have scored a 5-9% reduction in health [12] in individuals with a diagnosis of SSD.

Current SSD interventions
The most commonly used treatments for SSD restore two-sided (bilateral) access to sounds by re-routing sounds from the impaired ear to the hearing ear [13]. This can be achieved with the help of a specialised hearing aid system known as the CROS (Contralateral Routing of Signals) aid [14]. Bone Anchored Hearing Aids (BAHA) have also been utilised as interventions for SSD [15]. Alternatively, an auditory prosthesis such as a cochlear implant can deliver information about sounds directly to the auditory pathway on the side of the impaired ear, thus creating a sensation of true 'binaural' hearing [16].

Efficacy and safety of current SSD interventions
Existing literature has highlighted inconsistencies in what benefits and risks are assessed when evaluating these interventions [17]. The different sorts of benefits and risks are collectively called 'outcome domains'. For example researchers have measured aspects such as speech understanding in quiet or noise [18], sound localisation [19], the impact on the recipients' quality of life [12] or tinnitus suppression [20]. These inconsistencies hinder decisions about the choice of outcome measures for health and social care trials of clinical efficacy [21].

Triallists should ideally base the choice of outcome measures on what is important, not on what outcome instruments are available or most commonly used [22]. If evidence is lacking for an important outcome, this should be acknowledged, rather than ignoring the outcome. A Core Outcome Set (COS) developed from the perspectives of healthcare users, healthcare professionals and other relevant stakeholders would overcome this problem. A COS is a standardised collection of outcome domains that should be reported in all controlled trials within a research area [23]. Perspectives of healthcare users with lived experience of the condition are important for understanding what matters to them, as demonstrated by the IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) study [24] for chronic pain. It is vital that all stakeholders such as patients, healthcare professionals or budget holders are involved in the development of relevant COS [1].

How the results might affect future clinical practice
An agreement on a set of outcome domains of what is critical and important for deciding whether an intervention is efficacious will drive up the quality and relevance of research by ensuring that the most relevant outcomes are consistently measured and reported in every clinical trial relating to SSD. This would make it much easier for people with SSD and their intervening clinicians to make sense of all the knowledge produced and consequently minimise bias when making decisions about healthcare. This should subsequently lead to improvements in SSD interventions and in turn management and clinical outcomes of patients with SSD. On the basis of the recommended outcome domains, further research will then be needed to identify measurement instruments that assess the outcomes domains in the minimum set.

STUDY OBJECTIVES AND PURPOSE

PURPOSE

The aim of the Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) study is to identify what outcomes are crucial and important to measure when designing clinical trials to evaluate the effects of the various SSD interventions. A list of 'outcome domains' that should be assessed when evaluating SSD interventions will be compiled. An agreement on a set of outcome domains of what is critical and important for deciding whether an intervention is efficacious will drive up the quality and relevance of research by ensuring that the most relevant outcomes are consistently measured and reported in every clinical trial relating to SSD.

PRIMARY OBJECTIVE

To establish a Core Domain Set (COS) for interventions for adults with SSD. This will be achieved by prioritising and identifying the most important outcomes that should be measured from the perspectives of the key stakeholders, clinical practitioners, clinical researchers, commercial representatives, funders, and members of the public with lived experience of SSD.

SECONDARY OBJECTIVES

To compare and contrast outcome domains and instruments reported for interventions that restore bilateral / binaural hearing. Also, to identify what instruments have been utilised to date, as a function of the time-point after intervention, to measure outcomes for the various available SSD interventions and identify any 'gaps'. This information will be used to inform any future definitions of short-term and long-term treatment-related changes. Finally, to obtain participants' feedback on their experience in participating to construct the COS.

STUDY DESIGN

STUDY CONFIGURATION

A two-round international e-Delphi (consensus) survey, co-ordinated and managed by a single-centre in the UK, NIHR Nottingham Biomedical Research Centre (BRC).

All participants will be identified only by a Unique Identifier Code. Designated members of the study team (the Data Custodian) and two software programmers will maintain the only access to a record of personal data (name and email address) corresponding to this Unique Identifier Code for the e-Delphi survey. The Unique Identifier Code enables personalised feedback to be generated in e-Delphi survey round 2, as well as reminder emails to reduce and track attrition between rounds.

STUDY MANAGEMENT

The project will be managed by the members of the Study Management Team at Hearing Sciences, Division of Clinical Neuroscience, National Institute for Health Research (NIHR) Nottingham Biomedical Research Centre (BRC).

The Chief Investigator has overall responsibility for the study and shall oversee all study management, including working with the software programmers to ensure that the software can be configured to fit the study requirements and recruiting appropriate facilitators for the final consensus meetings.

The Study Co-Investigators (Deborah A. Hall & Roulla Katiri) will oversee and manage the e-Delphi survey, including its full implementation, overall management of the two e-Delphi rounds within the bespoke online e-management system and organising the final consensus meetings.

The data custodian will be the Chief Investigator, Pádraig T. Kitterick, who has responsibility for data integrity and monitoring of study data as an ongoing activity. Roulla Katiri will be responsible for managing the analysis of the data at each e-Delphi survey round and for presentation of the scores as anonymised feedback in Round 2 and at the consensus meetings.

The PhD student and Co-Investigator (Roulla Katiri) will co-ordinate the project advertisement, screening eligibility and recruitment of participants, communicating with participants throughout and collating feedback from participants from each e-Delphi round within the bespoke online e-management system.

The PhD student and Co-Investigator (Roulla Katiri), overseen by the Study Management Team, will have primary responsibility for creating a long list of outcome domains for use in the e-Delphi survey. Definitions for each outcome domain will be generated by the Study Management Team, the Patient and Public Involvement (PPI) manager and the two Public Representatives from the Research Steering Group (see below).

Research Steering Group

A Research Steering Group has been appointed to oversee the project. The group is comprised of the Study Management Team, a PPI manager, two Public Representatives and three professionals who provide SSD interventions and are independent from the NIHR Nottingham Hearing BRC.

The role of Research Steering Group is:

- To participate in telephone conferences to set-up, guide and discuss progress on the study.
- To read, review, comment and support the development of the study protocol, specifically commenting on the feasibility of the e-Delphi process.
- To review the CROSSSD study documentation, including information sheets for patients, professionals, supporting video explanations of the survey and intended advertisements.
- To participate in the testing of the e-Delphi study to review the list of outcomes and associated descriptions, specifically:
  - (i) Comment on the readability of the outcome descriptions,
  - (ii) Comment on the appropriateness of the grouping of outcomes to overall domains,
  - (iii) Provide any additional outcomes that individuals believe should be included in the first round,
  - (iv) Advise how best to recruit and keep participants engaged throughout the whole study.
- To engage in dissemination activities, such as contributing to publications on the e-Delphi process and results.
- All steering group members will have the option to attend the final consensus meetings. Attendance at these meetings will be voluntary.

PPI Involvement

The study PPI manager has reviewed PPI-related study documentation such as Patient Information leaflets and will be involved in training, support and payment to the Public Representatives for undertaking the activities in the Research Steering Group.

A small group of members of the public with lived experience of SSD will be invited to:

(i) Review and comment on the definitions for each outcome domain in the list and the suitability of the overall domains under which outcome domains are grouped; and to

(ii) Participate in a pilot of Round 1 of the e-Delphi survey to comment on the information provided and usability. This is an important aspect of PPI which is included to improve the quality of this research study. It is not a direct component of, but an important adjunct to, the Research Steering Group since individuals have the status of Public Research Partners.

None of the Research Steering groups will be allowed to vote on domains in the final consensus meeting. Any conflicts of interest within the Study Management Team will be described in the final report, including a brief summary of how these were managed. The recommendations by the Core Outcome Set–STAndards for Reporting (COS-STAR) Statement as a reporting guideline for COS studies will be followed [25].

DURATION OF THE STUDY AND PARTICIPANT INVOLVEMENT

Study Duration: up to 12 months

When the e-Delphi survey is launched participant recruitment will commence and immediately after the study team has completed screening those interested in the study via email or telephone, participants will be invited to complete the first round of the e-Delphi, with an embedded link via email.

The recruitment period to participate in the e-Delphi survey will be at least two months long. Analyses to inform the second round will only commence when all participants have completed the first round. It is anticipated that, once started, the e-Delphi will take up to six months, with a time interval of 6 weeks between the first and second round due to recruitment. The consensus meeting will take place as soon as practicable following the final round.

Participant Duration for e-Delphi Survey: involved up to 12 months

Study participants will commit to participating in two separate e-Delphi questionnaire rounds, with each round estimated to take approximately 60 minutes. Therefore, completion of both rounds is estimated to take up to two hours (120 minutes). Each participant will be given three weeks to complete each round of the e-Delphi, with a reminder email sent at the end of the second week.

After completion of the second round of the e-Delphi survey, a questionnaire, anticipated to take up to 10 minutes to complete, will be emailed to all participants to collect feedback on their experience of being a participant.

Participant Duration for Consensus Meeting: involved up to 20 participants in total

The consensus meeting will consist of a separate face-to-face group meeting that will take place over a whole day (approximately 7 hours including lunch). Up to 20 participants (who have completed both Round One and Round Two of the e-Delphi) will be invited to participate in the group meetings. Each participant will only be required to actively participate in discussions with a commitment to attend the entire day.

Participant Duration for Follow-Up Workshop: involved up to 10 participants in total

The follow-up workshop will consist of a subsequent face-to-face group meeting that will take place over a whole day (approximately 7 hours including lunch). Up to 10 participants (who have completed both Round One and Round Two of the e-Delphi) will be invited to participate in this group meeting.

Each participant will only be required to actively participate in discussions with a commitment to attend the entire day.

End of the Study

The end of the study will be the date of the final follow-up workshop, anticipated to take place approximately six months after the launch of the first round of the e-Delphi survey.

SELECTION AND WITHDRAWAL OF PARTICIPANTS

Recruitment

We will use non-probabilistic purposive sampling to recruit healthcare users and professionals with experience in SSD interventions, aiming to recruit at least 20 participants in each of three key stakeholder groups (healthcare user, healthcare practitioner, clinical researchers) who complete both rounds of the e-Delphi survey. The PhD Student and Co-Investigator (Roulla Katiri) will be responsible for recruitment and study communication with all participants throughout the two e-Delphi survey rounds.

A range of recruitment strategies will be used to raise awareness about the CROSSSD study so that potential participants can contact the Study Management Team and request a Participant Information Sheet, which explains all aspects pertaining to participation in the study, including detailed information on the requirement for participation, and also to purposively identify potential participants to invite by direct contact through email invitations. It will be explained to the potential participant that entry into the study is entirely voluntary. It will be explained to healthcare users that their treatment and care will not be affected by their decision. It will also be explained that they can withdraw at any time but attempts will be made to avoid this occurrence. In the event of their withdrawal it will be explained that their data collected so far cannot be erased and we will seek consent to use the data in the final analyses where appropriate. Participants will be informed to direct any questions or queries to the PhD Student and Co-Investigator (Roulla Katiri).

Recruitment strategies for e-Delphi surveys will include the following methods:

General:

1. A dedicated webpage on NIHR Nottingham Hearing BRC website (http://www.hearing.nihr.ac.uk/research/crosssd-study-core-rehabilitation-outcome-set-for-single-sided-deafness)
2. A dedicated webpage on the University of Nottingham's website, Hearing Sciences Projects section www.nottingham.ac.uk/go/CROSSSD.
3. Distribution of CROSSSD Study advertising posters in the Audiology / ENT Departments of identified Participant Identification Sites.
4. If deemed appropriate and if possible, a CROSSSD Study Participant Invitation Letter can be posted by their clinical team to identified adults diagnosed with SSD at collaborating Participant Identification Centres (PICs)
5. Newsletter articles and announcements published by relevant patient and professional organisations (e.g. British Society of Audiology, ENT & Audiology News, British Academy of Audiology)
6. Invitation emails to known distribution lists (e.g. British Society of Audiology, British Acoustic Neuroma Association, Ménière's Society, NIHR Nottingham Hearing BRC participant database)
7. Posts on social media channels (e.g. Twitter @hearingnhir, @CROSSSD_, @UoNHearSci) and Facebook
8. Video advertisements promoting the study.

Professionals with experience in SSD interventions:

1. Identify from existing connections with the Nottingham Hearing BRC
2. Manual searches of relevant hearing-related organisations
3. Identify authors of clinical trials from the relevant research publications in the trials systematic review being conducted
4. Manual search of reference lists of relevant Cochrane and other systematic reviews of SSD interventions
5. Online search of relevant journals and members of Cochrane ENT to identify editors with relevant experience / occupations
6. Manual search of relevant conference proceedings in last 3 years (e.g. Implantable Devices Meeting, Cochlear Implants International Meeting Ci2018.org, OSSEO International Congress on Bone Conduction Hearing and Related Technologies)
7. Email queries sent to representatives from each additional stakeholder organisations from commercial sectors and funding bodies, asking for recipients to nominate any colleagues with expertise in SSD interventions.
8. Via the CROSSSD Study Steering Group members who as experts in clinical practice and research; based in Europe, United States and United Kingdom.

Eligible professionals will be identified and invited to participate and will be asked a number of questions that will confirm

1. Their stakeholder group (i.e. job role or medical specialty)
2. That they meet the eligibility criteria for their stakeholder group (see eligibility section below).

Professional stakeholder groups include individuals involved in the management / care / field of SSD. These include "Healthcare Practitioners", "Clinical Researchers" and "Commercial Representatives and Funders". These groups have been identified as those representing the main professional categories in SSD research and clinical trials. Journal editors will not be included as a separate stakeholder group because it would not be possible to meet the minimum sample size requirement due to smaller population size. However, given that, in some cases, professional stakeholders within existing groups will have a secondary occupation of journal editor, this profession is still likely to be represented.

Healthcare Users **(UK and International):**

1. Poster advertisements and participant information sheets in relevant NHS clinics.
2. Participant information sheets will be handed to healthcare users by a care team member in relevant NHS clinics. Note that the care team member will not hold any responsibility for deciding if the respondent is eligible to take part (UK alone).
3. Poster advertisements and participant information sheets in relevant international Audiology or ENT clinics, dependent on the international clinician gaining appropriate local approvals.

Eligible healthcare users will be asked to confirm that they either have experience of receiving an SSD intervention or that they have the intention of utilising one of the interventions in the future. Participants will be sent an embedded link to the e-Delphi survey based on their confirmed expertise. Purposive sampling will be used to balance the healthcare users group as far as is practicable in terms of their experience using devices that restore either bilateral access to sounds or using binaural access to sounds.

Reporting of the e-Delphi surveys will fully describe the relevant characteristics of the participants involved at all stages of the COS as per COS-STAR guidance [25]. Examples of relevant characteristics are experience with the SSD intervention, gender, ethnic background, socioeconomic status, country and region (e.g. United Kingdom (Manchester), America (St Louis), Belgium (Antwerp) etc), since these factors affect how representative the consensus might be of the target population.

Recruitment strategies for Consensus Meeting and Follow-Up Workshop will include the following methods:

General:

1. The participant information sheets will inform participants to register their interest in attending the consensus meeting with the research team. Participants will be informed that there are only a limited number of places available.
2. For the e-Delphi round one, participants will be reminded at the end of the survey to register for the meeting if they wish to attend. They will be informed that travel expenses will only be reimbursed for UK or Ireland healthcare users. If the required number of participants have not registered following the first round, they will also be reminded to register at the end of the second round.
3. Allocation of places will be based on participants who completed both rounds of the e-Delphi survey, responded to at least 90% of the outcome domains in Round Two and registered an interest first.

Allocation into e-Delphi surveys:

In order to be allocated in the e-Delphi survey, both professional and healthcare users will be asked to self-certify as being an 'expert' in SSD interventions

Retention of Participants

Various strategies can be implemented to maintain the input of participants over time thus reducing attrition [26]. Managing expectations from the outset about the need to complete both e-Delphi rounds and about the timescales, building a rapport, keeping participants informed of progress, and showing appreciation for their contributions have all been highlighted by healthcare users [27].

The Study Management Team will thus create multimedia (video) explanations to convey these messages and links to these will be embedded into the online survey throughout the process. These multimedia explanations that we create will:

1. Provide a clear overview of the purpose of the study highlighting these messages such as importance of the study and time commitment and;
2. Guide participants through using the online survey by giving an overview of what to expect.

This will include an overview of what the survey looks like, how to access the plain language descriptions, what the scoring options mean, and how to exit and return to the survey, allowing them to take breaks. Anonymised results from the first e-Delphi round will be presented graphically as well as numerically to improve visual appeal. While these methods make the process more accessible to healthcare users, they may be contradicted by the disadvantage of having to complete a long questionnaire. All aspects will be reviewed and approved by the CROSSSD Study Steering Group.

To further increase attrition, reminder e-mails will be sent at the end of the second week, following the launch of each round, to aid completion. Furthermore design characteristics and contributing factors such as panel size and number of items included, as discussed by Gargon *et al.* (2018), will be considered to ensure as high response rates as possible [28]; and/or recruitment of at least 20 participants in each of three key stakeholder groups (healthcare user, healthcare practitioner, clinical researchers) who complete both rounds of the e-Delphi survey.

It will be explained to the potential participant that entry into the study is entirely voluntary and that their treatment and care will not be affected by their decision. It will also be explained that they can withdraw at any time but attempts will be made to avoid this occurrence. In the event of their withdrawal it will be explained that their data collected so far cannot be erased and we will seek consent to use the data in the final analyses where appropriate.

Eligibility Criteria

Inclusion criteria

- Men and women ≥18 years
- All participants are computer literate
- All participants are required to have a sufficient command of English to read, understand and complete questionnaires
- Ability to give informed consent

For each stakeholder group the specific inclusion criteria are provided below:

Healthcare users with lived experience of SSD:

- Experience of living with SSD for 12 months or more
- Have received or considered receiving an SSD intervention

Professional with experience in SSD interventions:
Healthcare Practitioners

- Have a clinical qualification
- Are currently employed by a public or private institution that provides a SSD interventions to patients
- Experience of assessing, diagnosing or managing SSD in adults

Clinical Researchers:

- Have an academic qualification
- Are currently employed by a research organisation
- Have current or 'recent past' experience with studies that focus on questions of clinical efficacy (benefit) of a SSD interventions in humans
- *Evidence of 'recent past' experience in clinical research will be defined as having been a co-author on a relevant peer-reviewed journal publication in the past 3 years.*

Commercial Representatives:

- Are currently employed by a company that develops, manufactures or sells product(s) that may be used an SSD intervention

Funders:

- Are currently employed by an organisation that funds SSD research
- Experience of reviewing funding applications for SSD interventions research in the last 3 years

Expected duration of participant participation

Study participants will be participating in the study for the timeframe of approximately 6 months but less than 12 months.

Participant Withdrawal

Participation is entirely voluntary. Participants may be withdrawn from the study either at their own request or at the discretion of the Investigator. Healthcare users will be made aware that this will not affect their future care. Participants will be made aware (via the information sheet and consent form) that should they withdraw the data collected to date cannot be erased and may still be used in the final analysis. Participants who withdraw will not be replaced. Responses will be weighted so that each stakeholder group has an equal overall contribution to the mean rating for each domain.

Informed consent

Prior to receiving a personalised link to the survey, all participants will have received and read through the detailed information sheets relevant to them (versions for Healthcare users and professionals).

Participants will be informed to direct any queries or concerns about participation to the PhD student and Co-Investigator (Roulla Katiri).

Before consenting, video explanations and the participant information sheet will be presented as a reminder of the purpose of the e-Delphi and time commitment required.

Participants will consent to participate by agreeing to the 'consent to participate' button shown on the introductory e-Delphi survey screen.

Consent will be obtained from each participant on the first page of their online survey. By clicking "continue", to move on to the questions within the main survey, their consent will be captured electronically by the e-Delphi survey database. Separate written informed consent will not be sought for the e-Delphi surveys.

The PhD student and Co-Investigator (Roulla Katiri) will re-consent the subset of participants who are recruited to join the final Consensus Meeting and/or Follow-Up Workshop. Consent will be recorded in written form.

STUDY REGIMEN

An international e-Delphi survey will be delivered online, using the Delphi Manager software developed by the Core Outcome Measures in Effectiveness Trials (COMET) initiative at The University of Liverpool [1].

Delivering this study online allows for us to capture the opinions of a diverse population of stakeholders with an interest in shaping outcome measures for SSD interventions. If any healthcare users do not have home access to a computer or a tablet then they will be able to visit the NIHR Nottingham Hearing BRC to complete each online round using one of the centre's computers.

The e-Delphi technique can minimise response bias as individual feedback is anonymised and not affected by views of influential individuals [29]. Research has shown that e-Delphi surveys could help to widen participation and help to minimise the influence of power differentials between different stakeholder groups. However, they can also be perceived as intimidating for members of the public as a result of the long number of outcomes included in some e-Delphi surveys that lay participants would have to go through and score at every round [27]. Methodological features highlighted by Smith *et al.* (2018), such as shortening and renaming the long list of domains and plain language descriptions will be adhered to where possible [30]. Evaluations discussed by Hall *et al.* (2018) will be considered to ensure robust recruitment and retention of healthcare users [26].

The development of the Core Domain Sets will involve three key phases:

Phase 1:
Generation of a list of outcomes and outcome domains for e-Delphi

An initial 'long list' of potential outcomes will be generated by the systematic review of the literature (PROSPERO http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018084274) which is presently being conducted. The study management team is currently extracting the precise primary and secondary outcome domains and outcome measures identified in suitable studies as defined by the systematic review PROSPERO protocol. It is anticipated that this process will be completed by mid- May 2019. The list of outcomes yielded will help inform the generation of the definitions.

The initial long list of outcomes will be inspected and reviewed by the Study Management Team. Domains that have numerous different conceptualisations, or reflect complex composite complaints, may be removed based on discussions with the Public Representatives and the Study Management Team. 'Quality of Life' is an example of the former since definitions can vary from broad (e.g. 'global quality of life', 'capability') to narrow (e.g. 'health-related quality of life', 'psychological well-being') [31]. 'Cognition' is an example of the latter since they reflect broad complex complaints, where fine grain elements will already be represented in the list. Any possible duplications of outcomes between data sources will be condensed, producing a final list of domains.

The remaining outcome domains in this final list will each be given a plain language description as recommended by the COMET handbook [1] and highlighted by the COMIT'ID study team [30] to ensure a meaningful COS is constructed. This is to ensure that the items are understandable and accessible for all stakeholders. Each outcome description will be using words previously used by patients in interviews e.g. language used by SSD participants in work published by Lucas *et al.* (2018)[11]; and via an iterative process during workshop sessions with members of the Study Management Team and the two Public Representatives. The purpose of the plain language descriptions is to ensure that all domains are correctly interpreted by all stakeholders, including public participants, therefore facilitating accurate and consistent understanding of domains across participant groups. To facilitate presentation of the final long list, outcome domains will be categorised into over-arching domains.

The final long list of categorised outcome domains will be operationalised into questionnaire items (with the plain language description) and will be piloted by our Research Steering Group and two public representatives for face validity, understanding and acceptability, and will be modified as a result of this feedback.

Reporting of the e-Delphi surveys will fully describe how outcomes were added, dropped or condensed, with reasons. It will also list all outcome domains considered at the start of the consensus process, as per COS-STAR [25].

Phase 2:
Prioritise outcomes through gaining consensus from key stakeholders using a modified e-Delphi survey

The study consists of an e-Delphi survey comprising of a series of two sequential questionnaires or 'rounds' aiming to obtain a consensus of opinion from professional and healthcare user stakeholder groups.

Each Delphi survey will be managed using a bespoke online e-management system (Delphi Manager) maintained by the COMET Initiative [1]. This system has previously been used successfully to obtain consensus on outcome measures in healthcare including dermatology [32], rheumatology [33] and women's health studies [34] as well as a hearing theme study, the COMIT'ID - Core Outcome Measures in Tinnitus: International Delphi study [35].

Both survey rounds will contain a questionnaire that includes the final long list of categorised outcome domains developed in Phase 1. International professionals and healthcare users with experience in receiving or managing SSD interventions will be identified via advertisements online and in clinics, existing email distribution lists and a list created from searches for professional information. Those who respond to any of these sources will register for the survey. Both professionals and healthcare users will receive an embedded link to the survey via email. This link will route the respondent to the survey webpage.

Upon entering the online survey webpage, an introductory page will reiterate key information previously provided in the Participant Information Sheet, including an embedded link to a video explanation. Participants will then be asked to give informed consent. Participants registering will be provided with a Unique Identification Code which will allow for identification of individual responses in follow-up rounds. Video explanation will then be presented to guide participants through the proceeding round. Following this, participants will complete a checklist of relevant personal characteristics (as described in the Recruitment section).

The questionnaire will be piloted by lay persons; for face validity, understanding and acceptability. Following this, if needed, modifications will be made before finalising the questionnaire.

Participant response rates will be monitored throughout and the Study Management Team will keep clearly defined records of the number of participants that completed the rounds and those who did not [25].

For each questionnaire item, participants will be asked to think about the importance of each SSD intervention outcome domain and indicate how important it is to measure when deciding if an intervention is working. All outcome domains will be retained in both rounds. One reminder e-mail will

also be sent at the end of the second week, following the launch of the survey round, to aid completion. A flow diagram illustrating the e-Delphi surveys consensus and feedback process shown in Figure 1 below:

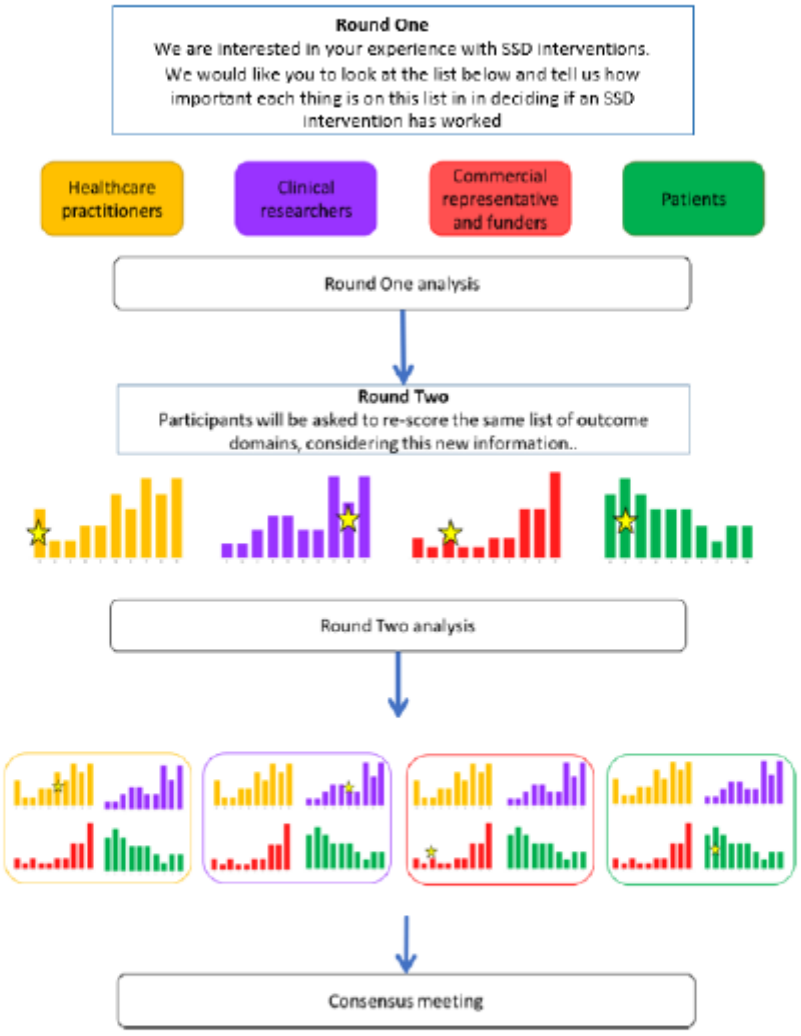


Figure 1. Flow Diagram illustrating the Delphi survey process

Round One:

The order of the questionnaire items will be decided having in mind recommendations by Williamson *et al.* (2017) [1] and Gargon *et al.* (2018) [28], to eliminate any impact on response rates e.g. the items will be listed alphabetically. The commonly used 9-point Likert scoring system will be utilised. Outcomes will be graded in accordance to their level of importance. Typically, 1 to 3 signifies an

outcome is of 'limited importance', 4 to 6 'important but not critical', and 7 to 9 'critical'. This method has been successfully utilised in the past in hearing-related core outcome set development studies e.g. mOMEnt (Management of Otitis Media with Effusion in childreN with cleft palaTe) study [36] and the COMIT'ID study [37]. If a participant feels that they did not understand a particular outcome, they will be able to select 'unable to score'.

Participants will have the option to suggest additional outcomes domains for inclusion in round two. These additional outcomes will be reviewed and coded by two Study Management Team members to ensure they represent new outcomes. Where uncertainty exists, the rest of the team will be consulted. Definitions will be generated for the new outcomes and reviewed by the Research Steering Group. Reporting of the e-Delphi surveys will describe any new outcomes introduced into the consensus process at the end of round one, with reasons [25].

Following each outcome and at the end of the questionnaire, each participant will be offered an open-text box to add any comments about particular outcome domains. This is optional, but participants will be encouraged to provide a reason for their scores on individual outcomes as recommended by the COMET handbook [1]; these comments will be summarised as part of the feedback after the first round.

The distribution of the scores for each outcome domain will be calculated for each stakeholder group, as shown in Figure 2 below.

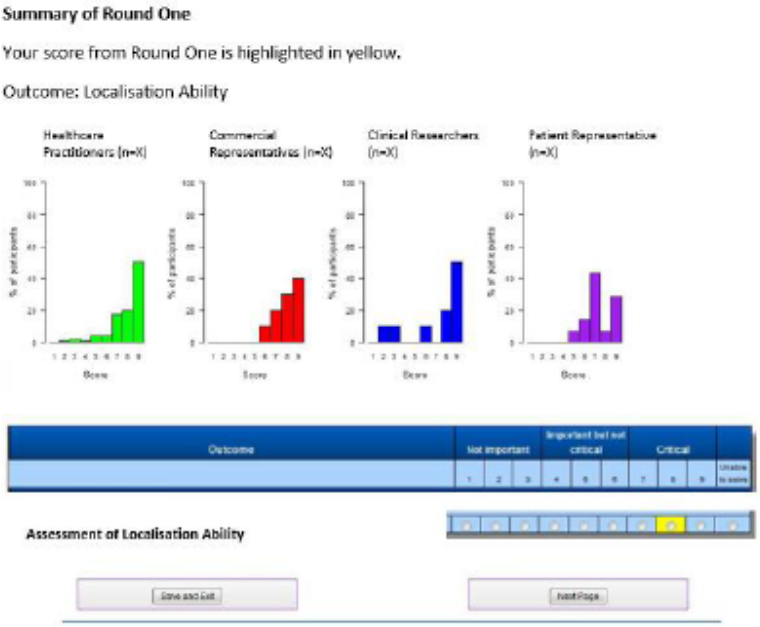


Figure 2. An example of outcomes from a Round Two questionnaire presenting the percentage distribution of scores across all stakeholder groups

Round Two:
The purpose of Round Two is to enable participants to reflect on their scores in light of feedback or the viewpoint of their stakeholder group and the other stakeholder groups in the e-Delphi survey.

In the second round, participants will be presented the same list of outcome domains from the first round; plus any new additional outcomes identified and approved by the Study Management Team. For each time period, participants will see their own previous score plus the anonymised distribution

of scores across the rest of the participants from the first round. Results will be presented graphically as well as numerically to be readily understood by participants. Participants will be asked to re-score the same list of outcome domains, considering this new information. To help give meaning to the 9-point Likert scoring system scale, participants will be reminded that any outcome domain will only be considered for inclusion in the Core Domain Set, if 70% of all participants select points 7-9 on the scale [1].

If the initial list of identified outcomes is too large (over 50), including them in each e-Delphi round may impose sufficient burden on participants [1]. Therefore discussion and consensus among the Steering Group will be obtained about adopting methods described in e.g. an oesophageal cancer surgery COS study by Blazeby *et al.* (2015), where they only retained items for Round Two if they were rated 7 to 9 on the Likert scale by 50% or more participants and 1 to 3 by no more than 15% of participants in at least one stakeholder group [38]. Fackrell *et al.* (2017), also identified the need to reduce the long list of outcome domains to improve the likelihood of their participants completing all items in the e-Delphi [37] e.g. by excluding 'out-of-scope' domains that were associated to comorbidities like 'speech perception' or 'depression' but were not specific to their topic, tinnitus interventions.

The distribution of the new scores for each outcome domain will then be calculated for each stakeholder group. Other aspects of design and analysis are the same as for Round One.

Consensus:
The '70 / 15%' consensus approach as described by Williamson *et al.* (2012) [23], and Williamson *et al.* (2017) [1]; and successfully utilised by Harman *et al.* (2015) [36] and Hall *et al.* (2018) [35], will be utilised.

Inclusion of the domain in Core Domain Set if:
70% or more of the participants in each stakeholder groups score 7-9,
and fewer than 15% score 1-3.

Exclusion of the domain for the Core Domain Set if:
50% or less of the participants in each stakeholder groups score 1-7.

Phase 3:

Consensus meeting to integrate healthcare users and professional perspectives on outcomes, providing final recommendations on an agreed SSD interventions Core Domain Set
Professionals and healthcare users who have completed the two rounds of the e-Delphi survey, responded to at least 90% of the outcome domains in Round Two; and register an interest in participating in the consensus meeting will be eligible to participate. Places will be allocated on a first come, first served basis. Recruitment will be guided by methods successfully adopted by Fackrell *et al.* (2017), [37] e.g. as far as possible, allocated places will maintain the balance across stakeholder groups, such as 50% healthcare users with SSD / 50% professionals; and will aim to include non-UK, non-native English language speakers.

After confirming their attendance to the meeting, participants will be sent an email with information on how to get to meeting and what to expect, as well as the information sheet again as a reminder. At the consensus meeting, the research team will discuss the aim of the meeting and what will happen with the participants, ensuring that all participants understand before starting the meeting.

An experienced independent moderator will be recruited to facilitate the consensus meeting discussions to agree a final Core Domain Set. Discussion within each meeting will include anonymised voting on each outcome as either "In" or "Out" (e.g. using electronic keypads which will create histograms and descriptive statistics 'live', to be displayed in the meeting). Participants will be given materials summarising the anonymised Round Two results.

A guide for the structure of the meeting is as follows:

- For outcomes recommended to be included based on the Round Two analysis (70% scored 7-9), the moderator will establish whether anyone has a major reason to want any to be excluded. The

moderator will focus the discussion and voting on these outcomes. Domains will be included if at least 70% of participants vote 'In'. All other outcomes recommended for inclusion will be 'In', without further discussion.

- For outcomes where at least 50% of more than one stakeholder group scored 7-9 on the Round Two analysis, the moderator will focus discussion and voting. Domains will be included if at least 70% of participants vote 'In'.
- For outcomes where less than 50% of the participants in all stakeholder groups scored 1-7 on the Round Two analysis, the moderator will establish whether anyone has a major reason to want any to be included. Domains will only be included if at least 70% of participants vote 'In'.

If consensus is not reached after two rounds of voting, a 'majority rules' approach will be applied. Because time for discussion will be limited, there will be no discussion about outcomes whereby the Round Two data meets the criteria for exclusion based on the pre-defined consensus definition.

The final consensus meeting will be audio recorded and transcribed to facilitate reporting. The PhD student or a member of the study team will type up the transcriptions. These will be classed as source data and will be retained in the study archives, using Unique Identifier Codes for each talker. Reporting of the Delphi surveys will list the outcomes in the final COS [25].

Finally, we will evaluate the participants' experience of the consensus meeting using an evaluation form. This was adapted and modified from the recommended template developed by the COMET Initiative group (Accessible here: http://www.comet-initiative.org/ppi/researchers). It is anticipated that completion of this will take approximately 10 minutes and completion is entirely voluntary.

Follow-Up Workshop to discuss the outcomes identified in the consensus meeting.
Outcomes identified at the consensus meeting as requiring additional input, e.g. 'content analysis' will be discussed with healthcare users and professionals at a subsequent meeting. The workshop will include discussion and, if needed, further explanation of each outcome. Methods utilised by Harman *et al.* (2015) will be utilised: Each outcome will be scored anonymously using an electronic scoring system for immediate feedback. The scores from the workshop will be combined with the scores from the consensus meeting and the definition of consensus applied [39].

The Follow-Up meeting will be audio recorded and transcribed to facilitate reporting. The PhD student or a member of the study team will type up the transcriptions. These will be classed as source data and will be retained in the study archives, using Unique Identifier Codes for each talker.

Compliance

Compliance will be defined according to the number of participants completing both Round One and Round Two of the e-Delphi survey. Attrition, referring to the percentage of participants who withdrew or dropped out between Rounds One and Two will be analysed and reported using similar methods used by Hall *et al.* (2019) [40].

Criteria for terminating the study

Two criteria for terminating the study as a whole are:

- Unable to recruit no more than 10 participants in at least two stakeholder groups.
- Loss of the Chief Investigator (e.g. by resignation or long-term illness) which precludes his active involvement in the Study Management Team.

No further criteria are specified for terminating the study. It is not expected to have any unused study materials since the e-Delphi survey will be managed online.

ANALYSES

Methods

A designated member of the Study Management Team (Roulla Katiri) will conduct the analysis of numerical data collected in the e-Delphi survey, using the UoN license for Statistical Package for the Social Sciences (SPSS) and Microsoft Excel.

The data from both rounds will be subjected to descriptive statistics, such as the distribution of the relevant participant characteristics, distribution of rating scores across stakeholder groups (including the "unable to score" option), and attrition rate from round to round.

Attrition will be analysed and reported, using similar methods adopted by the mOMEnt team [36] and COMIT'ID team [40]: The number of participants in each stakeholder group who respond to Round One will be assessed following Round One closure and parameters like 'number of registrations', 'number of respondents that were emailed', 'percentage of respondents from other sources', 'total number of respondents in each stakeholder group' will be captured. Similar to methods utilised by the mOMEnt team, if the number of responders (<10) is observed for one or more stakeholder groups the e-Delphi Round Two will be reviewed and revised, e.g. might consider grouping with another stakeholder group. All revisions considered with be will be brought to the CROSSSD steering group for discussion prior to finalisation. The total number of participants invited to take part in Round Two will be recorded.

A separate analysis will assess the shifts in scores across the two rounds as a consequence of considering the anonymised feedback from other participants. Also, attrition bias which might occur if participants who do not respond in Round Two have different views from their stakeholder group peers who participate at both rounds [1] will be considered and analysed. To do this, methods used by Bruce *et al.* (2015) [41] can be adopted: response distributions of withdrawn and completing participants can be drawn. Graphical representations by stakeholder group (healthcare users, healthcare practitioners, clinical researchers) can be drawn too, as presented by Hall *et al.* (2019), [40] to indicate if attrition bias is likely to have affected the outcome domain recommendations.

Round Two score distributions for each outcome domain will be considered at the final consensus meeting using a nominal group technique to evaluate individual perspectives. For example, like Harman *et al.* (2013) did, the results of the stakeholder group responses will be compared with the whole group response and percentage agreement will be considered to plan the focus of the consensus meeting [36].

Sample size and justification

As discussed by Hall *et al.* (2018), the numbers of participants recruited and retained remain highly variable in COS studies; it is documented that the size of several recent international e-Delphi surveys recruiting multi-stakeholder groups that include healthcare users (members of the public) can range from 39 to 838 participants completing the final round, with retention rates of 19.5% to 87.1% [26].

There is no agreed method to statistically calculate a sample size for e-Delphi surveys or for consensus meetings. However one of the key deciding factor is that the participant panel membership should adequately represent their corresponding stakeholder group.

Adult SSD is a relatively rare hearing disorder, with approximately 7000 to 9000 new cases diagnosed in the UK per year [42]. SSD interventions is also a relatively new field, especially cochlear implantation which has only been introduced in the last decade [43].

Therefore, the number professionals and members of the public with knowledge and experience of these interventions is limited and so based on the number identified professionals in this field, the aim is to recruit a sufficient number of participants so that a minimum of 20 participants complete the two rounds of the e-Delphi survey in each of the key stakeholder groups (healthcare users, healthcare practitioners, clinical researchers)

The consensus meetings require in-depth discussions and therefore a smaller group of up to 20 participants will be recruited for the meeting.

Similarly, the follow-up workshop, mostly comprised by healthcare users; and will require in-depth discussions about specific outcomes. Therefore an even smaller group of approximately 10 participants will be recruited.

ADVERSE EVENTS

The occurrence of an adverse event as a result of participation within this study is not expected and no adverse event data will be collected.

ETHICAL AND REGULATORY ASPECTS

We do not foresee any particular ethical concerns and according to the low risk of the study the proposal will be submitted to the Proportionate Review Service.

ETHICS COMMITTEE AND REGULATORY APPROVALS

The study will not be initiated before the protocol, consent forms and participant information sheets have received approval / favourable opinion from the Research Ethics Committee (REC), the respective National Health Service (NHS) or other healthcare provider's Research & Development (R&D) department, and the Health Research Authority (HRA) if required.

Should a protocol amendment be made that requires REC approval, the changes in the protocol will not be instituted until the amendment and revised informed consent forms and participant information sheets have been reviewed and received approval / favourable opinion from the REC and R&D departments.

A protocol amendment intended to eliminate an apparent immediate hazard to participants may be implemented immediately providing that the REC are notified as soon as possible and an approval is requested. Minor protocol amendments only for logistical or administrative changes may be implemented immediately; and the REC will be informed.

The study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, 1996; the principles of Good Clinical Practice and the UK Department of Health Policy Framework for Health and Social Care (2017), (https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/).

INFORMED CONSENT AND PARTICIPANT INFORMATION

The participant information sheet will inform participants that their participation is entirely voluntary and that they can withdraw at any time, and that the anonymous information collected might be used to support other research or shared with other researchers. The investigator or their nominee shall emphasize to them that consent regarding study participation may be withdrawn at any time without penalty or affecting the quality or quantity of their future medical care, or loss of benefits to which the participant is otherwise entitled. No study-specific interventions will be done before informed consent has been obtained.

All participant information and survey text be provided in English and will not be translated into other languages. In order to participate in the e-Delphi, all participants need to have a sufficient command of English and be able to complete the survey independently.

The e-Delphi survey is delivered and managed through an online e-management system. The process of obtaining informed consent will be carried out within the survey. Participants will consent to participate by agreeing to the 'consent to participate' button shown on the introductory screen. By clicking 'continue', to move on to the questions within the main survey, their consent will be captured electronically on the survey database. Separate written informed consent will not be sought for the e-Delphi surveys.

We will re-consent the subset of participants who are recruited to join the final consensus meeting and follow-up workshop. This paper consent form will be filed in the Case Report Form (CRF). The process for obtaining participant informed consent will be in accordance with the REC guidance, and Good Clinical Practice (GCP) and any other regulatory requirements that might be introduced. The investigator and the participant shall both sign and date the Consent Form before the person can participate in the study.

The investigator will inform the participant of any relevant information that becomes available during the course of the study, and will discuss with them, whether they wish to continue with the study. If applicable they will be asked to sign revised consent forms.

If the Consent Form is amended during the study, the investigator shall follow all applicable regulatory requirements pertaining to approval of the amended Consent Form by the REC and use of the amended form (including for ongoing participants).

RECORDS

Case Report Forms

Each participant will be assigned a study identity code number, for use on CRFs, other study documents and the electronic database. The documents and database will also use their date of birth (dd/mm/yyyy).

A designated member of the study team (the Data Custodian) and two software programmers will maintain the only access to a record of this Unique Identifier Code with corresponding personal data (name and email address) and the e-Delphi survey.

CRFs will be treated as confidential documents and held securely in accordance with regulations. CRFs shall be restricted to those personnel approved by the Chief or Local Investigator and recorded as such in the study records.

All paper forms used for consensus meetings shall be filled in using black ballpoint pen. Errors shall be lined out but not obliterated by using correction fluid and the correction inserted, initialled and dated.

The Chief or Local Investigator shall sign a declaration ensuring accuracy of data recorded in the CRF.

Source documents

Electronic source documents pertaining to the e-Delphi survey shall be filed within the bespoke online e-management system maintained by the COMET Initiative (University of Liverpool) [1]. The details of this collaboration have been discussed with the study management team and the COMET Initiative. Data is backed up to the University of Liverpool servers, with paper copies filed at the University of Nottingham investigator's site. These may include but are not limited to, consent records, study records, and written feedback. A Consultancy Agreement has been drawn with the Department of Biostatistics at the University of Liverpool and has been submitted to the University of Nottingham.

Audio records, transcriptions and consent forms from the final Consensus Meeting and/or Follow-Up Workshop will be filed at the investigator's site only. A CRF may also completely serve as its own

source data. Only the Study Management Team, two System Administrators from the University of Liverpool (Richard Crew and Keith Kennedy) and staff identified on the delegation log shall have access to study documentation other than the regulatory requirements listed below.

Direct access to source data / documents

The CRF and all source documents shall made be available at all times for review by the Chief Investigator, Sponsor's designee and inspection by relevant regulatory authorities.

DATA PROTECTION

All study staff and investigators will endeavour to protect the rights of the study's participants to privacy and informed consent, and will adhere to the Data Protection Act (1998). The CRF will only collect the minimum required information for the purposes of the study. CRFs will be held securely, in a locked room (authorised personal only) and locked cupboard or cabinet. Access to the information will be limited to the study staff and investigators and any relevant regulatory authorities (see above). Computer held data including the study database will be held securely and password protected. All data will be stored on a secure dedicated web server. Access will be restricted by user identifiers and passwords (encrypted using a one way encryption method).

The study documents held by the Chief Investigator on behalf of the Sponsor shall be archived at secure archive facilities at the University of Nottingham. This archive shall include all study data and associated meta-data encryption codes.

All personal data (email addresses of those who wish to receive study results) will be deleted as soon as the study results have been disseminated or after 2 years, whichever happens first. No personal data will be retained for long-term storage and archiving.

The Consensus Meeting and Follow-Up Workshop will be held within the same University of Nottingham unit, audio recordings will be saved in the same office area and will be transcribed within three weeks. In the process of transcribing only non-identifiable information will be transcribed e.g. identity of any of the talkers or anything said that identifies an individual will be removed.

Information about the study in the participant's medical records / hospital notes will be treated confidentially in the same way as all other confidential medical information.

Electronic data will be backed up every 24 hours to both local and remote media in encrypted format. The bespoke online e-management system maintained by the COMET Initiative (University of Liverpool) complies with these Data Protection requirements.

QUALITY ASSURANCE & AUDIT

INSURANCE AND INDEMNITY

Insurance and indemnity for clinical study participants and study staff is covered within the NHS Indemnity Arrangements for clinical negligence claims in the NHS, issued under cover of HSG (96)48. There are no special compensation arrangements, but study participants may have recourse through the NHS complaints procedures.

The University of Nottingham as research Sponsor indemnifies its staff, research participants and research protocols with both public liability insurance and clinical trials insurance. These policies include provision for indemnity in the event of a successful litigious claim for proven non-negligent harm.

STUDY CONDUCT

Study conduct may be subject to systems audit for inclusion of essential documents; permissions to conduct the study; CVs of study staff and training received; local document control procedures; consent procedures and recruitment logs; adherence to procedures defined in the protocol (e.g. inclusion / exclusion criteria, timeliness of visits); and accountability of study materials.

STUDY DATA

Monitor of the study data shall include confirmation of informed consent; source data verification, data storage and data transfer procedures; local quality control checks and procedures, back-up and disaster recovery of any local databases and validation of data manipulation. The Chief Investigator (Pádraig T. Kitterick) will carry out monitoring of study data as an ongoing activity and specifically at the end of each e-Delphi survey round prior to data analysis. Chief Investigator (Pádraig T. Kitterick) and Study Coordinator (Roulla Katiri) are the data custodians and will have full rights of access to the electronic source data.

Entries on CRFs will be verified by inspection against the electronic source data stored within the bespoke online e-management system maintained by the COMET Initiative (University of Liverpool). A sample of CRFs (10% or as per the study risk assessment) will be checked on a regular basis for verification of all entries made. In addition the subsequent capture of the data on the study database will be checked. Where corrections are required these will carry a full audit trail and justification, presented and approved by the Study Management Team.

Study data and evidence of monitoring and systems audits will be made available for inspection by the REC as required.

RECORD RETENTION AND ARCHIVING

In compliance with the International Conference on Harmonisation (ICH) / Good Clinical Practice (GCP) guidelines, regulations and in accordance with the University of Nottingham Code of Research Conduct and Research Ethics, the Chief or local Principal Investigator will maintain all records and documents regarding the conduct of the study.

Personal, identifiable information (i.e. names and email addresses) will be kept for 2 years after the End of Study report has been submitted to the Ethics Committee and the Study Sponsor. This time-scale will allow for thorough results' analysis and dissemination in publications.

All personal data (email addresses of those who wish to receive study results) will be deleted as soon as the study results have been disseminated or after 2 years, whichever happens first. No personal data will be retained for long-term storage and archiving.

Non-personal data will be retained for at least 7 years or for longer if required. If the responsible investigator is no longer able to maintain the study records, a second person will be nominated to take over this responsibility.

The study documents held by the Chief Investigator on behalf of the Sponsor shall be finally archived at secure archive facilities at the University of Nottingham. This archive shall include all anonymised audio recordings, study databases and associated meta-data encryption codes.

DISCONTINUATION OF THE STUDY BY THE SPONSOR

The Sponsor reserves the right to discontinue this study at any time for failure to meet expected enrolment goals, for safety or any other administrative reasons. The Sponsor shall take advice as appropriate in making this decision.

STATEMENT OF CONFIDENTIALITY

Individual participant medical or personal information obtained as a result of this study are considered confidential and disclosure to third parties is prohibited with the exceptions noted above.

Participant confidentiality will be further ensured by utilising identification code numbers to correspond to treatment data in the computer files.

Such medical information may be given to the participant's medical team and all appropriate medical personnel responsible for the participant's welfare.

If information is disclosed during the study that could pose a risk of harm to the participant or others, the researcher will discuss this with the Chief Investigator and where appropriate report accordingly.

Data generated as a result of this study will be available for inspection on request by the participating physicians, the University of Nottingham representatives, the REC, local R&D Departments and the regulatory authorities.

PUBLICATION AND DISSEMINATION POLICY

The project proposal has already been registered in the database of the COMET initiative http://www.comet-initiative.org/studies/details/1084?result=true.

Data from the final analysis of the e-Delphi, consensus meeting and feedback questionnaire will be presented at relevant national and international conferences, e.g. British Society of Audiology.

Peer-reviewed publications resulting for the research are also planned. We intend to publish the final COS; addressing all primary objectives, anticipated summer 2020.

This research will be further disseminated to members of the public and clinicians through specialist magazine articles and support groups. Participants will not be identified in any publications.

USER AND PUBLIC INVOLVEMENT

This study will have substantive user and public involvement. Details are given throughout the protocol description: Membership of the Study Management Team and Research Steering Group, reviewing study design, written study materials (i.e. participant information sheets) for face validity, understanding and acceptability, piloting and reviewing Round One of the e-Delphi survey providing any additional outcome domains that they believe should be included, and promoting participation in the e-Delphi surveys and disseminating study results.

STUDY FINANCES

Funding source

The main body of work is funded by the NIHR Nottingham Hearing Biomedical Research Centre.

Additional grants obtained:

- Graham Frazer Foundation Travel Grant (£500) to attend the 15th International Conference on Cochlear Implants and other Implantable Auditory Technology (Ci2018.org), where the study was first launched.
- Oticon Medical (£850 + VAT) to purchase the e-Delphi Manager from the University of Liverpool.

Participant stipends and payments

Participants will not be paid to participate in the e-Delphi survey.

Public Research Collaborators who are members of the Research Steering Group, or who are undertaking patient involvement in the study will be reimbursed at a rate commensurate with NIHR INVOLVE payment guidelines: http://www.invo.org.uk/posttypepublication/what-you-need-to-know-about-payment.

Travel expenses will be offered for any visits required by the study, such as for attending the final consensus meeting.

SIGNATURE PAGES

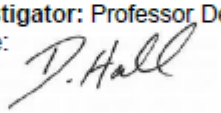
Signatories to Protocol:

Chief Investigator: Dr Pádraig T. Kitterick

Signature: 

Date: 20/05/2019

Co-Investigator: Professor Deborah A. Hall

Signature: 

Date: 20/05/2019

Co-Investigator: Sotira (Roulla) Katiri

Signature: 

Date: 20/05/2019

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Appendix 6. Healthcare user participant information sheet.

University of Nottingham
UK | CHINA | MALAYSIA

Local Letterhead to be added

PARTICIPANT INFORMATION SHEET
(Final Version 2.0: 06/07/2019)

IRAS Project ID: 239750

Title of Study: Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) Study

Name of Chief Investigator: Dr Pádraig Kitterick

Local Researcher(s): Roulla Katiri

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish. Ask us if there is anything that is not clear.

What is the purpose of the study?

Single Sided Deafness (SSD) refers to the condition where there is normal or near-normal hearing in one ear and a severe- to-profound hearing impairment in the other ear.

Good hearing in both ears is important for everyday listening tasks such as understanding speech in noisy environments, locating where sounds are, and identifying threats such as oncoming traffic.

Researchers don't yet agree on what aspects (benefits and harms, known as 'outcomes') should always be assessed when evaluating whether or not a treatment for SSD is effective. Different outcomes are measured in different studies. This makes it difficult to compare results, slowing progress in finding the most effective treatment for SSD.

We are seeking to change this by developing a fixed list of aspects of SSD, known as a **'Core Outcome Set'** that should be measured and reported in all future trials of SSD treatments.

We will work closely with people living with SSD and those with a professional interest across the world. We will find agreement on what outcomes are critical and important to measure when assessing how effective treatments are.

This study is part of a PhD undertaken by Roulla Katiri.

Why have I been invited?

You are being invited to take part because you have been diagnosed with Single Sided Deafness (SSD). We want you to have your say in what is measured in future SSD research. We would like at least 20 people with SSD, 20 healthcare professionals and 20 researchers to take part. There is no set upper limit on the number of people taking part.

Can I take part?
You can complete the surveys if you:

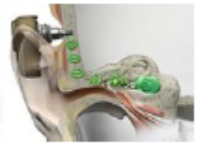
- ✓ Are aged 18 years or over,
- ✓ Have been diagnosed with SSD 12 months ago, or more
- ✓ Are able to read, understand and complete questionnaires in English
- ✓ You have received or considered trying treatment for your SSD

Taking part is voluntary. You will not receive any payment for completing the surveys.

Which treatments must I have received or considered trying?
They can be any of the types below:

1. Contralateral Routing of Sounds (CROS) hearing aid
2. Bone Anchored Hearing Aid (BAHA)
3. Middle Ear Implant (MEI)
4. Cochlear Implant (CI)
5. SoundBite™


1. CROS Aid


2. BAHA


3. MEI


4. CI


5. SoundBite™

Do I have to take part?
No. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to give consent. If you decide to take part you are still free to withdraw at any time and without giving a reason. This would not affect your legal rights.

What will happen to me if I take part?
You will complete an online survey made up of two questionnaire rounds, about what is important when deciding if Single Sided Deafness (SSD) treatments work.

You will be asked to answer general questions about what you feel is important, based on your own experiences. What would you want a treatment to help you with? The survey will not ask you about whether you liked or disliked SSD treatments or how well they work or worked. The survey is not about assessing existing treatments.

What is involved in completing the survey?

1. The survey will ask you what you think are the most important aspects of SSD to measure when deciding if a treatment is working.
2. Each survey involves two rounds of questions which will each take about 60 minutes to complete. You will be able to take breaks. See Figure 1 for details.
3. Each round of questions will be sent separately, over a period of 4 months.
4. After you have received the link, you will have up to 3 weeks to complete each round of questions.

Round One:

1. You will be asked to rate the importance of each aspect of SSD in deciding whether a treatment is effective. To do this you will use a simple 1-9 scoring system.
2. You will be given the chance to add any aspects of SSD that you feel we have missed from the list.

Round Two:

1. We will remind you of the previous scores you gave and show you a summary of others' scores.
2. Based on this information, you will have the chance to change or keep your score the same.
3. No one else will be able to see your individual score or know who you are.
4. You will have the option to complete a short feedback questionnaire about your experiences in taking part following completion of Round Two.

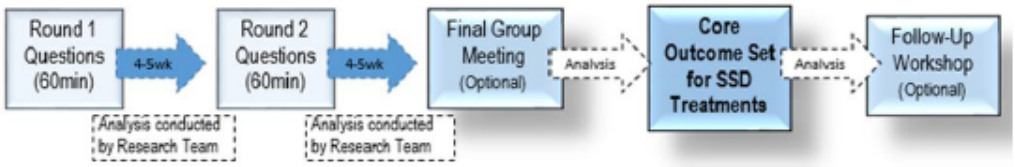
Group Meeting (Optional):

There will be a group meeting to discuss and agree on the list of the most important aspects to measure, based on the survey results. A group of approximately 20 healthcare users diagnosed with SSD and professionals working in the field of SSD will be invited to take part. It is anticipated that the meeting will take 7 hours, lunch and breaks will be provided. The meeting will be held in Nottingham (expected January 2020). The meeting discussions will be audio-recorded and transcribed by the study management team. The recordings will be destroyed as soon as the transcriptions are obtained and the transcriptions will be stored as per local policies. There will be limited places so please register your interest in attending the meeting with the research team. If you do decide to take part and a place is available then you be sent the details of the meeting location and will be asked to sign a consent form. You will have the option to complete a short evaluation form about your experiences in taking part following completion of the group meeting.

Follow-Up Workshop (Optional):

When the most important aspects to measure are identified and analysed; a subsequent group meeting will be organised. The focus of this meeting will be to discuss the list of outcomes and define them so they can be utilised in future studies. A group of approximately 10 healthcare users diagnosed with SSD and professionals working in the field of SSD will be invited to take part. It is anticipated that the meeting will take 7 hours, lunch and breaks will be provided. The meeting will be held in Nottingham (expected March 2020). The meeting discussions will be audio-recorded and transcribed by the study management team. The recordings will be destroyed as soon as the transcriptions are obtained and the transcriptions will be stored as per local policies. There will be limited places so please register your interest in attending the workshop with the research team. If you do decide to take part and a place is available then you will be sent the details of the workshop location and will be asked to sign a consent form.

Figure 1: Steps involved in CROSSSD study plan.



Expenses and payments

Participants will not be paid to participate in the online surveys. Travel expenses will be offered for any visits incurred as a result of participation in the group meetings or the follow-up workshop. Travel expenses will be reimbursed for UK or Ireland participants only.

What are the possible disadvantages and risks of taking part?

We do not foresee any particular risks.

What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get from this study may help future SSD studies. Researchers working in the field of SSD will adopt the final agreed list of aspects for measuring the effect of SSD treatments in every clinical trial. In the long run, this will make it easier and quicker to find out which treatments work best and why.

What happens when the research study stops?
The results collected from the two online surveys, the group meeting and workshop will be used to develop a 'Core Outcome Set' for SSD.

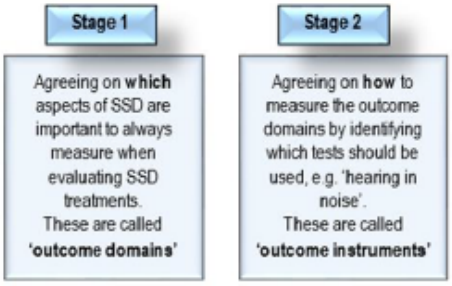
What is an 'Outcome'?
An 'outcome' refers to a single aspect experienced by people with SSD. To test how well treatments work, we measure one or more of these outcomes. For example we might measure how well someone with SSD can hear speech in background noise.

What is a 'Core Outcome Set'?
A 'Core Outcome Set' refers to a list of the most important aspects agreed following the survey rounds and group meeting mentioned above. It is made up of a list of outcomes and outcome instruments (tests) that should be used, measured and reported in clinical research.

Why is a 'Core Outcome Set' important to improving SSD treatments?
Studies testing similar SSD treatments often measure different outcomes. If one measures 'hearing in noise' and the other measures 'quality of life' we cannot compare the results. It would be like trying to compare 'apples and pears'. Researchers may also choose what they publish and may not include outcome results that were disappointing. This does not give a complete picture of the effect of a treatment. If studies reported results for a set number of outcomes, data could be compared and combined correctly. This would help us to make sense of treatments and improve the way we manage SSD.

How is a Core Outcome Set Defined?
The 'Core Outcome Set' must be relevant to health professionals working in the field of SSD and to people with lived experience of SSD. We want to make sure that everyone is involved and agrees on the core outcomes. Defining outcomes has two major parts (Figure 2):

Figure 2: The two stages involved in defining outcomes.



What are we doing to define a Core Outcome Set for SSD?
We are currently concerned with Stage 1; identifying and agreeing which aspects of SSD to measure. To do this, we are running these online surveys, referred to as 'Delphi (consensus) surveys'. Individuals taking part will either have been diagnosed with SSD (patients), treat SSD (healthcare professionals) or research SSD (researchers).

Following the survey, there will be a face-to-face group meeting and follow-up workshop to finalise and define the Core Outcome Set. This will involve the research team and a number of participants who completed the surveys (taking part is optional). By doing this, we will ensure that all key parties' views are taken into account.

By taking part in this study you will help to produce a Core Outcome Set for SSD.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. The researchers' contact details are given at the end of this information sheet. If you remain unhappy and wish to complain formally, you can do this by contacting [please provide the contact details of PALS for the hospital (different for each PIC)]

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against the University of Nottingham but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence.

If you join the study, we will use information collected from you during the course of the research. This information will be kept **strictly confidential**, stored in a secure and locked office, and on a password protected database at the University of Nottingham. Under UK Data Protection laws the University is the Data Controller (legally responsible for the data security) and the Chief Investigator of this study (named above) is the Data Custodian (manages access to the data). This means we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited as we need to manage your information in specific ways to comply with certain laws and for the research to be reliable and accurate. To safeguard your rights we will use the minimum personally – identifiable information possible.

You can find out more about how we use your information and to read our privacy notice at:
https://www.nottingham.ac.uk/utilities/privacy.aspx.

The data collected for the study will be looked at and stored by authorised persons from the University of Nottingham who are organising the research. Electronic data generated by the online questionnaires will be accessible and will be maintained by the COMET Initiative (http://www.comet-initiative.org/) which is located at the University of Liverpool. These may include but are not limited to, consent records, study records, and written feedback. Only two System Administrators from the University of Liverpool and staff identified on the delegation log shall have access to study documentation other than the regulatory requirements listed below.

Data may also be looked at by authorised people from regulatory organisations to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

Where possible information about you which leaves the Nottingham Biomedical Research Centre will have your name removed and a unique code will be used so that you cannot be recognised from it. However sometimes we need to ensure that we can recognise you to link the research data with your records so in these instances we will need to know your name and email address.

Your contact information will be kept by the University of Nottingham for two years after the end of the study so that we are able to contact you about the findings of the study and possible follow-up studies (unless you advise us that you do not wish to be contacted).

This information will be kept separately from the research data collected and only those who need to will have access to it. All other data obtained from the online surveys, group meetings and follow-up workshop will be kept

securely for 7 years. After this time your data will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team given permission by the data custodian will have access to your personal data.

In accordance with the University of Nottingham's, the Government's and our funders' policies we may share our research data with researchers in other Universities and organisations, including those in other countries, for research in health and social care. Sharing research data is important to allow peer scrutiny, re-use (and therefore avoiding duplication of research) and to understand the bigger picture in particular areas of research. Data sharing in this way is usually anonymised (so that you could not be identified) but if we need to share identifiable information we will seek your consent for this and ensure it is secure. You will be made aware then if the data is to be shared with countries whose data protection laws differ to those of the UK and how we will protect your confidentiality.

Although what you say to us is confidential, should you disclose anything to us which we feel puts you or anyone else at any risk, we may feel it necessary to report this to the appropriate persons.

What will happen if I don't want to carry on with the study?

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw we will no longer collect any information about you or from you but we will keep the information about you that we have already obtained as we are not allowed to tamper with study records and this information may have already been used in some analyses and may still be used in the final study analyses. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Who is organising and funding the research?

This research is being organised by the University of Nottingham and is being funded by the NIHR Nottingham Biomedical Research Centre and will be managed by researchers based at this centre.

Who has reviewed the study?

All research in healthcare is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the Nottingham 2 Research Ethics Committee.

Further information and contact details

The research team are happy to answer any questions you have before you agree to take part or when you are taking part in the survey:

Roulla Katiri
PhD Student CROSSSD Study
Roulla.Katiri@nottingham.ac.uk

Dr Pádraig Kitterick
Associate Professor in Hearing Sciences
Padraig.Kitterick@nottingham.ac.uk

Professor Deborah A. Hall
Professor of Hearing Sciences
Deborah.Hall@nottingham.ac.uk

You can also get through via our reception on: +44 (0) 115 8232600 or by post at: Biomedical Research Centre (BRC), Ropewalk House, 113 The Ropewalk, Nottingham. NG1 5DU.

You can find more information about the study on:
-University of Nottingham Website: www.nottingham.ac.uk/go/CROSSSD or,
-NIHR Nottingham BRC Website: https://nottinghambrc.nihr.ac.uk/hearing/.

Follow us on Twitter:

@CROSSSD_
#CROSSSD

Appendix 7. e-Delphi survey consent form.

University of Nottingham
UK | CHINA | MALAYSIA

(Form will be online)

CONSENT FORM
(Final Version 1.0: 22/05/2019)

IRAS Project ID: 239750

Title of Study: Core Rehabilitation Outcome Set in Single Sided Deafness (CROSSSD) Study

Name of Researcher: Roulla Katiri

Before proceeding to Round One, please read and confirm your agreement with the following information:

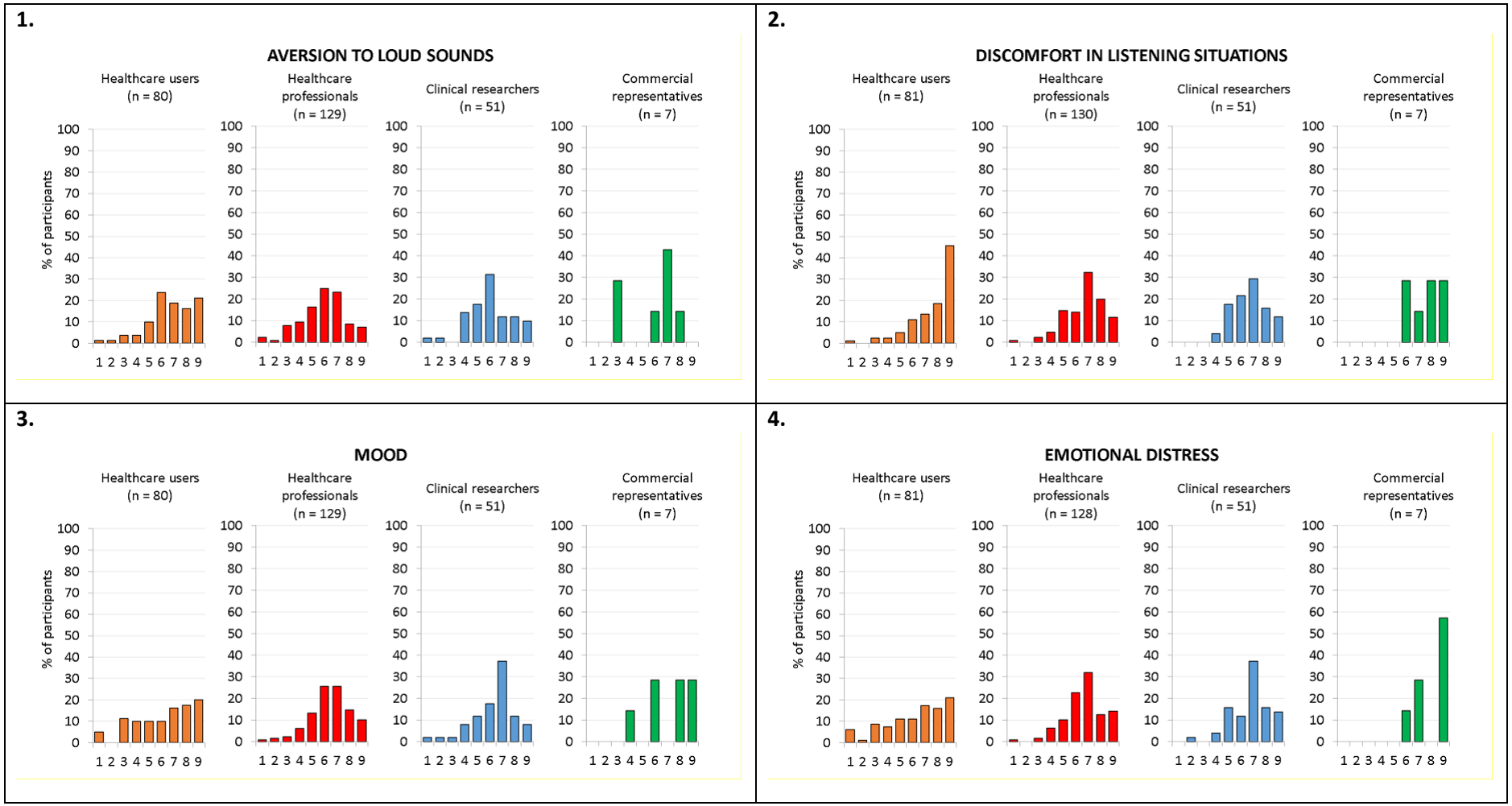
1. I confirm that I have read and understand the information sheet Final Version 1.0 dated 22/05/2019 for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care (if appropriate) or legal rights being affected. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis.
3. I understand that data collected in the study will be looked at by the research group and possibly reviewed by authorised individuals from the University of Nottingham, University of Liverpool and regulatory authorities. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential.
4. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.
5. I understand that the survey involves completing two rounds of questions on two separate occasions over 4-6 months.
6. By ticking this box I agree to take part in the above study on the basis of the statements above. ☐

Please Tick Box

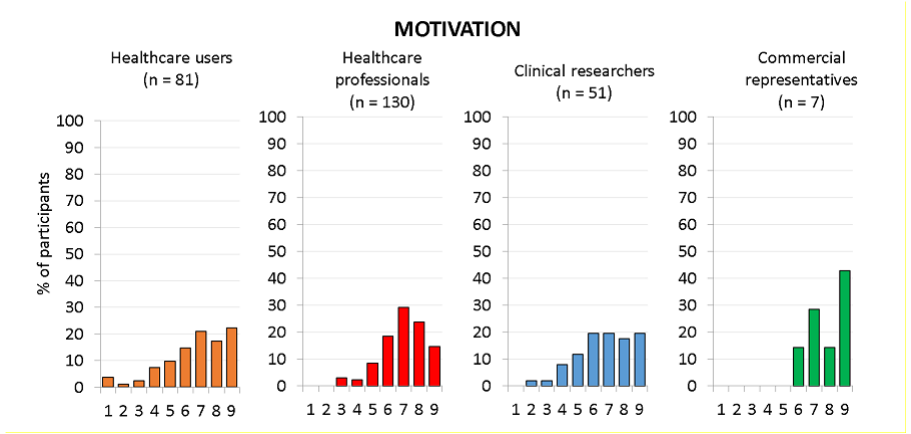
CROSSSD

Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) Study
Participant Consent Form for Online Survey: Final Version 1.0, 22/05/2019

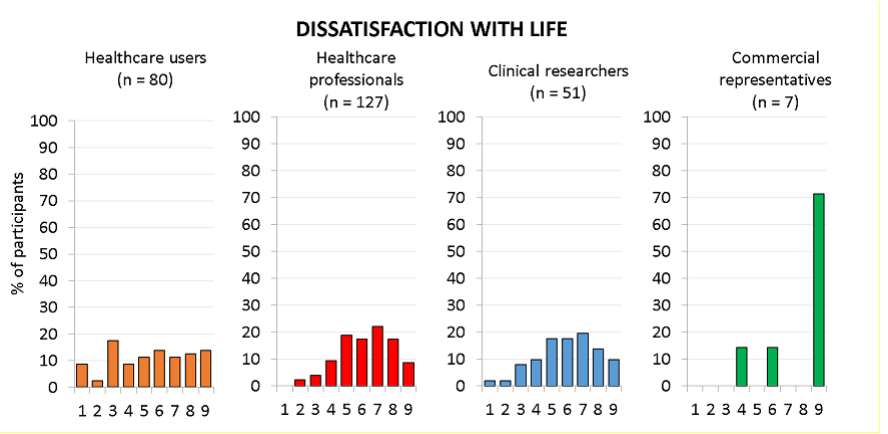
Appendix 8. Histograms of the Round 1 e-Delphi ratings for the 44 outcome domains.



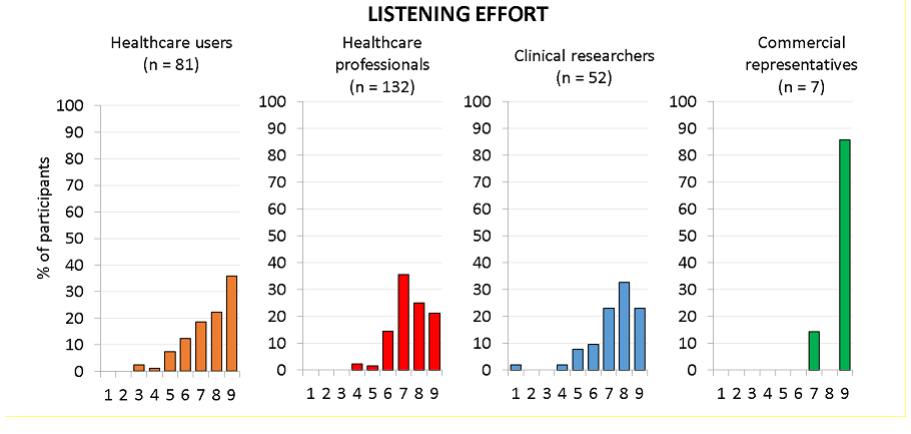
5.


MOTIVATION
Healthcare users (n = 81)
Healthcare professionals (n = 130)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

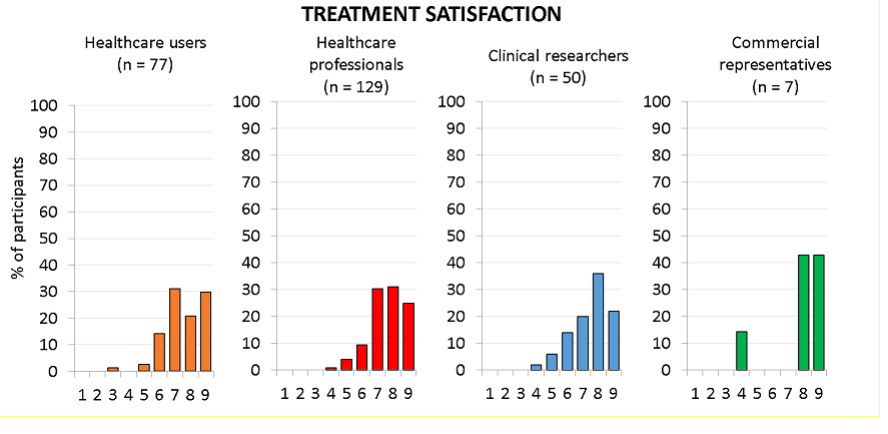
6.


DISSATISFACTION WITH LIFE
Healthcare users (n = 80)
Healthcare professionals (n = 127)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

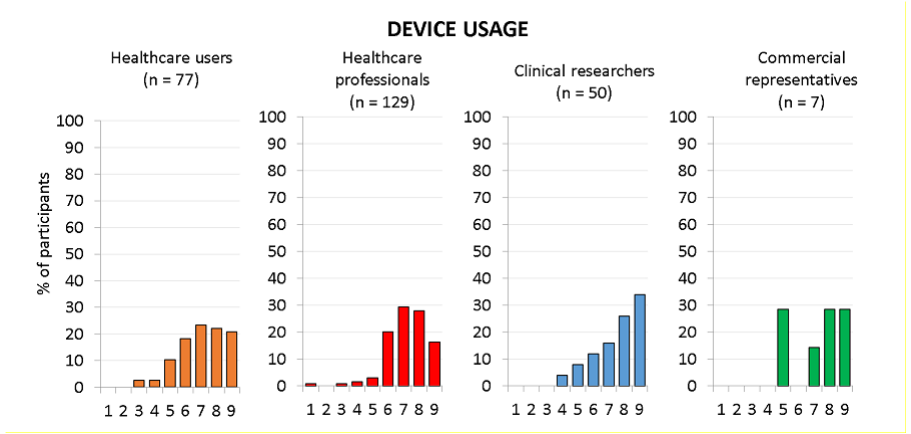
7.


LISTENING EFFORT
Healthcare users (n = 81)
Healthcare professionals (n = 132)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

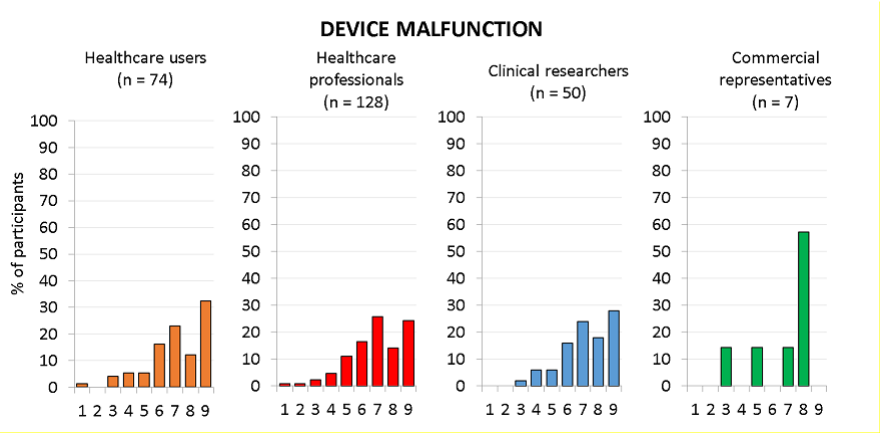
8.


TREATMENT SATISFACTION
Healthcare users (n = 77)
Healthcare professionals (n = 129)
Clinical researchers (n = 50)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

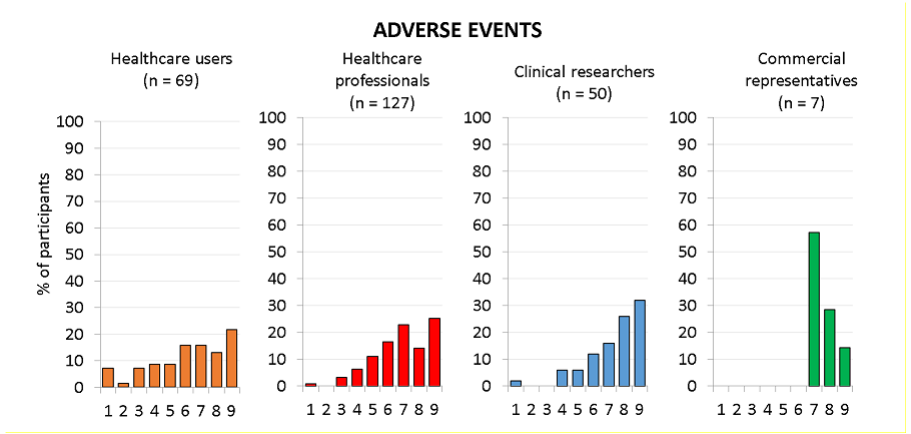
9.


DEVICE USAGE
Healthcare users (n = 77)
Healthcare professionals (n = 129)
Clinical researchers (n = 50)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

10.


DEVICE MALFUNCTION
Healthcare users (n = 74)
Healthcare professionals (n = 128)
Clinical researchers (n = 50)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

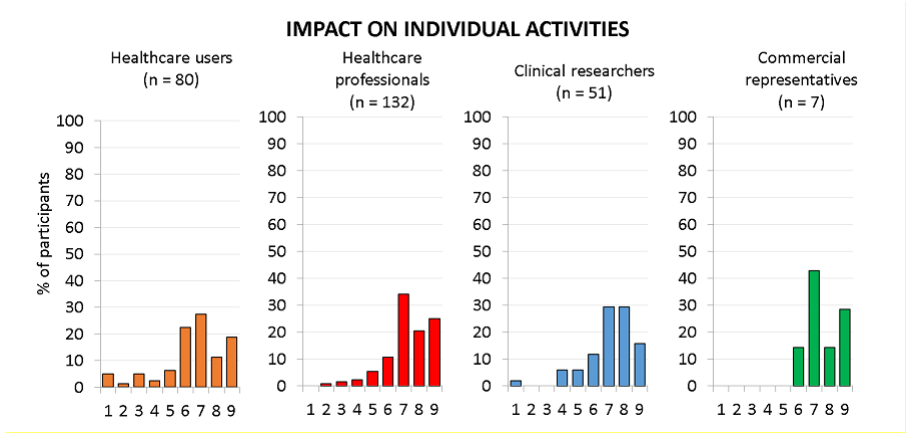
11.


ADVERSE EVENTS
Healthcare users (n = 69)
Healthcare professionals (n = 127)
Clinical researchers (n = 50)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

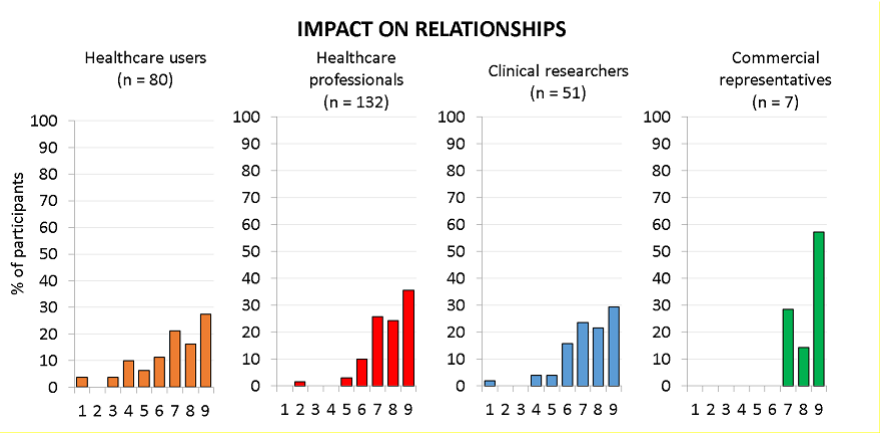
12.


AVOIDING SOCIAL SITUATIONS
Healthcare users (n = 81)
Healthcare professionals (n = 132)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

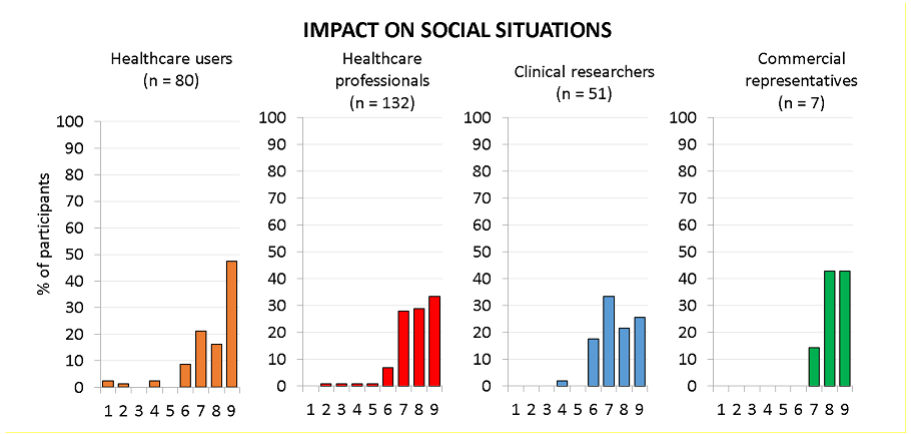
13.


IMPACT ON INDIVIDUAL ACTIVITIES
Healthcare users (n = 80)
Healthcare professionals (n = 132)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

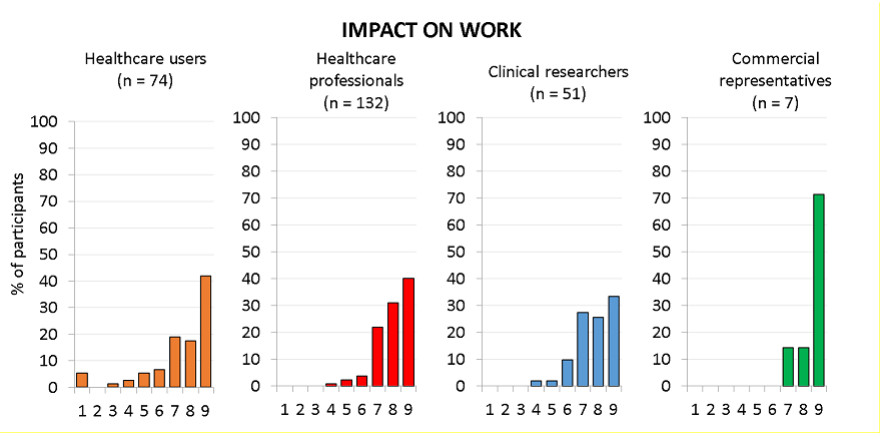
14.


IMPACT ON RELATIONSHIPS
Healthcare users (n = 80)
Healthcare professionals (n = 132)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

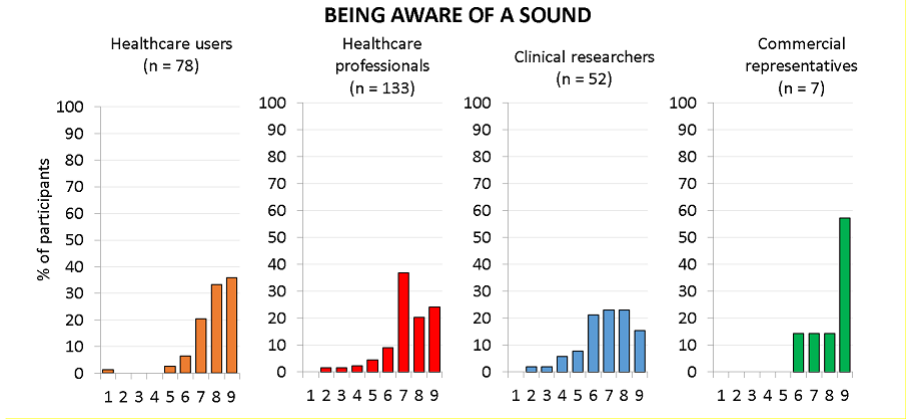
15.


IMPACT ON SOCIAL SITUATIONS
Healthcare users (n = 80)
Healthcare professionals (n = 132)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

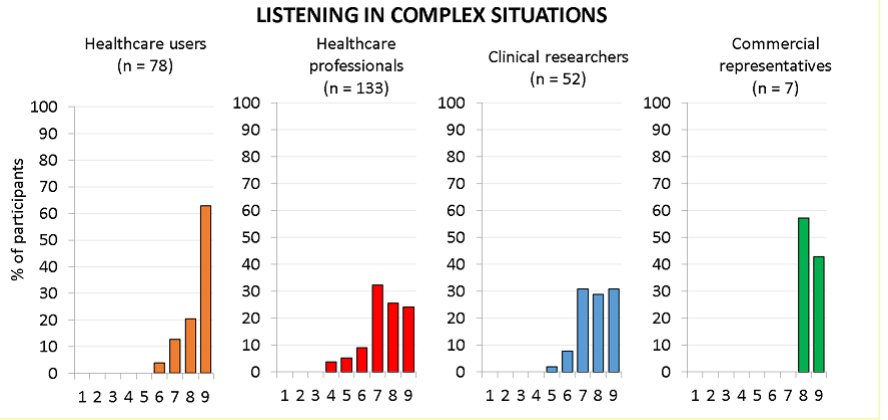
16.


IMPACT ON WORK
Healthcare users (n = 74)
Healthcare professionals (n = 132)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

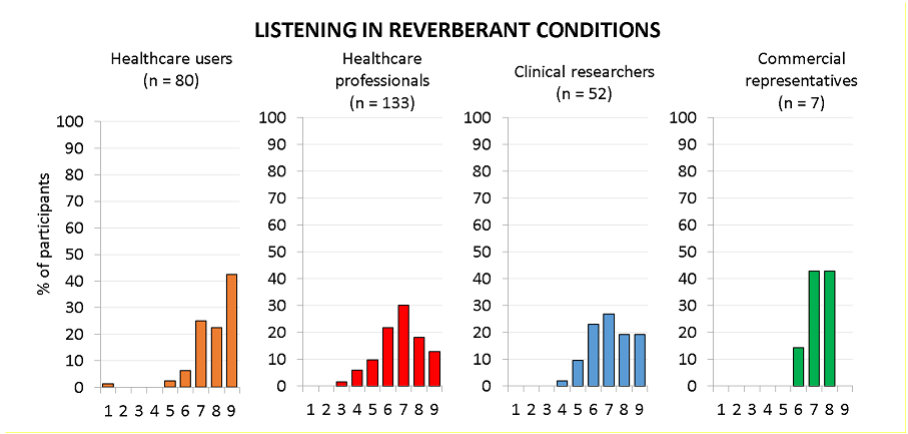
17.


BEING AWARE OF A SOUND
Healthcare users (n = 78)
Healthcare professionals (n = 133)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

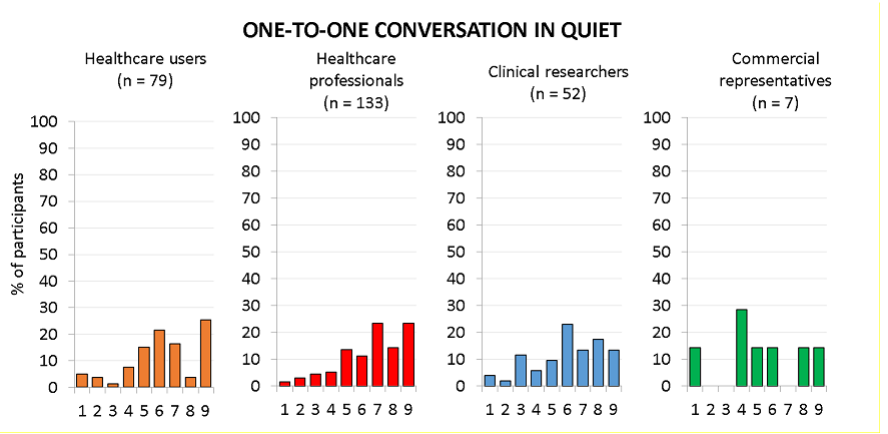
18.


LISTENING IN COMPLEX SITUATIONS
Healthcare users (n = 78)
Healthcare professionals (n = 133)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

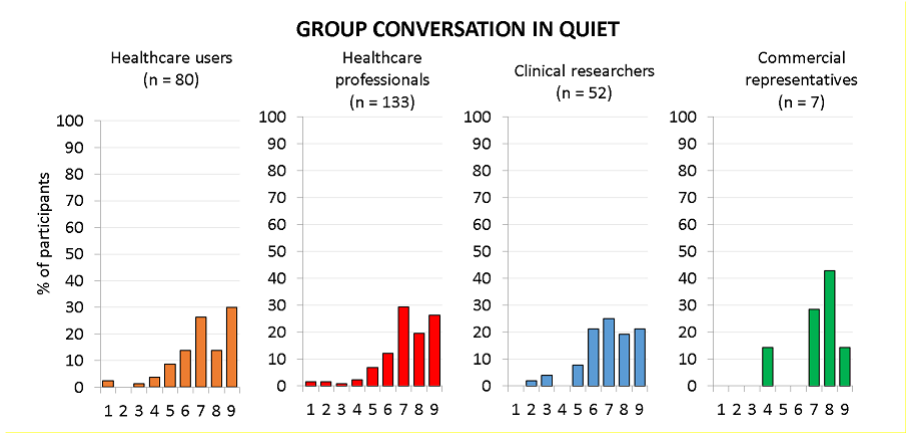
19.


LISTENING IN REVERBERANT CONDITIONS
Healthcare users (n = 80)
Healthcare professionals (n = 133)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

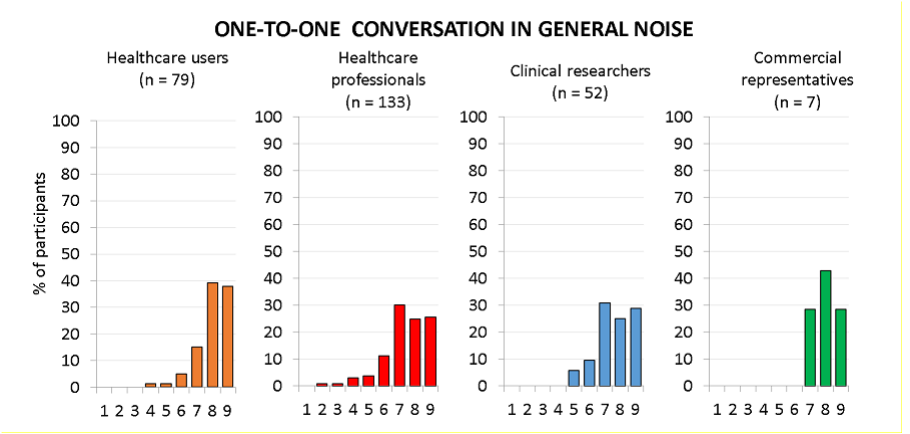
20.


ONE-TO-ONE CONVERSATION IN QUIET
Healthcare users (n = 79)
Healthcare professionals (n = 133)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

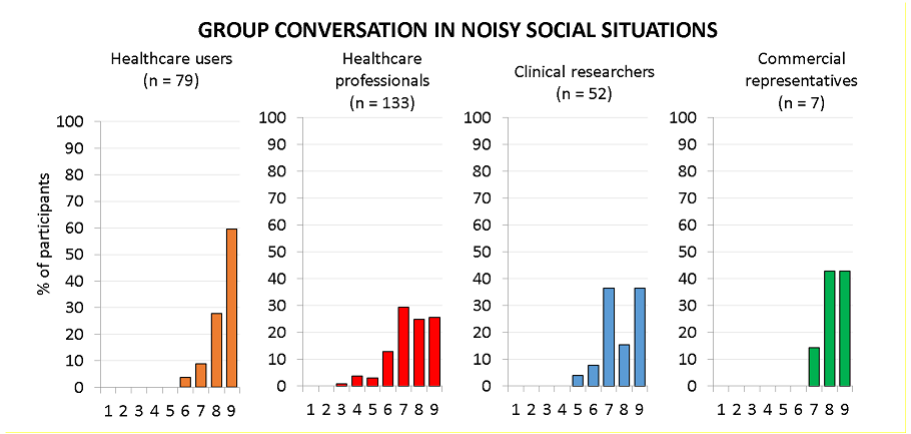
21.


GROUP CONVERSATION IN QUIET
Healthcare users (n = 80)
Healthcare professionals (n = 133)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

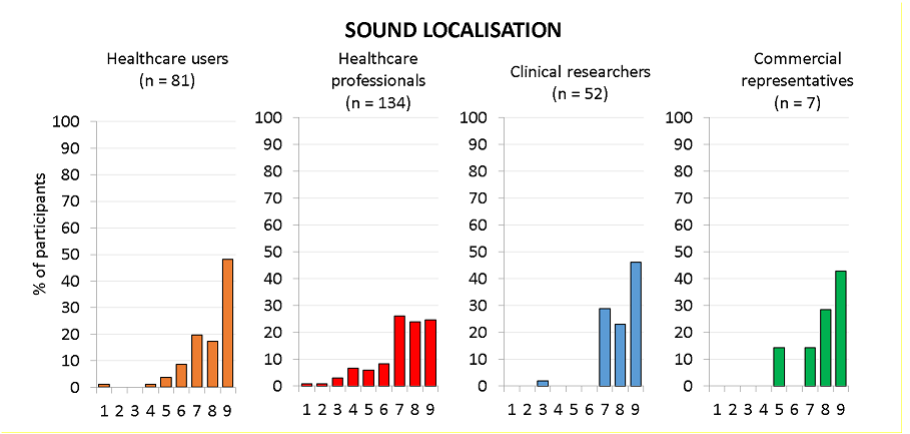
22.


ONE-TO-ONE CONVERSATION IN GENERAL NOISE
Healthcare users (n = 79)
Healthcare professionals (n = 133)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

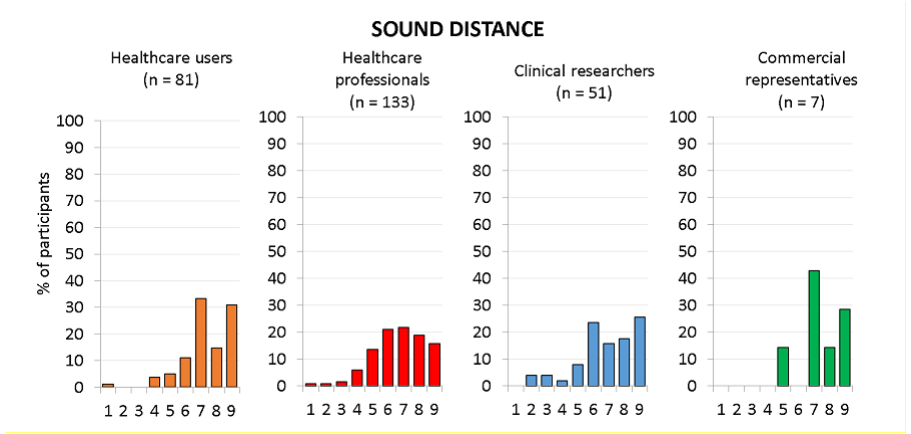
23.


GROUP CONVERSATION IN NOISY SOCIAL SITUATIONS
Healthcare users (n = 79)
Healthcare professionals (n = 133)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

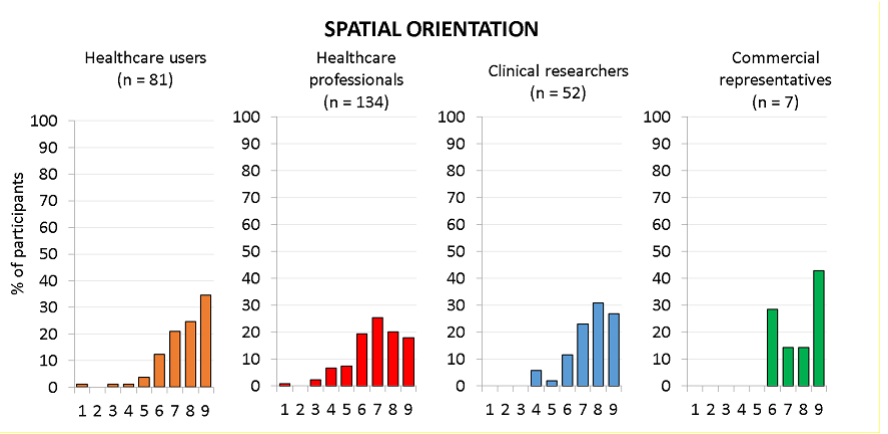
24.


SOUND LOCALISATION
Healthcare users (n = 81)
Healthcare professionals (n = 134)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

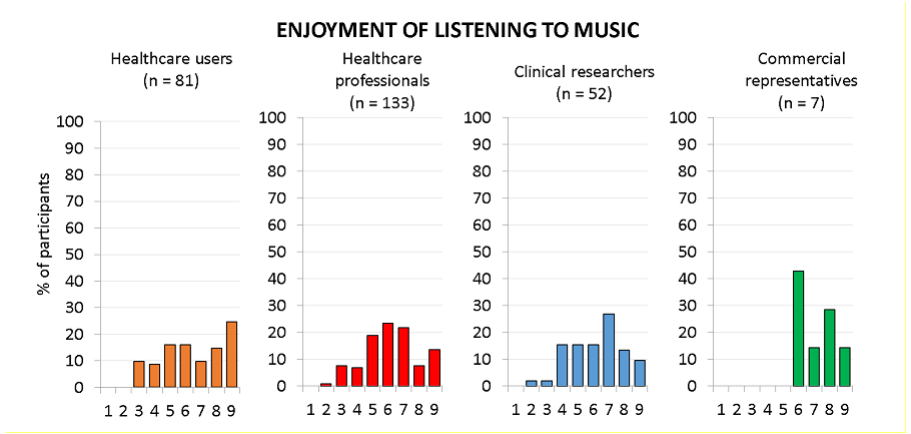
25.


SOUND DISTANCE
Healthcare users (n = 81)
Healthcare professionals (n = 133)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

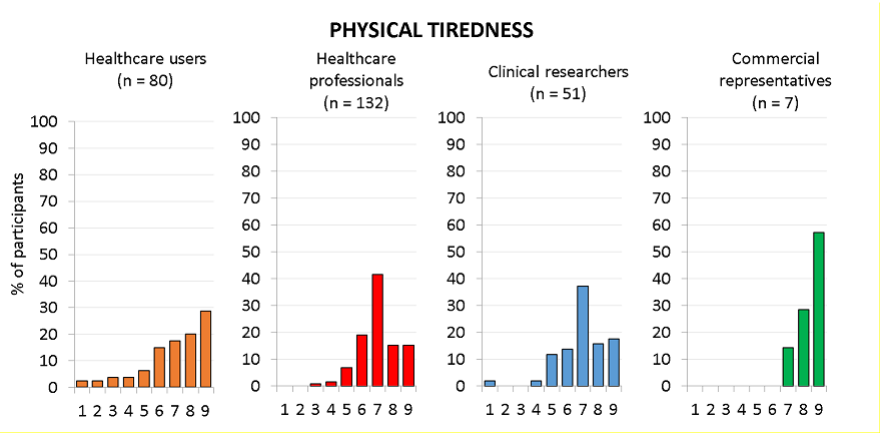
26.


SPATIAL ORIENTATION
Healthcare users (n = 81)
Healthcare professionals (n = 134)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

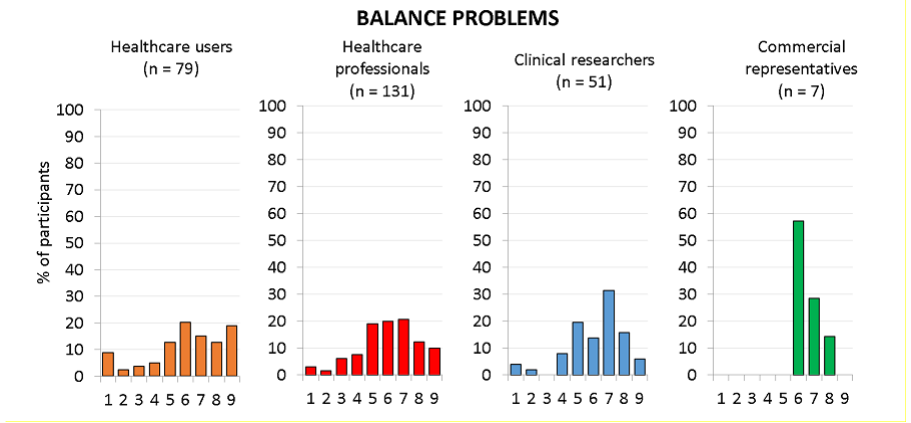
27.


ENJOYMENT OF LISTENING TO MUSIC
Healthcare users (n = 81)
Healthcare professionals (n = 133)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

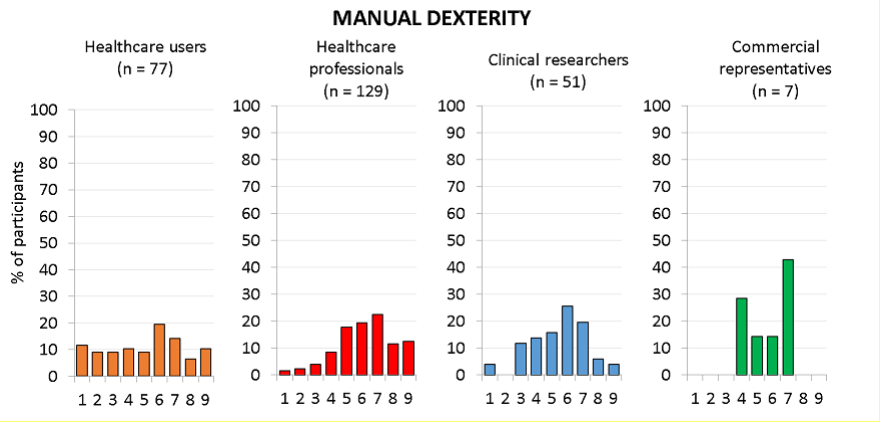
28.


PHYSICAL TIREDNESS
Healthcare users (n = 80)
Healthcare professionals (n = 132)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

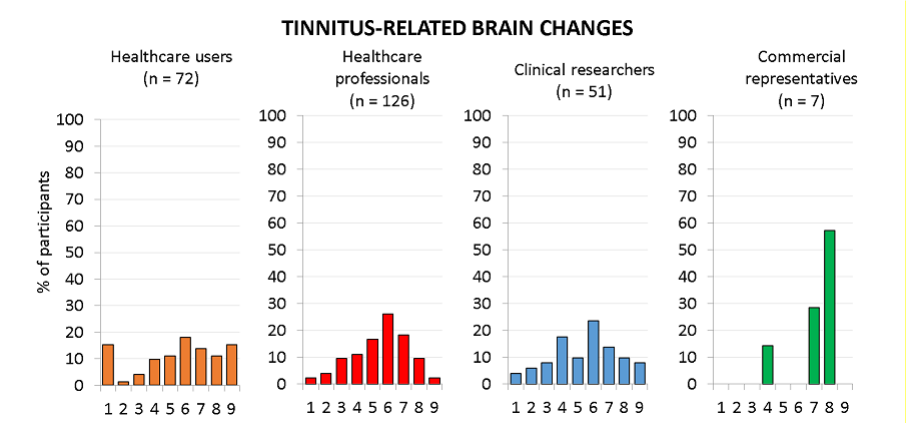
29.


BALANCE PROBLEMS
Healthcare users (n = 79)
Healthcare professionals (n = 131)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

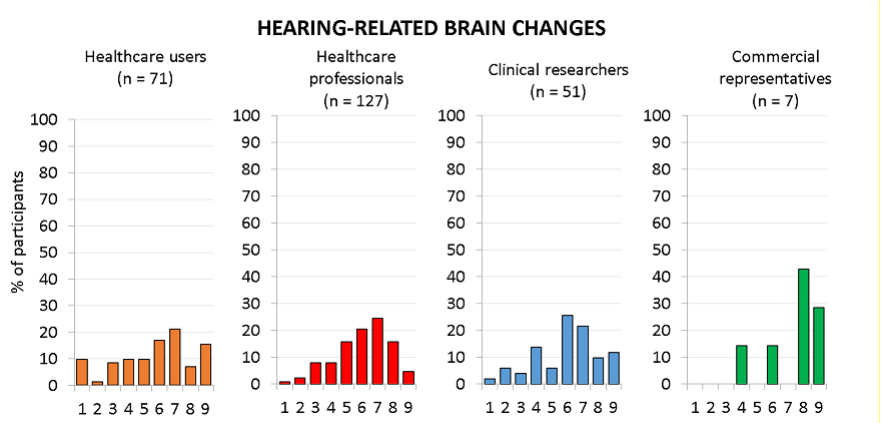
30.


MANUAL DEXTERITY
Healthcare users (n = 77)
Healthcare professionals (n = 129)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

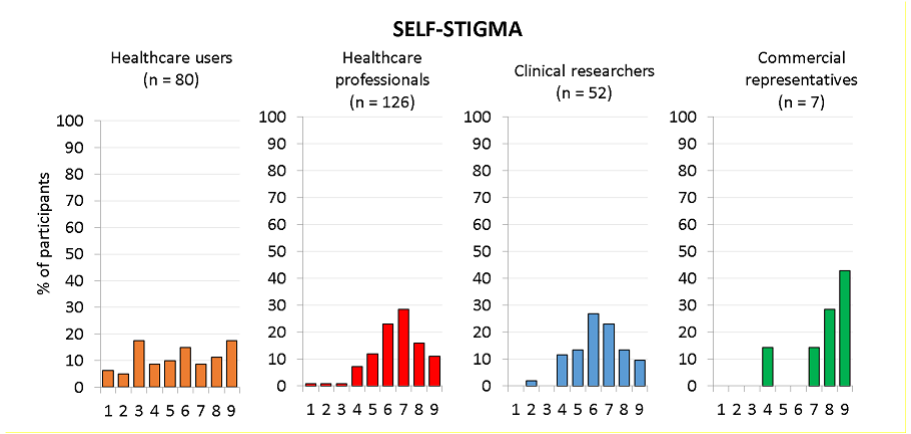
31.


TINNITUS-RELATED BRAIN CHANGES
Healthcare users (n = 72)
Healthcare professionals (n = 126)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

32.


HEARING-RELATED BRAIN CHANGES
Healthcare users (n = 71)
Healthcare professionals (n = 127)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

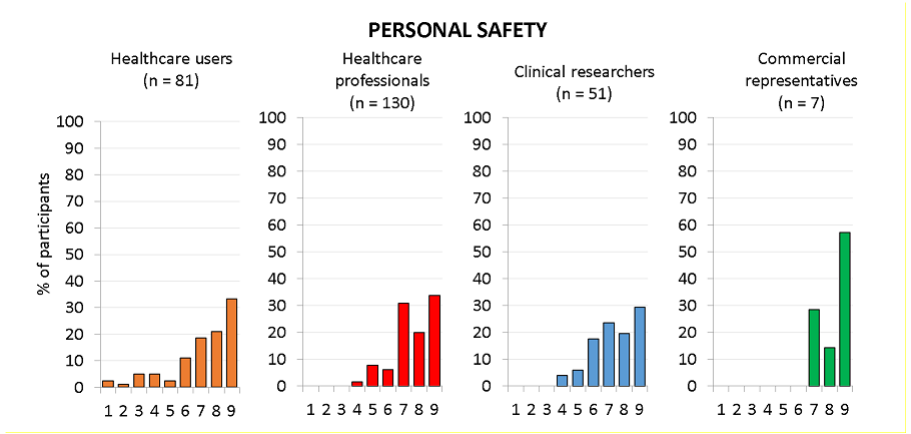
33.


SELF-STIGMA
Healthcare users (n = 80)
Healthcare professionals (n = 126)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

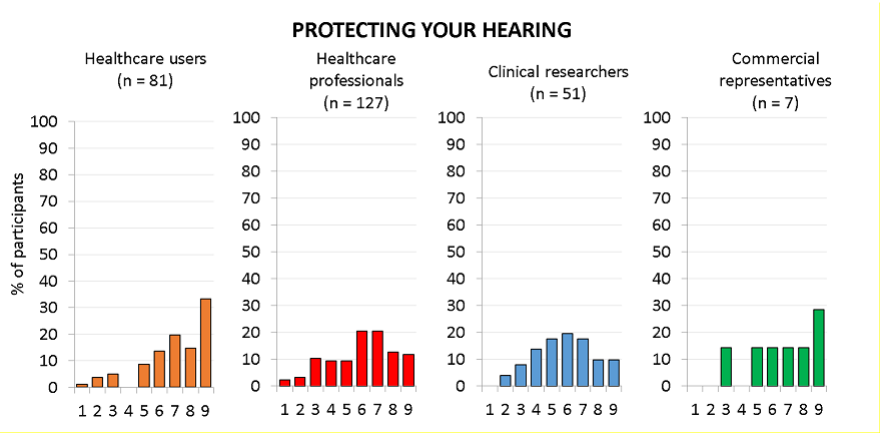
34.


SELF-IMAGE
Healthcare users (n = 80)
Healthcare professionals (n = 128)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

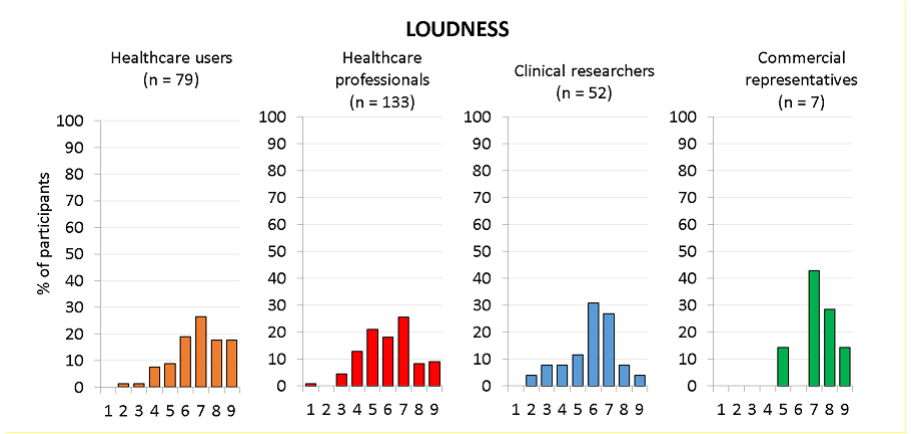
35.


PERSONAL SAFETY
Healthcare users (n = 81)
Healthcare professionals (n = 130)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

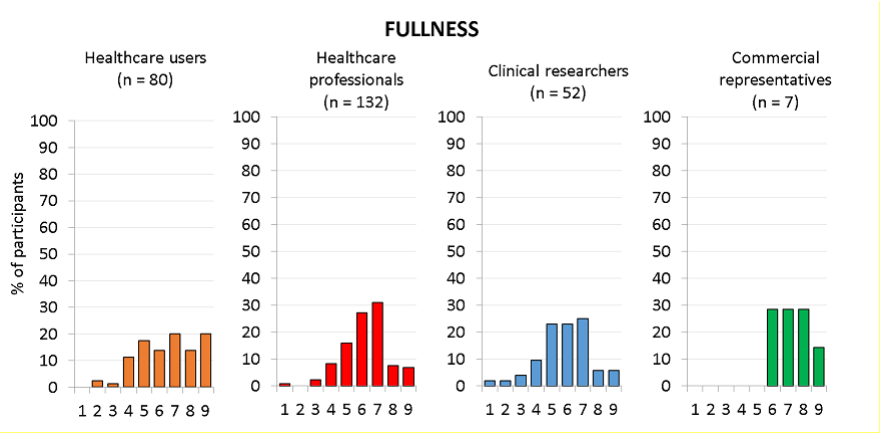
36.


PROTECTING YOUR HEARING
Healthcare users (n = 81)
Healthcare professionals (n = 127)
Clinical researchers (n = 51)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

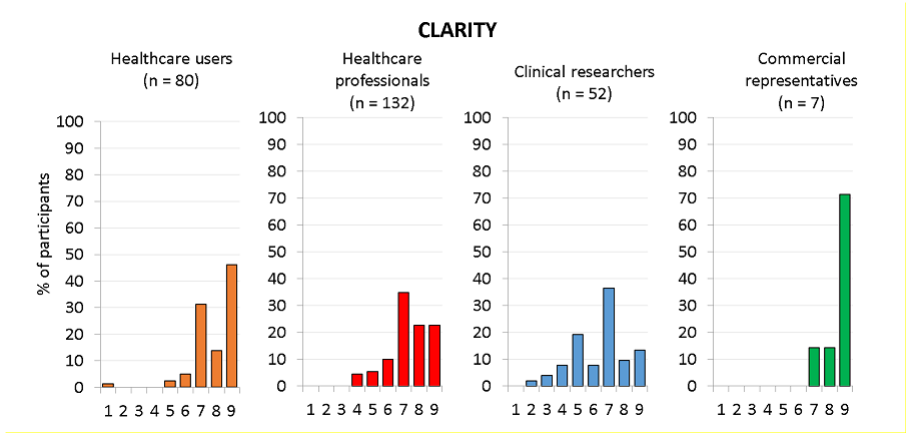
37.


LOUDNESS
Healthcare users (n = 79)
Healthcare professionals (n = 133)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

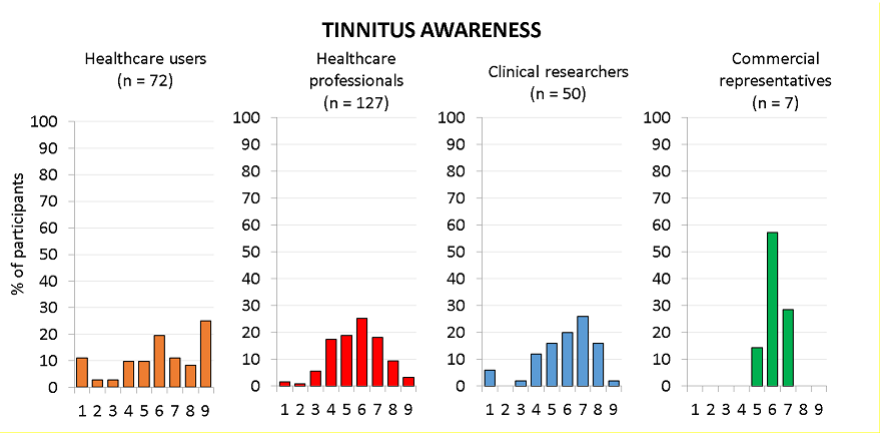
38.


FULLNESS
Healthcare users (n = 80)
Healthcare professionals (n = 132)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

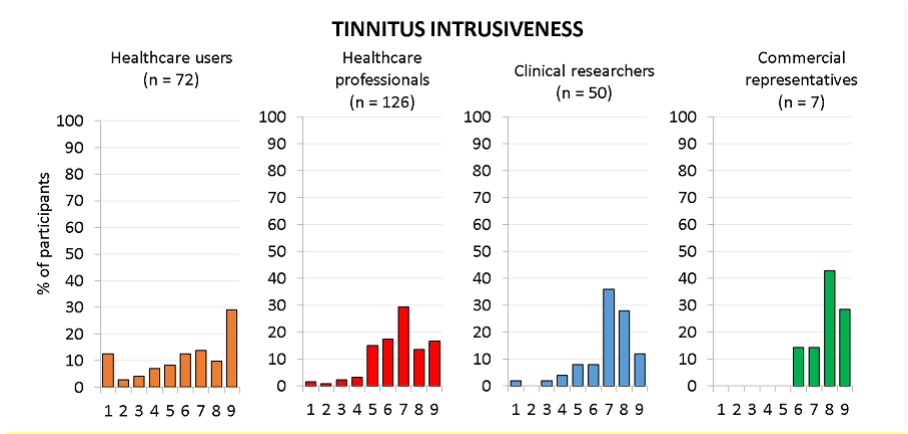
39.


CLARITY
Healthcare users (n = 80)
Healthcare professionals (n = 132)
Clinical researchers (n = 52)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

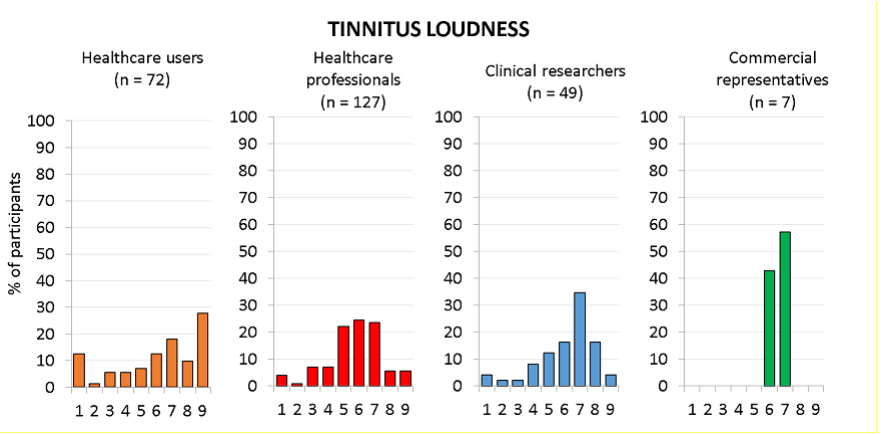
40.


TINNITUS AWARENESS
Healthcare users (n = 72)
Healthcare professionals (n = 127)
Clinical researchers (n = 50)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

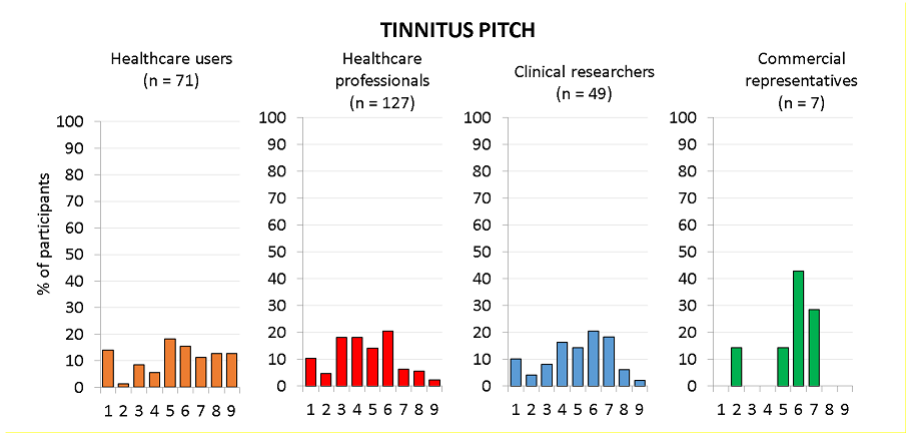
41.


TINNITUS INTRUSIVENESS
Healthcare users (n = 72)
Healthcare professionals (n = 126)
Clinical researchers (n = 50)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

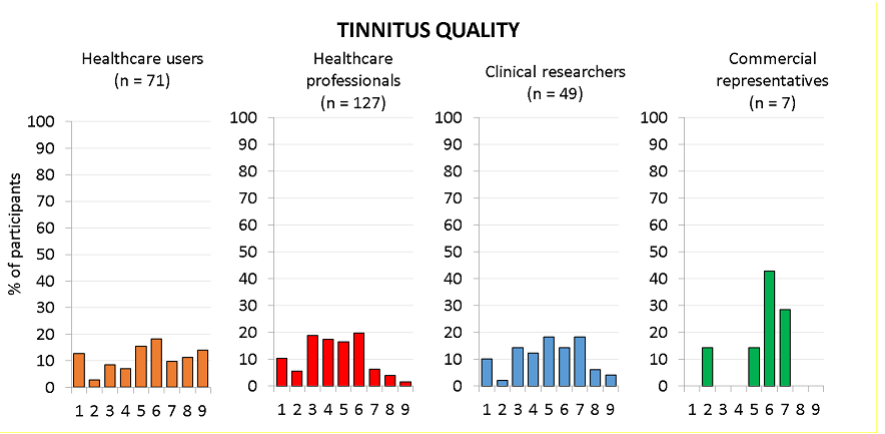
42.


TINNITUS LOUDNESS
Healthcare users (n = 72)
Healthcare professionals (n = 127)
Clinical researchers (n = 49)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

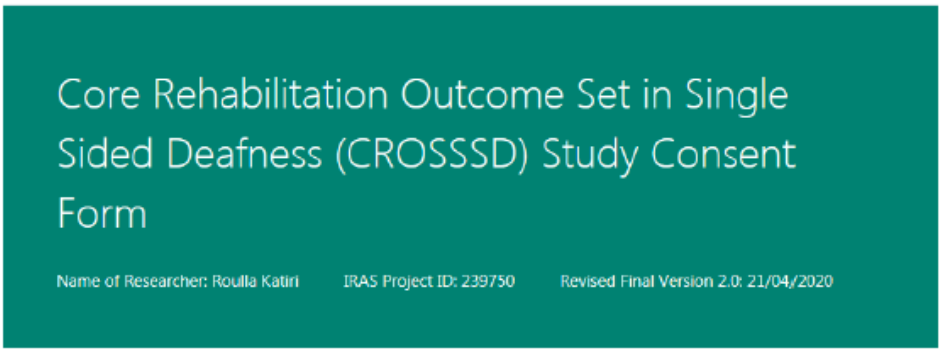
43.


TINNITUS PITCH
Healthcare users (n = 71)
Healthcare professionals (n = 127)
Clinical researchers (n = 49)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

44.


TINNITUS QUALITY
Healthcare users (n = 71)
Healthcare professionals (n = 127)
Clinical researchers (n = 49)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

Appendix 9. Consensus meeting and follow-up focus groups consent form.



1. Please type in your name and surname

2. I confirm that I have read and understand the information sheet Revised Final Version 3.0 dated 21/04/2020 for the above study and have had the opportunity to ask questions. (If you consent please type your initials in the box below)

3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care (if appropriate) or legal rights being affected. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis. (If you consent please type your initials in the box below)

4. I understand that relevant data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential. (If you consent please type your initials in the box below)

5. I understand that the consensus meeting will be audio recorded and that anonymous direct quotes from the consensus meeting may be used in the study reports. (If you consent please type your initials in the box below)

6. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers. (If you consent please type your initials in the box below)

7. I agree to take part in the above study. (If you consent please type your initials in the box below)

8. Optional I am willing to take part in a follow-up workshop if a space is available. I understand that the workshop will be audio recorded and that anonymous quotes may be used in the study reports. (If you would like to take part please type your initials in the box below)

9. Please type your name and date in the box below

Submit

Appendix 10. Facilitator pack for the consensus meeting.

Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) Study
Virtual Consensus Meeting to agree a Core Outcome Set (COS) for Single Sided Deafness (SSD) Interventions

Aim:
To bring together a sample of healthcare users and healthcare professionals who have completed both Rounds of the CROSSSD Study e-Delphi survey to discuss and agree on the final set of outcome domains for SSD interventions.

Date:
Tuesday 7th of July 2020, 9am-5pm.

Platform:
Microsoft Teams.

Study Management Team:
Roulla Katiri, PhD Student CROSSSD Study.
Deborah Hall, Professor of Hearing Sciences & PhD student supervisor.
Pádraig Kitterick, Associate Professor in Hearing Sciences & CROSSSD study chief investigator.

Facilitators:
Derek Hoare, Associate Professor in Hearing Sciences.
Kathryn Fackrell, NIHR Post-Doctoral Research Fellow (Hyperacusis).
Deborah Hall, Professor of Hearing Sciences.

Technical support:
Roulla Katiri, Participant training on online platform, set-up of meeting invites and address technical issues.
Pádraig Kitterick, Uploading and amendments of voting forms, assist with technical issues during the day.

Patient & Public Involvement (PPI) team:
Adele Horobin, Patient & Public Involvement manager NIHR Nottingham Hearing BRC.
Nora Buggy, PPI collaborator and healthcare user with SSD using a CROS aid.
Nicholas (Nicky) Hogan, PPI collaborator and healthcare user with SSD using a BAHA.
PPIs are allowed to participate in discussions throughout the day but *cannot* vote.

Participants:
Stakeholder representatives: healthcare users, healthcare professionals (audiologists and ENT surgeons), clinical researchers and commercial representatives.
Observers: Two commercial representatives (Oticon Medical); and a healthcare professional and clinical researcher.
Observers are *not* allowed to participate in discussions *nor* vote.

SSD, impact and interventions:
SSD: Normal or near-normal hearing in one ear and a severe to profound hearing impairment in the other ear.
Impact: Most significant functional consequences include difficulties understanding speech in noisy environments and locating where sounds are coming from.
'Rerouting' Interventions: Contralateral Routing of Signals (CROS) and Bone Anchored Hearing Aid (BAHA) which transfer signals from the poor side to the better hearing ear.
'Restoring' interventions: Cochlear Implants (CI) and Middle Ear Implants which get implanted on the poor side. Historically CI was first implanted to address incapacitating tinnitus following sudden-onset SSD.

1

Participant sub-groups:

Groups and facilitators	Group A Derek Hoare	Group B Kathryn Fackrell	Group C Deborah Hall
Study team helpers	Roulla	Pádraig	Adele
PPIs	Nicky	Nora	Adele
Healthcare users	Carly Sygrove Richard Bowles	Chris Parker Peter Toth	Lewis Williams Roger Bayston
Healthcare professionals	Penny Feltham	Richard Nicholson	Paul James
Commercial representative	N/A	Cherith Campbell-Bell	Paddy Boyle
Clinical researchers	Ad Snik	N/A	N/A
Observer	Tove Rosenbom	Daniel Zeitler	Maxine Oxford

Participant expertise:
Carly Sygrove, Madrid. SSNHL, trialed CROS, no benefit. Blogged during recruitment https://bit.ly/2OFCubY.
Richard Bowles, Kent. SSD due to neuroma. CROS user.
Chris Parker, Preston. SSD due to neuroma. CROS user.
Peter Toth, Surrey. Congenital SSD. CROS user. Keen musician.
Lewis Williams, London. SSD due to labyrinthitis, implanted with CI in Berlin to address tinnitus.
Roger Bayston, Nottingham. CROS trial in the past but not using any intervention now. Prof of surgical infection, UoN.
Penny Feltham, Manchester Audiologist. PhD. Works in BAHA/CI. Member www.auronet.org/.
Richard Nicholson, Nottingham Audiologist. Expert on CROS aids.
Paul James, Berlin Audiologist. Involved in Lewis's CI implantation. Used to work at RNTNE.
Cherith Campbell-Bell, Cochlear commercial representative.
Paddy Boyle, Advanced Bionics commercial representative.
Ad Snik, Nijmegen Audiologist & Clinical researcher. Renowned in the SSD field www.snikimplants.nl.
Daniel Zeitler, Seattle, Virginia Mason, ENT & Clinical researcher https://bit.ly/31dlTCc.
Tove Rosenbom, Smørum. Oticon Medical Denmark Senior Director Clinical Audiology and Research, BAHS.
Maxine Oxford, Oxford. Oticon Medical UK Sales and Marketing Director.

Social Media:
If you'd like to Tweet about the consensus meeting you can use the following tags:

Study UoN team	@CROSSSD_ @RouKat @padraig_hearing @HorobinAdele @Derek_J_Hoare @FackrellKathryn @DebHallNBRUH
Study organisation	@hearingnihr @UoNHearSci @NottsSPHL
Other related	@NIHRresearch @NIHRtakepart @NIHRinvolvement @Sharebank1 @COMETinitiative @COMITIDStudy @GlobalPPINet
Participants	@myhearingloss @PennyF_UK @radboudumc @DrDanielZeitler
Commercial reps	@oxford_maxine @OticonMedical @AdvancedBionics @CochlearUK @phonak
Charities	@BANAUK @MenieresSociety @ActionOnHearing @BritishTinnitus
Professional bodies	@BSAudiology1 @ENTUKGlobal @BCIG_UK @ENTANewsround
Steering group	@Prof_IainBruce @MFT_Research @Pvandeheyning @UAntwerpen @WUSTL_ENT

Please do not upload photos unless you obtain consent from the participants in your group to do so on the day.

Introductory presentation:
An introductory pre-recorded presentation was emailed to all participants, observers and PPI team on 27/06/2020. It covers the scope of the meeting, aims and objectives as well as the plan of the meeting. It will also provide details on COS development, including the results of the e-Delphi rounds. They were asked to watch the presentation prior to the meeting and email queries or questions to Roulla. Individual queries will be addressed by email and will also be mentioned on the day of the consensus meeting for the benefit of other attendees, as appropriate.

Consent forms:
All participants were asked to complete the consent form electronically after they watch the introductory presentation. They are able to fill this in online via O365 Forms. The consent form states that the discussions will be recorded. Roulla will ensure everyone has submitted their signed consent form by Monday 6th of July.

Outcome domains:
A total of 44 domains were chosen and defined at a workshop with Pádraig, Deb, Roulla, Adele, Nora and Nicky in Dublin (July 2019). An additional 5 domains were added to Round 2 of the e-Delphi following analysis of Round 1 participant suggestions. A total of 49 outcome domains were rated during Round 2 e-Delphi.

Rating scale and rules for outcome domain inclusion / exclusion:

1	2	3	4	5	6	7	8	9
Not at all important			*Important but not critical*			*Critical*		

- **IN** unless voted out on day: Outcomes where at least 70% of participants scored 7-9 and less than 15% scored 1-3, in all stakeholder groups.
- **OUT** unless voted in on the day: Outcomes where at least 50% of participants scored 7-9 in more than 1 stakeholder group.
- **MAYBE OUT** unless voted in on the day: Outcomes where less than 50% of participants scored 7-9 in all stakeholder groups.

A total of 14 domains were voted IN by at least 70% of the stakeholders in all stakeholder groups.

Domains (n=14) that fitted the INclusion rule: -the 'clear winners', should definitely always be included in a COS

Domain category	Outcome domain	Outcome domain definition
Other effects	**7. Listening effort**	Exerting greater effort to listen and follow a conversation. This might consequently lead to feelings of tiredness and fatigue; but those feelings would be a separate outcome domain
Factors related to the treatment being tested	**8. Treatment satisfaction**	How the treatment meets your expectations or how pleased you are after receiving the treatment; or how likely you are to recommend the treatment
	9. Device usage	How you use the device (for example; in what situations; for how long)
	10. Device malfunction	The device does not work as it should or it stops working
Health-related quality of life	**12.Avoiding social situations**	Choosing not to go to particular social situations because of your hearing loss
	15. Impact on social situations	Your hearing loss or device limiting your ability to fully participate in the social world; especially in challenging situations or where a lot of effort is needed to follow the conversation (for example; at a restaurant; at the park; in a bar or at a party)
	16. Impact on work	Effect of your hearing loss or device on your ability to carry out work tasks or job roles; or advancing your career
Hearing disability	**17. Being aware of a sound**	Being aware of a sound and recognising what that sound is (for example; being aware that someone has started to speak)
	18. Listening in complex situations	The difficulty experienced when listening to a sound while separating it out from a background of other sounds
	19. Listening in reverberant conditions	The difficulty experienced when listening in places where the sound reflects off the walls; floor or ceiling (echoes); creating a blurred sound. For example; understanding announcements in train stations or airports
	21. Group conversation in quiet	Listening and following a conversation between a group of people; in a quiet environment
	22. One-to-one conversation in general noise	Listening and understanding one person; in a noisy environment
	23. Group conversation in noisy social situations	Listening and following a conversation between a group of people; when others are talking in the background

Spatial hearing	**24. Sound localisation**	Knowing where a sound is coming from
	26. Spatial orientation	Knowing where you are in relation to the position of a sound source
Physical effects	**28. Physical tiredness**	Tiredness or fatigue from the effort of listening or when you need to turn your head repeatedly to listen in social situations
Self	**35. Personal safety**	How your hearing loss effects your awareness of potential hazards and threats in your daily life (for example; moving traffic; hazards at the workplace) and those you may not be able to see or hear (for example; other people behind you)

Domains (n=8) that didn't fit inclusion nor exclusion rules: -'maybes' or undecided, important but not essential in a COS

Domain category	Outcome domain	Outcome domain definition
Psychological effects	**6. Dissatisfaction with life**	Being unhappy because you feel you should be achieving or should have achieved more in your life
Physical effects	**30. Manual dexterity**	Having the fine motor skills needed to use your device effectively (for example; putting the device on; changing the batteries)
	31. Tinnitus-related brain changes	Changes in brain structure or function associated with tinnitus
	32. Hearing-related brain changes	Changes in brain structure or function associated with hearing loss
Self	**33. Self-stigma**	Negative perception of yourself due to your hearing loss and feeling stigmatised for using a hearing aid
Tinnitus	**40. Tinnitus awareness**	Noticing the sound of tinnitus is there
	43. Tinnitus pitch	Whether your tinnitus has a note-like quality; for example high pitch like whistling or low pitch like humming
	44. Tinnitus quality	What type of sound is heard (for example; hissing; buzzing; ringing; whistling etc)

Domains (n=19) that fitted the EXclusion rule: -the 'clear losers'

Domain category	Outcome	Outcome definition
Psychological effects	**2. Discomfort in listening situations**	Finding yourself in listening situations that you feel you can't adequately control (for example; when you can't choose a favourable listening position); or situations in which you don't feel comfortable (for example when interacting with people who don't know you have a hearing loss)
	3. Emotional distress	A negative unpleasant emotional reaction which may include fear; anger; frustration; anxiety; and suffering
	4. Mood	General sense of well-being; ranging from feeling very low or negative to very positive
	5. Motivation	A willingness to engage in challenging listening situations
Factors related to the treatment being tested	**11. Adverse events**	Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial
Health-related quality of life	**13. Impact on individual activities**	Effect of your hearing loss or your device on your choice to engage in individual activities (for example; travelling alone; swimming or watching TV / films / movies)
	14. Impact on relationships	Effect of your hearing loss or your device on making new relationships and maintaining relationships with a spouse or partner; family; friends and colleagues
Spatial hearing	**25. Sound distance**	Knowing if a sound is close by or far away
Self	**35. Self-Image**	Feeling incomplete or incapable because you are unable to do all the things that you want to do
Sound quality	**37. Loudness**	How 'loud' a sound seems to you
	38. Fullness	How 'full' a sound seems to you. This can also be described as the 'richness'; 'warmth' or 'depth' of a sound

	39. Clarity	How 'clear' a sound seems to you
Tinnitus	**41. Tinnitus intrusiveness**	Being acutely aware of the sounds of tinnitus; feeling that it is invading your life or your personal space; changing your thoughts or actions and negatively impacting on your life
	42. Tinnitus loudness	How loud your tinnitus sounds
Factors related to the treatment being tested	**45. Device usability**	How easy it is to learn; use; and maintain the device (for example; changing the batteries; cleaning)
Health-related quality of life	**46. Impact on learning**	Effect of your hearing loss or device on your ability to acquire new knowledge or skills; or further your education
Psychological effects	**47. Independence**	How your hearing loss affects how much you need to rely on other people in daily life
Self	**48. Concern about your hearing**	Feeling worried about the hearing in your better ear and the thought that it may decline
	49. Valnerability	Feeling insecure because your hearing loss affects your awareness of potential hazards and threats in your daily life (for example; moving traffic; hazards at the workplace) and those you may not be able to see or hear (for example; other people behind you)

N.B. Dilemma: what we do with the small number of commercial representatives (n=7) results. The key concern was that some of the rules for considering outcome domains at the consensus meeting require consistency across all groups, and therefore the scores of a very small number of commercial reps could ultimately determine whether certain outcomes are even discussed (the maybes will be affected). See https://bit.ly/2NcrDVH.

'Top 3 Outcome Domains':
All participants will be asked to choose their Top 3 outcome domains and submit them by completing a short survey prior to the meeting. The results should be submitted by Friday 3rd of July and will be analysed; and will be uploaded in the CROSSSD Virtual Consensus Meeting folder in Teams, under Files.

Group discussions:
Roulla, Pádraig and Adele will help and support small sub-group discussions, monitor the chat and address participants' queries. If discussions are getting intense, then consider breaking the session for 5 minutes or so. Please be sure to ask the group 'have we missed anything?' before voting. Participants should feel free to ask questions, and no question is trivial.

Reaching an agreement:
Please ensure that members of all stakeholder groups play an equal role in prioritising the outcomes. Be sure to invite and listen to dissenting voices when agreeing the choices, but remember that agreement is ≥70% (not everyone has to agree!). Make sure you stick to the task and not get completely diverted by other issues that will have a space to be raised at other times in the meeting.

Communication between facilitators and study team:
Roulla will monitor the chat in the CROSSSD Virtual Consensus Meeting folder in Teams during the day. This is available to everyone in the study management team, the facilitators and the PPI manager. If any queries, questions or concerns are raised during the day please post them in the group chat. All relevant documentation can be found under 'Files' in the same folder.

Meeting links:
Everyone will be emailed meeting links to their calendar according to the group or sub-group they are meant to be participating in, according to the agenda. The introductory session Teams meeting link will be the same for all participants. The sub-group links will be different etc. It is therefore important that everyone keeps on time. If there is any concerns during the day re: timekeeping please inform the group in the study communication chat.

Agenda and activities:

Time slot	Introductory Session	Tool	Session lead	Chat helper(s)
09:00-09:15	Facilitators & Study Team can join the meeting and ask any questions / clarify last-minute queries	Calendar Teams Link	Roulla	N/A
09:15-09:30	Participants arrival	Calendar Teams Link	Roulla	Adele
09:30-09:35	Welcome, quick reminder of aims and Q&A	Intro section of slide deck	Roulla	Deb / Pádraig
09:35-09:45	Speedy ice-breaker activity, 30s intro for all participants	Table with all participants names	Roulla	Deb / Pádraig
09:45-09:55	Practice vote 1: Q: What stakeholder Grp are you in? (A: 4 choice)	Survey link	Pádraig	Roulla / Deb
09:55-10:00	Presentation of Pre-Meeting survey 'Top 3' results: outcome domains that were not in any of the participants' 'Top 3' choices	Top 3 Survey results of slide deck	Roulla	Deb / Pádraig

Time slot	Session 1: Decide which domains should be discussed during the day	Tool	Session lead	Chat helper(s)
10:00-10:05	Advise that will break into 3 sub-groups for discussion of 'Top 3' vote: *'These outcome domains were not in anyone's 'Top 3', remove them from COS?'*	Individual group 'Join meeting' links in chat + Slide with Survey Results	Roulla	Adele
10:05-10:30	Break into 3 sub-groups to discuss Group A: Nicky, Carly, Richard B, Penny, Ad, (Tove) Group B: Nora, Chris, Peter, Richard N, Cherith, (Daniel) Group C: Lewis, Roger, Paul, Paddy, (Maxine)	Slide with Survey Results + Chat helper's word document for notes	A: Derek B: Kathryn C: Deb	Take notes A: Roulla B: Pádraig C: Adele
10:30-10:45	Return to large group, each group's facilitator summarises discussion outcomes in less than 5 min each	Chat helper's word document with notes	A: Derek B: Kathryn C: Deb	Roulla
10:45-11:00	**Group VOTE:** *Agree with plan to EXCLUDE those outcome domains that were not in anyone's 'Top 3'?* -YES, agree -NO, disagree - Unsure If ≥70% (i.e. 9 out of 12) participants vote YES, proceed with those XX domains only.	UoN Survey Link	Pádraig	Roulla / Deb
11:00	**Session 1 Close –Break** (and preparation for next session)		Roulla	Roulla

Time slot	Session 2: Round 1 of domain exclusion	Tool	Session lead	Chat helper(s)
11:30-11:35	Advise that will break into 3 sub-groups to discuss and shorten list of domains –?aim for Top 5	Slide with all remaining domains following previous session vote	Deb	Roulla
11:35-12:15	Break into 3 sub-groups to discuss Group A: Nicky, Carly, Richard B, Penny, Ad, (Tove) Group B: Nora, Chris, Peter, Richard N, Cherith, (Daniel) Group C: Lewis, Roger, Paul, Paddy, (Maxine) Discuss shortened list of domains: *'Clear winners (always include), clear losers (low priority, drop from COS) and maybes (undecided, important but not necessary for a COS)?'*	Individual group 'Join meeting' links in chat + Slide with the red string	A: Derek B: Kathryn C: Deb	Take notes A: Roulla B: Pádraig C: Adele
12:15-12:30	Sub-groups return to large group and feedback on Group's ?Top 5 with reasons	Large group 'Join meeting' link in chat	A: Derek B: Kathryn	Roulla

		+ Chat helper's word document for notes	C: Deb	
12:35-12:40	Summary of domains: *Clear winners*, *Clear losers* and *Maybes*	Summary slide with list of domains	Roulla	Pádraig
12:30-12:40	**Group VOTE:** *Agree with plan to EXCLUDE those outcome domains that were not in anyone group's 'Top 5' (clear losers)?* -YES, agree -NO, disagree - Unsure If ≥70% (i.e. 9 out of 12) participants vote YES, proceed with those XX included domains only.	UoN Survey Link	Pádraig	Roulla / Deb
12:45	**Session 2 Close –Lunch** (and analysis / re-grouping of domains)	Presentation slide summarizing small group outcomes		
	Study team and facilitators: Reflect and feedback on aspects that are not going to plan? / need to address during afternoon session	Teams CROSSSD group chat	Roulla / Pádraig / Deb	Adele / Derek / Kathryn (25min each)

Time slot	Session 3: Round 2 of domain exclusion	Tool	Session lead	Chat helper(s)
13:30-13:35	Presentation of list of outcomes needing further discussion	Presentation slide with *clear winners* and *maybes*	Roulla	
13:35-14:00	Break into 3 sub-groups to discuss Group A: Nicky, Carly, Richard B, Penny, Ad, (Tove) Group B: Nora, Chris, Peter, Richard N, Cherith, (Daniel) Group C: Lewis, Roger, Paul, Paddy, (Maxine) Discuss shortened list of domains: *'Clear winners (always include), clear losers (low priority, drop from COS) and maybes (undecided, important but not necessary for a COS)?'*	Individual group 'Join meeting' links in chat + Slide with the red string	A: Derek B: Kathryn C: Deb	Take notes A: Roulla B: Pádraig C: Adele
14:00-14:15	Sub-groups return to large group and feedback on Group's ?Top 5 with reasons	Large group 'Join meeting' link in chat	A: Derek B: Kathryn C: Deb	Roulla
14:15-14:20	Summary of domains: *Clear winners*, *Clear losers* and *Maybes*	Summary slide with list of domains	Roulla	Pádraig
14:20-14:25	**Group VOTE:** *Agree with plan to EXCLUDE those outcome domains that were not in anyone group's 'Top 5'?* -YES, agree -NO, disagree - Unsure If ≥70% (i.e. 9 out of 12) participants vote YES, proceed with those XX included domains only.	UoN Survey Link	Pádraig	Roulla / Deb
14:30	**Session 3 Close –Break** (and preparation for next session)		Roulla	Roulla

Time slot	Session 4: Domain inclusion	Tool	Session lead	Chat helper(s)
15:00-15:05	Presentation of short list of remaining outcomes, the *'clear winners'*	Presentation slide with *clear winners* (and *Maybes?)*	Roulla	
15:05-15:15	**Group VOTE:** *Agree this list of outcome domains should always*	UoN Survey Link	Deb	Roulla

	be in a COS for SSD interventions? -YES, agree -NO, disagree - Unsure If ≥70% (i.e. 9 out of 12) participants vote YES, proceed with those XX included domains only.			
15:15-15:20	Presentation of *clear winners* to be included in the COS	Presentation slide	Deb	

Time slot	Session 5: Additional tasks if have time	Tool	Session lead	Chat helper(s)
15:30	Definitions of outcome domains? Everyone agrees that included domains definitions are clear?	Presentation slide with definitions		
15:45	Discussion regarding prioritization of outcome domains? Future research will be concentrating on instrument recommendations> which one is the best, there will be regardless > Q is where to start? Which one will be the Top 1 or 2 or 3	Slide with ranking of outcome domains? *Draft of a survey on what they are ranking*		
16:00	Q&A • Any other discussion points? • Participant feedback they'd like to share? • One positive aspect of the meeting / what to work on?	Can have a slide with bullet points, share screen 'take notes'?		
16:15	Thank you, Future Steps & Close	Presentation slides ?? / Reminder to complete evaluation form	Roulla	

Facilitators to have in mind for sub-group discussions:

- Use the presentation slide with the 17 Domains in Cards & 'Red String'.
- Discuss and jointly agree top 5 by moving the cards around to facilitate discussion (e.g. if put one in the top 5, need to take another out).
- Emphasise to the group that the more items considered to be important and critical at this stage, the less helpful this exercise will be in terms of guiding clinical trial designs.
- Participants should be encouraged to share their reasons for ranking near the top or bottom to help discussion.
- Discussion should relate to measuring the effect of the intervention in a clinical trial.
- Remind participants to focus on discussing 'the **WHAT**' should be included in COS. Don't worry about 'the HOW' it should be measured.
- Remind participants that the Top 5 list has got to include outcomes that are relevant to all interventions, and that will be most sensitive to change over the course of the treatment.
- Save your group's Top 5; the helper should make a note of any strong dissenting views or important comments using the word document for notes.

If we are going ahead with prioritization task:

- Explain why it's important to rank relative importance (To plan Phase 2 –the **HOW**).
- Start with those outcomes where ≥70% participants agree should be in the top 5. Remember that there may be fewer than 5 at this point. That's fine. 5 is only a maximum, not necessarily an absolute target.
- Arrange domains on the slide in an initial order according to the discussions so far??
- Try to achieve an ordered set (no ties allowed) through discussion and by moving the cards around.
- Once the group seem to have exhausted all discussion and there is an interim list, then cast this order to a vote?

Appendix 11. Consensus meeting evaluation form.

University of Nottingham
UK | CHINA | MALAYSIA

NIHR | National Institute for Health Research

(Form to be printed on local headed paper)

EVALUATION FORM
(Final Version 1.0: 22/05/2019)

IRAS Project ID: 239750

Title of Study: Core Rehabilitation Outcome Set in Single Sided Deafness (CROSSSD) Study

Name of Researcher: Roulla Katiri

Thank you for attending the CROSSSD study consensus meeting.

We would value your feedback about the consensus meeting, to help improve future core outcome set work. If you could take a few moments to let us know your thoughts, it would be much appreciated.

If you have any questions or would like more information, please contact Roulla Katiri (details below).

We would like to thank you for taking the time to complete this evaluation form.

Roulla Katiri, PhD Student
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Email: roulla.katiri@nottingham.ac.uk
Web: www.nottingham.ac.uk/go/CROSSSD
National Institute for Health Research
Nottingham Hearing Biomedical Research Centre

CROSSSD @CROSSSD_ #CROSSSD

1. Please choose the option which describes you best:
☐ Health care professional ☐ Patient

2. The information that the organisers provided me with in advance of the meeting was helpful.
☐ Strongly agree ☐ Agree ☐ Neither ☐ Disagree ☐ Strongly disagree
Comments:

3. I was satisfied with the process used to agree the core outcomes set on the meeting day.
☐ Strongly agree ☐ Agree ☐ Neither ☐ Disagree ☐ Strongly disagree
Comments:

4. I was satisfied with the way the meeting was facilitated.
☐ Strongly agree ☐ Agree ☐ Neither ☐ Disagree ☐ Strongly disagree
Comments:

5. I felt able to contribute to the meeting.
☐ Strongly agree ☐ Agree ☐ Neither ☐ Disagree ☐ Strongly disagree
Comments:

6. I felt comfortable in communicating my views.
☐ Strongly agree ☐ Agree ☐ Neither ☐ Disagree ☐ Strongly disagree
Comments:

7. The workshop produced a fair result.
☐ Strongly agree ☐ Agree ☐ Neither ☐ Disagree ☐ Strongly disagree
Comments:

8. Do you have any comments about the practical arrangements for the workshop (e.g. venue, timing of the meeting, catering, number of breaks, or anything else)?

9. Was there anything else that could have been done to improve the workshop?

Appendix 12. British Society of Audiology (BSA) Audacity magazine research round-up article.

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Developing outcome measures for Single-Sided Deafness (SSD) research

Authors and Correspondence

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Most audiologists working clinically would have at some stage been posed the question 'What can I do for my single-sided deafness'? In response, most NHS audiologists, would probably explain that we have three possible choices 1) try a Contralateral Routing of Signals (CROS) aid, failing that, 2) trial a Bone Anchored Hearing Aid (BAHA) or 3) use of alternative strategies without a hearing aid intervention.

Single-Sided Deafness (SSD) is defined as normal or near-normal hearing in one ear and a severe-to-profound sensorineural hearing impairment in the other ear [1]. SSD can be congenital, sudden or progressive. The most common causes of SSD in adulthood are sudden and idiopathic; including vestibular schwannoma and associated surgery, Ménière's disease and sudden onset sensorineural hearing loss. The incidence of SSD in the UK is estimated to be approximately 9000 new cases per year [2].

Difficulties in everyday life secondary to SSD vary considerably between individuals. It is well-established that SSD can have an impact on speech perception in noisy environments and reduce spatial awareness. These functional impairments can affect social and psychological well-being. Social consequences of SSD can result from activity limitations and participation restrictions including withdrawal from and within situations. Psychological effects in individuals with SSD include worrying about losing the hearing in their other ear and reduced confidence and belief in their abilities to participate [3]. The multi-dimensional burden on overall health is indicated by reductions in health-related quality of life in individuals with a diagnosis of SSD [4].

'Rerouting' interventions, like a CROS aid or a BAHA aim to alleviate the impact of SSD by diverting signals from the impaired side to the better-hearing ear [5]. In the last decade, we have seen the introduction of cochlear implantation, which is a 'restoring' intervention. In other words, we deliver information directly to the impaired side, thus creating a sensation of true 'binaural' hearing. The pioneering team in Antwerp, led by Professor Paul van de Heyning, first implanted a cochlear implant for SSD to address the impact of incapacitating tinnitus [6]. A variety of interventions (Figure 1) have been trialled in clinical and research settings to investigate their effects in alleviating the detrimental effects of SSD.

The challenge faced by both clinicians and patients is to ascertain which intervention (if any) is ideal in a world where we are striving for patient-centered care delivery [7]. How can we measure the benefits, or indeed, harms an intervention for SSD delivers?

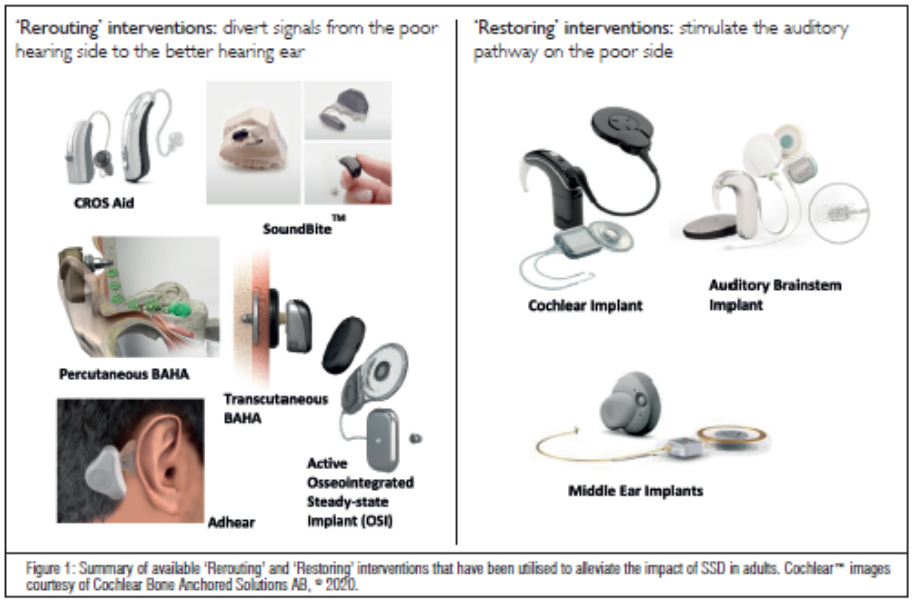

Figure 1: Summary of available 'Rerouting' and 'Restoring' interventions that have been utilised to alleviate the impact of SSD in adults. Cochlear™ images courtesy of Cochlear Bone Anchored Solutions AB, © 2020.

Existing literature has highlighted inconsistencies in what benefits and risks (side effects) are assessed when evaluating these interventions. The different sorts of benefits and risks are collectively called 'outcome domains'. For example studies that evaluate these interventions have sought to assess aspects like speech perception in quiet or noisy environments, sound localisation, tinnitus effects, or have attempted to quantify the impact on the recipient's quality of life. This diversity of chosen measures poses a challenge to both healthcare users and healthcare professionals when comparing and contrasting various study outcomes. In some cases, researchers choose available measures because they are standardised or easily accessible and not because of their importance to the healthcare users or professionals themselves.

Identifying appropriate outcome domains is crucial when designing clinical trials to evaluate the effects of different interventions. The selected outcomes need to be important to key stakeholders such as patients, healthcare professionals or budget holders to minimise bias when making decisions about healthcare. Furthermore, the choice of outcome measures should be based on what is important and of interest to people making decisions about healthcare, not on what outcome instruments are available or most commonly used. If evidence is lacking for an important outcome, this should be acknowledged, rather than ignoring that particular outcome [8].

The COMET (Core Outcome Measures in Effectiveness Trials) Initiative was launched in 2010 and brings together researchers interested in the development of agreed and standardised sets of outcomes, known as 'core outcome sets'. A Core Outcome Set (COS) is a recommendation of **'what'** should be measured and reported in all trials in a specific area, as a minimum. If developed from the perspectives of healthcare users, healthcare professionals, clinical researchers, and other relevant stakeholders a COS can overcome the problems imposed by utilisation of diverse measures.

In the field of Audiology and ENT, a group led by Professor Deborah A. Hall at the University of Nottingham have recently developed a COS for psychology, pharmacology and sound-based interventions for tinnitus [9]. Professor Iain A. Bruce and his team at the NIHR Manchester Biomedical Research Centre are currently working on the PONCHO study: Prioritising Outcomes iN Childhood Hearing lOss.

The CROSSSD (Core Rehabilitation Outcome Set for Single Sided Deafness) study group aims to develop a COS for SSD interventions. Since its inception in October 2017, the group is working closely with collaborators with lived experience of SSD and professionals across the world who are experts in the field. The group's objective is to find agreement on what outcomes are

critical and important to always measure when evaluating interventions for SSD, using the methodology proposed by the COMET initiative.

The methodology adopted involves the following steps (Figure 2):

1. The published literature reporting interventions for SSD has been systematically reviewed to identify what outcome domains and what measurement instruments have been used already [10].
2. The patient perspectives with regards to these outcomes were explored in workshops using a range of qualitative methods.
3. Key stakeholders were invited to participate in an interactive online consensus exercise known as a Delphi Survey, aiming to identify which outcome domains are critical and important for evaluating SSD interventions.
4. A subgroup of the stakeholders is due to meet up and during an interactive consensus meeting they will discuss the recommendations arising from the Delphi survey and they will agree on a minimum set of outcome domains that are relevant to all intervention options ('Rerouting' and 'Restoring') and stakeholder groups (healthcare users and professionals in the field).

Patient and Public Involvement (PPI) and stakeholder engagement and publicity have been integral to the design and delivery of the study. This promotional video was developed alongside collaborators with lived experience of SDD to increase awareness of the project and help with participant recruitment internationally.

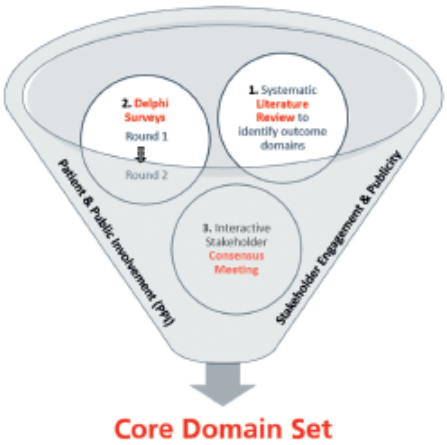

Figure 2: Steps adopted to develop a Core Outcome Set (COS) for SSD interventions in adults.

The systematic review of the literature yielded 72 articles that fitted the inclusion criteria. A total of 244 unique outcome domains were identified. Following categorisation using qualitative methods, this list was reduced to 44 outcome domains which were rated for their importance by healthcare users (n=81), healthcare professionals (n=135); and a group of clinical researchers, commercial representatives, funders and journal editors (n=61) via a two-round e-Delphi survey. Responses were international, representing a total of 30 countries. Five additional outcomes were included in the long list of candidate outcomes for rating in Round 2 following suggestions from participants who completed Round 1 of the e-Delphi. The e-Delphi concluded at the end of February and the consensus meeting is scheduled in late March 2020 to finalise the core outcome domain set.

Once a COS is developed, we would know ***'what'*** is important to measure in all studies; however researchers also need to consider ***'how'*** the included outcomes should be measured. The COSMIN (COnsensus-based Standards for the selection of health Measurement INstruments) international initiative has established criteria in developing and evaluating outcome measurement instruments. For example, if quality of life is an outcome in a COS, indicated to be critical and important to always measure for SSD interventions, COSMIN standards can help us establish what commonly agreed 'instrument' or questionnaire should everyone utilise to measure it. Ultimately, anyone designing a trial in this area will have a list of outcomes to measure, *as a minimum* alongside a list of recommended instruments to utilise. The COS will not prevent researchers from measuring additional outcomes or utilising supplementary instruments.

Future research studies in the field should then adopt the recommended COS to reduce the heterogeneity of measures utilised. Moreover, only outcomes meaningful to all stakeholders will be employed and as a result transparency will be established as both positive and negative outcomes will be reported on. Clinical researchers will be supported in thinking critically about the ***'what'*** they are trying to measure and they will not select their outcomes simply on the basis of the available instruments' popularity or accessibility. Uptake of the COS will be encouraged internationally to improve research quality, enhance clinical decision-making, and facilitate meta-analysis in systematic reviews.

When you as an audiologist are asked the question 'What can I do for my single-sided deafness'? the information from this study is intended to help you be able to provide an evidence-based response that may help patients make informed decisions.

If you would like to find out more please visit www.nottingham.ac.uk/go/CROSSSD or follow @CROSSSD_ on Twitter.

@CROSSSD_ #CROSSSD

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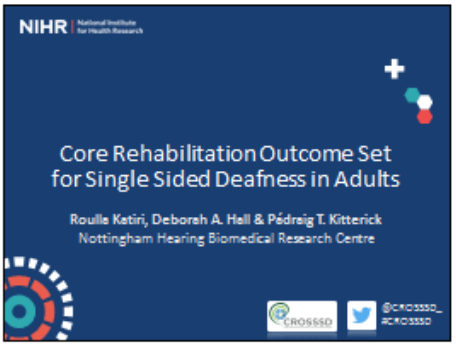
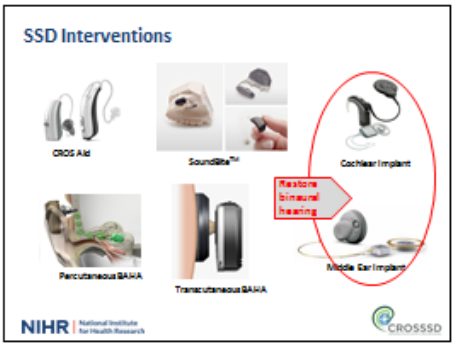
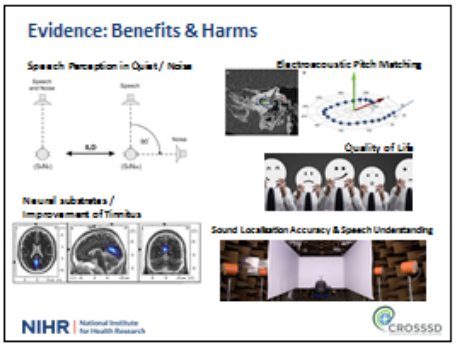
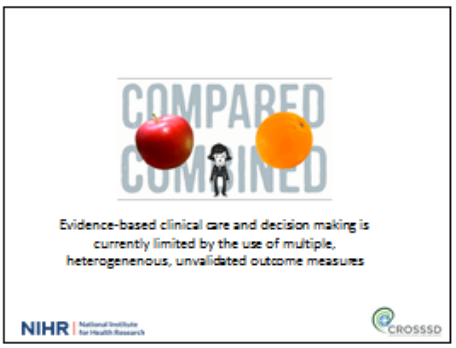
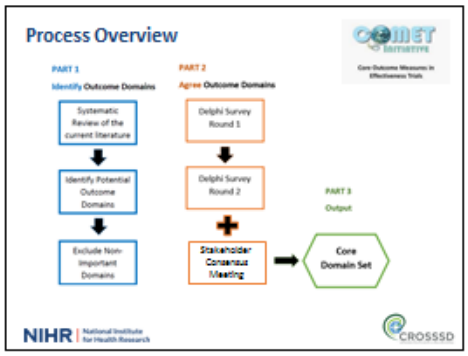
Appendix 13. Presentation slides used at healthcare professionals' journal clubs during recruitment.

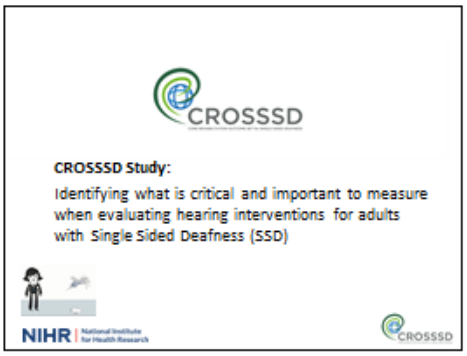








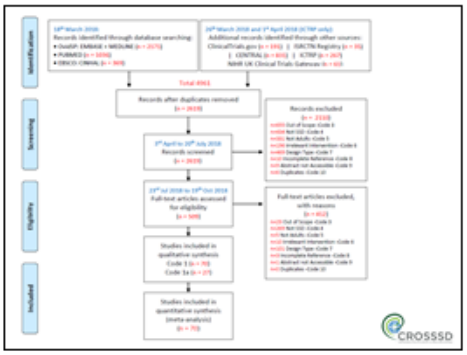

Process Overview
PART 1
Identify Outcome Domains
Systematic Review of the current literature
Identify Potential Outcome Domains
Exclude Non-Important Domains
PART 2
Agree Outcome Domains
Delphi Survey Round 1
Delphi Survey Round 2
Stakeholder Consensus Meeting
PART 3
Output
Core Domain Set
NIHR
CROSSSD


CROSSSD
CROSSSD Study:
Identifying what is critical and important to measure when evaluating hearing interventions for adults with Single Sided Deafness (SSD)
NIHR
CROSSSD


Study Management Team
Steering Group
Patient & Public Involvement
NIHR
CROSSSD


Objectives
Develop core sets of patient-centred outcome measures that:
Act as a standard of reporting in clinical trials
Guide individual clinical practice
Improve outcomes of patients with SSD
NIHR
CROSSSD


Systematic Review
PROSPERO
International prospective register of systematic reviews
Systematic review of outcome domains and instruments used in designs of clinical trials for interventions that seek to restore bilateral and binaural hearing in adults with unilateral sensorineural severe to profound hearing loss ('Single Sided Deafness')
WHAT?
HOW
NIHR
CROSSSD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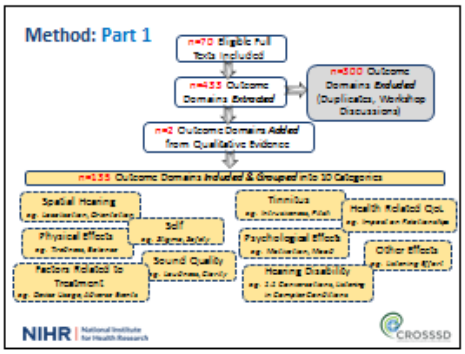
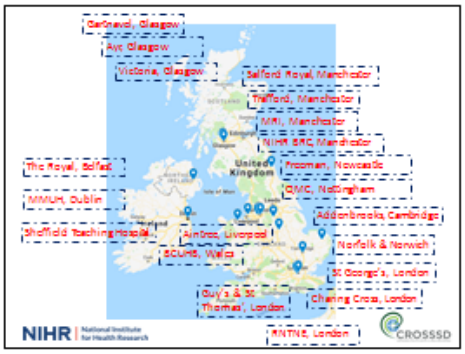
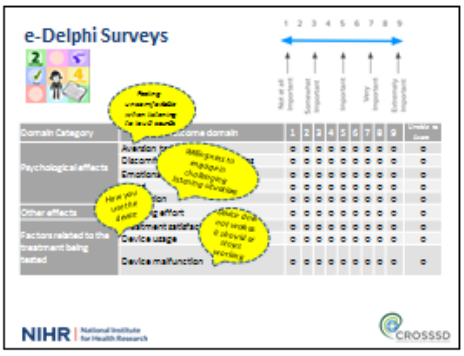

Method: Part 1
n=70 Eligible Full Texts Included
n=333 Outcome Domains Extracted
n=300 Outcome Domains Excluded (Duplicates, Workshop Discussions)
n=2 Outcome Domains Added from Qualitative Evidence
n=335 Outcome Domains Included & Grouped into 10 Categories
Spatial Hearing
Tinnitus
Health Related QoL
Self
Physical effects
Psychological effect
Other effects
Sound Quality
Hearing Disability
Factors Related to Treatment
NIHR
CROSSSD


YOU CAN HELP
NIHR
CROSSSD


Clatterbridge, Wirral
Aintree, Liverpool
Addenbrooke's, Cambridge
Norfolk & Norwich
St George's, London
Chelsea Cross, London
NIHR
CROSSSD


YOU CAN HELP
Adults with SSD
Delphi Survey Round 1
Delphi Survey Round 2
Stakeholder Consensus Meeting
Do you have very poor hearing in one ear only?
(Single-Sided Deafness)
NIHR
CROSSSD


YOU CAN HELP
Professionals working in the field of SSD
NIHR
CROSSSD


e-Delphi Surveys
Domain Category
Psychological effects
Other effects
Factors related to the treatment being tested
NIHR
CROSSSD

Consensus Meeting

Core Outcome Domain Set
for
Single Sided Deafness Interventions

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CROSSSD

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CROSSSD

Next Steps

- Posters & Leaflets Delivery
- Participant Identification

Early August | Mid-August | September | October | November

- Official HRA Approval Letter
- e-Delphi Round One web links emailed out
- Delphi Analysis
- e-Delphi Round Two Preparation
- e-Delphi Round Two
- Consensus Meeting Prep

NIHR | National Institute for Health Research

CROSSSD

Roulla Kalin
PhD Student, Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) Study
roulla.kalin@nottingham.ac.uk
@RouKat

CROSSSD www.nottingham.ac.uk/go/CROSSSD @CROSSSD_ #CROSSSD

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Appendix 14. CROSSSD study posters used at (i) Ci2018.org (June 2018), (ii) BAA conference in Liverpool (November 2019), (iii) BSA eConference and OSSEO conference in Miami (December 2019), and (iv) BAA conference in Manchester (November 2021) to help with healthcare professional engagement.

Towards an international consensus on core outcome measures for clinical trials in adult single sided deafness

Roulla Katiri[1,3], Deborah A. Hall[1,2] & Pádraig T. Kitterick[1,2]

[1]NIHR Nottingham Biomedical Research Centre, Ropewalk House, 113 The Ropewalk, Nottingham, NG1 5DU, UK; [2] Otology & Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, NG7 2UH; [3] Department of Audiology, Mater Misericordiae University Hospital, Dublin, Ireland.

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Background

Single-sided deafness (SSD) is described by the presence of a severe-to-profound hearing impairment in one ear only[1].

- SSD disrupts the spatial aspects of hearing and impairs the ability to understand speech in the presence of background noise[2].
- It can lead to functional, psychological and social consequences[3].

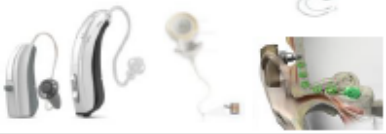
What can we do about it?

The most commonly used treatments for SSD restore bilateral access to sounds with:

- Contralateral Routing of Sounds (CROS) aids
- Bone Conduction Hearing Aids (BAHA);

or binaural access with:

- Middle Ear Implants (MEI)
- Cochlear Implants (CI)



What is the problem?

- Existing literature has highlighted inconsistencies in what benefits and risks are assessed when evaluating these interventions.
- The different sorts of benefits and risks are collectively called 'outcome domains'.

e.g. Studies that evaluate these interventions have sought to assess speech perception in quiet or noisy environments and sound localisation[4] or have attempted to quantify the impact on the recipient's quality of life[5]

- These inconsistencies hinder decisions about the choice of outcome measures for trials of clinical efficacy.

Why do we need a solution?

Identifying appropriate outcome domains is crucial when designing clinical trials to evaluate the effects of different interventions.

The selected outcomes need to be important to key stakeholders such as patients, healthcare professionals or budget holders in order to minimise bias when making decisions about healthcare.

What is CROSSSD?

CROSSSD

CORE REHABILITATION OUTCOME SET for SINGLE SIDED DEAFNESS

The aim of CROSSSD is to identify what outcomes are crucial and important to measure when designing clinical trials to evaluate the effects of the various SSD interventions.

Methods

Our methods for developing a set of minimum standards will follow the Core Outcome Measures in Effectiveness Trials (COMET) Handbook:[6]:

- The published literature reporting interventions for SSD will be systematically reviewed to identify what outcome domains and what measurement instruments have been used already.
- The patient perspective will be explored using a range of qualitative methods.
- Key stakeholders will be invited to participate in an interactive online consensus exercise known as a Delphi Survey.
- The outcome domains that are critical and important for evaluating SSD interventions will be identified.
- A subgroup of the stakeholders will be invited to an interactive consensus meeting to discuss the recommendations arising from the Delphi survey and to agree on a minimum set of outcome domains that are relevant to all intervention options and stakeholder groups.

The future:

An agreement on a set of outcome domains of what is critical and important for deciding whether an intervention is efficacious will drive up the quality and relevance of research by ensuring that the most relevant outcomes are consistently measured and reported in every clinical trial relating to SSD. On the basis of the recommended outcome domains, further research will then be needed to identify measurement instruments that assess the outcomes domains in the minimum set.

Follow @CROSSSD_ on Twitter

References: [1] Vincent, C., Arndt, S., Finet, J. B., Freyse, B., Kitterick, P. T., Papsin, B. C., Snik, A., Van de Heyning, P., Deguine, O. & Marx, M. (2015). Identification and evaluation of cochlear implant candidates with asymmetrical hearing loss. *Audiol Neurootol*, 20, 87-89. [2] Akeroyd, M. A. (2006). The psychoacoustics of binaural hearing. *IJA*, 45, 25-33. [3] Lucas, L., Katiri, R. & Kitterick, P. T. (2018). The psychological and social consequences of single-sided deafness in adulthood. *IJA*, 57, 21-30. [4] Kitterick, P. T., Smith, S. N., & Lucas, L. (2016). Hearing Instruments for Unilateral Severe-to-Profound Sensorineural Hearing Loss in Adults: a Systematic Review and Meta-analysis. *Ear Hear*, 37(5), 495. [5] Kitterick, P. T., Lucas, L., & Smith, S. N. (2015). Improving health-related quality of life in single-sided deafness: a systematic review and meta-analysis. *Audiol Neurootol*, 20, 79-86. [6] Williamson, P. R., Altman, D. G., Bagley, H. Barnes, K. L., Blazeby, J. M., Brookes, S. T., Clarke, M., Gargon, E., Gorst, S., Harman, N., Kirkham, J. J., McNair, A., Prinsen, C. A. C., Schmitt, J., Terwee, C. B. & Young, B. (2017). The COMET Handbook: version 1.0. *Trials*, 18, 280-330.

Author Name: Roulla Katiri, **Email:** roulla.katiri@nottingham.ac.uk

This is a summary of independent research funded by the National Institute for Health Research at its NIHR Nottingham Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

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- The CROSSSD study group are aiming to identify what are the most critical and important effects to measure when testing how good treatments are for adults who have SSD.
- Defining a list of these effects – or 'outcomes' – will help researchers design future clinical trials that measure what is most important.
- Ultimately this will reduce research waste and improve the evidence available for patients and professionals when deciding whether to use hearing aids or auditory implants for SSD.

Roulla Katiri, audiologist, PhD student and CROSSSD study lead

For more information and to check if you can take part, please contact us.

Email us at:
- Roulla.Katiri@nottingham.ac.uk

Visit our website at:
- nottingham.ac.uk/go/CROSSSD

Read Carly Sygrove's blog about taking part at:
- https://myhearinglossstory.wordpress.com/

Please complete our survey if you are:
- Member of the public with severe-profound SSD for over 12 months
- Healthcare professional treating SSD e.g. Audiologists / ENT doctors
- Clinical researcher working in the field
- Commercial representative working with hearing aids or auditory implant

Go to the survey at:
https://delphimanager.liv.ac.uk/CROSSSD/Delphi

You will be asked to score 44 different outcomes on a 1-9 importance scale. This should take around 30 minutes. You will be asked to complete a similar survey a few weeks after.

Hurry! Survey closes soon!

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An International Consensus on Outcome Measures for Single Sided Deafness Interventions

Roulla Katiri[1,3], Deborah A. Hall[1,2] & Pádraig T. Kitterick[1,2]

[1] NIHR Nottingham Biomedical Research Centre, 113 The Ropewalk, Nottingham, NG1 5DU, UK;
[2] Otology & Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, NG7 2UH;
[3] Audiology Department, Mater Misericordiae University Hospital, Dublin, D07 R2WY.

NIHR Nottingham Biomedical Research Centre

Background

Single-sided deafness (SSD) is described by the presence of a severe-to-profound hearing impairment in one ear only[1].

- SSD disrupts the spatial aspects of hearing and impairs the ability to understand speech in the presence of background noise[2].
- It can lead to functional, psychological and social consequences[3].

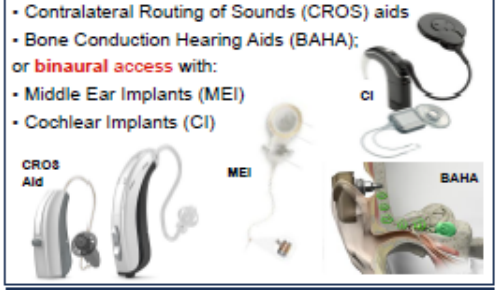
What can we do about it?

The most commonly used treatments for SSD restore **bilateral** access to sounds with:

- Contralateral Routing of Sounds (CROS) aids
- Bone Conduction Hearing Aids (BAHA);

or **binaural** access with:

- Middle Ear Implants (MEI)
- Cochlear Implants (CI)



What is the problem?

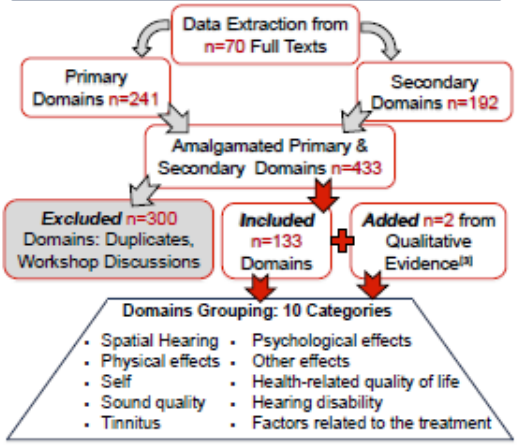
Existing literature has highlighted inconsistencies in what benefits and risks are assessed when evaluating SSD interventions.

Evidence-based clinical care and decision making is currently limited by the use of multiple, heterogeneous, unvalidated outcome measures.

How do we address the problem?

Our methods for developing a set of minimum standards will follow the Core Outcome Measures in Effectiveness Trials (COMET) Handbook:[4]

Systematic Review & Delphi Preparation



Where next?

@CROSSSD_ #CROSSSD

CROSSSD

International e-Delphi Surveys & Face-to-Face Stakeholder meetings to establish a consensus on core outcome set for SSD interventions

References: [1] Vincent, C., Arndt, S., *et al.* (2015). Identification and evaluation of cochlear implant candidates with asymmetrical hearing loss. *Audiol Neurootol*, 20, 87-89. [2] Akeroyd, M. A. (2006). The psychoacoustics of binaural hearing. *IJA*, 45, 25-33. [3] Lucas, L., Katiri, R. & Kitterick, P. T. (2018). The psychological and social consequences of single-sided deafness in adulthood. *IJA*, 57, 21-30. [4] Williamson, P. R., Altman, D. G., *et al.* (2017). The COMET Handbook: v 1.0. *Trials*, 18, 280-330.

Author Name: Roulla Katiri; **Email:** Roulla.Katiri@nottingham.ac.uk

This research was funded by the NIHR Nottingham Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

The NIHR Nottingham Biomedical Research Centre is a partnership between Nottingham University Hospitals NHS Trust and the University of Nottingham, supported by Nottinghamshire Healthcare NHS Foundation Trust and Sherwood Forest Hospitals NHS Foundation Trust. We are hosted by Nottingham University Hospitals.

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The CROSSSD study: Working together to overcome the challenges of evaluating treatments for SSD

Roulla Katiri, Deborah A. Hall, Derek J. Hoare, Kathryn Fackrell, Adele Horobin, Nicholas Hogan, Nóra Buggy, Paul H. Van de Heyning, Jill B. Firszt, Iain A. Bruce & Pádraig T. Kitterick for the Core Rehabilitation Outcome Set for Single-Sided Deafness (CROSSSD) initiative

How do we treat SSD?

What is the problem?

Existing literature has highlighted inconsistencies in what benefits and risks are assessed when evaluating SSD interventions.

Evidence-based clinical care and decision making is currently limited by the use of multiple, heterogeneous, unvalidated outcome measures.

The CROSSSD study:

@CROSSSD_
#CROSSSD
CROSSSD

International e-Delphi surveys and face-to-face stakeholder meetings helped to establish a consensus on a Core Outcome Set (COS) for SSD interventions

COMET INITIATIVE
Core Outcome Measures in Effectiveness Trials

Academic

Develop a COS of patient-centred outcome measures employing COMET initiative methods that:

- is shaped by opinions of Patient and Public Involvement (PPI) collaborators and all other relevant key stakeholders
- acts as a standard of reporting in clinical trials
- aims to reduce inconsistency / heterogeneity, of outcome measures used, which will aid review of clinical trials internationally
  - help journal editors evaluate manuscripts

Economic

Implementation of the COS will:

- allow for efficient and effective comparison of the benefits and risks of the various SSD interventions, increasing 'value for money'
- reduce 'research waste' by measuring only outcomes that are deemed critical, important and relevant by all key stakeholders

IMPACT

Assessing the domains in the core outcome set when evaluating SSD interventions will drive up the quality and relevance of research and will improve outcomes of patients

Society

Awareness of the COS will:

- minimise bias and guide charities and budget holders to allocate support to research encompassing outcome measures critical and important to all key stakeholders
- improve awareness of impact of SSD in everyday life
- improve the health of those diagnosed with SSD

Clinical

Adoption of the COS can:

- guide evidence-based clinical practice internationally
- empower healthcare users taking decisions about their healthcare

Researcher: Roulla Katiri; Part-time PhD student (Year 5), MSc in Audiology (University of Manchester), BSc Speech Sciences (University College London)

This research was funded by the NIHR Nottingham Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

The NIHR Nottingham Biomedical Research Centre is a partnership between Nottingham University Hospitals NHS Trust and the University of Nottingham, supported by Nottinghamshire Healthcare NHS Foundation Trust and Sherwood Forest Hospitals NHS Foundation Trust. We are hosted by Nottingham University Hospitals.

Appendix 15. Recruitment poster designed to display in audiology and ENT clinical rooms or waiting areas at participant identification sites.

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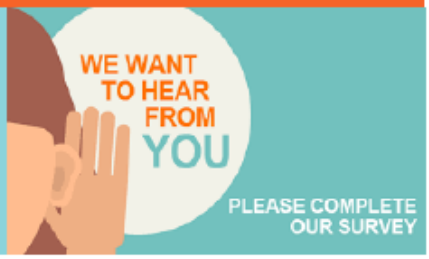
Do you have very poor hearing in one ear only?

(Single-Sided Deafness)

Are you interested in having your opinions about single-sided deafness treatments heard?



The CROSSSD Study aims to work out what should always be measured to help decide if a treatment is effective

You can take part if you:

- ✓ are over 18 years old
- ✓ have had single-sided deafness for at least 12 months
- ✓ have received or considering treatment for single-sided deafness

To take part all you have to do is complete an anonymous electronic survey

For more details, or to register your interest please contact:

Roulla Katiri, PhD Student
Tel: +44 (0) 115 823 2600
Email: roulla.katiri@nottingham.ac.uk
Web: www.nottingham.ac.uk/go/CROSSSD
National Institute for Health Research
Nottingham Hearing Biomedical Research Centre

CROSSSD @CROSSSD_ #CROSSSD

This study is being undertaken for educational purposes IRAS Project ID:239750

CROSSSD

Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) Study
Participant Recruitment Poster: Final Version 1.0, 22/05/2019

Appendix 16. Optional participant invitation letter.

(Letter to be printed on local headed paper)

Audiology / ENT Department
Insert:
Department Location
Department Hospital
Department Street
Department Post Code

Insert:
Participant Name
Participant Address
Participant Town
Participant Post Code

Insert: Date Month 2019

Dear Ms/Mr *Insert: Name*,

Re: Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) Study

You are invited to take part in a research study. The CROSSSD Study aims to work out what should always be measured to help decide if a treatment for single-sided deafness is effective.

You can take part if you:

- are over 18 years old
- have had single-sided deafness for at least 12 months
- have received or are considering treatment for single-sided deafness

To take part all you have to do is complete an anonymous electronic survey.

If you think that you might be interested in taking part in this study, please contact the study team directly, who will be able to send you some more information:

Roulla Katiri, PhD Student
Tel: +44 (0) 115 823 2600
Email: roulla.katiri@nottingham.ac.uk
Web: www.nottingham.ac.uk/go/CROSSSD
National Institute for Health Research
Nottingham Hearing Biomedical Research Centre

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Yours sincerely,

Insert: Clinical Team's Name

Appendix 17. Systematic review data extraction protocol.

CROSSSD data extraction protocol

CROSSSD Study:
Core Rehabilitation Outcome Set for Single Sided Deafness Study

Aim:
Towards a Consensus on Outcome Measures for Interventions that Seek to Restore Bilateral and Binaural Hearing in Adults with Unilateral Severe-to-Profound Hearing Loss

PROSPERO:
https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=84274

Scope:
This guidance document was developed to ensure consistency of data extraction procedures across reviewers.

Methodology:
Data collection will be conducted electronically on an Excel spreadsheet and will be initially piloted independently by RK and DAH with five studies. The two reviewers will then meet to discuss the suitability of the selected data fields. If indicated, the fields will be amended accordingly or additional fields will be included to capture additional information that is deemed important. A further five studies will then be piloted using the amended spreadsheet and if both reviewers deem the information captured adequate the 'finalised' version of the Data Extraction Spreadsheet will be developed. If not another five studies will be piloted until RK and DAH are happy with all the information captured.

Full data collection for all articles (n=70) that fit the PROSPERO described criteria will be conducted independently and in duplicate by RK, DAH and/or PTK and data will subsequently be compared and compiled into a single data extraction record. In cases of disagreement on data extracted, an arbitrator (DAH or PTK) will be asked to take a decision with regards to data extraction.

General framework:
The following four basic categories of data will be extracted:

a. **Methodological and substantive features:** Including source of the study, year of publication, type of research design etc. Documenting these features should help to relate these characteristics to the study findings (Brown *et al.*, 2003) and will help to explore relationships in the data (Popay *et al.*, 2006).
b. **Study quality:** Including assessment of the robustness of the study, such as the use of validated instruments (Kitterick *et al.*, 2016) utilised to evaluate the effects of interventions; and if the reported outcomes were on the basis of the instruments' measurement properties (Mokkink, *et al.*, 2010).
c. **Intervention descriptors:** Including the two types of hearing interventions (bilateral and binaural) as described by the CROSSSD study aims, and relevant clinical issues, such as cause of SSD, patients' age range, time between SSD diagnosis and implementation of intervention etc (Brown *et al.*, 2003).
d. **Outcome measures:** Based on PROSPERO, all outcomes relating to the interventions of interest will be considered; such as primary and secondary outcomes defined by study researchers, harms etc.

Specific Data Fields:
Selected data items were decided on the basis of the PICOS criteria as outlined in PROSPERO and guided by Popay *et al.*, (2006) principles and Hall *et al.*, (2016) methodology. The selected fields also relate to trial design and methodology adopted to measure the effects of a particular SSD intervention. The key headings (Table 1) for data extraction were developed using thematic analysis and with a scoping review of the current literature e.g. Van Zon *et al.*, (2015), Kitterick *et al.*, (2016), Van de Heyning *et al.*, (2016).

Table 1: Excel Spreadsheet dataset column headings and their descriptions

Col	Dataset column heading	Description
A	Study ID	As allocated by the original CROSSSD screening spreadsheet
B	Authors	As listed on the published article. For registered trials give the corresponding

		author
C	Year of publication	As listed on the published article. For registered trials give the date they were published online. If ePub give the date they were published online
D	Journal	Give the journal name the study was published in or the Name of the Registry for registered trials
E	Study Title	Full title of the article or registered trial
F	Corresponding author	As listed on the article or the principal investigator for registered clinical trials if a corresponding author is not listed
G	Email of Corresponding Author	As documented on the publication, or if not available endeavor to find online via the author's institution website
H	Country/ies Study Conducted	Write the country name only. If a multi-centre study indicate by writing 'multi-centre'. If the study is conducted at multiple countries list all countries e.g. *If in Lille / Lyon / Paris / Rennes / Tours, France write 'France, multi-centre' or if Lille / Rennes, France & Antwerp / Yvoir, Belgium write 'France & Belgium multi-centre'*
I	Study Start Date	Write in format MM/ YYYY e.g. *January 2009 is 01/2009*. If the month is not available write in format 00/YYYY
J	Study Design / Type of Study	Choose one of: Randomised Controlled Trials, Quasi-Randomised Controlled Trials, Before & After Study, Non-Randomised Controlled Trials, Cross-Over Studies, Clinical Trial Registration, Systematic Review. Any relevant / additional details should be noted in Column AJ (Notes Column)
K	SSD Cause / Participant Characteristics	Choose one of: Congenital, Acoustic Neuroma, Ménière's disease, Sudden Hearing Loss, Trauma, Unknown. If participants included have SSD due to different causes pls list all of the causes with number of participants noted e.g. *acoustic neuroma x5, Trauma x6* etc. If cause is not stated please document as 'Not stated'
L	Number of Participants	List the number of enrolled participants, if several groups, including controls; please write the number of participants in each group e.g. *Grp 1 trialing CROS in 10 patients and Grp 2 trialing a Cochlear Implant in 5 patients write CROS n=10 and CI n=5*
M	Participant Age Range	Record in years, if not stated please document as 'Not stated'. If several groups included please record for the SSD / UHL group only
N	Participant Mean Age	Record in years, if not stated please document as 'Not stated'
O	Age Standard Deviation	If able to calculate using participant characteristics please do so. If not calculated and unable to calculate please document as 'Not stated'. If several groups included please record for the SSD / UHL group only
P	Time since SSD Diagnosis	Record when the participants were diagnosed with SSD e.g. *5 years prior to recruitment in the study*. If several groups included please record for the SSD / UHL group only
Q	Study Primary Objective	Please copy exactly as defined by authors
R	Study Secondary Objective	Please copy exactly as defined by authors
S	Type of Intervention	Choose one of: Contralateral Routing of Signals (CROS) hearing aid devices, Bone Anchored Hearing Aids (BAHA), Middle Ear Implants (MEI), Cochlear Implants (CI), Auditory Brainstem Implant (ABI), Soundbite or Adhere. If specific details are given about the intervention e.g. for BAHA if Percutaneous or Subcutaneous (Attract) devices were used please specify which one in the Notes Section (Column AJ), if both were used please list both. For MEI if BoneBridge or SoundBridge was used please specify which one, if both were used please list both. If a Grp 1 was given a CI programmed with X algorithm and was compared to Grp 2 that was given CIs with Y algorithm please record as 'CI + X algorithm' in the Notes section (Column AJ). If there was several groups of participants, given different interventions please list all interventions used
T	Intervention	Choose one of: CROS, BAHA, MEI, CI, ABI, Soundbite or Adhere. If different

	Comparator	programming strategies were used please list them e.g. *If a Grp 1 was given a CI programmed with X algorithm and was compared to Grp 2 that was given CIs with Y algorithm please record as 'CI + Y algorithm'*
U	Implementation of Intervention	Please record in months or years, on average (mean value); how long after the onset of SSD the intervention was implemented. e.g. if a participant was diagnosed with SSD in 2002 and was enrolled in an interventions study and given an intervention in 2006, then record 4 years. If not stated please document as 'Not stated'
V	Primary Outcome Domain: The 'WHAT'	Please copy exactly as described by authors e.g. *Localisation*. If the authors do not explicitly describe the outcome domain as 'Primary' but it is assumed to be a primary outcome please indicate with a '?' e.g. *Localisation?*
W	Primary Outcome Measure: The 'HOW'	Record the Outcome Measure e.g. *AB Wordlists in Quiet*. If more than one measure was used e.g. *AB Wordlists in Quiet and QuickSIN testing*, please insert extra rows and record the data in different cells. Please keep the description of the instruments used succinct e.g. *Localisation with use of a 33-loudspeaker array at the horizontal plane*; no need for a full description e.g. *The ability to localize sounds in the horizontal plane was measured in a conventional room (not sound treated) typical of an office. For sound localization testing, all loudspeakers (1, 2, 3, 4, 5, 6) faced towards the participant. Thirty six responses were obtained for each participant.* If questionnaire subsections were measured separately as opposed to the global score please insert extra rows and record as separate Outcome Measures e.g. *If the SSQ questionnaire was used and they measured the Speech, Spatial and Qualities Domain record as 3 different measures i.e. Speech domain subscale of the SSQ, Spatial domain subscale of the SSQ, Qualities domain subscale of the SSQ.*
X	Primary Outcomes Measurement Time Frame	Record how long the participants had the intervention for before they were 'tested'. e.g. if participants were implanted with a CI and were enrolled in a study to measure CI outcomes 3 months post implantation please document as '*3 mths*'. If all measurements were conducted on the same day, record as 'Single session'. If several measurements were taken e.g. at 3 months, 6 months, 9 months please list all time frames i.e. *3, 6, 9 mths*. If exact time-frame was not stated please document as 'Not Stated'
Y	Secondary Outcome Domain: The 'WHAT'	As per Primary Outcome domain instructions (Column V), but for secondary
Z	Secondary Outcome Measure: The 'HOW'	As per Primary Outcome measure instructions (Column W), but for secondary
AA	Secondary Outcome Measurement Time Frame	As per Primary Outcomes Measurement Time Frame (Column X), but for secondary
AB	Is this a prospective trial registration or published protocol?	Choose Yes (Y) or No (N). Prospective Trial Registration is defined as e.g. https://clinicaltrials.gov/ct2/show/record/NCT02105441, a record in a Clinical Trails Registry. Published Protocol is defined as e.g. https://trialsjournal.biomedcentral.com/articles/10.1186/1745-6215-14-70, a publication in a peer reviewed journal
AC	Is this a report of study findings?	Choose Yes (Y) or No (N). Choose N if e.g. the record is a protocol of the intendent study
AD	Where there is multiple records for the same study, has the data extraction process been linked?	Choose Yes (Y) or No (N) or Not applicable (N/A). Chose Y if e.g. both the study protocol in the clinical trials registry and the peered reviewed published record were yielded
AE	Was quality assessed in terms of the consistency with which outcomes are	Choose Yes (Y) or No (N). Comment on details e.g. APHAB questionnaire was used to measure Listening Difficulty vs QoL

	reported and described within a manuscript?	
AF	Were outcomes reported prospectively through trial registration or a published protocol?	Choose Yes (Y) or No (N) or Not applicable (N/A). Choose Y if e.g. The research question and inclusion criteria were established and published before the study was conducted. Choose N/A if e.g. the record you are extracting data from is a publication of the protocol
AG	Are the outcomes reported consistently between protocol / registration and study report?	If applicable, comment on e.g. *Clinical Trial registration stated 80 target sample size, but only 56 recruited. Clinical Trial Registration states additional primary outcome is Tinnitus questionnaire (not defined, at 4 and 8 weeks) and additional secondary outcomes are 1- complication including headache measured using check list (not defined) at 4 weeks, 2- complication including vertigo measured using check list (not defined) at 4 weeks*
AH	Are there any conflicts of interest noted by the authors?	Choose Yes (Y), No (N) or Not stated, and please give details e.g. If declared that there were no conflicts of interest, record as N. If funding was provided by the hearing company involved e.g. *Funding provided by Sonitus Medical, Inc., San Mateo, CA. The authors have no other funding, financial relationships, or conflicts of interest to disclose*; please choose Y and copy the details as described by the authors
AI	Notes on Study Design	Any other study design features that were different e.g. *Recruited 9 but only analysed data for 8 participants*
AJ	Notes	Please note anything you feel is relevant to consider e.g. If a clinical trial registry did not recruit any participants or if you have any queries

Notes:
> If unable to find the data for columns as defined, please document as 'Cannot find'
> Generally, if data is not documented in the publication please record as 'Not Stated'

Systematic Reviews: The yielded systematic review records will be reviewed for the individual articles included. All included articles of each systematic review will be assessed independently for eligibility as per set CROSSSD study PICOS criteria. They will then be double-coded according to the original CROSSSD criteria. If any were missed by the original search the Titles / Abstracts will be coded and if necessary the full text PDFs will be retrieved and coded accordingly by two independent reviewers. Data will be extracted from all new (if any) identified records.

Quality Assessment:
The validity of the conclusions of a systematic review depend on the quality of the included primary studies (Downs & Black, 1998). Assessing the quality of studies is defined as an assessment of 'the likelihood of the trial design to generate unbiased results that are sufficiently precise and allow application in clinical practice' (Verhagen *et al.*, 2001). In their systematic review of management options for unilateral hearing loss in children, Appachi *et al.*, (2017) successfully utilised the validated Newcastle-Ottawa Scale (NOS) to assess the quality of the studies reviewed. When NOS is utilised, the reviewer is instructed to assign points when quality domains are present, thus permitting the calculation of overall 'quality scores'. However Oremus *et al.*, (2012) report 'poor to fair' inter-rater reliability only 'fair to excellent' test-rested reliability especially when inexperienced raters are scoring the studies. Furthermore, Higgins *et al.*, (2011) state that quality scales and scale scores are not appropriate tools to utilise when assessing study quality. It considered that the Cochrane Collaboration tool for assessing risk of bias is utilised, with the following types of bias recorded (Higgins *et al.*, 2017):

Table 8.4.a: A common classification scheme for bias

Type of bias	Description	Relevant domains in the Cochrane 'Risk of bias' tool
Selection bias	Systematic differences between baseline characteristics of the groups that are compared	• Sequence generation • Allocation concealment
Performance bias	Systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest	• Blinding of participants and personnel • Other potential threats to validity
Detection bias	Systematic differences between groups in how outcomes are determined	• Blinding of outcome assessment • Other potential threats to validity
Attrition bias	Systematic differences between groups in withdrawals from a study	• Incomplete outcome data
Reporting bias	Systematic differences between reported and unreported findings	• Selective outcome reporting (see also Chapter 10)

However, there is a large variability in study designs and types yielded by the search. These included Randomised Controlled Trials for which the Cochrane tool is tailored for; but also Quasi-Randomised Controlled Trials, Before and After Studies, Non-Randomised Controlled Trials, Cross-Over Studies, Clinical Trial Registrations and Systematic Reviews. Therefore, utilizing the Cochrane tool would not effectively address bias in all types of study designs.

Consequently, Risk of bias will be assessed by analysing the reporting of outcomes both within and across manuscripts reporting study findings. Quality will be assessed in terms of the consistency with which outcomes are reported and described within a manuscript (Column AE), whether outcomes were reported prospectively through trial registration or published protocol (Column AF), and whether outcomes are reported consistently between protocol / registration and study report (Column AG).

The quality of a pilot sample of articles (n=5) will be conducted initially to ensure that criteria are applied consistently by two independent reviewers and that consensus can be reached between reviewers. Following this the Data Extraction Protocol will be modified accordingly. A second batch of n=5 studies will be piloted next to ensure the revised protocol is thoroughly covering all aspects. If the reviewers are happy with the consistency and outcomes they will proceed with data extraction of the rest of the records.

The reviewers will consider blinding (to authors, institutions, journals and study results) when conducting the quality assessment. This will depend on the resources available at the time, although there is limited evidence that blinded assessments is significantly beneficial (Kjaergard *et al.*, 2011).

The consolidated record data (e.g. outcome descriptors, published primary / secondary findings) collated from the review will be qualitatively and critically analysed for consistency of outcome reporting by at least two independent reviewers. If consensus cannot be reached on whether outcomes have been reported consistently

then disagreements will be resolved by consensus with a third reviewer. Findings will be reported using a narrative synthesis. The quality of a study will not affect its inclusion in the synthesis.

Sensitivity Analysis:
A subgroup of studies (n=27) had minor differences form the PROSPERO protocol for example in the sample of actual recruited subjects a small number did not meet the explicit threshold criteria for SSD, despite the overall intention to recruit SSD patients. These have been coded as '1a' so that a sensitivity analysis can be conducted to identify whether this subgroup of studies differ in their outcomes measured. If not, then the outcomes information will be pooled across all studies.

Consolidation of Studies:
A single common extraction will be utilized for e.g. Clinical Trial Registrations and/or Protocols which describe the same study. These studies will be identified and clearly marked. Quality assessment will be undertaken and will be compared for these separately.

References:

Appachi, S., Specht, J.L., Raol, N., Lieu, J.E., Cohen, M.S., Dedhia, K. & Anne, S. (2017). Auditory outcomes with hearing rehabilitation in children with unilateral hearing loss: a systematic review. *Otolaryngol Head Neck Surg*, *157*(4), 565-571.

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Higgins, J.P., Altman, D.G., Gøtzsche, P.C., Jüni, P., Moher, D., Oxman, A.D., Savović, J., Schulz, K.F., Weeks, L. & Sterne, J.A. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*, *343*, p.d5928.

Higgins, J. P. T., Altman, D. G., Sterne, J. A. C. (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins, J. P. T., Churchill, R., Chandler, J., Cumpston, M. S. (editors), Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0 (updated June 2017), Cochrane, 2017. Available: www.training.cochrane.org/handbook.

Kitterick, P. T., Smith, S. N., & Lucas, L. (2016). Hearing instruments for unilateral severe-to-profound sensorineural hearing loss in adults: a systematic review and meta-analysis. *Ear Hear,* 37(5), 495-507.

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Mokkink, L.B., Terwee, C.B., Patrick, D.L., Alonso, J., Stratford, P.W., Knol, D.L., Bouter, L.M. & De Vet, H.C., (2010). The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. *Qual Life Res*, *19* (4), 539-549.

Oremus, M., Oremus, C., Hall, G.B., McKinnon, M.C. and ECT & Cognition Systematic Review Team (2012). Inter-rater and test–retest reliability of quality assessments by novice student raters using the Jadad and Newcastle–Ottawa Scales. *BMJ Open*, *2*(4), e001368.

Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., Britten, N., Roen, K. & Duffy, S., (2006). Guidance on the conduct of narrative synthesis in systematic reviews. *A product from the ESRC methods*

programme Version, 1, p.b 92.

Van de Heyning, P., Távora-Vieira, D, Mertens, G., Van Rompaey, V., Rajan, G. P., Müller, J., Hempel, J. M, Leander, D., Polterauer, D., Marx, M., Usami, S. I., Kitoh, R., Miyagawa, M., Moteki, H., Smilsky, K., Baumgartner, W. D., Keintzel, T. G., Sprinzl, G. M., Wolf-Magele, A., Arndt, S., Wesarg, T., Zirn, S., Baumann, U., Weissgerber, T., Rader, T., Hagen, R., Kurz, A., Rak, K., Stokroos, R., George, E., Polo, R., Medina, M. D. M., Henkin, Y., Hilly, O., Ulanovski, D., Rajeswaran, R., Kameswaran, M., Di Gregorio, M. F. & Zernotti, M. E. (2016). Towards a Unified Testing Framework for Single-Sided Deafness Studies: A Consensus Paper. *Audiol Neurootol*. 21(6): 391-398.

Van Zon, A., Peters, J.P., Stegeman, I., Smit, A.L. and Grolman, W. (2015). Cochlear implantation for patients with single-sided deafness or asymmetrical hearing loss: a systematic review of the evidence. *Otol Neurotol*, 36 (2), 209-219.

Verhagen, A.P., de Vet, H.C., de Bie, R.A., Boers, M. & van den Brandt, P.A. (2001). The art of quality assessment of RCTs included in systematic reviews. *J Clin Epidemiol*, *54*(7), 651-654.

Consulted:

Higgins, J. P. T. & Green S (2011). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1. The Cochrane Collaboration. Available from www.cochrane-handbook.org

Systematic Reviews, a Guide: Data Extraction. Available from:
http://researchguides.ebling.library.wisc.edu/systematic-reviews/author/data

Systematic Reviews: Reporting the quality / risk of bias. Available from:
http://libguides.gwumc.edu/c.php?g=27797&p=170451

Systematic Reviews & Meta-analyses: Data Extraction. Available from:
https://guides.lib.vt.edu/SystematicReviews/DataExtraction

Appendix 18. Participant plan and guide documents for virtual consensus meeting.

Core Rehabilitation Outcome Set for Single Sided Deafness (CROSSSD) Study

Consensus meeting to agree a Core Outcome Set (COS) for Single Sided Deafness (SSD) Interventions

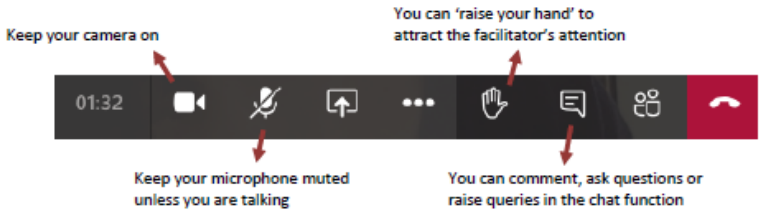
In preparation for the meeting, it would be helpful if you could read this document carefully.

Meeting focus:
The aim of the consensus meeting is to bring together a sample of healthcare users, healthcare professionals, clinical researchers and commercial representatives who have completed both Rounds of the e-Delphi survey; to discuss and agree the final minimum set of outcome domains for SSD interventions.

Date and time:
Tuesday 7th of July 2020, 9:30am to 4:30pm. Please log-into Microsoft Teams promptly just before 9:30am. We aim to wrap up the meeting by 4-4:30pm.

Virtual meeting platform:
We will be using Microsoft Teams for the meeting. You can join via the Teams App or on the web. To join simply click on the 'Join Microsoft Teams Meeting' link which will be send to your email calendar in due course. More details on the Teams software and on how to join can be found in this short video.

To improve the sound quality for all participants during the meeting please ensure your microphone is muted when you are not talking. It is preferable to have your camera turned on, to enhance communication for other participants who use lip-reading. Please 'raise your hand' and use the chat function to attract the facilitator's attention or post any comments or questions to the group. For details on how to use these features please refer to the diagram below, which will be on your screen. You can also enable captions on Microsoft Teams, if you feel that might be helpful. If you'd like any more details on these features please email roulla.katiri@nottingham.ac.uk.



Study management team:
Roulla Katiri, PhD student CROSSSD study
Deborah Hall, Professor of Hearing Sciences, expert in outcome measures & PhD student supervisor
Pádraig Kitterick, Associate Professor in Hearing Sciences, expert in SSD & CROSSSD study chief investigator

Facilitators:
Derek Hoare, Associate Professor in Hearing Sciences
Kathryn Fackrell, NIHR Post-Doctoral Research Fellow (Hyperacusis)
Deborah Hall, Professor of Hearing Sciences.

Patient & Public Involvement (PPI) team:
Adele Horobin, Patient & Public Involvement manager NIHR Nottingham Hearing BRC
Nora Buggy, PPI collaborator and healthcare user with SSD using a CROS aid
Nicholas (Nicky) Hogan, PPI collaborator and healthcare user with SSD using a BAHA
PPIs are allowed to participate in discussions throughout the day but *cannot* vote.

Participants:
Stakeholder representatives: Expert healthcare users, healthcare professionals, clinical researchers and commercial representatives.
Observers: Two commercial representatives (Oticon Medical); and a healthcare professional and clinical researcher. Observers are *not* allowed to participate in discussions *nor* vote.

Participant sub-groups:
To help with discussions throughout the day, we have split the larger group into three sub-groups as listed on the table below. You will have separate Microsoft Teams links saved in your email calendar, directing you to the correct group at the correct time on the day. If you have any queries with regards to your allocated group please get in touch.

Groups and facilitators	**Group A** Derek Hoare	**Group B** Kathryn Fackrell	**Group C** Deborah Hall
Study team helpers	Roulla Katiri	Pádraig Kitterick	Adele Horobin
Patient & Pubic Involvement (PPI) team	Nicky Hogan	Nora Buggy	Adele Horobin
Healthcare users Healthcare professionals Commercial representatives Clinical researchers Observers	Ad Snik Carly Sygrove Penny Feltham Richard Bowles Tove Rosenbom	Cherith Campbell-Bell Chris Parker Daniel Zeitler Peter Toth Richard Nicholson	Lewis Williams Maxine Oxford Paddy Boyle Paul James Roger Bayston

Draft Agenda (will be flexible during the day, will be guided by discussions):

Time in GMT	
09:15-09:30	Log-in & Join Microsoft Teams Meeting
09:30-10:00	Welcome, Introductions and Q&A
10:00-10:45	Group discussions on outcome domains to consider
10:45-11:15	*Coffee Break*
11:15-11:45	Small Group Workshop 1: Reducing the number of outcome domains for clinical trials
11:45-12:30	Workshop feedback to the larger group
12:30-13:00	*Lunch*
13:00-13:20	Small Group Workshop 2: Reducing the number of outcome domains for clinical trials
13:20-13:45	Workshop feedback to the larger group
13:45-14:15	*Coffee Break*
14:15-16:00	Discussion of workshop outcomes and agreement on final Core Outcome Set
16:00-16:30	Close & Feedback

What do I need to do on the day?
The study management team will briefly remind the group of the scope of the day and will answer any questions you may have. You will be expected to participate in small-group discussions to share your views; and voting exercises using Microsoft Forms. Links to these voting forms will be provided on the day of the meeting.

Preparation prior to the meeting:
To prepare for the meeting and to be aware of the Scope, Aims and Objectives please watch our 15 minute long introductory presentation.

The intention of the consensus meeting is to reduce the list of 17 outcome domains (see table below); but this will be confirmed with the group. These were scored as critical and important to include in a core outcome set for SSD interventions by at least 70% of the 241 participants, from 30 different countries, who took part in Round 2 of our online survey.

No	Outcome Domain	Outcome Domain Definition
7	Listening effort	Exerting greater effort to listen and follow a conversation. This might consequently lead to feelings of tiredness and fatigue; but those feelings would be a separate outcome domain
8	Treatment satisfaction	How the treatment meets your expectations or how pleased you are after receiving the treatment; or how likely you are to recommend the treatment
9	Device usage	How you use the device (for example; in what situations; for how long)
10	Device malfunction	The device does not work as it should or it stops working
12	Avoiding social situations	Choosing not to go to particular social situations because of your hearing loss
15	Impact on social situations	Your hearing loss or device limiting your ability to fully participate in the social world; especially in challenging situations or where a lot of effort is needed to follow the conversation (for example; at a restaurant; at the park; in a bar or at a party)
16	Impact on work	Effect of your hearing loss or device on your ability to carry out work tasks or job roles; or advancing your career
17	Being aware of a sound	Being aware of a sound and recognising what that sound is (for example; being aware that someone has started to speak)
18	Listening in complex situations	The difficulty experienced when listening to a sound while separating it out from a background of other sounds
19	Listening in reverberant conditions	The difficulty experienced when listening in places where the sound reflects off the walls; floor or ceiling (echoes); creating a blurred sound. For example; understanding announcements in train stations or airports
21	Group conversation in quiet	Listening and following a conversation between a group of people; in a quiet environment
22	One-to-one conversation in general noise	Listening and understanding one person; in a noisy environment
23	Group conversation in noisy social situations	Listening and following a conversation between a group of people; when others are talking in the background
24	Sound localisation	Knowing where a sound is coming from
26	Spatial orientation	Knowing where you are in relation to the position of a sound source
28	Physical tiredness	Tiredness or fatigue from the effort of listening or when you need to turn your head repeatedly to listen in social situations
35	Personal safety	How your hearing loss effects your awareness of potential hazards and threats in your daily life (for example; moving traffic; hazards at the workplace) and those you may not be able to see or hear (for example; other people behind you)

Ahead of the meeting you are required to consider your **'Top 3'** most important and critical domains to include in the core outcome set **from your own personal perspective** (as a healthcare user, healthcare professional, clinical researcher or commercial representative). Please remember that the core outcome set will be a recommendation to always measure *as a minimum* in all *clinical trials* that investigate SSD interventions in adults. At this stage of the process we are not concerned about how easy, time-consuming, fun, challenging or complicated it might be to measure this outcome; that is work for the future.
*Please submit your 'Top 3' outcome domains by **Friday 3rd of July** by completing this short survey.

Consent:
In order to take part you need to read and complete the study consent form, which can be accessed here. Please complete the consent form by **Friday 3rd of July**. If you need more information on the study prior to signing the consent form please read our information leaflets; for healthcare users and for professionals accordingly. Please contact Roulla Katiri at roulla.katiri@nottingham.ac.uk if you have any questions. Meeting observers do not need to complete the consent form.

Recordings:
To facilitate analysis, discussions will be recorded on Microsoft Teams. The recordings will be saved on University of Nottingham secure servers. In case they need to be transcribed, only non-identifiable information will be transcribed e.g. the identity of any of the talkers or anything said that identifies an individual will be removed.

Photography and Social Media:
The study team plan to take screen shots on the day, which will be shared on the internet and social media. If you do not wish to be included on social media posts, please let us know in advance. If you'd like to Tweet about the consensus meeting you may like to use the following tags:

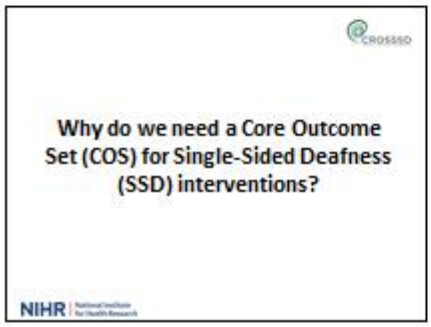
Study UoN team	@CROSSSD_ @RouKat @padraig_hearing @HorobinAdele @Derek_J_Hoare @FackrellKathryn @DebHallNBRUH
Study organisation	@hearingnihr @UoNHearSci @NottsSPHL
Other related	@NIHRresearch @NIHRtakepart @NIHRinvolvement @Sharebank1 @COMETinitiative @COMITIDStudy @GlobalPPINet
Participants	@myhearingloss @PennyF_UK @radboudumc @DrDanielZeitler
Commercial reps	@oxford_maxine @OticonMedical @AdvancedBionics @CochlearUK @phonak
Charities	@BANAUK @MenieresSociety @ActionOnHearing @BritishTinnitus
Professional bodies	@BSAudiology1 @ENTUKGlobal @BCIG_UK @ENTANewsround

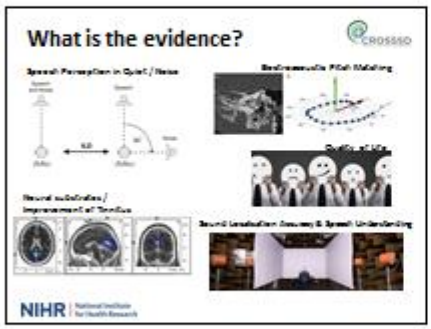
Meeting evaluation:
We would like to evaluate your experience of taking part in a virtual consensus meeting using an evaluation form. It is anticipated that completion of this will take approximately 5 minutes and completion is entirely voluntary.

Study contact:
Please get in touch with Roulla Katiri if any queries arise prior to the meeting or on the day.
Email: roulla.katiri@nottingham.ac.uk **Phone, WhatsApp or Viber:** +353 86 8966461 **Skype:** @roullak

Thank you for taking an interest in the CROSSSD study.

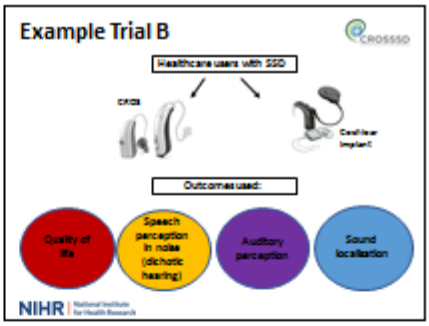
Appendix 19. Pre-consensus meeting introductory presentation slides.

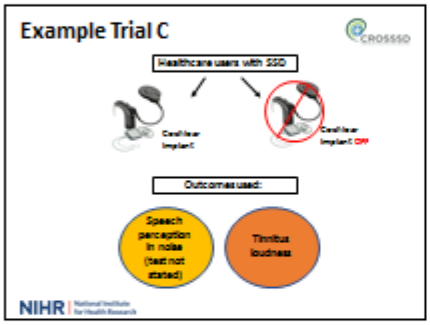




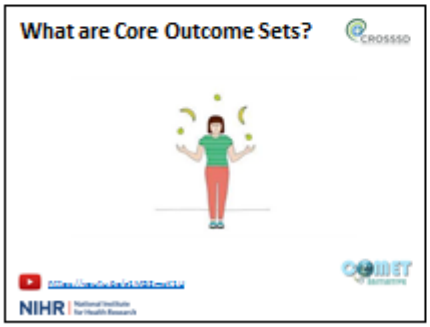
1


Example Trial A
CROSSSD
Healthcare users with SSD
CROS
BAHA
Outcomes used:
Speech perception in noise (sentences)
Speech perception in noise (single words)
Hearing disability questionnaire
NIHR


Example Trial B
CROSSSD
Healthcare users with SSD
CROS
Cochlear Implant
Outcomes used:
Quality of life
Speech perception in noise (dichotic hearing)
Auditory perception
Sound localisation
NIHR


Example Trial C
CROSSSD
Healthcare users with SSD
Cochlear Implant
Cochlear Implant OFF
Outcomes used:
Speech perception in noise (test not stated)
Tinnitus loudness
NIHR


CROSSSD
COMPARED
COMBINED
Evidence-based clinical care and decision making is currently limited by the use of multiple, heterogeneous, unvalidated outcome measures
NIHR


What are Core Outcome Sets?
CROSSSD
COMET
NIHR


CROSSSD
CROSSSD
CROSSSD Study:
Identifying what is critical and important to measure when evaluating hearing interventions for adults with Single-Sided Deafness (SSD)
NIHR

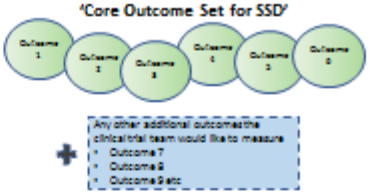
2

Consensus meeting aim

To finalise a list of outcomes which should be measured and reported, *as a minimum*, by researchers studying SSD interventions

NIHR

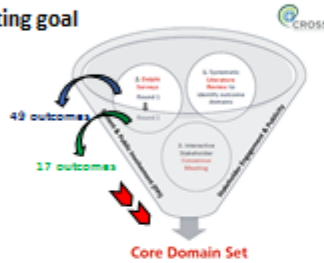
'Core Outcome Set for SSD'



Any other additional outcomes the clinical trial team would like to measure
- Outcome 7
- Outcome 8
- Outcome 9 etc

NIHR

Meeting goal



NIHR

Next Steps

Complete the consent form by Friday 3rd of July
(Check your email for link to the form)

Identify your Top 3 Outcome Domains by Friday 3rd of July
(Check your email for survey link)

Group Discussions and voting on Tuesday 7th of July

NIHR

Remember

- The derived COS is for *clinical trials* not clinical use
- We are concerned about *the 'WHAT'* to measure
- The 'HOW' to measure each outcome is work for the future
- All opinions matter, please share them, we are all equal in this meeting despite what group we represent

NIHR

Virtual 'Housekeeping'

- Sharp 9:30am start (GMT)
- Click on the 'Join Microsoft Teams Meeting' link in your calendar
- Breaks & Lunch
- Language use
- Mute your microphone
- Social Media
- Confidentiality
- Acknowledgements

NIHR

Don't forget...

Optional pre-consensus meeting coffee morning...
(Bring your own refreshment)

Thursday 2nd of July
join any time 9:30-11:30am

- Test the technology
- Meet the other participants

(Check your calendar for the Join Microsoft Teams Meeting link)

NIHR

Questions?

To ensure we address all questions effectively please email them to roulla.katiri@nottingham.ac.uk by Monday 6th of July 2020

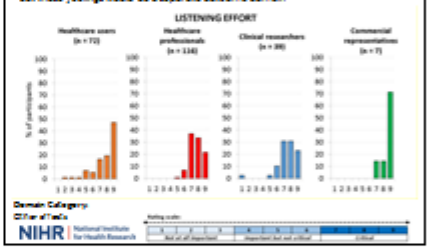
NIHR

List of the 17 outcome domains that were unanimously voted, by all stakeholder groups, as critical and important to be included in a core domain set for SSD

NIHR

7. LISTENING EFFORT

Evening greater effort to listen and follow a conversation. This might consequently lead to feelings of tiredness and fatigue; but those feelings would be a separate outcome domain



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8. TREATMENT SATISFACTION

How the treatment meets your expectations or how pleased you are after receiving the treatment; or how likely you are to recommend the treatment

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9. DEVICE USAGE

How you use the device (for example; in what situations; for how long)

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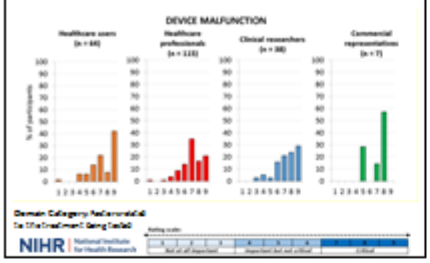
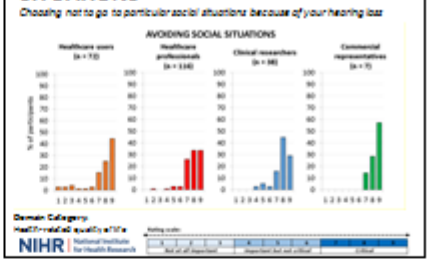
10. DEVICE MALFUNCTION

The device does not work as it should or it stops working



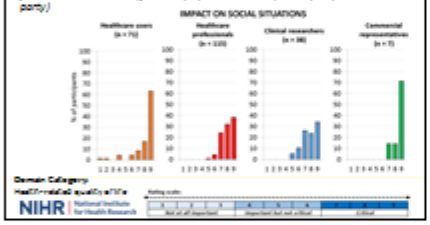
12. AVOIDING SOCIAL SITUATIONS

Choosing not to go to particular social situations because of your hearing loss



15. IMPACT ON SOCIAL SITUATIONS

Your hearing loss or device limiting your ability to fully participate in the social world; especially in challenging situations or where a lot of effort is needed to follow the conversation (for example; at a restaurant; at the park; in a bar or at a party)

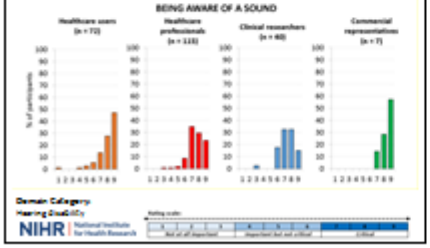


16. IMPACT ON WORK

Effect of your hearing loss or device on your ability to carry out work tasks or job roles; or advancing your career

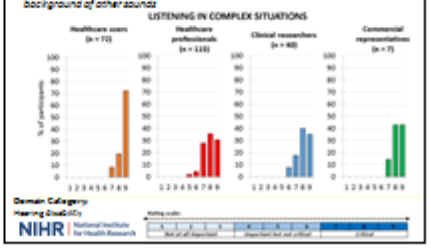
17. BEING AWARE OF A SOUND

Being aware of a sound and recognizing what that sound is (for example; being aware that someone has started to speak)



18. LISTENING IN COMPLEX SITUATIONS

The difficulty experienced when listening to a sound while separating it out from a background of other sounds



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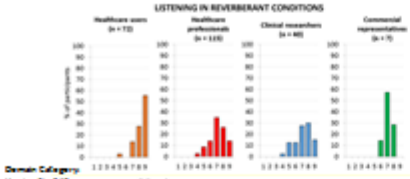
19. LISTENING IN REVERBERANT CONDITIONS

The difficulty experienced when listening in places where the sound reflects off the walls; floor or ceiling (echoes); creating a blurred sound. For example; understanding announcements in train stations or airports



Domain Category
Hearing Disability

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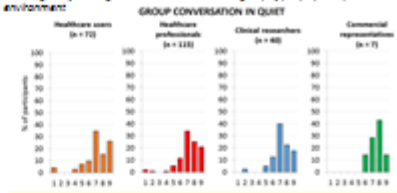
21. GROUP CONVERSATION IN QUIET

Listening and following a conversation between a group of people; in a quiet environment



Domain Category
Hearing Disability

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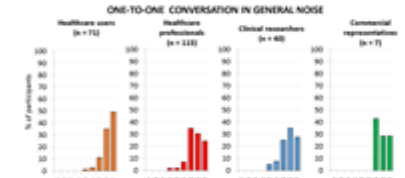
22. ONE-TO-ONE CONVERSATION IN GENERAL NOISE

Listening and understanding one person; in a noisy environment



Domain Category
Hearing Disability

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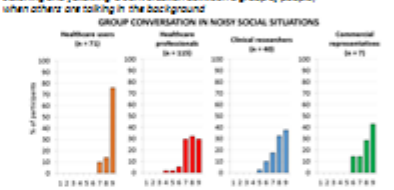
23. GROUP CONVERSATION IN NOISY SOCIAL SITUATIONS

Listening and following a conversation between a group of people; when others are talking in the background



Domain Category
Hearing Disability

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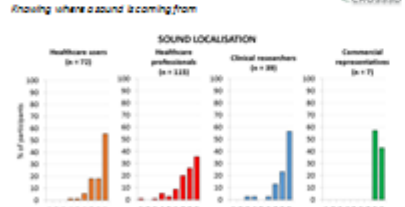
24. SOUND LOCALISATION

Knowing where a sound is coming from



Domain Category
Spatial Hearing

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26. SPATIAL ORIENTATION

Knowing where you are in relation to the position of a sound source

Domain Category
Spatial Hearing

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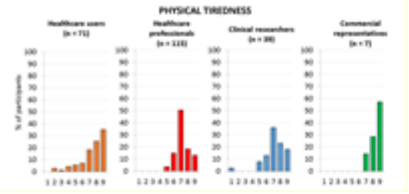
28. PHYSICAL TIREDNESS

Tiredness or fatigue from the effort of listening or when you need to turn your head repeatedly to listen in social situations



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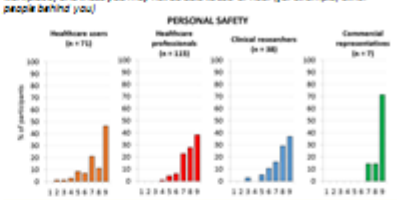
35. PERSONAL SAFETY

How your hearing loss affects your awareness of potential hazards and threats in your daily life (for example, moving traffic; hazards at the workplace) and those you may not be able to see or hear (for example, other people behind you)



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List of the 49 outcome domains that were rated during the second round of the Delphi survey for Inclusion, Exclusion or 'Maybe'

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e-Delphi survey results

Round 1 e-Delphi (9th Sept - 21st Nov):

n=44 outcome domains to rate
n=308 registrations
n=272 rated all domains
n=36 did not complete
n=95 suggested additional outcomes
n=5 outcomes added to Round 2

Round 2 e-Delphi (21st Nov - 24th Feb):

n=49 outcome domains to rate
n=232 rated all domains
n=44 did not complete
n=870 changes to Round 1 ratings

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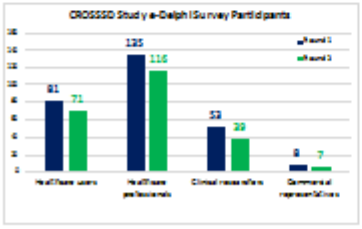
Stakeholder group participants



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Rules: Outcome Inclusion

Outcomes where at least 70% scored 7-9 and less than 15% scored 1-3 in all stakeholder groups

at least 70% scored it as 'critically important'

less than 15% scored it 'unimportant'

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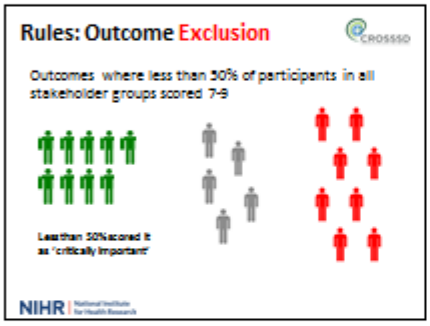
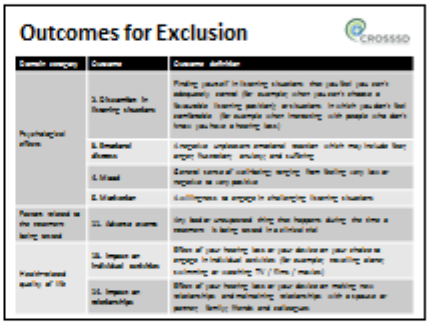
7

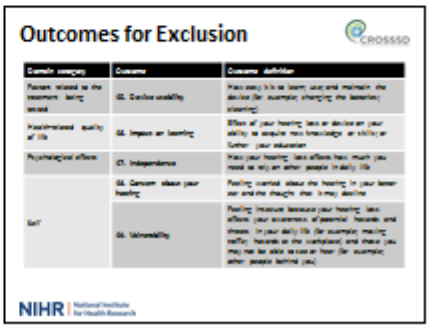

Outcomes for Inclusion
CROSSSD
NIHR


Outcomes for Inclusion
CROSSSD


Rules: Outcome Exclusion
CROSSSD
Outcomes where less than 50% of participants in all stakeholder groups scored 7-9
Less than 50% scored it as 'critically important'
NIHR


Outcomes for Exclusion
CROSSSD


Outcomes for Exclusion
CROSSSD
NIHR


Outcomes for Exclusion
CROSSSD
NIHR

8

Maybes? No consensus

Domain category	Outcome	Outcome definition
Psychological effects	6. Discomfort/burden with life	Being unhappy because you feel you should be achieving or should have achieved more in your life
Physical effects	12. Manual dexterity	Having the fine motor skills needed to use your devices effectively (for example, pushing the device and changing the batteries)
	13. Tinnitus-related brain changes	Changes in brain structure or function associated with tinnitus
	14. Hearing-related brain changes	Changes in brain structure or function associated with hearing loss
QoL	15. Self-stigma	Negative perception of yourself due to your hearing loss and feeling embarrassed for using a hearing aid
Tinnitus	16. Tinnitus awareness	Hearing the sound of tinnitus is there
	17. Tinnitus pitch	Whether your tinnitus has a repetitive quality (for example high pitch like whistling or low pitch like humming
	18. Tinnitus quality	What type of sound is heard (for example: hissing buzzing ringing whistling etc)

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Appendix 20. Round 1 participant comments about potential additional outcome domains and decisions to include in Round 2.

	Additional suggested outcome / feedback comment	Suggested by	Scored	Existing' / 'Rejected' / 'Neither'	If 'Existing' what domain does it match?	If 'Rejected ' why?	If 'Neither' include?	FINAL DECISION - Add outcome?	Comment
1	Wireless functionality of intervention (Bi/CROS; BAHA)	Healthcare professional	6	Existing	**DEVICE MALFUNCTION** - The device does not work as it should or it stops working		N/A	N	
2	Size of the hearing aid (Bi/CROS; BAHA)	Healthcare professional	6	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
3	Re-current ear infections after using Bi/CROS system	Healthcare professional	7	Existing	**ADVERSE EVENTS** - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial		N/A	N	
4	Ability to manage treatment option (change batteries; clean slim tubes) has the client dexterity or visual impairment which may impact on their ability to use a particular treatment type	Healthcare professional	6	Neither	**MANUAL DEXTERITY** - Having the fine motor skills needed to use your device effectively (for example, putting the device on, changing the batteries)			Y (see 19)	Visual acuity is not an outcome domain for SSD interventions. See also additional outcome no 19
5	The fact wearing a hearing aid reveals having a (hearing) handicap previously not seen by people around. If they want to wear the device despite the fact revealing their handicap is must be worthwhile	Healthcare professional	6	Existing	**DEVICE USAGE** - How you use the device (for example, in what situations, for how long) & **TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment & **SELF-STIGMA** - Negative perception of yourself due to your hearing loss and feeling stigmatised for using a hearing aid		N/A	N	
6	Long term follow-up (declined device use over time)	Healthcare professional	7	Existing	**DEVICE MALFUNCTION** - The device does not work as it should or it stops working & DEVICE USAGE - How you use the		N/A	N	

					device (for example, in what situations, for how long)				
7	How robust the device is (waterproof; shock proof; etc)	Healthcare user	8	Existing	**DEVICE MALFUNCTION -** The device does not work as it should or it stops working & **ADVERSE EVENTS** - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial		N/A	N	
8	Battery life	Healthcare user	6	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
9	re word the outcome that I gave feedback on	Healthcare user	8	Reject	N/A	This is a comment , not a suggested outcome domain	No	N	
10	The ability to be able to hear and understand low voices eg. on radio; children or people with accents	Healthcare user	7	Existing	LOUDNESS - How 'loud' a sound seems to you & CLARITY - How 'clear' a sound seems to you & BEING AWARE OF A SOUND - Being aware of a sound and recognising what that sound is (for example, being aware that someone has started to speak) & ONE-TO-ONE CONVERSATION IN QUIET - Listening and understanding one person, in a quiet environment		N/A	N	
11	Physical comfort e.g., strain on neck	Healthcare professional	3	Existing	TREATMENT SATISFACTION - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment & PHYSICAL TIREDNESS - Tiredness or fatigue from the effort of listening or when you need to turn your head repeatedly to listen in		N/A	N	

					social situations & ADVERSE EVENTS - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial				
12	Data-logging on trial of device	Healthcare professional	8	Reject	**DEVICE USAGE** - How you use the device (for example, in what situations, for how long)	Dataloggi ng on *trial* device is not an outcome	No	N	
13	The reason for one sided hearing loss needs consideration	Healthcare user	7	Reject	N/A	Not an outcome domain for SSD interventi ons	No	N	
14	Feeling a sense of auditory balance	Healthcare professional	7	Existing	**SOUND LOCALISATION** - Knowing where a sound is coming from & **SOUND DISTANCE** - Knowing if a sound is close by or far away & **SPATIAL ORIENTATION** - Knowing where you are in relation to the position of a sound source		N/A	N	
15	Patient satisfaction with treatment	Healthcare professional	8	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
16	Stigma - Other (i.e., stigma and discrimination from society; media; employers; family; friends; colleagues etc; as opposed to self-stigma. Stigma doesn't just come from the self - there is genuine discrimination against people with disabilities)	Clinical researcher	6	Reject	**IMPACT ON RELATIONSHIPS** - Effect of your hearing loss or your device on making new relationships and maintaining relationships with a spouse or partner, family, friends and colleagues & **IMPACT ON RELATIONSHIPS** - Effect of your hearing loss or your device on making new relationships and maintaining relationships with a spouse or partner, family, friends and colleagues	Stigma and discrimin ation *from* society is not an outcome for SSD interventi on itself	No	N	

17	Impact on romantic/intimate relationships (i.e., impact on conversations with partner; spending time with partner etc Quite different from relationships with relatives; friends; colleagues etc However; it is a problematic one to measure as it may not apply to all)	Clinical researcher	4	Existing	**IMPACT ON RELATIONSHIPS** - Effect of your hearing loss or your device on making new relationships and maintaining relationships with a spouse or partner, family, friends and colleagues		N/A	N	
18	Comfort of device (i.e., whether the device/intervention is uncomfortable such as itchy; painful; loud etc)	Clinical researcher	6	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment & **ADVERSE EVENTS** - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial		N/A	N	
19	Ease of use (This should replace 'manual dexterity'; which is a characteristic of the patient; not an outcome of the intervention. Dexterity is not changed by an audiology intervention. Instead its better to measure if the device is feasible or simple for the target population to use or whether it is too complex; inaccessible etc.)	Clinical researcher	6	Neither	N/A			Y	New outcome domain: **DEVICE USABILITY** - How easy it is to learn, use, and maintain the device (for example, changing the batteries, cleaning)
20	Communication (Too many of the outcomes focus on listening; which is one-way/passive. Its important to know whether they can take part in back-and-forth conversations. Can they communicate; as well as absorb; information?)	Clinical researcher	9	Existing	**LISTENING IN COMPLEX SITUATIONS** - The difficulty experienced when listening to a sound while separating it out from a background of other sounds & **ONE-TO-ONE CONVERSATION IN QUIET** - Listening and understanding one person, in a quiet environment & **GROUP CONVERSATION IN QUIET** - Listening and following a conversation between a group of people, in a quiet environment & **ONE-TO-ONE CONVERSATION IN**		N/A	N	

					GENERAL NOISE - Listening and understanding one person, in a noisy environment & **GROUP CONVERSATIONS IN NOISY SOCIAL SITUATIONS** - Listening and following a conversation between a group of people, when others are talking in the background				
21	Independence (i.e., maintain their ability to live relatively independently; including buying groceries; communicating at the bank; speak on the phone etc)	Clinical researcher	7	Neither	N/A			Y	New outcome domain: **INDEPENDENCE** - How your hearing loss affects how much you need to rely on other people in daily life
22	Pastimes (i.e., carrying out activities they enjoy like watching television; going to cinema/theatre; listening to music). This may overlap with some other outcome domains. Worth considering whether music needs its own domain or whether it's a sub-domain)	Clinical researcher	7	Existing	**ENJOYMENT OF LISTENING TO MUSIC** - Appreciating 'stereo', '3-dimensional' or 'surround sound' quality of live or recorded music & **LISTENING IN COMPLEX SITUATIONS** - The difficulty experienced when listening to a sound while separating it out from a background of other sounds & **IMPACT ON INDIVIDUAL ACTIVITIES** - Effect of your hearing loss or your device on your choice to engage in individual activities (for example, travelling alone, swimming or watching TV / films / movies)		N/A	N	
23	Flexibility of treatment to move from one environment to another; e.g., Leave a noisy restaurant and then enter a quiet movie theatre	Healthcare user	5	Existing	**DISCOMFORT IN LISTENING SITUATIONS** - Finding yourself in listening situations that you feel you can't adequately control (for example, when you can't choose a favourable listening position); or situations in which you don't feel comfortable (for example when interacting with people who don't know you have a hearing loss) & **TREATMENT SATISFACTION** - How the treatment		N/A	N	

					meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment & **LISTENING IN COMPLEX SITUATIONS** - The difficulty experienced when listening to a sound while separating it out from a background of other sounds				
24	"echo" heard using CROS aid	Healthcare user	7	Reject	ADVERSE EVENTS - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial	Echo is not an outcome for all SSD interventions	No	N	
25	Any negative effects of treatment (esp surgical options) - pain; infection etc	Healthcare user	9	Existing	**ADVERSE EVENTS** - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial		N/A	N	
26	Consistency of use (every day all day; just in certain situations etc)	Healthcare user	7	Existing	**DEVICE USAGE** - How you use the device (for example, in what situations, for how long)		N/A	N	
27	How much negative impact on personal life .i.e., social exclusion; frustration	Healthcare user	9	Reject	**IMPACT ON INDIVIDUAL ACTIVITIES** - Effect of your hearing loss or your device on your choice to engage in individual activities (for example, travelling alone, swimming or watching TV / films / movies) but this does not assess 'social exclusion' & **EMOTIONAL DISTRESS** - A negative unpleasant emotional reaction which may include fear, anger, frustration, anxiety, and suffering	Concept description too general, already covered by another domain	No	N	
28	Receive support for tinnitus	Healthcare user	9	Reject	N/A	Not an outcome domain for SSD interventions	No	N	

29	Being able to use Loop System in public places eg. church; theatre; train station etc	Healthcare user	9	Existing	**DEVICE MALFUNCTION** - The device does not work as it should or it stops working - for BAHA you need the Mini Mic 2+ device to connect to the Loop: i.e., you need an extra device -not entirely sure we are capturing this in existing outcomes & **TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment & **MANUAL DEXTERITY** - Having the fine motor skills needed to use your device effectively (for example, putting the device on, changing the batteries)		N/A	N	
30	Ability to hear speech specifically through CI side (in case hearing drops in the good ear)	Healthcare professional	7	Reject	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment	Not applicable to all SSD interventions, specific to restoring interventions	N/A	N	
31	Cosmetic aspects of the device	Healthcare professional	7	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
32	Management efforts involved - rechargeable batteries / cost of maintenance	Healthcare professional	7	Existing	**DEVICE MALFUNCTION** - The device does not work as it should or it stops working & **TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to	Cost is not an outcome measure for SSD	N/A	N	

					recommend the treatment & **MANUAL DEXTERITY** - Having the fine motor skills needed to use your device effectively (for example, putting the device on, changing the batteries)	interventions			
33	Impact of hearing loss on significant others	Healthcare professional	6	Existing	**IMPACT ON RELATIONSHIPS** - Effect of your hearing loss or your device on making new relationships and maintaining relationships with a spouse or partner, family, friends and colleagues		N/A	N	
34	General Quality of Life	Clinical researcher	9	Reject	N/A	Concept too general	N/A	N	
35	The reason for one sided hearing loss needs consideration	Healthcare user	5	Reject	N/A	Not an outcome domain for SSD interventions	No	N	
36	The worry that one might lose the hearing on the functional side also	Healthcare user	9	Neither	?**PROTECTING YOUR HEARING** - Making a conscious decision to avoid loud sounds or other risks to your hearing, or taking steps to protect your hearing. Comment: ('worry' is something different since protecting your hearing is a behavioural consequence of worry but not the worry itself)			Y	New outcome domain: **CONCERN ABOUT YOUR HEARING** - Feeling worried about the hearing in your better ear and the thought that it may decline
37	Effect on physical tensions in e.g., neck and upper back pain or headaches due to strained listening positions when not being able to hear on deaf side	Commercial representative	6	Existing	**PHYSICAL TIREDNESS** - Tiredness or fatigue from the effort of listening or when you need to turn your head repeatedly to listen in social situations & **ADVERSE EVENTS** - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial		N/A	N	
38	Perceiving speech from the 'deaf'(shadow) side	Healthcare professional	9	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or	This is about	N/A	N	

					how pleased you are after receiving the treatment, or how likely you are to recommend the treatment	'how' speech understanding is assessed			
39	Economic factors (cost of surgery; rehabilitation; support with spares etc.)	Clinical researcher	9	Reject	**DEVICE MALFUNCTION** - The device does not work as it should or it stops working	Cost is not an outcome measure for SSD interventions	N/A	N	
40	Existence / Involvement of hearing loss support groups	Clinical researcher	6	Reject	N/A	Not an outcome domain for SSD interventions	N/A	N	
41	Taking part in auditory training with speech therapist	Clinical researcher	9	Reject	N/A	Not an outcome domain for all SSD interventions, only applicable to cochlear implantation	N/A	N	
42	Doing auditory training everyday in home	Clinical researcher	9	Reject	N/A	Not an outcome domain for all SSD interventions, only applicabl	N/A	N	

						e to cochlear implantation			
43	How easy it is to use and live with the treatment on a daily basis	Clinical researcher	7	Existing	**DEVICE USAGE -** How you use the device (for example, in what situations, for how long) **& TREATMENT SATISFACTION -** How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatme		N/A	N	
44	Ease and practicability of use - availability of batteries etc; ease of cleaning and care; usability with glasses or during physical activity	Healthcare user	9	Existing	**MANUAL DEXTERITY** - Having the fine motor skills needed to use your device effectively (for example, putting the device on, changing the batteries)		N/A	N	
45	Social acceptability and aesthetics of treatment - can it be hidden or flaunted as desired?	Healthcare user	6	Existing	**DEVICE USAGE -** How you use the device (for example, in what situations, for how long) **& TREATMENT SATISFACTION -** How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
46	The ability to use a device in all desired situations e.g., exercising; swimming; at night; playing with children	Healthcare professional	6	Existing	**DEVICE USAGE -** How you use the device (for example, in what situations, for how long) **& TREATMENT SATISFACTION -** How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
47	Longevity of device e.g., need for reviews; revision surgeries; clinical commitments; contraindications to medical interventions in future i.e., MRI	Healthcare professional	6	Existing	**ADVERSE EVENTS** - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial		N/A	N	
48	Value based judgement; whether the treatment is better or worse	Healthcare professional	8	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or		N/A	N	

	relative to either (i) no treatment (those trialling first intervention) or (ii) previous treatment e.g., that used currently. This conclusion is generally led by synthesis of multiple domains but I wonder if patient self-report value judgement might also be an over-arching theme?				how pleased you are after receiving the treatment, or how likely you are to recommend the treatment				
49	Wide availability for people with SSD to obtain a BAHA in this country and not have to wait until they are in a critical situation. The BAHA implant is life changing	Healthcare user	9	Reject	N/A	Not an outcome domain of SSD interventi on, relating to healthcar e system	No	N	
50	Effect of not having a visible disability of SSD (no one can see)	Healthcare user	9	Existing	**SELF-STIGMA** - Negative perception of yourself due to your hearing loss and feeling stigmatised for using a hearing aid		N/A	N	
51	Emotional effect of wearing an SSD device	Healthcare user	6	Existing	**SELF-STIGMA** - Negative perception of yourself due to your hearing loss and feeling stigmatised for using a hearing aid		N/A	N	
52	Concerns over future good ear hearing loss	Healthcare user	9	Neither	N/A	See 36 above		N (see 36)	See 36 above
53	Meeting Pts expectations	Healthcare professional	9	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
54	Speech perception AND comprehension of linguistic units longer than a single sentence	Clinical researcher	9	Reject	**ONE-TO-ONE CONVERSATION IN QUIET** - Listening and understanding one person, in a quiet environment & **GROUP CONVERSATION IN QUIET** - Listening and following a conversation between a group of people, in a quiet environment	Not a sufficientl y new concept to add as a new		N	

					& **ONE-TO-ONE CONVERSATION IN GENERAL NOISE** - Listening and understanding one person, in a noisy environment & **GROUP CONVERSATIONS IN NOISY SOCIAL SITUATIONS** - Listening and following a conversation between a group of people, when others are talking in the background	outcome domain, too broad			
55	Being able to sleep on my deaf side without becoming dizzy	Healthcare user	6	Existing	**BALANCE PROBLEMS** - Feeling unbalanced and the effect it has on your ability to walk or move normally		N/A	N	
56	Improved balance in general and confidence in being able to do activities that involve movement and previously have left me dizzy for days	Healthcare user	7	Existing	**BALANCE PROBLEMS** - Feeling unbalanced and the effect it has on your ability to walk or move normally & **AVOIDING SOCIAL SITUATIONS** - Choosing not to go to particular social situations because of your hearing loss		N/A	N	
57	Impact of device on good ear	Healthcare user	7	Existing	**PROTECTING YOUR HEARING** - Making a conscious decision to avoid loud sounds or other risks to your hearing, or taking steps to protect your hearing & **TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment & **HEARING-RELATED BRAIN CHANGES** - Changes in brain structure or function associated with hearing loss -am not sure what they mean by 'impact' & **ADVERSE EVENTS** - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial & **BEING AWARE OF A SOUND** - Being aware of a sound and recognising what that sound is (for example, being aware that someone has started to speak)		N/A	N	

58	sturdiness; wearability; discreetness of device	Healthcare user	6	Existing	Sturdiness is: **DEVICE MALFUNCTION** - The device does not work as it should or it stops working; Wearability is: **DEVICE USAGE** - How you use the device (for example, in what situations, for how long); Discreteness is: **TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
59	Hearing quiet whispered voice from SSD side	Healthcare professional	6	Existing	**BEING AWARE OF A SOUND** - Being aware of a sound and recognising what that sound is (for example, being aware that someone has started to speak)		N/A	N	
60	Feeling of "vulnerability" or "insecurity" on deaf side	Healthcare user	7	Neither	**PERSONAL SAFETY** - How your hearing loss effects your awareness of potential hazards and threats in your daily life (for example, moving traffic, hazards at the workplace) and those you may not be able to see or hear (for example, other people behind you)			Y	New outcome doamain: **VULNERABILITY** - Feeling insecure because your hearing loss affects your awareness of potential hazards and threats in your daily life (for example, moving traffic, hazards at the workplace) and those you may not be able to see or hear (for example, other people behind you)
61	Need to position oneself when conversing with others; either at a table (not always possible; so destroys the interaction) or when walking	Healthcare user	7	Existing	**PHYSICAL TIREDNESS** - Tiredness or fatigue from the effort of listening or when you need to turn your head repeatedly to listen in social situations & **DISCOMFORT IN LISTENING SITUATIONS**		N/A	N	

					- Finding yourself in listening situations that you feel you can't adequately control (for example, when you can't choose a favourable listening position); or situations in which you don't feel comfortable (for example when interacting with people who don't know you have a hearing loss) & **TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment				
62	Jxxxxxx Mxxxxxx	Healthcare user	9	Reject	N/A	Error	N/A	N	
63	How education / learning is impacted	Healthcare professional	8	Neither	N/A			Y	New outcome domain: **IMPACT ON LEARNING** - Effect of your hearing loss or device on your ability to acquire new knowledge or skills, or further your education
64	Differences to language comprehension caused by side individual is deaf	Healthcare professional	8	Existing	**LISTENING IN COMPLEX SITUATIONS** - The difficulty experienced when listening to a sound while separating it out from a background of other sounds & **ONE-TO-ONE CONVERSATION IN QUIET** - Listening and understanding one person, in a quiet environment & **GROUP CONVERSATION IN QUIET** - Listening and following a conversation between a group of people, in a quiet environment & **ONE-TO-ONE CONVERSATION IN GENERAL NOISE** - Listening and understanding one person, in a noisy environment & **GROUP CONVERSATIONS IN NOISY SOCIAL SITUATIONS** - Listening		N/A	N	

					and following a conversation between a group of people, when others are talking in the background				
65	Access to support groups to share experiences of SSD	Healthcare professional	4	Reject	N/A	Not an outcome domain for SSD interventions	No	N	
66	Ease of quick access to Audiologist for adjustments or help with problem solving with CROS device	Healthcare professional	7	Reject	N/A	Not an outcome domain for SSD interventions	No	N	
67	Awareness and support from family; friends and work colleagues to help develop and utilise communication strategies	Healthcare professional	4	Existing	**IMPACT ON RELATIONSHIPS** - Effect of your hearing loss or your device on making new relationships and maintaining relationships with a spouse or partner, family, friends and colleagues -although not sure if 'awareness' covered by this outcome		N/A	N	
68	Affordability of hearing aid and CROS device	Healthcare professional	4	Reject	N/A	Cost is not an outcome measure for SSD interventions	N/A	N	
69	Perceived stress in different hearing situations	Healthcare professional	8	Existing	**EMOTIONAL DISTRESS** - A negative unpleasant emotional reaction which may include fear, anger, frustration, anxiety, and suffering		N/A	N	
70	Reaction of family members/ colleagues to your problem	Healthcare professional	7	Existing	**IMPACT ON RELATIONSHIPS** - Effect of your hearing loss or your device on making new relationships and maintaining relationships with a spouse or partner, family, friends and colleagues		N/A	N	

					-although not sure if 'awareness' covered by this outcome				
71	How comfortable the device is to wear - e.g., irritation to the ear	Healthcare user	9	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment & **ADVERSE EVENTS** - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial		N/A	N	
72	Whether its possible to wear a hat or other hair accessories without impacting on the functioning of the device (e.g., BAHA)	Healthcare user	9	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
73	The quality of the sound produced; e.g., natural vs stereo (e.g., BAHA Vs CROSS aid)	Healthcare user	8	Existing	**ENJOYMENT OF LISTENING TO MUSIC** - Appreciating 'stereo', '3-dimensional' or 'surround sound' quality of live or recorded music & **LISTENING IN COMPLEX SITUATIONS** - The difficulty experienced when listening to a sound while separating it out from a background of other sounds		N/A	N	
74	The visibility of the device to others (e.g., can other people see it or is it hidden?)	Healthcare user	6	Existing	**SELF-STIGMA** - Negative perception of yourself due to your hearing loss and feeling stigmatised for using a hearing aid		N/A	N	
75	The length of time that the person has gone without using the device (i.e., have they found other ways to adapt to these listening situations)	Healthcare user	6	Reject	N/A	Not an outcome domain for SSD intervention itself	No	N	
76	The complexity of the device (e.g., can someone who is cognitive impaired or has a learning disability access the device?)	Healthcare user	7	Reject	N/A	Not an outcome domain for SSD interventions		Y (see 19)	Depends on the level of cognition the person has. If the person's cognition is low then maybe there is a

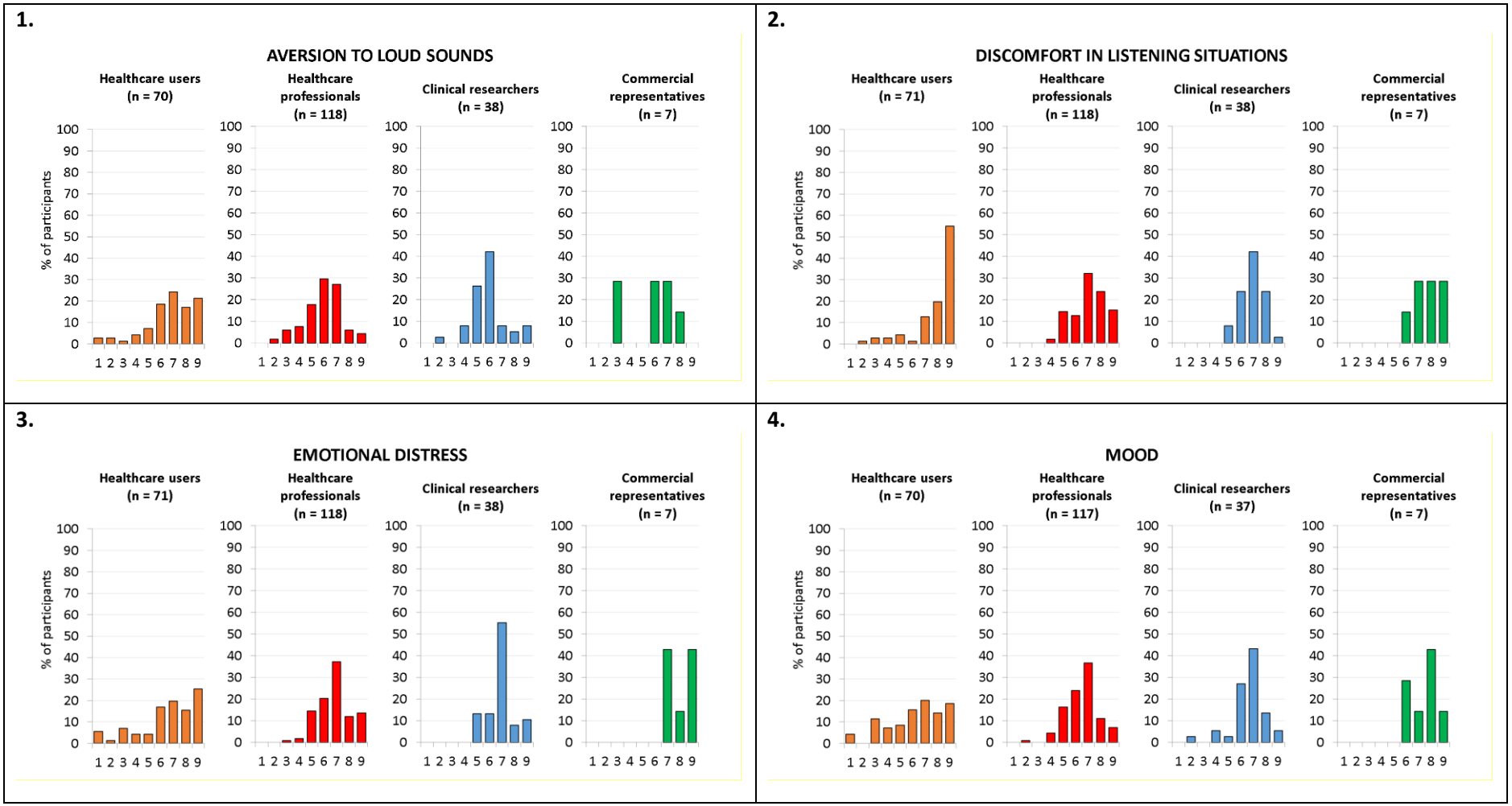
									role for the parents, OT, nurse, carer etc.
77	The cost of the device	Healthcare user	7	Reject	N/A	Cost is not an outcome measure for SSD interventions	N/A	N	
78	The availability of the device	Healthcare user	7	Reject	N/A	Not an outcome domain of SSD intervention, relating to healthcare system	No	N	
79	In the future would you be able to manage without your new aid?	Healthcare user	7	Reject	N/A	Not an outcome measure for the SSD intervention itself		N	
80	How satisfied are you with your SSD treatment?	Healthcare user	9	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
81	How effective was your SSD treatment/ technological intervention?	Healthcare user	9	Existing	**TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment & **DEVICE MALFUNCTION** - The device does not work as it should or it stops working		N/A	N	

82	Have you stopped using your SSD treatment/ technological device and if so why?	Healthcare user	9	Existing	**DEVICE USAGE** - How you use the device (for example, in what situations, for how long) - but the 'why' part is to an outcome measure is it?		N/A	N	
83	Did you experience any negative side effects of using a technological device (eg., CROS). If so what were they?	Healthcare user	9	Existing	**ADVERSE EVENTS** - Any bad or unexpected thing that happens during the time a treatment is being tested in a clinical trial		N/A	N	
84	Speech and language availability (for children)	Clinical researcher	8	Reject	N/A	Out of scope for the CROSSSD study Delphi		N	
85	Comparison to previous intervention for SSD	Healthcare professional	6	Reject	N/A	Comparison with 'other' interventions is not an outcome domain		N	
86	Cost of intervention	Healthcare professional	6	Reject	N/A	Cost is not an outcome measure for SSD interventions	N/A	N	
87	Ease of obtaining intervention (i.e., process for obtaining a cochlear implant versus BAHA)	Healthcare professional	6	Reject	N/A	Not an outcome domain of SSD intervention, relating to		N	

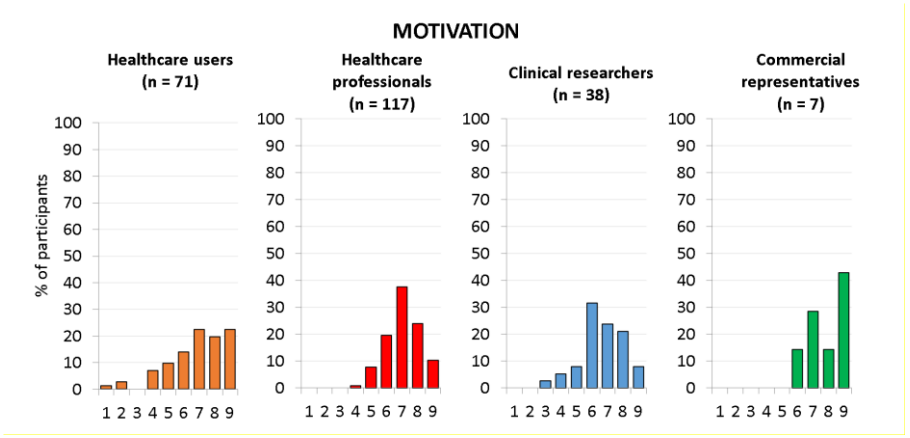
						healthcare system			
88	Sound fusion across ears	Clinical researcher	7	Existing	**SOUND LOCALISATION** - Knowing where a sound is coming from & **SOUND DISTANCE** - Knowing if a sound is close by or far away & **SPATIAL ORIENTATION** - Knowing where you are in relation to the position of a sound source	Not relevant for rerouting interventions	N/A	N	
89	Confidence when meeting new people	Healthcare user	7	Existing	**IMPACT ON RELATIONSHIPS** - Effect of your hearing loss or your device on making new relationships and maintaining relationships with a spouse or partner, family, friends and colleagues & **EMOTIONAL DISTRESS** - A negative unpleasant emotional reaction which may include fear, anger, frustration, anxiety, and suffering		N/A	N	
90	Medical professions awareness of SSD (when a patient goes to the doctor with hearing loss in an ear; directing the to ER for steroid treatment straight away)	Healthcare user	9	Reject	N/A	Not an outcome domain for SSD interventions		N	
91	Public awareness of SSD (public to understand what SSD is and what to do if it happens to them)	Healthcare user	9	Reject	N/A	Not an outcome domain for SSD interventions		N	
92	Language acquisition in children with SSD	Healthcare professional	9	Reject	N/A	Out of scope for the CROSSSD study Delphi		N	
93	If had to undergo surgical intervention, has there been any	Healthcare professional	8	Existing	**ADVERSE EVENTS** - Any bad or unexpected thing that happens during		N/A	N	

	complication which could impact on use of the device?				the time a treatment is being tested in a clinical trial				
94	Telephone use	Healthcare professional	6	Existing	**DEVICE USAGE** - How you use the device (for example, in what situations, for how long) & **TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	
95	Ease of using assistive listening device	Healthcare professional	6	Existing	**DEVICE USAGE** - How you use the device (for example, in what situations, for how long) & **TREATMENT SATISFACTION** - How the treatment meets your expectations or how pleased you are after receiving the treatment, or how likely you are to recommend the treatment		N/A	N	

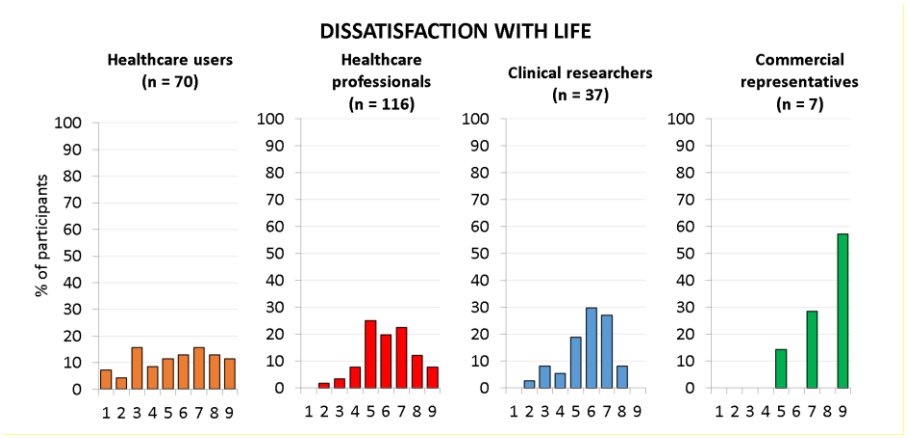
Appendix 21. Ratings for the 49 outcome domains included in Round 2.



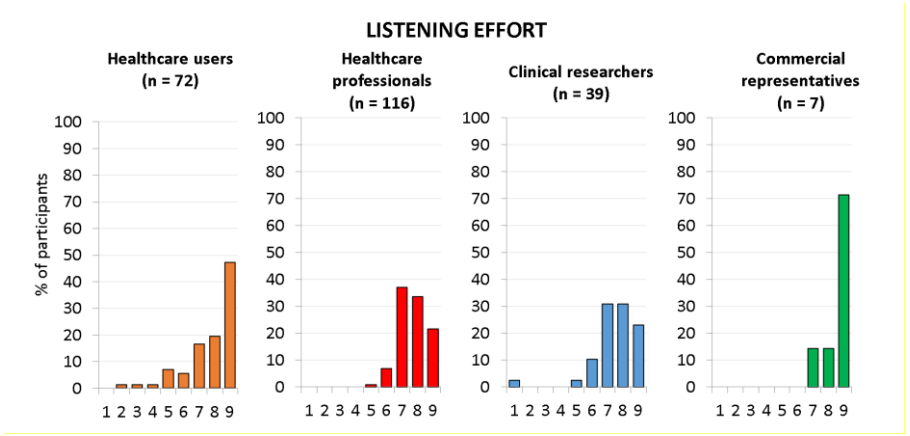
5.


MOTIVATION
Healthcare users (n = 71)
Healthcare professionals (n = 117)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

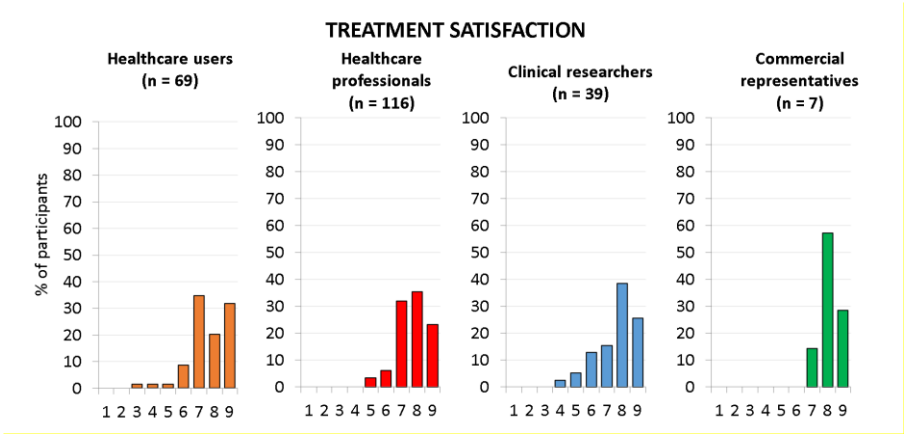
6.


DISSATISFACTION WITH LIFE
Healthcare users (n = 70)
Healthcare professionals (n = 116)
Clinical researchers (n = 37)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

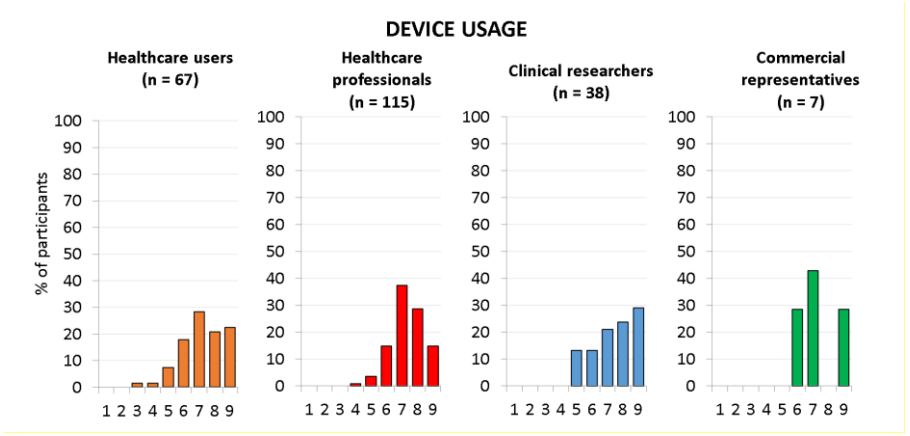
7.


LISTENING EFFORT
Healthcare users (n = 72)
Healthcare professionals (n = 116)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

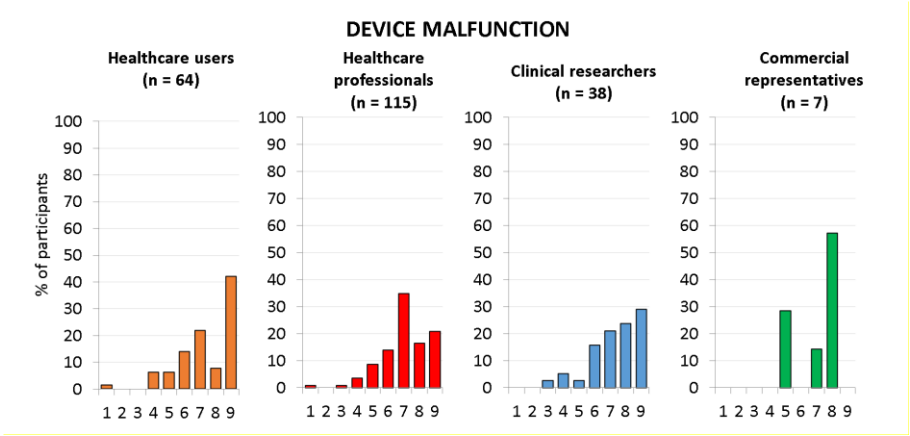
8.


TREATMENT SATISFACTION
Healthcare users (n = 69)
Healthcare professionals (n = 116)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

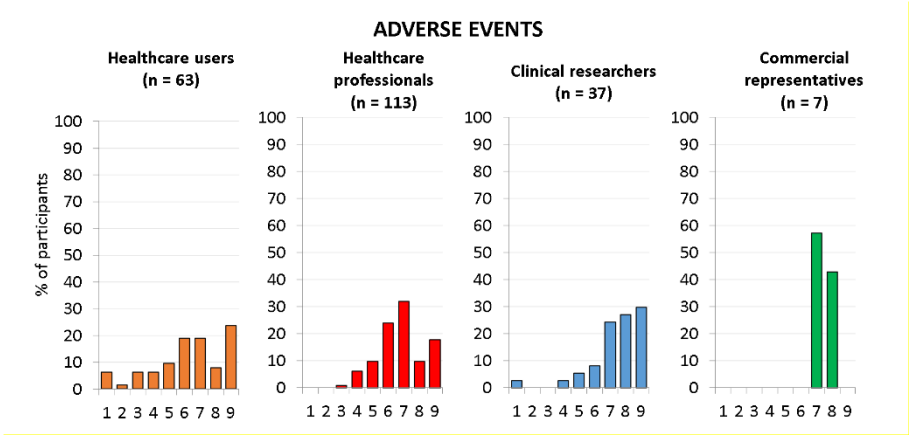
9.


DEVICE USAGE
Healthcare users (n = 67)
Healthcare professionals (n = 115)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

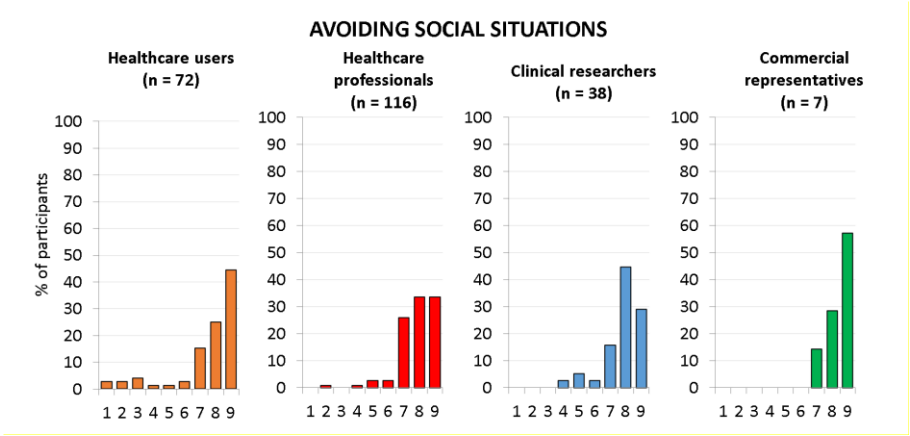
10.


DEVICE MALFUNCTION
Healthcare users (n = 64)
Healthcare professionals (n = 115)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

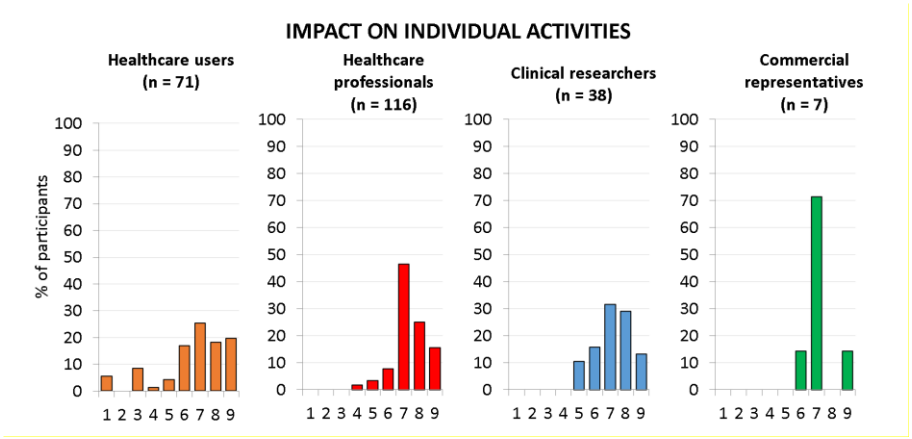
11.


ADVERSE EVENTS
Healthcare users (n = 63)
Healthcare professionals (n = 113)
Clinical researchers (n = 37)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

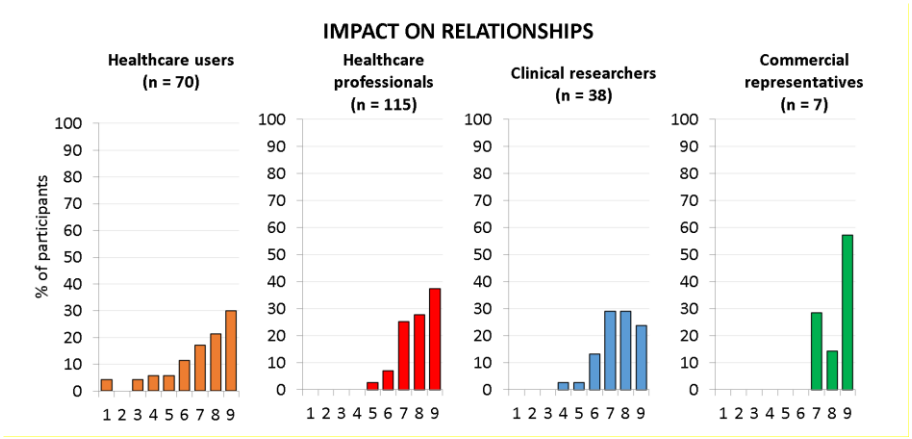
12.


AVOIDING SOCIAL SITUATIONS
Healthcare users (n = 72)
Healthcare professionals (n = 116)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

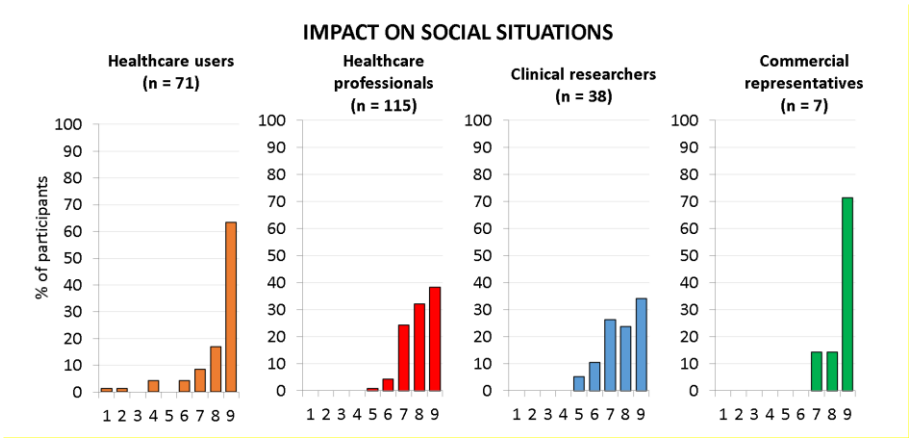
13.


IMPACT ON INDIVIDUAL ACTIVITIES
Healthcare users (n = 71)
Healthcare professionals (n = 116)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

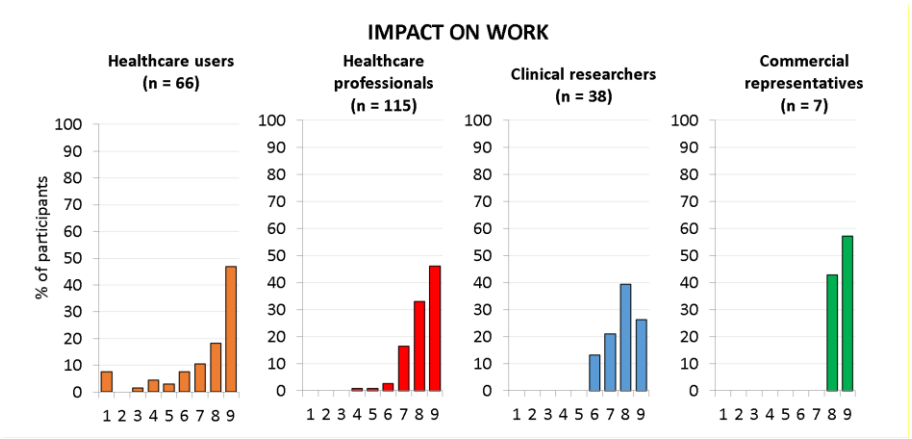
14.


IMPACT ON RELATIONSHIPS
Healthcare users (n = 70)
Healthcare professionals (n = 115)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

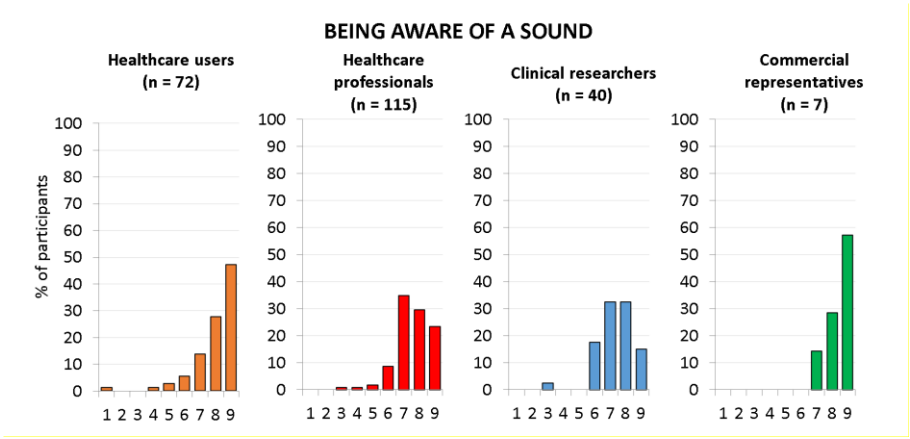
15.


IMPACT ON SOCIAL SITUATIONS
Healthcare users (n = 71)
Healthcare professionals (n = 115)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

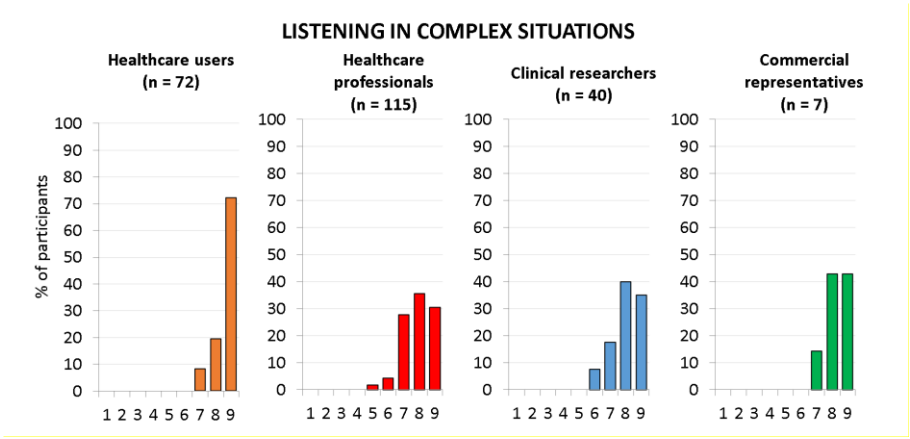
16.


IMPACT ON WORK
Healthcare users (n = 66)
Healthcare professionals (n = 115)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

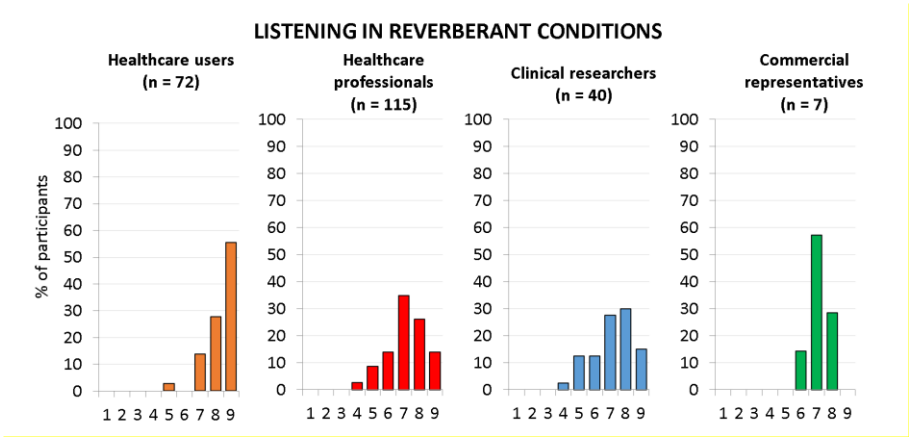
17.


BEING AWARE OF A SOUND
Healthcare users (n = 72)
Healthcare professionals (n = 115)
Clinical researchers (n = 40)
Commercial representatives (n = 7)
% of participants

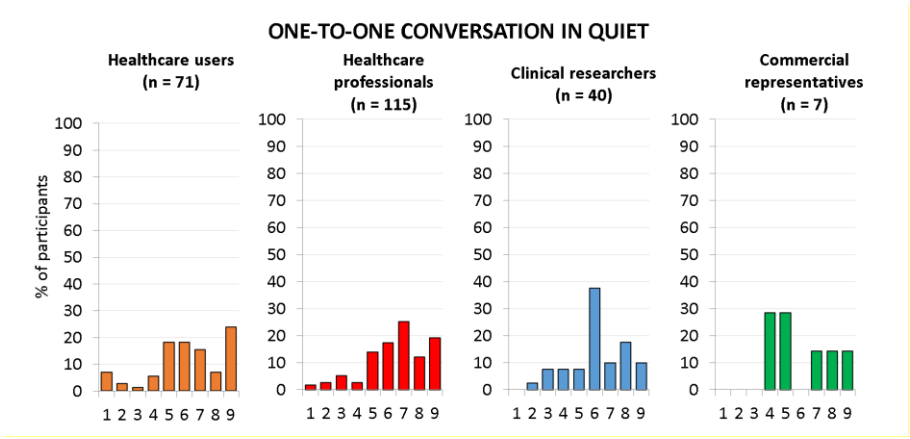
18.


LISTENING IN COMPLEX SITUATIONS
Healthcare users (n = 72)
Healthcare professionals (n = 115)
Clinical researchers (n = 40)
Commercial representatives (n = 7)
% of participants

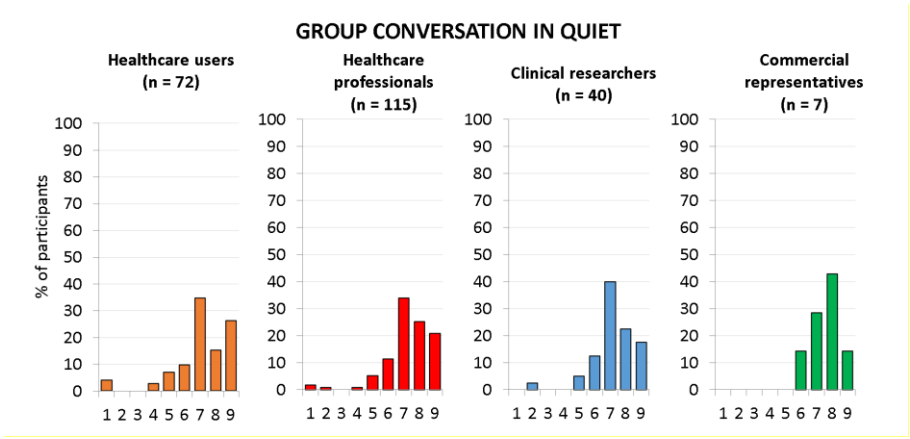
19.


LISTENING IN REVERBERANT CONDITIONS
Healthcare users (n = 72)
Healthcare professionals (n = 115)
Clinical researchers (n = 40)
Commercial representatives (n = 7)
% of participants

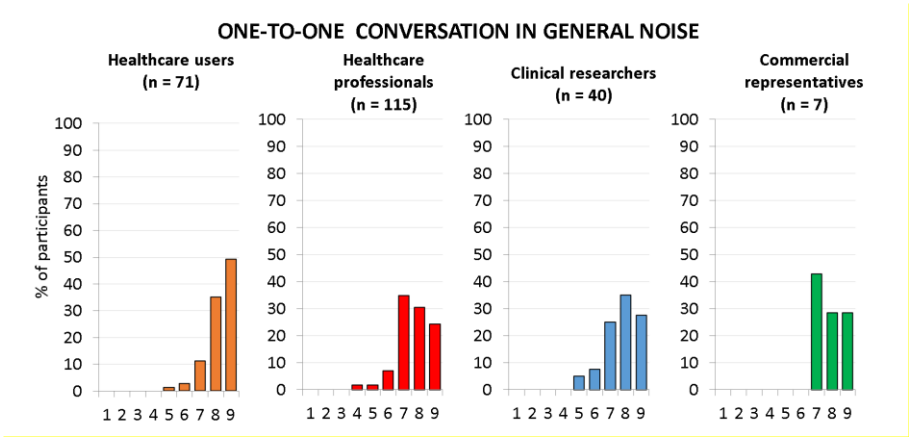
20.


ONE-TO-ONE CONVERSATION IN QUIET
Healthcare users (n = 71)
Healthcare professionals (n = 115)
Clinical researchers (n = 40)
Commercial representatives (n = 7)
% of participants

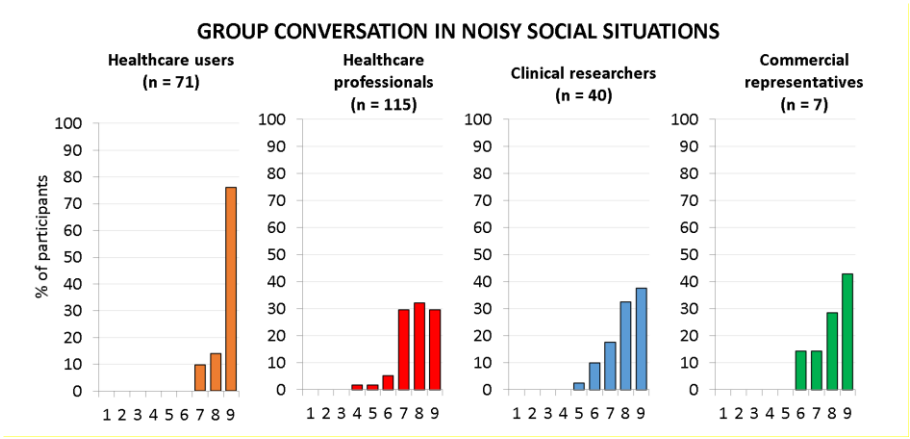
21.


GROUP CONVERSATION IN QUIET
Healthcare users (n = 72)
Healthcare professionals (n = 115)
Clinical researchers (n = 40)
Commercial representatives (n = 7)
% of participants

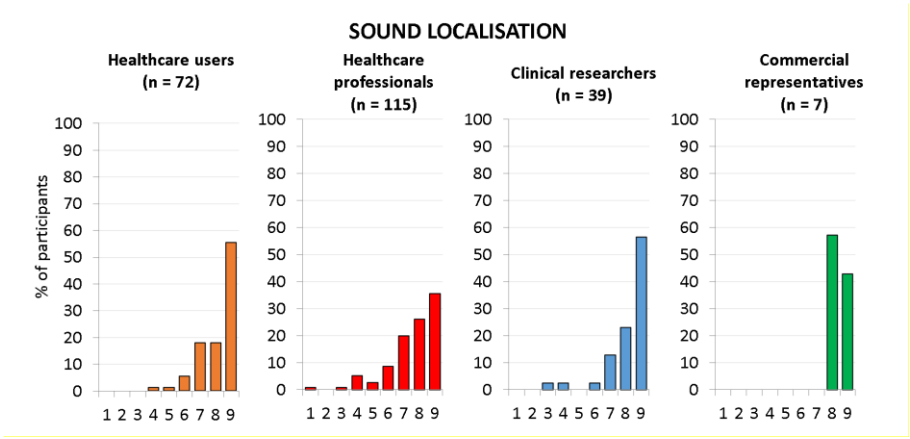
22.


ONE-TO-ONE CONVERSATION IN GENERAL NOISE
Healthcare users (n = 71)
Healthcare professionals (n = 115)
Clinical researchers (n = 40)
Commercial representatives (n = 7)
% of participants

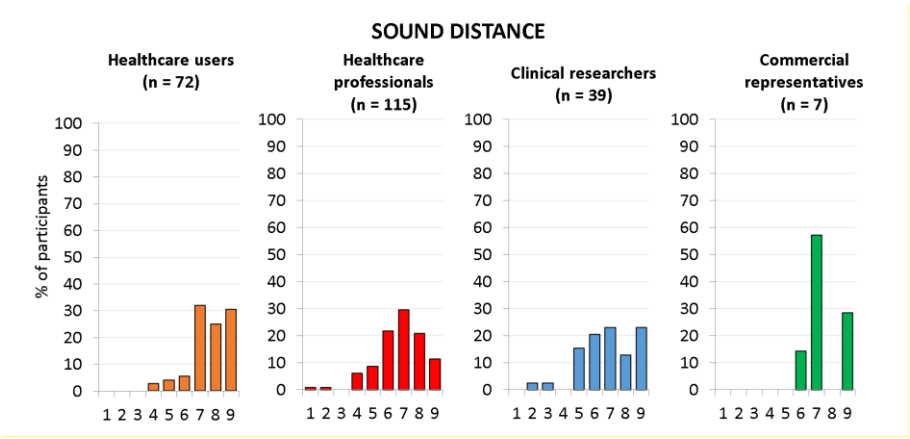
23.


GROUP CONVERSATION IN NOISY SOCIAL SITUATIONS
Healthcare users (n = 71)
Healthcare professionals (n = 115)
Clinical researchers (n = 40)
Commercial representatives (n = 7)
% of participants

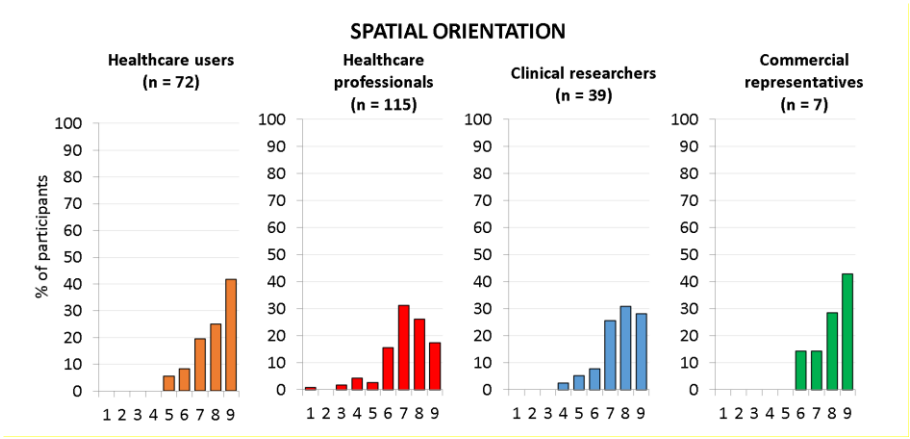
24.


SOUND LOCALISATION
Healthcare users (n = 72)
Healthcare professionals (n = 115)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants

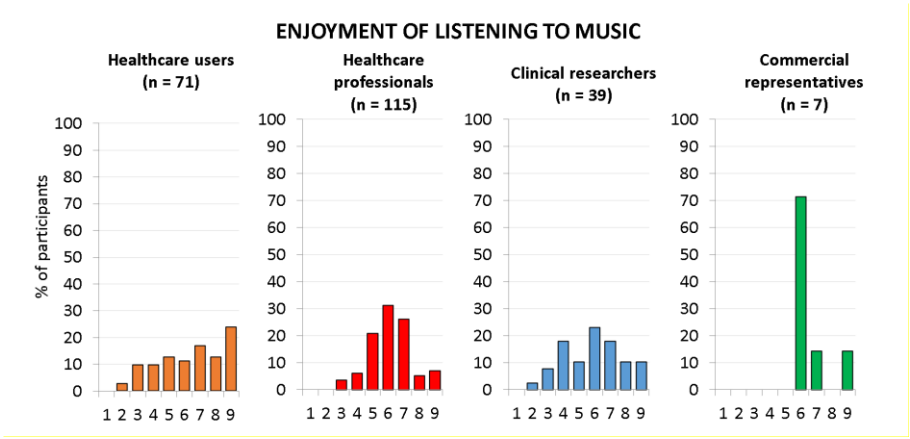
25.


SOUND DISTANCE
Healthcare users (n = 72)
Healthcare professionals (n = 115)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

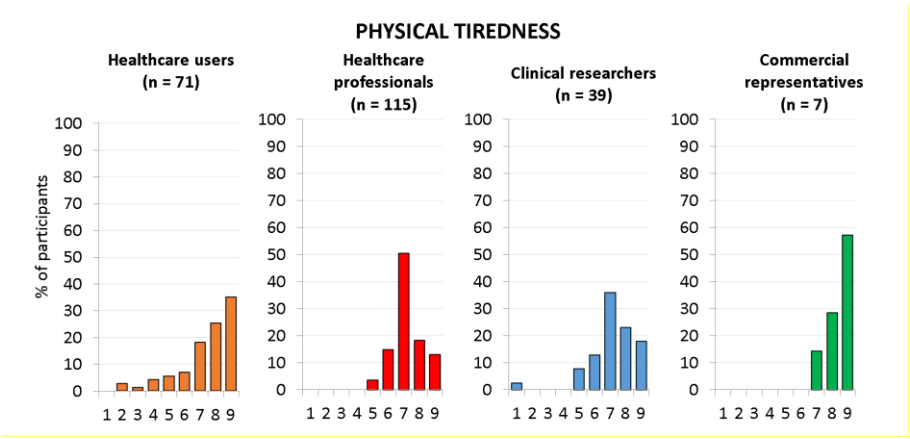
26.


SPATIAL ORIENTATION
Healthcare users (n = 72)
Healthcare professionals (n = 115)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

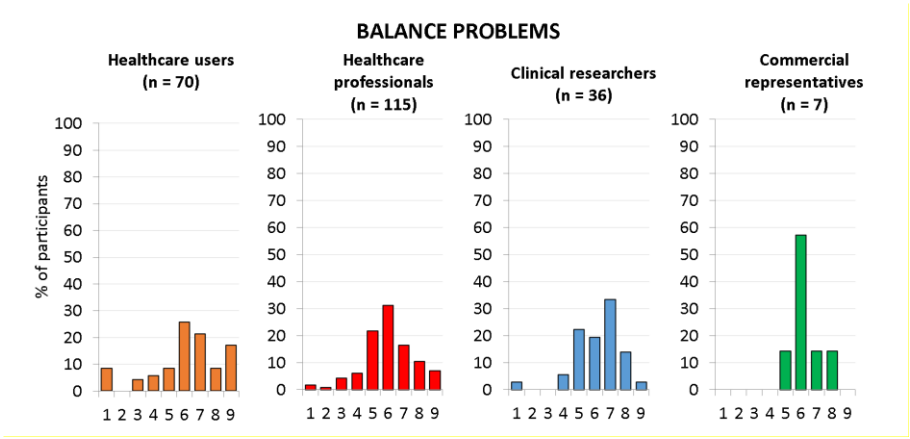
27.


ENJOYMENT OF LISTENING TO MUSIC
Healthcare users (n = 71)
Healthcare professionals (n = 115)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

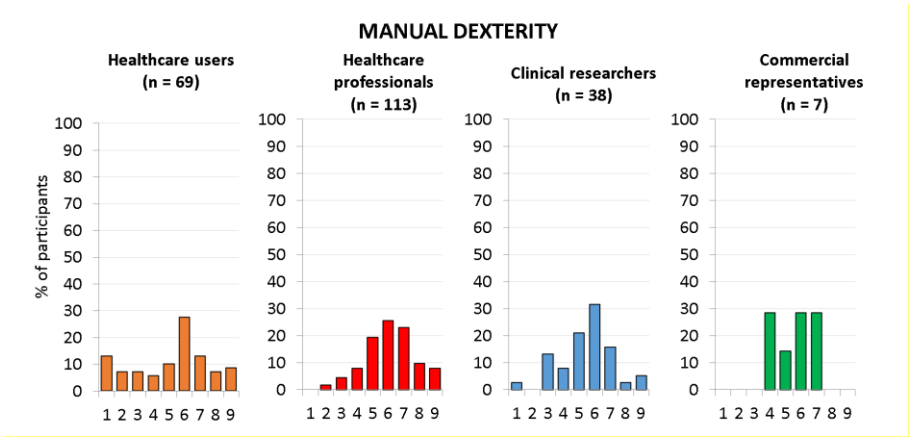
28.


PHYSICAL TIREDNESS
Healthcare users (n = 71)
Healthcare professionals (n = 115)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

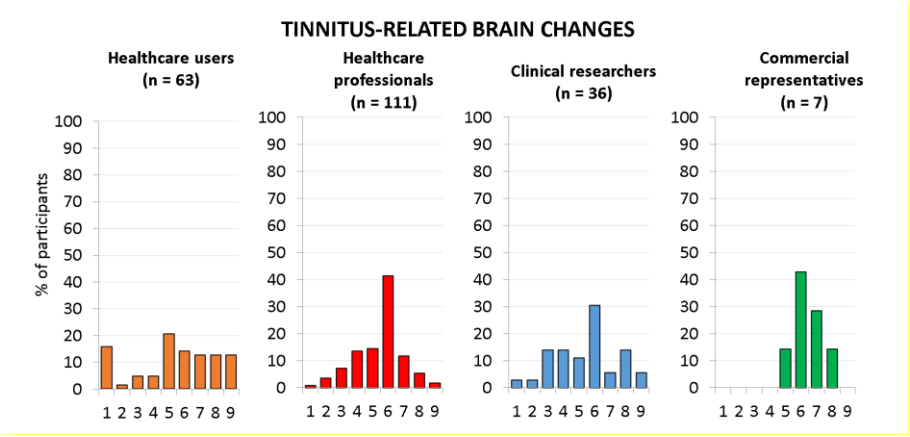
29.


BALANCE PROBLEMS
Healthcare users (n = 70)
Healthcare professionals (n = 115)
Clinical researchers (n = 36)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

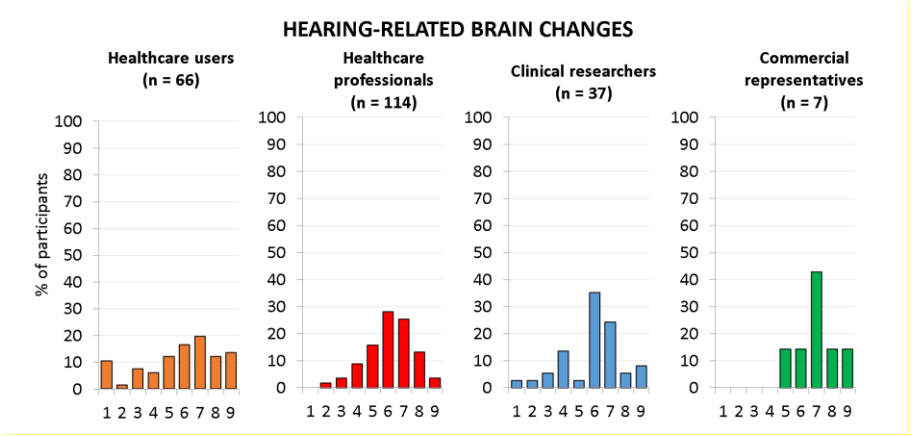
30.


MANUAL DEXTERITY
Healthcare users (n = 69)
Healthcare professionals (n = 113)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

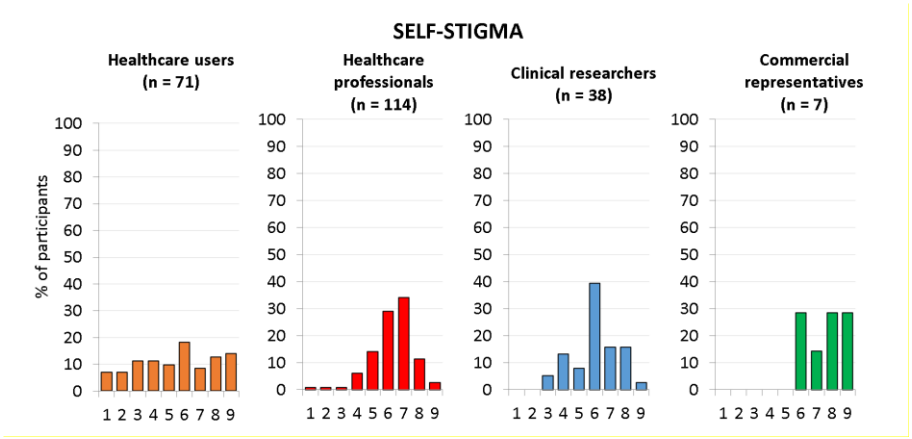
31.


TINNITUS-RELATED BRAIN CHANGES
Healthcare users (n = 63)
Healthcare professionals (n = 111)
Clinical researchers (n = 36)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

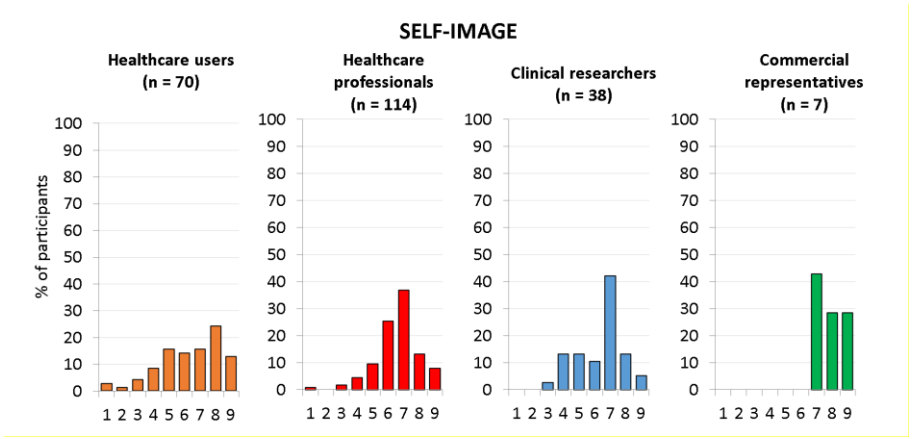
32.


HEARING-RELATED BRAIN CHANGES
Healthcare users (n = 66)
Healthcare professionals (n = 114)
Clinical researchers (n = 37)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

33.


SELF-STIGMA
Healthcare users (n = 71)
Healthcare professionals (n = 114)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

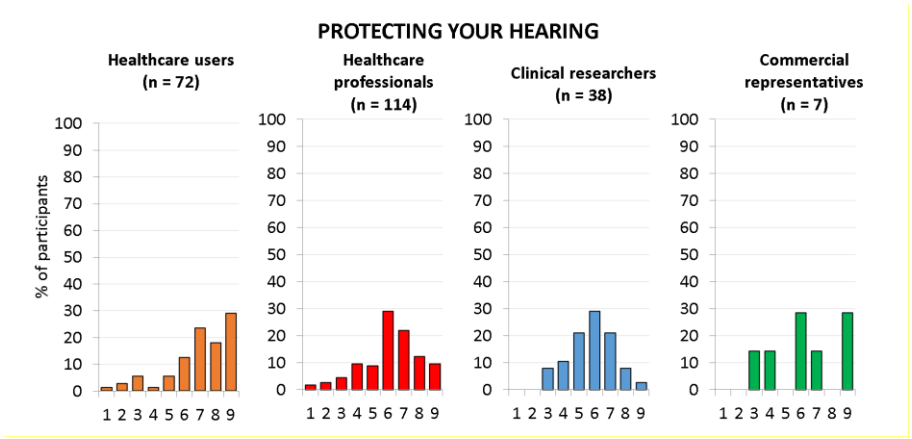
34.


SELF-IMAGE
Healthcare users (n = 70)
Healthcare professionals (n = 114)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

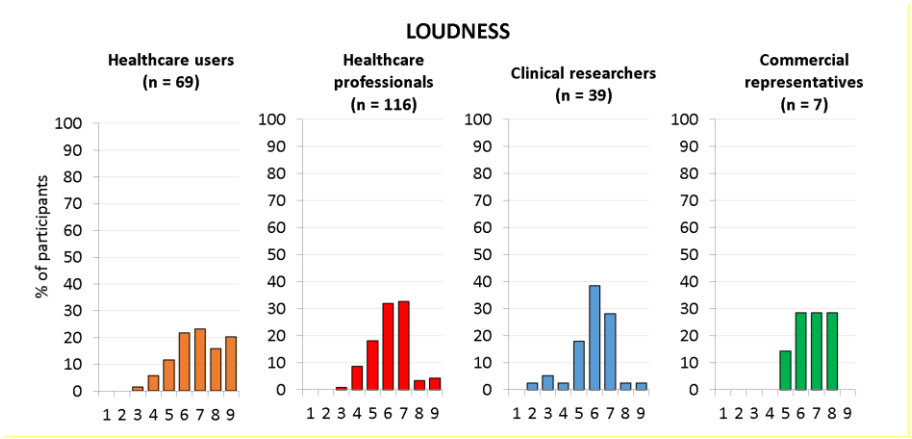
35.


PERSONAL SAFETY
Healthcare users (n = 71)
Healthcare professionals (n = 115)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

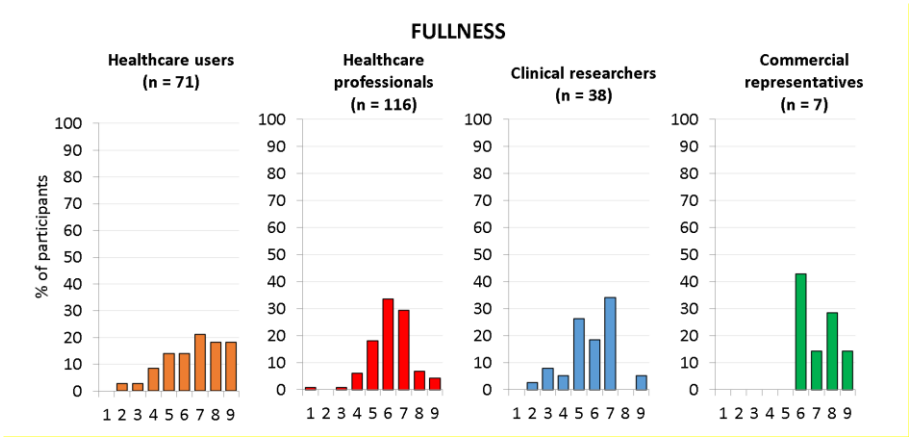
36.


PROTECTING YOUR HEARING
Healthcare users (n = 72)
Healthcare professionals (n = 114)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

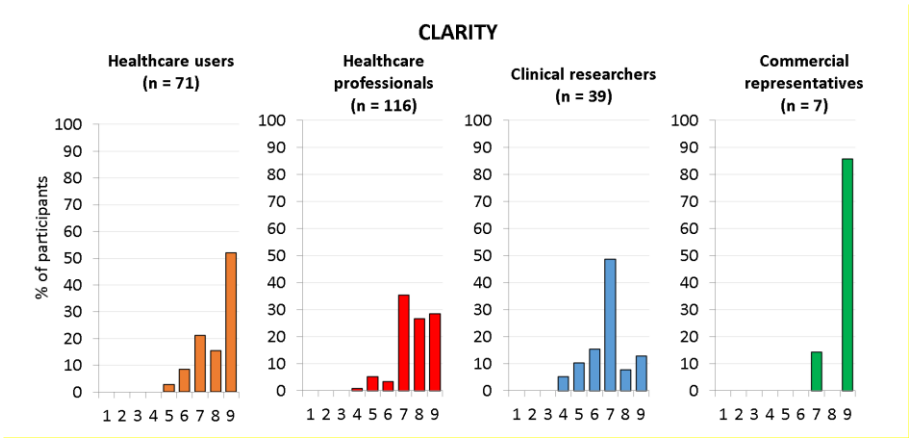
37.


LOUDNESS
Healthcare users (n = 69)
Healthcare professionals (n = 116)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants

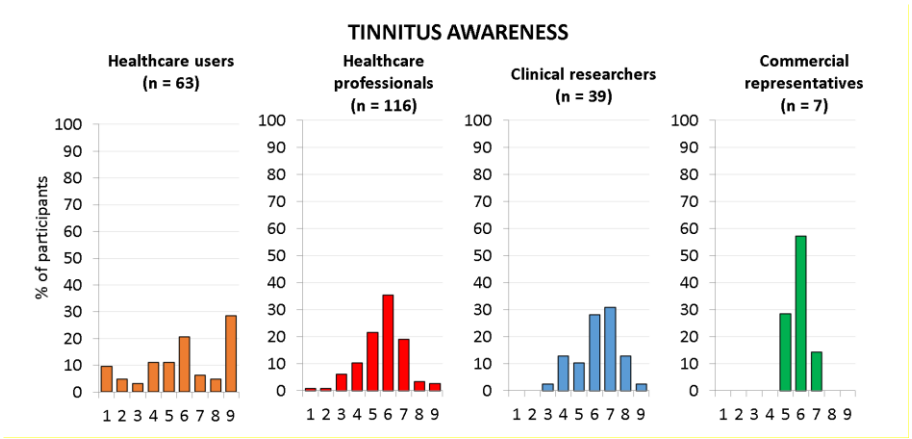
38.


FULLNESS
Healthcare users (n = 71)
Healthcare professionals (n = 116)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

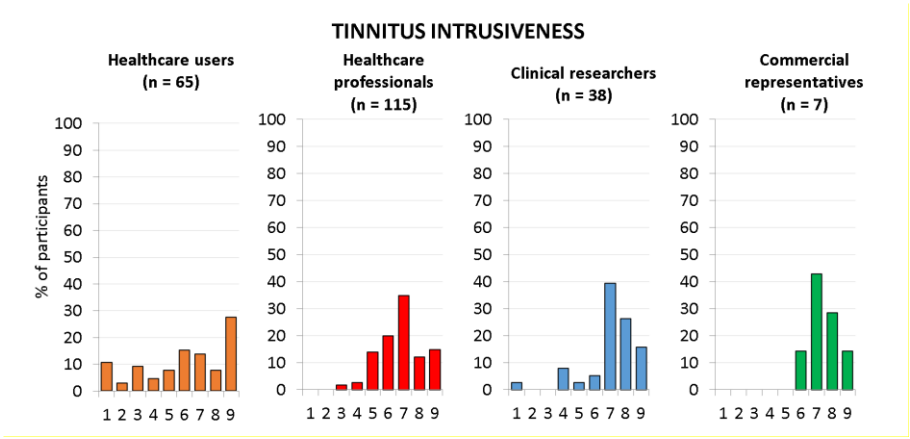
39.


CLARITY
Healthcare users (n = 71)
Healthcare professionals (n = 116)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants

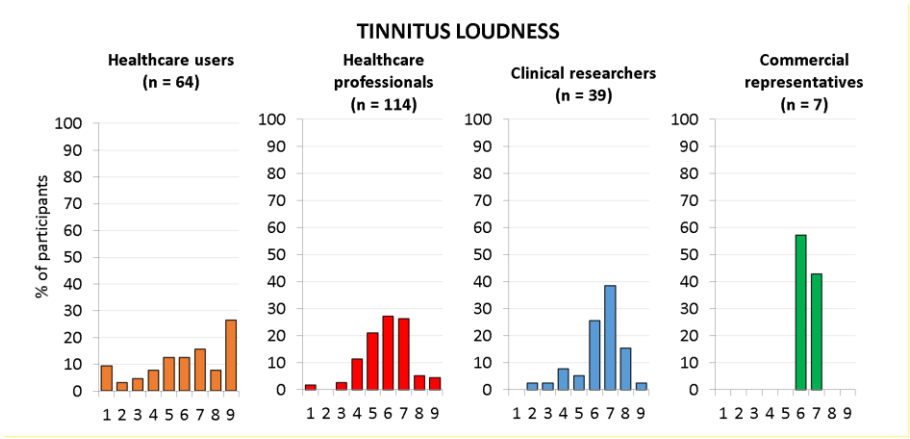
40.


TINNITUS AWARENESS
Healthcare users (n = 63)
Healthcare professionals (n = 116)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants

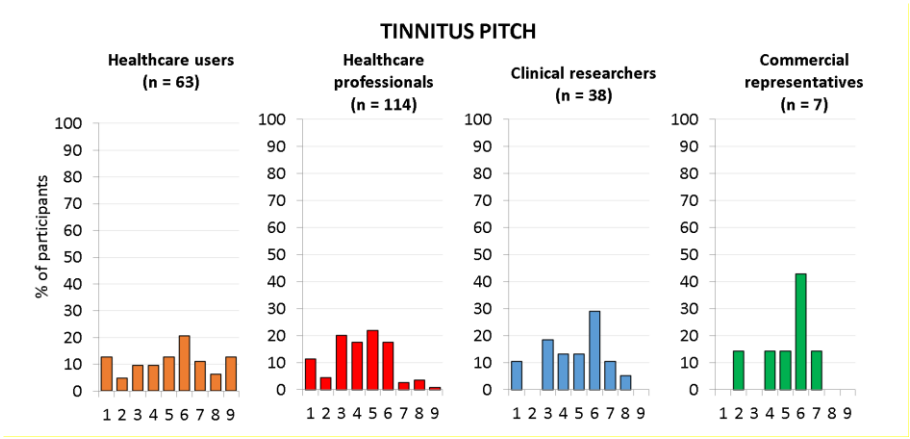
41.


TINNITUS INTRUSIVENESS
Healthcare users (n = 65)
Healthcare professionals (n = 115)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

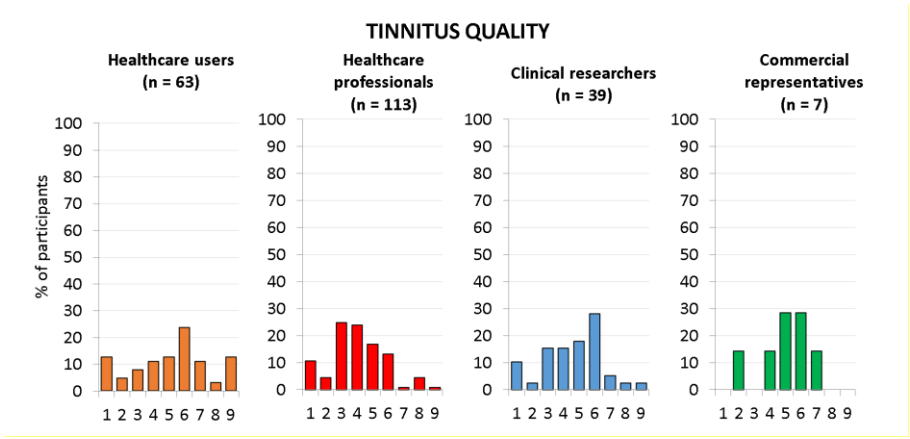
42.


TINNITUS LOUDNESS
Healthcare users (n = 64)
Healthcare professionals (n = 114)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants

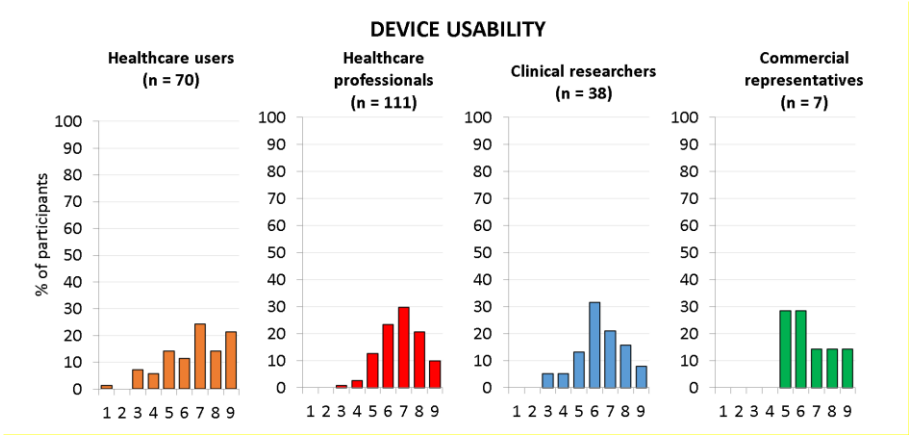
43.


TINNITUS PITCH
Healthcare users (n = 63)
Healthcare professionals (n = 114)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants

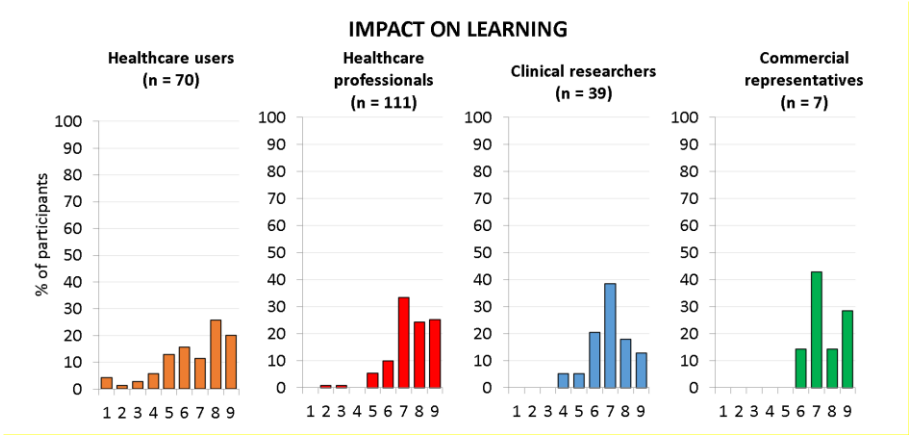
44.


TINNITUS QUALITY
Healthcare users (n = 63)
Healthcare professionals (n = 113)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants

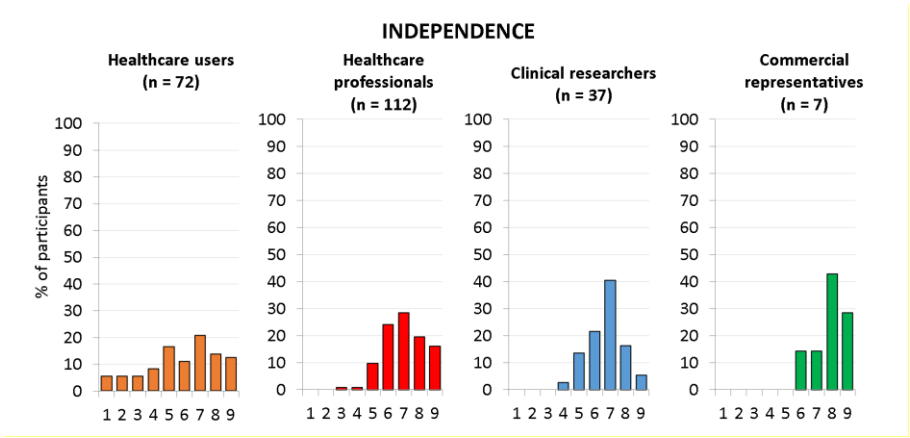
45.


DEVICE USABILITY
Healthcare users (n = 70)
Healthcare professionals (n = 111)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

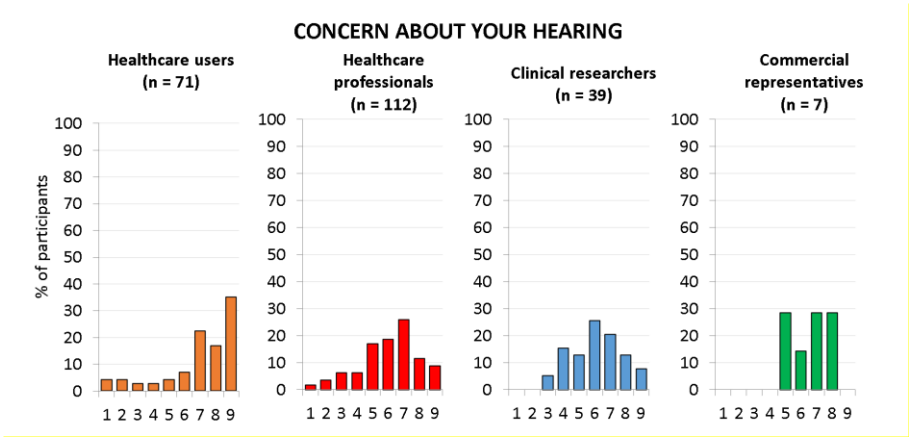
46.


IMPACT ON LEARNING
Healthcare users (n = 70)
Healthcare professionals (n = 111)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

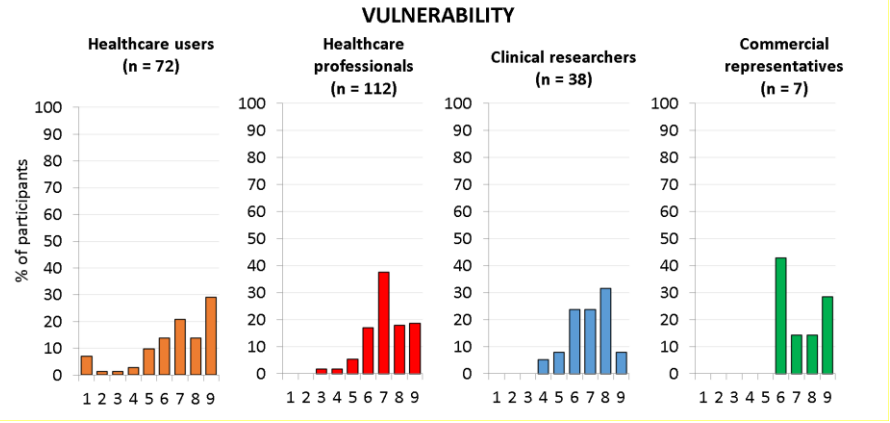
47.


INDEPENDENCE
Healthcare users (n = 72)
Healthcare professionals (n = 112)
Clinical researchers (n = 37)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

48.


CONCERN ABOUT YOUR HEARING
Healthcare users (n = 71)
Healthcare professionals (n = 112)
Clinical researchers (n = 39)
Commercial representatives (n = 7)
% of participants
0 10 20 30 40 50 60 70 80 90 100
1 2 3 4 5 6 7 8 9

49.


VULNERABILITY
Healthcare users (n = 72)
Healthcare professionals (n = 112)
Clinical researchers (n = 38)
Commercial representatives (n = 7)
% of participants
0
10
20
30
40
50
60
70
80
90
100
1 2 3 4 5 6 7 8 9

Appendix 22. Comprehensive list of the 76 Patient Reported Outcome Measures (PROMs) assessed and relevant details for each.

Instr Ax No	Measurement instrument	Developers / Reference	Year developed	PROM type	n of items	Structure	SSD specific?
1	Abbreviated Hearing Aid Benefit Profile (APHAB)	Cox, R. M., & Alexander, G. C. (1995). The Abbreviated Profile of Hearing Aid Benefit. *Ear Hear*, 16(2), 176–186. doi: 10.1097/00003446-199504000-00005.	1995	Questionnaire	24	Consists of everyday situations. Requires Pt to circle the answer that is closest to their own experiences A (Always, 995%) to G (Never, 1%) with and without their hearing aid.	No
2	Audio Processor Satisfaction Questionnaire (APSQ)	Billinger-Finke, M., Bräcker, T., Weber, A., Amann, E., Anderson, I., & Batsoulis, C. (2020). Development and validation of the audio processor satisfaction questionnaire (APSQ) for hearing implant users. *Int J Audiol*, 59(5), 392–397. doi: 10.1080/14992027.2019.1697830.	2018?	Questionnaire	21	Consists of a 5-point Likert scale with a range from 'never' to 'always' plus a 'not applicable' field.	No
3	Bern Benefit in Single-Sided Deafness (BBSS) questionnaire	Kompis, M., Pfiffner, F., Krebs, M., & Caversaccio, M. D. (2011). Factors influencing the decision for Baha in unilateral deafness: The Bern benefit in single-sided deafness questionnaire. *Adv Otorhinolaryngol,* 71, 103–111. doi: 10.1159/000323591.	2011	Questionnaire	10	Consists of a 11-point Likert scale with a range from -5 ('much better without the aid') to +5 ('much better with the aid').	Yes
4	Bone Anchored Cochlear Stimulator (BAHA) satisfaction questionnaire	Ghossaini, S. N., Spitzer, J. B., & Borik, J. (2010). Use of the Bone-Anchored Cochlear stimulator (Baha) and satisfaction among long-term users. *Semin Hear*, 31(01), 3–14.	2010	Questionnaire	30	Consists of a 5-point Likert scale with a range from 'strongly agree' to 'strongly disagree' plus a 'not applicable' field.	No
5	Brief- Coping Orientation to Problems Experienced (COPE) questionnaire	Carver, C. S. (1997). You want to measure coping but your protocol's too long: Consider the brief COPE. *Int J Behav Med*, 4(1), 92–100. doi: 10.1207/s15327558ijbm0401_6.	1997	Questionnaire	28	Consists of a 4-point Likert scale with a range from 'I haven't been doing this at all' to 'I've been doing this a lot'.	No
6	Center for Epidemiologic Studies Depression Scale (CES-D) English adaptation of ADS-L	Lewinsohn, P. M., Seeley, J. R., Roberts, R. E., & Allen, N. B. (1997). Center for Epidemiologic Studies Depression Scale (CES-D) as a screening instrument for depression among community-residing older adults. 12(2), 277–287. doi: 10.1037//0882-7974.12.2.277.	1997	Questionnaire	20	Response options range from 0 to 3 for each item (0 = Rarely or None of the Time, 1 = Some or Little of the Time, 2 = Moderately or Much of the time, 3 = Most or Almost All the Time). Scores range from 0 to 60, with high scores indicating greater depressive symptoms.	No
7	Client Orientated Scale of Improvement (COSI)	Dillon, H., James, A., & Ginis, J. (1997). Client Oriented Scale of Improvement (COSI) and its relationship to several other measures of benefit and satisfaction provided by hearing aids. *J Am Acad Audiol,* 8(1), 27–43.	1997	Questionnaire	16	Consists of a 5-point Likert scale with a range from 'worse' to 'much better'. Contains a choice of 16 categories.	No

8	Communication profile for hearing impaired (CPHI)	Demorest, M. E., & Erdman, S. A. (1987). Development of the communication profile for the hearing impaired. *J Speech Hear Disord*, 52(2), 129–143. doi: 10.1044/jshd.5202.129.	1987	Questionnaire	145	Consists of 3 parts. Part I covers communication with others (Qn 1-18), Part II covers 'experiences when communicating with others (Qn 19-76). Part III covers 'feelings, attitudes, beliefs' (Qn 77-145). Responses are gathered with a 5-point rating scale.	No
9	Diary record: Characterized their tinnitus in a diary. Each day, they were asked to rate the loudness and stress caused by the tinnitus in a visual analogue scale, as well as their mood and their ability to influence the tinnitus. In the evaluation, visual analogue scale was translated to a scale from 0 to 10. The ratings were averaged for each subject over all 4 questions and each month	Buechner, A., Brendel, M., Lesinski-Schiedat, A., Wenzel, G., Frohne-Buechner, C., Jaeger, B., & Lenarz, T. (2010). Cochlear implantation in unilateral deaf subjects associated with ipsilateral tinnitus. *Otol Neurotol*, 31(9), 1381–1385. doi: 10.1097/MAO.0b013e3181e3d353.	2010	VAS	4	Consists of a 10-point Likert scale from 0 to 10, with 10='better'. Categories were: loudness, stress, mood, ability to influence tinnitus. Ratings of all four categories were averaged monthly.	Not sure
10	Diary record: During this evaluation period, Pt were asked to switch devices daily and to complete a diary in which they had to rate overall satisfaction, clearness of sound (CS), and effort of listening in background noise (BN) on a scale from 1 to 10. Free space was provided for personal comments of the patient	Desmet, J. B. J., Wouters, K., De Bodt, M., & Van de Heyning, P. (2012). Comparison of 2 implantable bone conduction devices in Pt with single-sided deafness using a daily alternating method. *Otol Neurotol*, 33(6), 1018–1026. doi: 10.1097/MAO.0b013e31825e79ba.	2012	Diary	4	Diary record: During this evaluation period, Pt were asked to switch devices daily and to complete a diary in which they had to rate overall satisfaction, clearness of sound (ranging from 0=unclear to 10=very clear), and effort of listening in background noise (ranging from 0=no effort to 10=very much effort) on a scale from 1 to 10. Free space was provided for personal comments for 9 situations (Positive numbers=improvement, negative numbers=deterioration).	Not sure
11	Dizziness Handicap Inventory (DHI)	Jacobson, G. P., & Newman, C. W. (1990). The development of the Dizziness Handicap Inventory. *Arch Otolaryngol Head Neck Surg*, 116(4), 424–427. doi: 10.1001/archotol.1990.01870040046011.	1990	Questionnaire	25	Consists of 3 subscales P=Physical, E=Emotional and F=Functional. Pt are presented with questions and asked to mark if they experience it 'Always', 'Sometimes' or 'No'. Top score is 100 (maximum perceived disability). Bottom score is 0 (no perceived disability).	No
12	Entific Medical System Questionnaire (EMSQ)	Dutt, S. N., McDermott, A.-L., Jelbert, A., Reid, A. P., & Proops, D. W. (2002). Day to day use and service-related issues with the bone-anchored hearing aid: The Entific Medical Systems	2002	Questionnaire	13	Investigates 'Day to day usage', 'wear and tear concerns', 'service related issues' themes. Consists of 2 demographics questions, 8 questions with multiple choice answers, and 3 questions asking for general views on the	No

		questionnaire. *J Laryngol Otol Suppl*, 28, 20–28. doi: 10.1258/0022215021911301.				service, repairs, surgical, nursing, outpatient visits.	
13	EQ-5D-3L of the EuroQol Group with a Visual Analogue Scale (VAS)	Rabin, R., & de Charro, F. (2001). EQ-5D: A measure of health status from the EuroQol Group. *Ann Med*, 33(5), 337–343. doi: 10.3109/07853890109002087.	2001	Questionnaire	6	The Pt is presented with 5 headings ('mobility', 'self-care', 'usual activities', 'pain/discomfort' and 'anxiety/depression') and is asked to choose out of 3 answers how their health can be described today. The last Qn is a rating scale of 0 (the worst health you can imagine) to 100 (the best health you can imagine) in 5 point increments and they are asked to write in a box the number on the scale of how their health is today.	No
14	EQ-5D-5L of the EuroQol Group with a Visual Analogue Scale (VAS) v1.2	Janssen, M. F., Bonsel, G. J., & Luo, N. (2018). Is EQ-5D-5L better than EQ-5D-3L? A head-to-head comparison of descriptive systems and value sets from seven countries. *Pharmacoeconomics*, 36(6), 675–697. doi: 10.1007/s40273-018-0623-8.	2018	Questionnaire	6	The Pt is presented with 5 headings ('mobility', 'self-care', 'usual activities', 'pain/discomfort' and 'anxiety/depression') and is asked to choose out of 5 answers how their health can be described today. The last Qn is a rating scale of 0 (the worst health you can imagine) to 100 (the best health you can imagine) in 5 point increments and they are asked to write in a box the number on the scale of how their health is today.	No
15	Expected Consequences of Hearing aid Ownership (ECHO)	Cox, R. M., & Alexander, G. C. (2000). Expectations about hearing aids and their relationship to fitting outcome*. J Am Acad Audiol,* 11(7), 368–382; quiz 407.	2000	Questionnaire	18	Consists of statements about hearing aids. Pt are asked to circle on a 7-point scale the letter A (not at all') to G ('tremendously') that indicates the extent to which they agree with each statement.	No
16	Generalized Anxiety Disorder questionnaire (GAD-7)	Spitzer, R. L., Kroenke, K., Williams, J. B. W., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch Intern Med,* 166(10), 1092–1097. doi: 10.1001/archinte.166.10.1092.	2006	Questionnaire	8	Consists of 2 Qn. Qn 1 asks over the last 2wk how often have they been bothered by a series of 7 problems. Pt rate the 7 problems on a 4-point scale of 0 ('not at all sure') to 3 ('nearly every day'). Qn 2 asks to rate impact on work, home, and people on a 4-point scale of 0 'not difficult at all' to 3 'extremely difficult'. A score of 10 or higher means significant anxiety is present. Score over 15 are severe.	No
17	Glasgow Benefit Inventory (GBI)	Robinson, K., Gatehouse, S., & Browning, G. G. (1996). Measuring patient benefit from otorhinolaryngological surgery and therapy. *Ann*	1996	Questionnaire	18	Consists of 18 change in health status Qn which assess how the intervention has altered their QoL. The response to each Qn is based on a 5-point Likert scale (1='much worse' to 5='much	No

		Otol Rhinol Laryngol, 105(6), 415–422. doi: 10.1177/000348949610500601.				better'), ranging from a large deterioration in health status through to a large improvement in health status.	
18	Glasgow Health Status Inventory (GHSI)	Hawthorne, G., & Hogan, A. (2002). Measuring disability-specific patient benefit in cochlear implant programs: Developing a short form of the Glasgow Health Status Inventory, the Hearing Participation Scale. *Int J Audiol,* 41(8), 535–544. doi: 10.3109/14992020209056074.	2002	Questionnaire	18	Consists of 18 health status Qn which ask specific Qn about how the health problem has affected their QoL. The response to each Qn is based on a 5-point Likert scale (1=''frequently or all of the time' to 5='never'), ranging from 'high health status' through to 'low health status'. It has 3 subscales: general (12 Qn), social support (3 Qn) and physical health (3 Qn). Scores range from 0 to +100.	No
19	Glasgow Hearing Aid Benefit Profile (GHABP)	Gatehouse, S. (1999). Glasgow hearing aid benefit profile: Derivation and validation of a client-centered outcome measure for hearing aid services. *J Am Acad Audiol*, 10, 80–103.	1999	Questionnaire	5	Consists of 4 everyday situations that can lead to difficulty with hearing. The Pt is asked to rate them on a 6-point Likert scale (0=N/A, 1='no difficulty' to 5='cannot manage at all') in terms of difficulty, worry, proportion of the time wearing their hearing aid, how much the hearing aid helps, and satisfaction with aid. Pt can also nominate up to 4 new situations in which it is important for them to be able to hear as well as possible and rate them as above.	No
20	Health Utilities Index Mark 3 (HUI-3)	Furlong, W. J., Feeny, D. H., Torrance, G. W., & Barr, R. D. (2001). The Health Utilities Index (HUI) system for assessing health-related quality of life in clinical studies. *Ann Med*, 33(5), 375–384. doi: 10.3109/07853890109002092.	2001	Questionnaire	11	Asks about various aspects of your health. Pt are asked to think about their health and ability to do things on a day-to-day basis, during the past 4wks. Each Qn has up to 6 multiple-choice answers. The Pt is asked to choose 1. Qn 11 is a QoL rating scale with 10-point increments from 0 ('worst imaginable quality of life') to 100 ('best imaginable quality of life'). The Pt is asked to mark anywhere on the scale how good or bad their overall QoL is.	No
21	Hearing Handicap Inventory (HHIA)	Newman, C. W., Weinstein, B. E., Jacobson, G. P., & Hug, G. A. (1991). Test-retest reliability of the hearing handicap inventory for adults. *Ear Hear*, 12(5), 355–357. doi: 10.1097/00003446-199110000-00009.	1991	Questionnaire	25	Pt is presented with everyday situations and is asked to check 'Yes' (=4 points), 'Sometimes' (=2 points) or 'No' (=0 points) for the way they hear without a hearing aid. Scored for 'social', 'emotional' and 'total'. Score of 0=no handicap, to 100=total handicap. Percentage of 0-16%=no handicap, 18-42%=mild/moderate handicap and 44%+=significant handicap.	No

22	Hearing Implant Sound Quality Index (HISQUI-NL)	Amann, E., & Anderson, I. (2014). Development and validation of a questionnaire for hearing implant users to self-assess their auditory abilities in everyday communication situations: The Hearing Implant Sound Quality Index (HISQUI19). *Acta Otolaryngol,* 134(9), 915–923. doi: 10.3109/00016489.2014.909604.	2014	Questionnaire	19	Provides subjective feedback about sound quality of hearing implants experienced by the user.	No
23	Hospital Anxiety and Depression Scale (HADS)	Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatr Scand*, 67(6), 361–370. doi: 10.1111/j.1600-0447.1983.tb09716.x.	1983	Questionnaire	14	Contains two 7-item scales: one for anxiety and one for depression both with a score range of 0-21.	No
24	Hyperacusis Questionnaire (Khalfa et al, 2002)	Khalfa, S., Dubal, S., Veuillet, E., Perez-Diaz, F., Jouvent, R., & Collet, L. (2002). Psychometric normalization of a hyperacusis questionnaire. *ORL J Otorhinolaryngol Relat Spec*, 64(6), 436–442. doi: 10.1159/000067570.	2002	Questionnaire	14	Assesses sensitivity to sound and other noises in the environment. Pt is asked to mark out of 4 answers ('no'=0, 'yes a little'=1, 'yes quite a lot'=2, 'yes a lot'=3) which one best applies to them. Total scores range from 0-45, higher scores representing greater hypersensitivity.	No
25	International Outcome Inventory for Hearing Aids (IOI-HA)	Cox, R. M., & Alexander, G. C. (2002). The International Outcome Inventory for Hearing Aids (IOI-HA): Psychometric properties of the English version. *Int J Audiol,* 41(1), 30–35. doi: 10.3109/14992020209101309.	2002	Questionnaire	7	Consists of general Qn and situations. Pt is asked to choose out of 5 answers which best describes their experience with their hearing aids.	No
26	Monaural auditory capacity assessment scale (MACAS)	McLeod, B., Upfold, L., & Taylor, A. (2008). Self reported hearing difficulties following excision of vestibular schwannoma. *Int J Audiol*, 47(7), 420–430. doi: 10.1080/14992020802033083.	2008	Questionnaire	18	Asks some demographic Qn. Then the Pt is presented with a number of Qn on the difficulties they may be experiencing with their hearing. For each Qn the Pt is asked to circle the number in an 11-point Likert scale of 0 ('not at all') to 10 ('perfectly). The last Qn presents 4 types of hearing difficulty and the Pt is asked to rank them in order of importance to them (1='most important' to 4 'least important').	Yes
27	Multi-item, multi-domain questionnaire (author's own)	Schafer, E. C., Baldus, N., D'Souza, M., Algier, K., Whiteley, P., & Hill, M. (2013). Behavioral and subjective performance with digital CROS / BiCROS hearing instruments. 46, 62–93.	2013	Questionnaire	43	Pt are presented with listening conditions (hearing at home, hearing at work or school, hearing in social situations, satisfaction and instrument). They are asked to circle on a 7-point Likert scale of 0 ('can function fine') to 6 ('cannot function at all') the level of difficulty they have in each condition with no hearing instrument and with a (Bi)CROS instrument. The	Yes

						last section (Qn 30-43) collects general information about the hearing aid.	
28	Nijmegen Cochlear Implant Questionnaire (NCIQ)	Hinderink, J. B., Krabbe, P. F., & van den Broek, P. (2000). Development and application of a health-related quality-of-life instrument for adults with cochlear implants: The Nijmegen cochlear implant questionnaire. *Otolaryngol Head Neck Surg*, 123(6), 756–765. doi: 10.1067/mhn.2000.108203.	2000	Questionnaire	60	Pt are presented with situations and they are asked to choose out of 5 possibilities 'never' to 'always' how they hear with their CI. A 'not applicable' choice is also available. Qn 56-60 have 5 different categories 'no' to 'quite well', with a 'not applicable' choice too. Situations include physical, psychological, and social.	No
29	Number of days the patient has missed work: Data linked to the number of days the patient has missed work will also be gathered from the French health insurance databases	Marx, M., Costa, N. N., Lepage, B., Taoui, S., Molinier, L., Deguine, O., & Fraysse, B. (2019). Cochlear implantation as a treatment for single-sided deafness and asymmetric hearing loss: a randomized controlled evaluation of cost-utility. *BMC Ear Nose Throat Disord*, 19(1), 1. doi: 10.1186/s12901-019-0066-7.	2019	Diary	1	Counted the number of days missed work.	No
30	Numeric rating scale (0-10): Tinnitus loudness rated by the patient on a 0-10 scale	Lee, D. J. (2015). Cochlear implantation for treatment of single-sided deafness. ClinicalTrials.Gov. https://clinicaltrials.gov/ct2/show/record/NCT02532972	2015	Numeric rating scale	1	Tinnitus loudness rated by the patient on a 0-10 scale (no more info).	Not sure
31	Numeric rating scale (max score 10): Tinnitus loudness on a numeric rating scale	Song, J.-J., Punte, A. K., De Ridder, D., Vanneste, S., & Van de Heyning, P. (2013). Neural substrates predicting improvement of tinnitus after cochlear implantation in Pt with single-sided deafness. *Hear Res*, 299, 1–9. doi: 10.1016/j.heares.2013.02.001.	2013	Numeric rating scale	1	Tinnitus loudness on a numeric rating scale with max score of 10 (no more details).	Not sure
32	Numeric rating scale: Tinnitus loudness on a numeric rating scale	Song, J.-J., Kim, K., Sunwoo, W., Mertens, G., Van de Heyning, P., De Ridder, D., Vanneste, S., Lee, S.-Y., Park, K.-J., Choi, H., & Choi, J.-W. (2017). A quantitative electroencephalography study on cochlear implant-induced cortical changes in single-sided deafness with tinnitus. *Front Hum Neurosci*, 11, 210. doi: 10.3389/fnhum.2017.00210.	2017	Numeric rating scale	1	Tinnitus loudness on a numeric rating scale with max score of 10 (no more details).	Not sure
33	Numerical rating scales (author's own): The specific questions included ease of use, local discomfort or pain, accidental uncoupling, and user friendliness	Leterme, G., Bernardeschi, D., Bensemman, A., Coudert, C., Portal, J. J., Ferrary, E., Sterkers, O., Vicaut, E., Frachet, B., & Grayeli, A. B. (2015). Contralateral routing of signal hearing aid versus transcutaneous bone conduction in single-sided	2015	Numeric rating scale	4	Consists of a 5-point scale from 0 to 5, with 1='deterioration', and 5='improvement': Questions included ease of use, local discomfort or pain, accidental uncoupling, and user friendliness.	Not sure

	and were evaluated on a Likert scale ranging from 1 (deterioration) to 5 (improvement)	deafness. *Audiol Neurotol*, 20(4), 251–260. doi: 10.1159/000381329.					
34	Patient report (parasthesia / dysesthesia)	Nevoux, J., Coudert, C., Boulet, M., Czajka, C., Tavernier, L., Daval, M., Ayache, D., Meller, R., Rossetto, S., Papon, J. F., & Deveze, A. (2018). Transcutaneous Baha Attract system: Long-term outcomes of the French multicenter study. *Clin Otolaryngol*, 43(6), 1553–1559. doi: 10.1111/coa.13214.	2018	Single question	1	Pt reported parasthesia.	No
35	Patient report of hours / day	Newman, C. W., Sandridge, S. A., & Wodzisz, L. M. (2008). Longitudinal benefit from and satisfaction with the Baha system for Pt with acquired unilateral sensorineural hearing loss. *Otol Neurotol*, 29(8), 1123–1131. doi: 10.1097/MAO.0b013e31817dad20.	2008	Diary	2	Pt recorded in a diary the number of hours/ day and the number of hours/week they used the device over a period of 18 months.	Not sure
36	Patient report of tinnitus relief or severity	Sladen, D. P., Frisch, C. D., Carlson, M. L., Driscoll, C. L. W., Torres, J. H., & Zeitler, D. M. (2017). Cochlear implantation for single-sided deafness: A multicenter study. *Laryngoscope*, 127(1), 223–228. doi: 10.1002/lary.26102.	2017	Single question	1	Subjective presence of tinnitus was recorded pre- and postoperatively ('improvement' or 'no change' in tinnitus after surgery).	Not sure
37	Patient report: Pt reported use of their BAHA processor (hours / day)	Wazen, J. J., Spitzer, J. B., Ghossaini, S. N., Fayad, J. N., Niparko, J. K., Cox, K., Brackmann, D. E., & Soli, S. D. (2003). Transcranial contralateral cochlear stimulation in unilateral deafness. *Otolaryngol Head Neck Surg*, 129(3), 248–254. doi: 10.1016/S0194-5998(03)00527-8.	2003	Questionnaire	9	Pt are asked to choose out of 5 answers (more than 8hr, 4-8hr, 2-4hr, less than 2hr) how many hours per day they use their device.	Not sure
38	Perceived Stress Questionnaire (PSQ)	Levenstein, S., Prantera, C., Varvo, V., Scribano, M. L., Berto, E., Luzi, C., & Andreoli, A. (1993). Development of the Perceived Stress Questionnaire: A new tool for psychosomatic research. *J Psychosom Res*, 37(1), 19–32. doi: 10.1016/0022-3999(93)90120-5.	1993	Questionnaire	30	Pt are presented with sentences and they are asked to circle the number 1 ('almost never'), 2 ('sometimes', 3 ('often') or 4 ('usually') how often it applies to them in general during the last year or two. A 'recent' version asks the same Qn but asks Pt to 'consider only the last month'. PSQ Score = (Raw score -30) / 90.	No
39	Qn: 'How many years of your life would you exchange for getting normal hearing in your deaf ear?'	Louza, J., Hempel, J. M., Krause, E., Berghaus, A., Müller, J., & Braun, T. (2017). Patient benefit from cochlear implantation in single-sided deafness: A 1-year follow-up. *Eur Arch*	2017	Single question	1	Pt were asked 'How many years of your life would you exchange for getting normal hearing in your deaf ear?' The Burstrom et al (2007) time trade-off method for determining quality	Not sure

		Otorhinolaryngol, 274(6), 2405–2409. doi: 10.1007/s00405-017-4511-1.				adjusted life years (QUALY.) was used to calculate the results	
40	Questionnaire (author's own)	Härkönen, K., Kivekas, I., Kotti, V., Sivonen, V., & Vasama, J.-P. (2017). Hybrid cochlear implantation: quality of life, quality of hearing, and working performance compared to Pt with conventional unilateral or bilateral cochlear implantation. *Eur Arch Oto-Rhino-Laryngology*, 274(10), 3599–3604. doi: 10.1007/s00405-017-4690-9.	2017	Questionnaire	6	Pt are presented with Qn addressing their working performance with the CI. They can choose out of 5 answers ('very much', 'moderately', 'a little', 'no change' and 'worsened' / 'decreased activity' / 'increased fatigue'.	No
41	Questionnaire (author's own)	Snapp, H. A., Fabry, D. A., Telischi, F. F., Arheart, K. L., & Angeli, S. I. (2010). A clinical protocol for predicting outcomes with an implantable prosthetic device (Baha) in Pt with single-sided deafness*. J Am Acad Audiol*, 21(10), 654–662. doi: 10.3766/jaaa.21.10.5.	2010	Questionnaire	4	Pt are presented with situations regarding speech or direction of sounds and are asked to rate them by choosing one of 5 answers ('always', 'most of the time', 'occasionally', 'seldom' and 'never'). The Pt is also asked to mark if answering the Qn pre-op, post-op for Rt or Lt ear.	Yes
42	Questionnaire about the use of the system (author's own): The custom-made questionnaire regarding the use of the adhesive hearing system was used to assess the following specific topics: 1) ‘‘How often did you need to change the adhesive adaptor?,’’ 2) ‘‘Did you experience feedback?,’’ 3) ‘‘Did the adhesive adaptor fall off during normal use?,’’ 4) ‘‘Did you experience skin irritation?,’’ 5) ‘‘How do you rate the sound quality?,’’ 6) ‘‘How do you rate the appearance of the hearing system?,’’ 7) ‘‘During the trial, was the hearing system a useful hearing tool for you?’’	Mertens, G., Gilles, A., Bouzegta, R., & Van de Heyning, P. (2018). A prospective randomized crossover study in single sided deafness on the new non-invasive adhesive bone conduction hearing system. *Otol Neurotol*, 39(8), 940–949. doi: 10.1097/MAO.0000000000001892.	2018	Questionnaire	7	Pt were asked regarding the use of the adhesive hearing system during the their trial using these Qn: 1) 'How often did you need to change the adhesive adaptor?', 2) 'Did you experience feedback?', 3) 'Did the adhesive adaptor fall off during normal use?', 4) 'Did you experience skin irritation?', 5) 'How do you rate the sound quality?', 6) ‘‘How do you rate the appearance of the hearing system?', 7) 'During the trial, was the hearing system a useful hearing tool for you?'	Not sure
43	Questionnaire concerning Phonak Audeo Smart IX model CROS	Busk Linnebjerg, L., & Wetke, R. (2014). The benefits of CROS aids for individuals with unilateral sensorineural hearing loss. *Hear*	2014	Questionnaire	37	Pt are presented with general Qn about their hearing, a few are open, others have a choice of answers. The second part has 11-point Likert	Not sure

		Balanc Commun, 12(1), 36–40. doi: 10.3109/21695717.2013.794593.				point rating scales of 0 ('very poor') to 10 ('very good') where the Pt is asked to rate the use of aids in various situations. The option to comment is also available.	
44	Satisfaction with Amplification in Daily Life (SADL)	Cox, R. M., & Alexander, G. C. (2001). Validation of the SADL questionnaire. *Ear Hear*, 22(2), 151–160. doi: 10.1097/00003446-200104000-00008	2001	Questionnaire	15	Pt are presented with a list of Qn and are asked about their opinions about their hearing aids. For each Qn they are asked to circle one out of 7 letters A ('not at all') to G ('tremendously') that represents the best answer for them regarding the hearing aids they are wearing now.	No
45	Short Form Health Survey (SF-36)	Ware, J. E. (1999). SF-36 Health Survey. In M. E. Maruish (Ed.), The use of psychological testing for treatment planning and outcomes assessment. Lawrence Erlbaum Associates Publishers.	1999	Questionnaire	36	Pt are presented with general health Qn, Qn about activities, physical health, emotional problems. Each Qn has multiple choice answers ranging from 2 to 6 possible answers. A scoring tool is available.	No
46	Short Tinnitus Questionnaire (Goebel & Hiller)	Goebel, G., & Hiller, W. (1994). The tinnitus questionnaire. A standard instrument for grading the degree of tinnitus. Results of a multicenter study with the tinnitus questionnaire. *HNO*, 42(3), 166–172.	1994	Questionnaire	33	Consists of 4 subscales (distress and intrusiveness, sleep disturbances, auditory perceptual difficulties, irrational beliefs. Scoring is out of 3 answers 'true', 'partly true' or 'not true'. Normative data is provided.	No
47	Short version of the Speech, Spatial and Qualities (SSQ-12) scale	Noble, W., Jensen, N. S., Naylor, G., Bhullar, N., & Akeroyd, M. A. (2013). A short form of the Speech, Spatial and Qualities of Hearing scale suitable for clinical use: The SSQ12. *Int J Audiol,* 52(6), 409–412. doi: 10.3109/14992027.2013.781278.	2013	Questionnaire	12	Consist of Qn about aspects of Pt's ability and experience hearing and listening in different situations. Pt are asked to mark on an 11-point Likert scale of 0 ('quite unable to do or experience what is described') to 10 ('would be perfectly able to do or experience what is described'). Pt have the choice to mark 'not applicable'.	No
48	Single feedback question (author's own): Upon completion of the study, Pt were asked, 'Taking everything into consideration, would you do it again? That is, would you still proceed with the Baha?'	Newman, C. W., Sandridge, S. A., & Wodzisz, L. M. (2008). Longitudinal benefit from and satisfaction with the Baha system for Pt with acquired unilateral sensorineural hearing loss. *Otol Neuro,* 29(8), 1123–1131. doi: 10.1097/MAO.0b013e31817dad20.	2008	Single question	1	Pt were asked at the end of the study: 'Taking everything into consideration, would you do it again? That is, would you still proceed with the Baha?' (no more details)	Not sure
49	Spatial Hearing Questionnaire (SHQ)	Tyler, R. S., Perreau, A. E., & Ji, H. (2009). Validation of the Spatial Hearing Questionnaire. *Ear Hear*, 30(4), 466–474. doi: 10.1097/AUD.0b013e3181a61efe.	2009	Questionnaire	24	Pt are presented with situations and they are asked to respond to each Qn with a number from 0 ('very difficult') to 100 ('very easy').	Yes

50	Speech, Spatial and Qualities 12 Comparative (SSQ-12-C)	Gatehouse, S., & Noble, W. (2004). The Speech, Spatial and Qualities of hearing scale (SSQ*). Int J Audiol*, 43(2), 85–99. doi: 10.1080/14992020400050014.	2004	Questionnaire	12	Consist of Qn about aspects of the Pt's ability and experience hearing and listening in different situations. Pt are asked to compare their ability and experience with their current aids vs their previous aids. Pt are asked to mark on an 11-point Likert scale of -5 ('things are much worse') through 0 ('things are no different') to +5 ('if things are much better'). Pt have the choice to mark 'not applicable'.	No
51	Speech, Spatial and Qualities 12 of Hearing Scale for Benefit Questionnaire (SSQ-12-B) pre and post	Gatehouse, S., & Noble, W. (2004). The Speech, Spatial and Qualities of hearing scale (SSQ*). Int J Audiol*, 43(2), 85–99. doi: 10.1080/14992020400050014.	2004	Questionnaire	12	Consist of Qn about aspects of the Pt's ability and experience hearing and listening in different situations. Pt are asked to compare their ability and experience with their current aids vs before getting the aids. Pt are asked to mark on an 11-point Likert scale of -5 ('things are much worse') through 0 ('things are no different') to +5 ('if things are much better'). Pt have the choice to mark 'not applicable'.	No
52	Speech, Spatial and Qualities 18 Comparative (SSQ-18-C)	Gatehouse, S., & Noble, W. (2004). The Speech, Spatial and Qualities of hearing scale (SSQ). *Int J Audiol*, 43(2), 85–99. doi: 10.1080/14992020400050014.	2004	Questionnaire	49	Consist of Qn about aspects of the Pt's ability and experience hearing and listening in different situations. Pt are asked to compare their ability and experience with their current aids vs their previous aids. Pt are asked to mark on an 11-point Likert scale of -5 ('things are much worse') through 0 ('things are no different') to +5 ('if things are much better'). Pt have the choice to mark 'not applicable'.	No
53	Speech, Spatial, and Qualities of Hearing Scale 5 Questions (SSQ-5)	Gatehouse, S., & Noble, W. (2004). The Speech, Spatial and Qualities of hearing scale (SSQ). *Int J Audiol*, 43(2), 85–99. doi: 10.1080/14992020400050014.	2004	Questionnaire	5	Consist of Qn about aspects of the Pt's ability and experience hearing and listening in different situations. Pt are asked to compare their ability and experience with their current aids vs their previous aids. Pt are asked to mark on an 11-point Likert scale of -5 ('things are much worse') through 0 ('things are no different') to +5 ('if things are much better'). Pt have the choice to mark 'not applicable'.	No
54	Subjective Tinnitus Severity Scale (STSS)	van Veen, E. D., Jacobs, J. B., & Bensing, J. M. (1998). Assessment of distress associated with tinnitus. *J Laryngol Otol,* 112(3), 258–263. doi: 10.1017/s002221510015830x.	1998	Questionnaire	16	Pt are presented with Qn about the severity of their tinnitus and the related distress. They respond with a Yes/No.	No

55	Time trade off (not specified) comprises one question about how many years of their lives Pt would sacrifice for living with perfect hearing for the rest of their lives. TTO (%) = ((life expectancy – number of years to give up for perfect hearing) / life expectancy) * 100	Peters, J. P., van Zon, A., Smit, A. L., van Zanten, G. A., de Wit, G. A., Stegeman, I., & Grolman, W. (2015). CINGLE-trial: cochlear implantation for siNGLE-sided deafness, a randomised controlled trial and economic evaluation. *BMC Ear Nose Throat Disord,* 15, 3. doi: 10.1186/s12901-015-0016-y.	2015	Single question	1	Pt were asked 'How many years of their lives would they sacrifice for living with perfect hearing for the rest of their lives' during the baseline and follow up visits.	Not sure
56	Tinnitus Burden Questionnaire (TBQ): A self-developed questionnaire assessing various aspects of tinnitus burden. It consists of 12 visual analogue scales (VAS), ranging from '0' (no tinnitus burden) to '10' (maximum tinnitus burden)	Peters, J. P., van Zon, A., Smit, A. L., van Zanten, G. A., de Wit, G. A., Stegeman, I., & Grolman, W. (2015). CINGLE-trial: cochlear implantation for siNGLE-sided deafness, a randomised controlled trial and economic evaluation. *BMC Ear Nose Throat Disord,* 15, 3. doi: 10.1186/s12901-015-0016-y.	2015	Questionnaire	12	Pt are asked Qn about various aspects of tinnitus burden. It consists of 12 visual analogue scales, ranging from 0 ('no tinnitus burden') to 10 ('maximum tinnitus burden').	Not sure
57	Tinnitus Functional Index (TFI)	Meikle, M. B., Henry, J. A., Griest, S. E., Stewart, B. J., Abrams, H. B., McArdle, R., Myers, P. J., Newman, C. W., Sandridge, S., Turk, D. C., Folmer, R. L., Frederick, E. J., House, J. W., Jacobson, G. P., Kinney, S. E., Martin, W. H., Nagler, S. M., … Vernon, J. A. (2012). The Tinnitus Functional Index: Development of a new clinical measure for chronic, intrusive tinnitus. *Ear Hear,* 33(2), 153–176. doi: 10.1097/AUD.0b013e31822f67c0.	2012	Questionnaire	25	Pt are presented with Qn about their tinnitus and are asked to rate on an 11-point Likert scale of 0 to 10 or 10% to 100%. Includes 8 subscales (intrusiveness, sense of control, cognitive, sleep, auditory, relaxation, QoL, emotional). Detailed instructions on scoring are provided.	No
58	Tinnitus Handicap Inventory (THI)	Newman, C. W., Jacobson, G. P., & Spitzer, J. B. (1996). Development of the Tinnitus Handicap Inventory. *Arch Otolaryngol Head Neck Surg,* 122(2), 143–148. doi: 10.1001/archotol.1996.01890140029007.	1996	Questionnaire	25	Pt are presented Qn about difficulties they may be experiencing because of their tinnitus. They are asked to answer each Qn with a 'yes', 'sometimes' or 'no' response. A severity scale is provided for interpretation (0-16=slight, 18-36=mild, 38-56=moderate, 58-76=severe and 78-100=catastrophic).	No
59	Tinnitus Handicap Questionnaire (THQ)	Kuk, F. K., Tyler, R. S., Russell, D., & Jordan, H. (1990). The psychometric properties of a tinnitus handicap questionnaire. *Ear Hear,* 11(6), 434–445. doi: 10.1097/00003446-199012000-00005.	1990	Questionnaire	27	Consists of statements about tinnitus. Pt are asked to indicate with a 0 ('strongly disagree') up to 100 ('strongly agree') their agreement with the statement.	No

60	Tinnitus Questionnaire (Hallam et al, 1988)	Hallam, R. S., Jakes, S. C., & Hinchcliffe, R. (1988). Cognitive variables in tinnitus annoyance. *Br J Clin Psychol,* 27(3), 213–222. doi: 10.1111/j.2044-8260.1988.tb00778.x.	1988	Questionnaire	52	Consists of statements about tinnitus. Pt are asked to score each with an A ('always'), B ('sometimes') or C 'never'.	No
61	Tinnitus Rating Scale (TRS)	Ahmed, M. F. ., & Khater, A. (2017). Tinnitus suppression after cochlear implantation in Pt with single-sided deafness. *Egypt J Otolaryngol,* 33(1), 61. doi: 10.4103/1012-5574.199404.	2017	Numeric rating scale	5	Pt are asked to rate their tinnitus on a 5-point Likert scale (1='not present' through to 5='present and debilitating').	Not sure
62	Tinnitus Reaction Questionnaire (TRQ)	Wilson, P. H., Henry, J., Bowen, M., & Haralambous, G. (1991). Tinnitus reaction questionnaire: psychometric properties of a measure of distress associated with tinnitus. *J Speech Hear Res,* 34(1), 197–201.	1991	Questionnaire	26	Pt are presented with statements about effects of tinnitus on their lifestyle, general well-being etc. Pt are asked to circle a number on a 5-point Likert rating scale of 0 ('not at all') to 4 ('almost all of the time') that best describes how their tinnitus affects them.	No
63	Visual Analogue 6-point scale: Sound quality and annoying background noise were assessed using a six-item visual analogue scale (VAS), where 0 represented being unable to hear and 5 indicated hearing perfectly	Choi, J. E., Ma, S. M., Park, H., Cho, Y. S., Hong, S. H., & Moon, J. (2019). A comparison between wireless CROS / BiCROS and soft-band BAHA for Pt with unilateral hearing loss. *PLoS One,* 14(2), e0212503. doi: 10.1371/journal.pone.0212503.	2019	VAS	2	Consists of a 6-item VAS from 0 to 5, with 0='unable to hear' and 5='hearing perfectly'. Categories included Sound quality and Annoying background noise.	Not sure
64	Visual Analogue Scale (0-10 points): Subjects scored the loudness of the scale was assigned a score of 0 (no tinnitus), and the right-hand side of the scale was assigned a score of 10 (very loud, disturbing tinnitus). The subjects had to mark with an X where they perceived the loudness of their tinnitus to be	Van de Heyning, P., Vermeire, K., Diebl, M., Nopp, P., Anderson, I., & De Ridder, D. (2008). Incapacitating unilateral tinnitus in single-sided deafness treated by cochlear implantation. *Ann Otol Rhinol Laryngol,* 117(9), 645–652. doi: 10.1177/000348940811700903.	2008	VAS	1	Consists of a 10-point Likert scale from 0 to 10, with 0='no tinnitus' and 10='very loud, disturbing tinnitus'. Pt had to mark with an X where they perceived the loudness of their tinnitus to be. The VAS was completed for 2 conditions: with the CI activated, and with the CI deactivated.	Not sure
65	Visual Analogue Scale (1-10): Skin safety was evaluated by a visual analogue scale (between 1 and 10 from very bad to excellent) to rate cutaneous tolerance	Schmerber, S., Deguine, O., Marx, M., Van de Heyning, P., Sterkers, O., Mosnier, I., Garin, P., Godey, B., Vincent, C., Venail, F., Mondain, M., Deveze, A., Lavieille, J. P., & Karkas, A. (2017). Safety and effectiveness of the Bonebridge transcutaneous active direct-drive bone-conduction hearing implant at 1-year device use. *Eur Arch Otorhinolaryngol,* 274(4), 1835–1851. doi: 10.1007/s00405-016-4228-6.	2017	VAS	1	Skin safety was evaluated by the surgeon using a 1-10 VAS, with 1='very bad' to 10='excellent' rating of 'cutaneous tolerance'. Skin safety was evaluated up to 12 months post-op.	No

66	Visual Analogue Scale (VAS)	Pfiffner, F., Kompis, M., Flynn, M., Asnes, K., Arnold, A., & Stieger, C. (2011). Benefits of low-frequency attenuation of Baha® in single-sided sensorineural deafness. *Ear Hear,* 32(1), 40–45. doi: 10.1097/AUD.0b013e3181ecd002.	2011	VAS	6	Subjective sound quality was evaluated using questionnaires with an 11-point Likert scale from -5 to +5 VAS, rating brightness, softness, clarity, fullness, loudness (Ovegard et al. 1997), and reverberation. Two questionnaires were administered for each subject, one after completing the tests with the lowest cutoff frequency of 270 Hz, and the other after completing the tests with the highest cutoff at 1500 Hz.	Not sure
67	Visual Analogue Scale (VAS): An evaluation of the discomfort related to the possible tinnitus associated with the deafness will rely on a visual analogue scale (VAS) ranging from 0 to 10. This scale is presented as a 17 cm plastic ruler with a vertical arrow on one side and a graduated scale on the other side (0 to 10 cm). The subject first indicates the level of annoyance generated by the tinnitus on the vertical arrow using a cursor and the corresponding numeric value is reported by the evaluator. Then, the intensity of tinnitus is assessed using another ruler with the same dimensions	Marx, M., Costa, N. N., Lepage, B., Taoui, S., Molinier, L., Deguine, O., & Fraysse, B. (2019). Cochlear implantation as a treatment for single-sided deafness and asymmetric hearing loss: a randomized controlled evaluation of cost-utility. *BMC Ear Nose Throat Disord,* 19(1), 1. doi: 10.1186/s12901-019-0066-7.	2019	VAS	2	Discomfort related to the possible tinnitus associated with the deafness was measured on a VAS ranging from 0 to 10 presented as a 17 cm plastic ruler with a vertical arrow on one side and a graduated scale on the other side (0 to 10 cm). The subject first indicates the level of annoyance generated by the tinnitus on the vertical arrow using a cursor and the corresponding numeric value is reported by the evaluator. Then, the intensity of tinnitus is assessed using another ruler with the same dimensions.	Not sure
68	Visual Analogue Scale (VAS): Each day, they were asked to rate the loudness and stress caused by the tinnitus in a visual analogue scale, as well as their mood and their ability to influence the tinnitus. In the evaluation, visual analogue scale was translated to a scale from 0 to 10. The ratings were	Buechner, A., Brendel, M., Lesinski-Schiedat, A., Wenzel, G., Frohne-Buechner, C., Jaeger, B., & Lenarz, T. (2010). Cochlear implantation in unilateral deaf subjects associated with ipsilateral tinnitus. *Otol Neurotol,* 31(9), 1381–1385. doi: 10.1097/MAO.0b013e3181e3d353.	2010	Diary	4	Pt rated loudness, stress caused by tinnitus, mood, ability to influence tinnitus on a VAS of 0-10 (higher numbers =better). Ratings were averaged over the 4 questions each month.	Not sure

	averaged for each subject over all 4 questions and each month						
69	Visual Analogue Scale (VAS): Subjective hearing handicap on a Visual Analogue Scale (VAS) 0-10 - Hearing handicap: as described by the experiencing of hearing problems in various everyday situations	Andersen, H. T., Schrøder, S. A., & Bonding, P. (2006). Unilateral deafness after acoustic neuroma surgery: subjective hearing handicap and the effect of the bone-anchored hearing aid. *Otol Neurotol,* 27(6), 809–814. doi: 10.1097/01.mao.0000227900.57785.ec.	2006	VAS	1	Pt are asked to rate their subjective hearing handicap in various everyday hearing situations on a VAS of 0 to 10.	Not sure
70	Visual Analogue Scale (VAS): Subjects were asked to mark the tinnitus severity on a 10-cm line anchored with the extreme labels “No tinnitus at all” and “Worst tinnitus imaginable.”	Galvin, J. J., Fu, Q. J., Wilkinson, E. P., Mills, D., Hagan, S. C., Lupo, J. E., Padilla, M., & Shannon, R. V. (2019). Benefits of cochlear implantation for single-sided deafness: Data from the House Clinic-University of Southern California-University of California, Los Angeles Clinical Trial. *EarHear,* 40(4), 766–781. doi: 10.1097/AUD.0000000000000671.	2019	VAS	1	Pt are asked to mark their tinnitus severity on a 10-cm line anchored with the extreme labels 'no tinnitus at all' and 'worst tinnitus imaginable'.	Not sure
71	Visual Analogue Scale (VAS): The VAS, assessing tinnitus loudness, is a simple ‘‘analogue’’ line, 10 cm in length, anchored by ‘‘quiet’’ and ‘‘very loud, cannot get any worse’’	Mertens, G., Punte, A. K., De Ridder, D., & Van De Heyning, P. (2013). Tinnitus in a single-sided deaf ear reduces speech reception in the non tinnitus ear. *Otol Neurotol,* 34(4), 662–666. doi:	2013	VAS	1	Pt are asked to rate their tinnitus loudness using a simple 'analogue' line, 10 cm in length, anchored by 'quiet' and 'very loud, cannot get any worse'. The VAS score is determined by measuring in millimetres from the Lt-hand end of the line to the marked point.	Not sure
72	Visual Analogue Scale (VAS): The Visual Analogue Scale (VAS), assessing tinnitus loudness and disturbance, is a simple analogue line, 10 cm in length	Mertens, G., Hofkens, A., Punte, A. K., De Bodt, M., & Van de Heyning, P. (2015). Hearing performance in single-sided deaf cochlear implant users after upgrade to a single-unit speech processor. *Otol Neurotol,* 36(1), 51–60. doi: 10.1097/MAO.0000000000000653.	2015	VAS	2	Pt are asked to rate their tinnitus loudness and disturbance, on a simple analogue line, 10 cm in length, anchored by 'absolutely not' and 'absolutely'. The Lt-hand end represents 'complete disability' and the Rt-hand end 'complete ability'.	Not sure
73	Visual Analogue Scale (VAS): Tinnitus distress was measured with the visual analogue scale (VAS) before and 6 months after CI activation. The Pt had to mark the tinnitus strength on a scale from 0 (no tinnitus) to 10 (maximum strength)	Arndt, S., Aschendorff, A., Laszig, R., Beck, R., Schild, C., Kroeger, S., Ihorst, G., & Wesarg, T. (2011). Comparison of pseudobinaural hearing to real binaural hearing rehabilitation after cochlear implantation in Pt with unilateral deafness and tinnitus. *Otol Neurotol,* 32(1), 39–47. doi: 10.1097/MAO.0b013e3181fcf271.	2011	VAS	1	Pt are asked to rate their tinnitus distress on a VAS before and 6 months after CI activation. Pt had to mark the tinnitus strength on a scale from 0 ('no tinnitus') to 10 ('maximum strength').	Not sure
74	Visual Analogue Scale (VAS): VAS assessment of tinnitus annoyance	Poncet-Wallet, C., Mamelle, E., Godey, B., Truy, E., Guevara, N., Ardoint, M., Gnansia, D., Hoen,	2020	VAS	2	Pt are asked to rate their tinnitus annoyance before and 13 months after surgery on a VAS	Not sure

	scores could range from 0 (not intense/not annoying) to 10 (intense/annoying)	M., Saaï, S., Mosnier, I., Lescanne, E., Bakhos, D., & Vincent, C. (2020). Prospective multicentric follow-up study of cochlear implantation in adults with single-sided deafness: Tinnitus and audiological outcomes. *Otol Neurotol,* 41(4), 458–466. doi: 10.1097/MAO.0000000000002564.				ranging from 0 ('not intense/not annoying') to 10 ('intense/annoying').	
75	World Health Organisation Quality of Life Short Form Survey (WHOQOL-BREF)	The WHOQOL Group (1998). Development of the World Health Organisation WHOQOL-BREF quality of life assessment. *Psychol Med,* 28(3), 551–558. doi: 10.1017/s0033291798006667.	1998	Questionnaire	26	Pt are presented with Qn about their QoL, health, and other areas of their life. Pt are asked to choose out of 5 answers which appears more appropriate.	No
76	Yes/No Answer to 'Beneficial to Hearing?' Question: Pt were asked whether they felt that the CROS amplification had been worthwhile and which of the three CROS devices (if any) took their preference	Hol, M. K. S., Kunst, S. J. W., Snik, A. F. M., & Cremers, C. W. R. J. (2010). Pilot study on the effectiveness of the conventional CROS, the transcranial CROS and the BAHA transcranial CROS in adults with unilateral inner ear deafness. *Eur Arch Otorhinolaryngol,* 267(6), 889–896. doi: 10.1007/s00405-009-1147-9.	2010	Single question	1	Pt are asked whether they felt the intervention has been worthwhile with 'Beneficial to Hearing?. A Yes/No answer was expected.	Not sure

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