Optimising Contextual Factors in the Practitioner-Patient Encounter in the Management of Osteoarthritis

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Thesis submitted to the University of Nottingham for the degree of Doctor of Philosophy

May 2023

Declaration

I hereby declare that this thesis is the result of original research. This work has not been submitted for any other degree or qualification. I have largely conducted it, and any assistance received is detailed below.

- The supervisors of the research project Professor Weiya Zhang, Professor Michael Doherty, and Dr Michelle Hall, provided guidance and supervision in all aspects of this thesis. In addition, Professor Weiya Zhang and Dr Michelle Hall contributed to the eligibility assessment of full-text studies in the quantitative systematic review. They also assisted in circulating the online survey through emailing relevant networks.
- Dr Catrin Evans collaborated in co-supervising the qualitative systematic review study. She guided me throughout the stages of the qualitative review (i.e., from the protocol registration to writing the chapter), provided relevant examples and reviewed my work on that chapter.
- Khalid Yaseen participated in the validation process of the two systematic reviews.
- Ramadan Musa, the former PhD researcher, conducted the Delphi exercise in 2016. I have utilised the unpublished Delphi results to guide the development of the systematic reviews search strategy with agreement from the research team.

Abstract

Background

Contextual factors (CFs) related to the patient, healthcare practitioners, and their therapeutic relationship are integral to the overall treatment effect of any given intervention. In osteoarthritis (OA), around 75% of the treatment effect is directly attributable to CFs. Identifying and understanding the role of CFs may encourage healthcare practitioners to develop and enhance the contextual aspects of care, and thus enhance the overall treatment benefit.

Objectives

The overall aim of this research project is to develop a contextual enhancement package (CEP) that can be used to optimise the management of OA. To achieve this aim, the studies in this thesis aimed to realise the following objectives: [1] to identify and evaluate the current evidence for modifiable CFs that can improve clinical outcomes using quantitative systematic review and meta-analysis of randomised controlled trials (RCTs); [2] to explore and understand the experience and perspectives of patients and health practitioners about contextual enhancers in consultations for OA using qualitative systematic review and meta-aggregation; and [3] to obtain views and perspectives from clinicians, researchers, and public and patients on the identified CFs using an online survey and Public and Patient Involvement and Evaluation (PPI/E) meetings.

Methods

Quantitative systematic review: A systematic search was carried out, up until April 18th, 2019, on the following databases: MEDLINE via Ovid, EMBASE, AMED, PsycINFO and Cochrane library. RCTs comparing contextual enhanced interventions versus non-enhanced control in adults for any health conditions were searched. The outcomes included both self-reported outcomes and objectively measured outcomes. The effect size and 95% confidence interval were calculated using the standardised mean difference. Risk of bias was evaluated using the modified Cochrane tool. The random effects model was used to pool the results. The GRADE approach was used to assess the confidence in the body of evidence for each outcome assessed.

Qualitative systematic review: A systematic search was conducted between March 15 and May 18, 2020, on the following databases: MEDLINE via Ovid, EMBASE, AMED, PsycINFO and CINAHL. The search for unpublished studies included ProQuest Dissertations and Google Scholar. The search was not limited to any language or publication year. The Joanna Briggs Institute (JBI) methodology for quality assessment, study selection, data extraction and synthesis were used. Findings were assessed for credibility, categorised based on similarity in meaning and subjected to a meta-aggregation. The ConQual approach was used to assess the confidence of the synthesised findings.

Stakeholders' involvement: An online survey was conducted using Microsoft Forms software. The responses to the survey were collected between September 20 and October 15, 2021. Results were tabulated and analysed utilising Microsoft Excel. The study sought anonymous stakeholders' ratings and opinions. The survey involved a Likert scale question to rate the importance of each of the eight contextual factors identified in this project and an optional open-ended question about additional contextual factors related to practitioner-patient interaction that need to be considered.

PPI/E meetings: The PPI/E process in this research project took two forms of involvement. In the early stages of the project, in November 2019, the in-person PPI/E meeting aimed to consider the relevance of the research topic to the public and patients. The meeting communicated the research information (i.e., research question and topic) to patients with OA. Whereas, at the later stage of the research, in September 2021, patients exchanged information and participated by providing their opinion and input on the research outcomes in the online meeting.

Results

Quantitative systematic review: Of 3928 records generated from the systematic search, 25 trials (5632 participants) met the inclusion criteria, and 20 were included in this meta-analysis. Conditions studied included musculoskeletal [6], cardiovascular [3], asthma [2], irritable bowel syndrome [1], diabetes [1], chronic pain [1], acute pain [3], gynaecological conditions requiring day-care surgery [1], postoperative nausea [1], and in GP or hospital-based patients [6]. Three CFs were identified from these trials: empathy, patient involvement and positive communication. All were found to be effective for patient experience (i.e., satisfaction) (SMD 0.34; 95% CI 0.27, 0.42). Positive communication was also effective for symptoms (SMD 0.17, 95%CI 0.06, 0.28) but not objective outcomes (SMD 0.10, 95%CI -0.14, 0.34). According to the GRADE guidelines for assessing confidence in the findings of systematic reviews of interventions, the certainty of the evidence was rated low for symptoms and objective outcomes and very low for patient experience outcomes.

Qualitative systematic review: Of 1808 records generated from the systematic search of databases and grey literature, eight studies were included in the meta-aggregation. All included papers were moderate to high quality based on the JBI qualitative critical appraisal tool. Meta-aggregation generated three synthesised findings. According to the ConQual criteria for assessing confidence in qualitative review findings, all the synthesised findings' level of evidence was rated as moderate. The key, potentially modifiable, factors identified were empathy and positive communication; clear and relevant information provided by the health practitioner; patient expectation concerning their outcome and the consultation experience; active involvement of the patient in the consultation; sufficient consultation time; easy access to consultations; and health providers confidence.

Stakeholder's involvement: Fifty healthcare providers from various professions and four patients with OA responded to the online survey.

The healthcare providers' professions included physicians, physiotherapists, health researchers, and podiatrist. All the respondents answered the Likert scale question, and 39 answered the optional open-ended question. The stakeholders' importance rating for each of the eight contextual factors identified from the quantitative and qualitative systematic reviews was high. Healthcare providers and patients with OA considered all factors essential and expanded their responses about how important these factors are in the open-ended question.

PPI/E meetings: The first meeting confirmed the importance and relevance of the research topic to a group of OA patients. Also, the PPI suggested some CFs (i.e., regular follow-up and referral) that were considered later in developing the search strategy for the qualitative systematic review. The second meeting obtained the PPI inputs on the CFs identified from previous reviews in the research project. The PPI/E supported the delivery of all the factors and suggested tailoring the factors to patient needs.

Conclusion

Eight contextual factors have been identified according to their therapeutic effects, clinical importance and stakeholders' perspectives. They are ready to be integrated to form a CEP. Further studies will be undertaken to develop an educational programme, test the feasibility of delivering CEP, and assess the clinical effectiveness and cost-effectiveness of CEP in people with osteoarthritis at the first instance.

COVID-19 Pandemic Impact Statement

The COVID-19 pandemic has affected people all over the world. Personally, the pandemic had impacted my life from different aspects. The stress of hearing people talking all day about the coronavirus news was overwhelming in the workplace and made it difficult for me to concentrate on my work in the shared office before the lockdown. I limited my use of public transportation and went less often to the main university campus for courses or studying in the library before the national lockdown was imposed. In the early stages of the pandemic (March 2020), I was infected by the virus, as was my son.

My mental health was profoundly affected during the lockdown, hence my physical well-being. The parental responsibilities increased, having my child in my care all the time due to nurseries shut down had greatly affected the study progression and the ability to work efficiently. It was challenging to maintain a balance between learning, research and meetings in the digital world and my other life responsibilities.

The research team has decided to cancel the feasibility study initially planned to be conducted at later project stages, as this was not COVID-related research, and it was not feasible during the pandemic to recruit participants for the feasibility study. We therefore considered a revised research plan to undertake a stakeholder survey that could be completed within the remaining time of the full-time registration for the PhD.

In order to minimise the impact, firstly, I scheduled my study hours with my husband, who was a final year PhD researcher. Secondly, I returned my son to the day nursery by the end of 2020. Thirdly, I have discussed my worries and concerns, and I obtained advice from:

- My principal supervisor (through regular meetings) and the supervisory team discussion and support
- Coffee and catch up for ROD PGR weekly meeting (with Dr Sonia Gran)
- ROD Divisional Meeting (I raised the issue, and the Dean of the Medical School, Prof Brigitte Scammell, commented on mothers' productivity being affected by the pandemic and possible ways to compensate for their impact).
- I have applied for the COVID-19 pandemic extension, and I have been awarded a six-month extension to my study period.

Irrespective of the challenges, I was able to work on a modified research plan and complete my research remotely. Working from home, I completed the analysis of the first systematic review, conducted the qualitative systematic review, conducted the stakeholders' online survey and an online PPI meeting, wrote my thesis, obtained the required training points for the second and third academic years, participated in national and international scientific meetings and conferences, and had regular meetings with the principal supervisor.

Acknowledgements

The journey towards achieving the PhD degree was challenging yet inspiring for me. I would not have been able to complete this thesis without the help of many people to whom I am very grateful.

First and foremost, I wish to express my sincere appreciation to my principal supervisor Professor Weiya Zhang and the supervisory team, Professor Michael Doherty and Dr Michelle Hall. It has been an honour to be supervised by some leader researchers in osteoarthritis, and I am grateful for learning from these excellent examples of successful researcher.

Special thanks to Dr Catrin Evans for her dedication in co-supervising the qualitative systematic review. It has been a great privilege to work with such an experienced and well-respected researcher.

Many thanks to my fellows in the division Academic Rheumatology, Dr Burak Kundakci, Khalid Yaseen and Dr Abasiama Obotiba, who were always supportive and generous in teaching and guiding me in conducting my research. I would like to thank the members of the Division of Rheumatology, Orthopaedics and Dermatology, who had taught me and helped me.

Gratitude goes to my sponsors, the Saudi Arabian Cultural Bureau and King Abdul-Aziz University, to fund my PhD study and provide this precious experience to pursue my postgraduate studies at the University of Nottingham.

From the bottom of my heart, I would like to thank the closest people in my life, my husband and my son, for their endless love and sacrifices. Last but not least, thanks to my parents, Nabeel Ismail and Hajar Abu-AlKhair, for their motivational support and prayers. Thank you is not enough.

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Abbreviations

CEs	Contextual Enhancers
CEP	Contextual Enhancement Package
CFs	Contextual Factors
CI	Confidence Interval
CMA	Conventional meta-analysis
CSP	Chartered Society of Physiotherapy
EBM	Evidence-Based Medicine
ENTREQ	Enhancing Transparency in Reporting the Synthesis of Qualitative Research
ES	Effect Size
EULAR	The European Alliance of Associations for Rheumatology
GPs	General Practitioners
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HCP	Healthcare provider
JAMA	Journal of American Medicine Association
JBI	Joanna Briggs Institute
JBI-QARI	Joanna Briggs Institute - Qualitative Assessment and Review Instrument
MRC	UK Medical Research Council
OA	Osteoarthritis
OR	Odds Ratio
PBA	Pearson-Based Approach
PCE	The Proportion attributable to Contextual Effect
PICO	Population, Intervention, Comparator, Outcome
PPI/E	Public Patient Involvement and Evaluation
PPI	Public Patient Involvement

PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analysis
RCT	Randomised Controlled Trial
RR	Risk Ratio
SD	Standard Deviation
SMD	Standardised Mean Difference
SR	Systematic Review
WHO	World Health Organisation

Chapter 1. Introduction and Background

1.1 Placebo and placebo effect

1.1.1 Definition and key terms

“Placebo” is one of the most widely used words in medicine. There are multiple definitions for placebo. From the biomedical perspective, it is defined as any inert substance or therapeutic procedure that does not have a direct specific effect on the disease process, so it is not expected to affect its manifestations (Shapiro, 1964, Abhishek and Doherty, 2016).

However, following the administration of a placebo, people might respond to the procedure or the process of receiving treatment. The “placebo effect” is therefore defined as a clinically beneficial effect that follows the administration of an inert treatment. It involves different biological mechanisms and affects different body systems that are triggered by the placebo therapy and the therapeutic context around the patient (Benedetti, 2014b). An additional definition proposed by Shapiro (1997) refers to “the changes produced by things objectively without specific activity for the condition being treated”. Therefore, the placebo effect should not be misinterpreted as patient bias, regression to the mean or spontaneous remission.

“Placebo response” is often used interchangeably with the placebo effect, but the main difference is that “placebo response” indicates the change from baseline. As illustrated in Figure 1-1, the placebo effect, however, is the difference in response between doing nothing (i.e., no treatment) and giving placebo treatment (i.e., giving a sham treatment) (Kirsch, 2013).

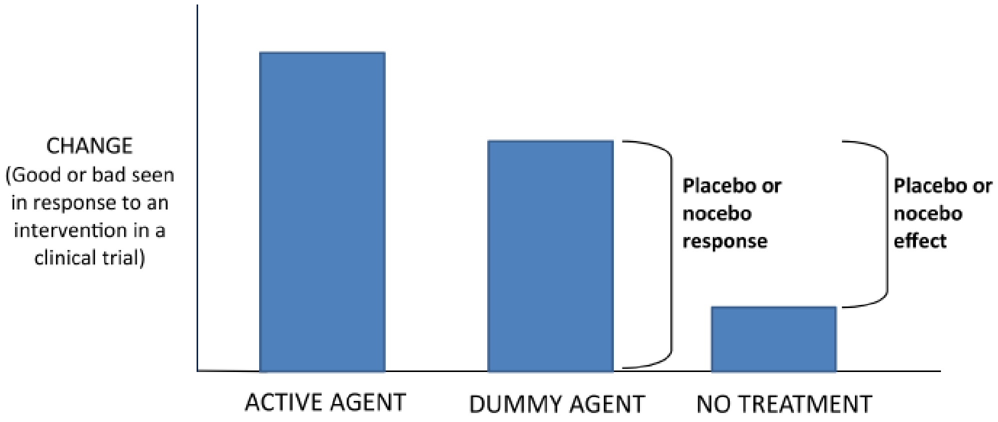


Figure 1-1. Diagrammatic representation of the meaning of placebo/nocebo response and placebo effect (Kirsch, 2013)

Daniel Moerman suggested to substitute the term “placebo response” with “meaning response”, to emphasize the importance to the individual of the surrounding context and the therapeutic ritual and not the inert treatment per se (Moerman, 2002). Meaning response, reflects the meaning that the individual attributes to a characteristic encountered in the treatment context, rather than the characteristic itself. A classic example of meaning response is the effect of tablet colour and number on patient response (Doherty and Dieppe, 2009). A study by De Craen et al. (1996) found that green and blue tablets caused sedation, while red and orange have stimulant effects, and this variation is reflected in the colour of marketed medications, perhaps boosting their efficacy. However, the colour effect is not generalisable, and colours have distinct meanings and effects in different cultures and contexts. In a study conducted in Italy on sedative placebos, blue tablets had the usual sedative effect in women but not in men (Cattaneo et al., 1970). It was suggested that this was possibly because blue is the national football team colour and associates in men with excitement feelings. Hence, the meaning given to a colour by an individual, not the colour itself, has an impact on the outcome.

This highlights the shift in the placebo concept from inert agents or pills to the concept of stimulation within a psychosocial context. Olesen (2015) suggested replacing the term placebo with “context-mediated effect”, which describes the effect of total care experience encompassing the treatment. Similarly, Enck et al. (2013) stated that placebo response is not restricted to placebo treatments but can also be an outcome of any active treatment. Di Blasi et al. (2001) claimed that the following terms are interchangeable: “placebo effects”, “non-specific effects” and “context effects”.

In broad terms, ‘context’ can be defined as the background relevant to a specific event, and it can be distinguished or defined through the characteristics of the event and the individuals experiencing the event (Anderton and Sellers, 1989). The term context in healthcare refers to the total environment surrounding the practitioner-patient encounter, the various rituals around the treatment and the practitioner-patient relation (Lucassen and Olesen, 2016). Therefore, “Contextual effects” suggests the influence of context characteristics on individuals. The following heading (1.2 Contextual factorsContextual factors) explores the concept in detail. Although different opinions still exist regarding the definition of placebo, there appears to be some consensus that it refers to inert interventions that have favourable outcomes.

In contrast to placebo effect, the term “nocebo effect” has been used to refer to the worsening of pre-existing symptoms or the start of new symptoms in response to negative expectations, experience, or communication. The phrases nocebo effect and nocebo response are relatively similar, but the latter phrase occurs as a result of deliberate negative suggestion and/or expectation (Abhishek and Doherty, 2016). Colloca and Miller (2011b) clarified that the nocebo effect refers to the negative psychosocial context around the subject and the treatment and its neurobiological bases, while the nocebo response suggests the expectancy-induced alterations in the subject’s brain-body unit. For instance, the information disclosure regarding potential side effects that can itself contribute to adverse effects (Colloca and Miller, 2011b).

1.1.2 Brief history of placebo

The history of placebo is integral to the history of medicine. The basis of early treatments predominantly emerged from social influences, religious and metaphysical beliefs, and scientific ignorance rather than scientific rationale or assessment of real efficacy (Benedetti, 2014b). Early shamans and physicians recognised that they often helped patients, even if they could not analyse how it all helped.

In their book “The Powerful Placebo: From Ancient Priest to Modern Physician”, Shapiro and Shapiro (1997) revealed illustrations of placebo use across history. Most treatments used in ancient tribes and civilisations were linked to religion and prayers to God(s), and spiritual healing was very commonly undertaken. Some of the medicaments and procedures were unusual. This is exemplified in the use of worms, ants, scorpions, hair, horns and so forth as ingredients to treat maladies. In addition, physicians applied various procedures, such as leeching, cutting, blistering, and heating. Seemingly, all these techniques were applied to please the patients rather than to heal the disorder. Many physicians often shared a strong belief and positive expectation of the effectiveness of such treatments, which in itself may have strengthened the expectancy of patients. These were in line with Latin history, the etymology of the word placebo suggests “I shall please” whereas nocebo means “I shall harm” (Colloca and Miller, 2011b, Benedetti et al., 2007).

The first use of a placebo in modern randomised controlled trials (RCTs) (to my knowledge) was in 1945 as a standard control to confirm the effect of streptomycin in pulmonary tuberculosis (Crofton and Mitchison, 1948). A famous anecdote in placebo literature is about the anaesthesiologist Henry Beecher, who was treating wounded soldiers during World War II. One day in a field hospital, while looking after injured soldiers, he ran out of morphine. A nurse suggested that he could administer a saline solution and tell the injured soldiers that they were getting a strong pain reliever. Surprisingly, the placebo saline was quite successful with the patients and allowed them to withstand the pain (Bensing and Verheul, 2010). Henry Beecher was amazed by that phenomenon, and after the war he focused his work on placebo research. In 1955, Beecher published “The Powerful Placebo” paper in the Journal of American Medicine Association (JAMA), which concluded that at least 35% of the treatment response is due to the placebo response (Beecher, 1955). Indeed, Hippocrates had recognised the effect of the physician on patient wellness. He said, “The patient, though conscious that his condition is perilous, may recover his health simply through his contentment with the goodness of the physician” (Hippocrates–Vol, 1923).

Later, in the 18th century, when it was recognised that most substances given to patients by doctors were ineffective, the term placebo became linked to any substance that the physician believed or knew was not remedial for the medical condition (i.e., powerless placebo) (Shapiro and Shapiro, 1997). The irrationality of many treatments are not features of the past, and various ineffective therapies may exist today. Most of them fall within the category of alternative and complementary medicine, which applies to physical procedures, pharmacological agents and psychological interventions (Benedetti, 2014b). However, over the last four decades, scientific interest in the placebo effect has grown considerably and the number of citations listed on PubMed for ‘the placebo effect’ has risen from 214 in the 1970s to 86607 at 2019. The primary basis for research on placebo is to harness the power of placebo effect to enhance the overall therapeutic outcomes in clinical practice.

1.1.3 Research and clinical practice

The use of placebo as an intervention in its own right has been controversial throughout history. Some medical organisations have endorsed it (Guess et al., 2002). However, Richard Cabot, in 1903, concluded that intentional use of placebo is deceptive and unprofessional and therefore should be avoided. The “placebo paradox” introduced by Newman (2009) argues that although the use of a placebo may be unethical, it is also unethically not to use something that heals. Afterwards, he suggested a solution for this dilemma which implies the adoption of the meaning response or placebo effect in medicine, as long as the administration is open, honest and believes in its potential healing power (Newman, 2009). Another possible resolution of the ethical dilemma might derive from the "open-labelled placebo" effect. Placebo interventions can influence symptoms even without concealment or deception. For example, patients with irritable bowel syndrome experienced a significant beneficial effect even though they were told they were taking placebo pills, compared to a control group who received no pills (Kaptchuk et al., 2010). In order to improve the treatment outcomes by using the placebo properties, Enck et al. (2013) suggested that once a drug effect is approved and in clinical use, the placebo effect should be maximised by harnessing patients’ expectations and learning methods. Moreover, they claim that placebo responses could be personalised by considering the individual’s personality, past medical history and treatment experience (Enck et al., 2013).

The randomised, double-blind clinical control trial establishes its own specific context. The invitation letter and informed consent that provide the participants with written information describing both the rationale and content of interventions can modify participants’ understanding of their condition and possible treatment. Also, assessment tools such as questionnaires might alter understanding or change expectations. The main interest in most of the published RCTs is to show that the “active treatment” is superior to “placebo” in regards to effectiveness (Price et al., 2008). In RCTs, the improvement manifested in the control groups may occur in response to non-specific effects. Hawthorne effect (i.e., the effect due to being observed) is an example of a non-specific effects in which the person’s behaviour changes when they know they are being observed (McCarney et al., 2007). Moreover, the mode of delivering the intervention to the study participants, the therapeutic rituals and the treatment context may all influence the outcomes.

Similarly, the previous effects could manifest in clinical practice, such as the Halo effect. The Halo effect is a form of cognitive bias whereby one specific characteristic or trait is used to make an overall judgement of that person (Kirsch, 1999). The Halo effect is one of the context factors that underpin patients' expectations of health practitioners (Kirsch, 1999). This effect is exemplified in the judgment about health practitioners' quality, such as experience and skilfulness, influenced by looking professional and having good communication skills. This contextual effect can also be detected in a person's expectancies and judgement of a positive individual as intelligent, trustworthy and friendly (Wade and DiMaria, 2003).

The placebo effect is variable depending on the context in which the placebo is administered. For instance, the Vase et al. (2002) meta-analysis found that greater placebo effects are detected when the placebo mechanism is specifically studied rather than included as a comparison intervention. In studies of placebo mechanisms, the instructions provided to the participants receiving placebo intend to enhance expectation for the effectiveness of the placebo (i.e., ‘the pill you have just received is known to powerfully reduce pain in some patients). In contrast, in placebo-controlled studies, the participants are instructed that they will receive either the studied intervention or a placebo. Vase et al. (2002) noted a large effect size (Cohen’s *d*=0.95) in studies designed to specifically investigate placebo mechanisms and a small effect size (Cohen’s *d*=0.15) in studies of placebo as a comparative intervention.

Indeed, a complex set of phenomena are responsible for any clinical improvement following treatment. Different explanatory psychological theories such as classical conditioning, expectancy, and learning and interaction could explain how contextual factors (CFs) trigger placebo and nocebo effects (Rossettini et al., 2018b). A brief explanation of these theories is available under the Psychological mechanisms subheading (page 19).

1.2 Contextual factors

1.2.1 What do the contextual factors represent?

The term context originates from the Latin “contexture” meaning “to weave together” and the term contextual enhancers/healing is used to express the circumstances that form the setting for an event and in terms that it can be fully understood. In 2008, Kaptchuk introduced the concept of ‘contextual healing’ to outline the clinical encounter benefits, which lead to the improvement of patient conditions (Miller and Kaptchuk, 2008). The factors which enhance the healing through the clinical context, as distinct from the treatment specific effect, are entitled “contextual enhancers” (Miller and Kaptchuk, 2008). The clinical context is influenced by five main dimensions: the practitioner, the patient, the practitioner-patient interaction, the treatment and its delivery, and the environment characteristics (Di Blasi et al., 2001) (Figure 1-2):

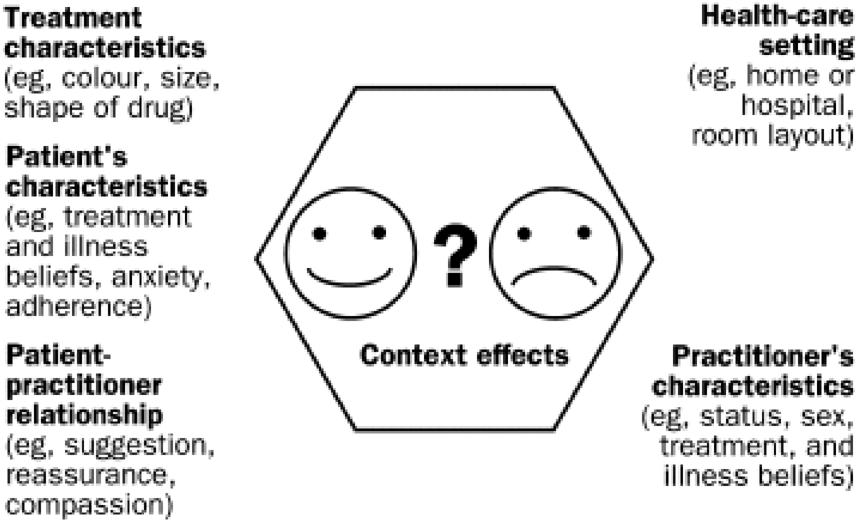


Figure 1-2. Contextual enhancers (Di Blasi et al., 2001)

Practitioner characteristics

The physician has even been called a placebo (Patel, 2017). The health-providers' words and suggestions have the power to promote patient recovery (Benedetti, 2002). For instance, how positively the suggestion "you should be better in a few days" would resonate with the patient in contrast to the negative words "I am not sure if the treatment I am going to give you will have an effect". In clinical practice, physicians may use affective communication (i.e., communication aimed at putting a patient at ease and releasing their emotions), and instrumental communication (i.e., communication aimed at providing information and influencing a patient's cognitions) (Van Dulmen and Bensing, 2002). Physicians who are confident, attentive, warm, optimistic about treatment, providing reassurance about prognosis, and displaying the desire to follow-up have a more substantial placebo response (Abhishek and Doherty, 2013).

Although some of the health practitioner’s characteristics could be innate intrapersonal skills, they can be developed through instruction and practice. For instance, clinical empathy can be accomplished by professional training on a set of skills or competencies rather than a personality trait that a person either has or not (Kiosses et al., 2016). Expressing empathy in clinical encounters involves four dimensions: cognitive dimension to identify another’s feeling; a moral dimension, which suggests the inner encouragement to empathise; emotive dimension to share feelings; and behavioural dimension to communicate an understanding response (Morse et al., 1992, Mercer and Reynolds, 2002). A systematic review (SR) of the effectiveness of empathy training in medical and nursing students found that 68% of the participants demonstrate statistically significant empathy improvement (Bas-Sarmiento et al., 2020). This finding must be interpreted with caution because the SR examined variable training programs (i.e., the dimension of empathy training and length of the intervention), and the included studies were variable in design (i.e., reviews, randomly controlled trials, and a qualitative study).

Patient characteristics

Patients’ beliefs and expectations of treatment outcomes are fundamental CFs (Colloca and Miller, 2011c). A SR of the literature reported that patients’ positive expectations of recovery were associated with better health outcomes (Mondloch et al., 2001). The review included various clinical conditions (i.e., chronic pain, cardiac conditions, and psychiatric conditions) and study designs. However, the systematic search was conducted in the MEDLINE database only and included moderate-quality primary studies dated before 1998.

The patient perception that the healthcare provider is competent and the knowledge of being treated are some of the determinants of CFs' effect (Abhishek and Doherty, 2013, Colloca et al., 2004, Linde et al., 2007). These factors were evident in testing the effect of anxiety-reducing drugs and pain killers. It was found these drugs were less effective when infused secretly than when the patient knows they are receiving them (Petrovic et al., 2005, Amanzio et al., 2001). Amanzio et al. (2001) assumed that the placebo in that study to be the equivalent of 0.14 mg of buprenorphine, 31 mg of tramadol, or 12 mg of ketorolac. Patient expectations were accountable for the variability of the response to analgesic agents and contributed to the effectiveness. Furthermore, some illness characteristics (i.e., pain level at baseline), and individuals' personality factors (i.e., anxiety and optimism) may impose an effect on placebo response(Zhang et al., 2008, Watson et al., 2012). An example is that the higher baseline pain, the higher the PR.

Practitioner-patient interaction

This is a special professional and social interaction whereby patient health, and well-being can be promoted. The quality of the interaction determines the magnitude of the placebo response (Hróbjartsson and

Gøtzsche, 2004). An essential aspect of the practitioner-patient interaction is the cognitive and affective reassurance the practitioner provides to patients. Nevertheless, affective reassurance alone may not be helpful or valued by some patients (Walsh, 2016). Although face-to-face communication is not necessary for providing information to patients, patients do prefer to receive information from their health practitioner directly compared to written or electronic information (Terry and Healey, 2000). This emphasizes the importance of the clinical encounter.

The utilisation of appropriate verbal and non-verbal communication with patients in clinical settings can significantly boost patients' expectations of the therapy (Bishop et al., 2011, Myers et al., 2008a, Linde et al., 2007). The secondary analyses of previous RCTs indicated that high expectations for recovery from low back pain were associated with greater functional improvement ($\beta = 0.96$, 95% CI = 0.56, 1.36) (Myers et al., 2008a, Linde et al., 2007). Greenfield et al. (2010) examined the meaning of caring from patients' perspectives undergoing physical therapy. The study disclosed that physiotherapists compromise care as a core value in their practice (Greenfield et al., 2010). The notion of care in health practice refers to empathy, concern and consideration for others' needs and values (APTA, 2004). One of the defining features of care offered by skilled healthcare providers is touch (Lauterstein, 2004). Touch may be one of the most powerful and personalised methods of communication (Fritz and Fritz, 2020). Healthcare providers utilise two forms of touch in their practice: therapeutic and non-therapeutic touch. The latter type of touch tends to be spontaneous in many cases (i.e., shaking hands, stroking, or touching during casual conversations). Patients reported that they felt treated as an individual person if their therapist had made interactions in the form of non-therapeutic touch (Hiller et al., 2015).

The opposite is also true. Weak interaction or using words that induce negative expectations in the patient could lead to nocebo effects and worsening of the condition (Benedetti, 2007). A RCT investigated the effect of verbal suggestion during the administration of epidural anaesthesia for childbirth pain (Varelmann et al., 2010). One hundred and forty healthy women at full term were randomised to two styles of procedure description: “We are going to give you a local anaesthetic that will numb the area, and you will be comfortable during the procedure”, or “You are going to feel a big bee sting; this is the worst part of the procedure”. The pain was assessed immediately after the injection using verbal analogue scale scores. Median pain scores were lower when reassuring words were used compared with the nocebo framing style (3 [2–4] vs 5 [3–6]; $P < 0.001$) (Varelmann et al., 2010).

Interestingly, the primary reason for lawsuits in the United States last century was not medical injury, but the doctors failure to communicate effectively with their patients (Beckman et al., 1994). A program evaluation for triage in orthopaedic services for patients with hip and knee OA reported that some patients were initially quite disappointed or potentially unsatisfied with the fact that they did not get to see an orthopaedic surgeon “...patients might feel fobbed off if the purpose of the consultation has not been explained to them” (GP) “ (Abbott et al., 2019). Hence, effective and clear communication with patients is needed to encourage compliance and recovery.

Healthcare providers’ implementation of a patient-centred approach in clinical consultations positively affects consultation processes on a range of measures. When providers focus on patient preferences situated within social contexts (in contrast to a focusing on the disease) and share control of management options with the patient, they can clarify patients’ concerns and beliefs, communicate about treatment options and express empathy for patients (Dwamena et al., 2012).

Treatment characteristics

The ritual of administering treatment might be better identification of the treatment characteristics of CFs. The treatment frequency of administration, costs, colour, and branding all affect the magnitude of placebo response. For instance, a greater number of tablets, renowned brands, and higher cost may all increase the placebo response (Zhang et al., 2008). Waber et al. (2008) studied the effect of commercial features (i.e., price) on analgesic response to placebo pills on 82 healthy paid volunteers. After randomisation, half of the participants were informed that the drug had a regular price and half were told that the price had been discounted. The randomised trial ensured the blinding of participants to the study purpose and researchers to group assignment. Experimental pain was applied to the wrist, and the mean change in visual analogue scale rating was assessed before and after taking the pill. On assessment, pain reduction was greater for the regular-price pill ($P < 0.001$) (Waber et al., 2008). The findings may justify the popularity of high-cost therapies over inexpensive alternatives.

Additionally, the route of delivering the treatment has a great placebo effect especially with invasive techniques (i.e., injection, acupuncture, and surgery) (Kaptchuk et al., 2006, Doherty and Dieppe, 2009). A relevant example of the effect of invasive methods is the arthroscopic debridement and arthroscopic partial meniscectomy for knee OA. In the early 2000s, rigorous studies with strict blinding of patients and assessors confirmed that arthroscopic debridement for knee OA was no better than a sham arthroscopy in relieving knee pain or improving functional status (Katz et al., 2014). Also, patients who underwent arthroscopic partial meniscectomy did not show more improvement than the sham procedure (Yim et al., 2013). Nevertheless, the role of knee arthroscopy is controversial. Although it provides symptom relief, studies suggest that such improvement could be attributable to a placebo effect. Perhaps, the patients' pain is relieved when they see and feel that something is applied at the site of symptoms.

Environment characteristics

The treatment context or environment mediates therapeutic effectiveness (Walsh, 2016). Medical visits appear to have health-promoting effects beyond that of the actual medical intervention (Van Dulmen and Bensing, 2002). The influence of the healthcare setting in promoting patient recovery (i.e., environment, architecture, interior design) has been considered in establishing healthcare centres from the medieval era (Taheri, 2021). Architectural engineers aim to design healthy environments that promote well-being in hospitals and health centres and consider the patients’ conditions attending various departments and clinics (i.e., oncology, paediatrics, women’s clinic, surgery) (Dilani, 2006, Walden, 2006). Also, the clinic’s interior design elements (i.e., room arrangement, colours, and light) can be adjusted according to the consumers’ physical and psychological needs (Forsgren, 2005). Pleasant outside landscapes, soothing sounds, artwork and aromas can convey positive distractions for patients and staff (Iyendo et al., 2016). Moreover, the social environment in health care centres should represent a pleasant and peaceful environment, and employing welcoming, professional, and supportive staff can help patients to feel comfortable (Bishop et al., 2017). The last section of the following heading (CFs physiotherapy management of osteoarthritis) demonstrates some strategies for improving the five dimensions of CFs in physiotherapy settings (see page 59).

1.2.2 How do the contextual factors work?

The CFs of the therapeutic encounter can trigger different changes at neurobiological, perceptual, and cognitive levels. The CFs directly influence the quality of the therapeutic outcomes, with positive CFs reducing pain through placebo effects and negative CFs aggravating pain through nocebo effects (Rossettini et al., 2018b). Placebo effects are genuine psychobiological influences attributable to the overall therapeutic context (Finniss et al., 2010). The placebo mechanism can best be explained by the following:

Psychological mechanisms

Cognitive factors are the primary mediators for placebo response (Enck et al., 2013). The principal mechanisms are expectation and conditioning (Meissner et al., 2011). Expectancy is a product of cognitive engagement, and it is influenced by environmental clues, previous experience, verbal instructions, emotional arousal, and interaction with care-providers (Benedetti and Amanzio, 2011). The anticipation of future outcomes triggers internal changes that result in specific experience (i.e., placebo analgesia or nocebo hyperalgesia).

To explain the hyperalgesia induced by the nocebo effect, patients with a chronic musculoskeletal condition may repeatedly seek care for the same subjective complaints, hence adopting unhelpful health-seeking behaviours (Rossettini et al., 2022). They mainly seek out information and symptom relief, and they trust health professionals to offer them. Besides, health professionals are in a strong position to influence their experience and beliefs (Darlow et al., 2013). However, healthcare providers may invalidate a patient’s experience (De Ruddere et al., 2013), provide contradictory explanations about the condition (Mannion et al., 2013), or give a generic diagnosis (Yunus, 2007), which alter the patient’s expectations regarding their illness and the likely outcomes (Thomaidou et al., 2021). Consequently, patients could experience negative emotions (i.e., anxiety, depression) and embrace negative coping strategies (i.e., avoidance of movement, catastrophizing), which lead to worsening of their clinical conditions and symptoms experience (i.e., increased pain and stiffness) (Darlow, 2016). On the other hand, the expectation of forthcoming pain can be modulated by some cognitive and emotional factors such as desire and self-efficacy (Benedetti and Amanzio, 2011).

Conditioning, as described initially by Pavlov (1906), is ‘The repeated occurrence of an unconditioned response to an unconditioned stimulus (salivation after the sight of food) with a conditioned stimulus (a bell ringing) induces a conditioned response (salivation that is induced by bell-ringing alone)’ (Siegel, 2002). Similarly, the clinical environment (hospital smell, white coats, or medications colour or shape) can act as a stimulus, prompting therapeutic responses in the absence of an active treatment (Benedetti and Amanzio, 2011). The role of expectation towards treatment benefits and the placebo effects on the immune response was examined in some trials. Behavioural conditioned immunosuppression was experimentally examined in healthy subjects, conditioned to receive the immunosuppressive drug cyclosporin with a green drink (conditioned stimulus) in four sessions over three consecutive days. A week later, re-exposure to the conditioned stimulus (green drink), but with placebo tablets, induced suppression of immune response as evaluated by the IL-2 and IFN-γ mRNA expression, intracellular production, and lymphocyte proliferation (Goebel et al., 2002). These findings provided evidence of brain-immune system interaction and immunosuppression by behavioural conditioning in humans.

In addition to the expectation and conditioning mechanisms, other coexisting psychological mechanisms may interact to deliver the placebo response, including: previous experience; verbal suggestion; reward mechanism; and observing the treatment effectiveness in others in a social context (Colloca and Benedetti, 2006, Colloca and Benedetti, 2009).

Neurobiological mechanisms

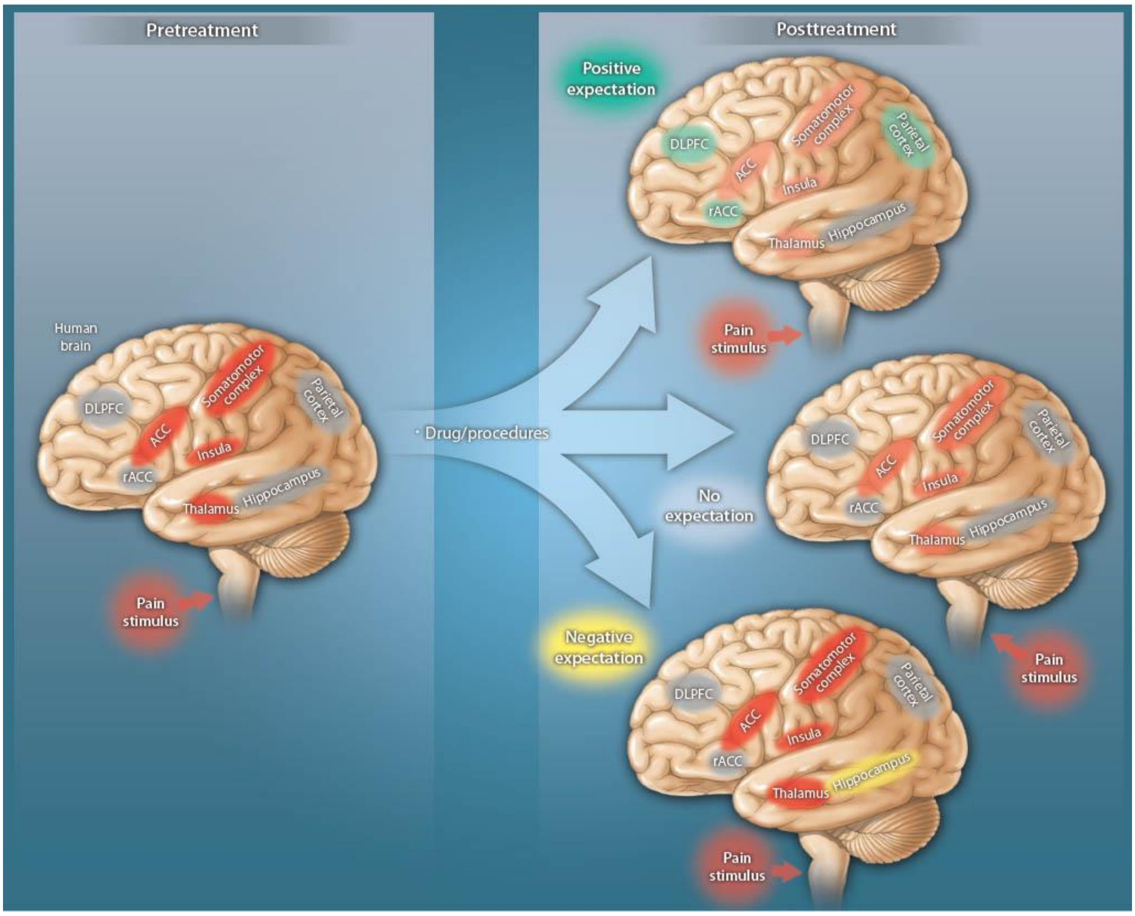
The placebo effect and contextual effect are not `a trick of the mind`. Instead, they result from objective biological changes within the patient (Doherty and Dieppe, 2009). Almost all the brain centres involved in pain processing are stimulated in placebo-induced analgesia (Wager et al., 2004), specifically:

- Frontal cortex
- Limbic system
- Subcortical reward mechanism
- Sub-cortical pain transmission centres
- Descending pain modulatory pathway
- Nociceptive pain processing pathways in the dorsal horn of the spinal cord.

Placebo analgesia implies the pain-relieving effect associated with administering a placebo, which may be a result of the individual's belief in the analgesic effect of an intervention (Levine et al., 1978). The available evidence reveals that placebo analgesia is mediated largely by an increase in endogenous opioids, dopamine and oxytocin and reduction in cholecystokinin and the placebo motor improvement by an increase in endogenous dopamine (Levine et al., 1978, Benedetti, 1996, De la Fuente-Fernández et al., 2001). Though, it should be noted that the mechanisms of placebo effect are generally extrapolated to explain the mechanism of CFs.

Whereas in nocebo response or nocebo hyperalgesia, a marked decrease in endogenous opioids and dopamine secretion occurs, resulting in a flare-up of symptoms (Scott et al., 2008). Since worsening of symptoms are often associated with anxiety, the neuro-hormone cholecystokinin often releases as part of the nocebo response (Benedetti et al., 2006).

A decade ago, the Bingel et al. (2011) brain functional magnetic resonance imaging study found that associated positive expectations and negative expectations activate additional areas in the brain. The response is rather complex than pain processing. Individual patient characteristics (i.e., past experiences, personality traits, emotional state, and genetic factors) could also influence the specific effect of a drug or procedure. Figure 1-3 depicts the brain areas activated by pain and altered expectations. All brains shown in the figure are when a person perceives a painful stimulus (left side of the figure: absence of treatment, right side of the figure: after an analgesic treatment has been given) (Gollub and Kong, 2011). The red colour indicates some brain areas activated by the pain stimulus (i.e., thalamus, insula, somatomotor complex, and anterior cingulate cortex). The pain-activated brain areas are diminished proportionately with pain relief as indicated by lighter colour (darker red = most highly active). Green shows the active brain regions (i.e., dorsolateral prefrontal cortex, parietal cortex, and rostral anterior cingulate cortex) during the positive expectation of treatment outcome, and yellow shows the active brain region (i.e., hippocampus) during negative expectation.



DLPFC: dorsolateral prefrontal cortex; ACC: anterior cingulate cortex; rACC: rostral anterior cingulate cortex.

Figure 1-3. Brain areas activated by pain and expectancy (Gollub and Kong, 2011)

1.2.3 **Previous publications about contextual factors**

The table in Appendix 1 depicts the conclusions of SRs (= 13), narrative reviews (= 2) and an expert consensus concerned with CEs in healthcare practice published in the last two decades (between 2001 and 2018). The reviews were obtained from searching the five databases used in the SR search, hand searching of key journals and snowballing -tracking down references in articles and following the suggestions which some databases provide (i.e., Elsevier). The two most recommended and mentioned CEs throughout the available literature are the meaningfulness of interaction between practitioners and patients and adopting an empathic behaviour when dealing with patients. Reviews also highlight the importance of practitioner communication skills and providing patients with information and management options and engaging them in shared decision-making. Furthermore, professionalism is one of the CEs that has been associated with higher patient satisfaction (see Figure 1-4).

Meaningfulness of interaction	**Empathy**	**Information provision**	**Positive communication**	**Professionalism**
• Kelley et al. (2014) • Derksen et al. (2013) • Pinto et al. (2012) • Henry et al. (2012) • Griffin et al. (2004) • Beck et al. (2002) • Van Dulmen and Bensing (2002)	• Howick et al. (2018b) • Evers et al. (2018) • Testa and Rossettini (2016) • Mistiaen et al. (2016) • Derksen et al. (2013) • Pinto et al. (2012) • Neumann et al. (2011)	• Evers et al. (2018) • Testa and Rossettini (2016) • Beck et al. (2002) • Van Dulmen and Bensing (2002) • Di Blasi et al. (2001)	• Howick et al. (2018b) • Mistiaen et al. (2016) • Pinto et al. (2012) • Henry et al. (2012) • Beck et al. (2002)	• Henry et al. (2012) • Pinto et al. (2012) • Di Blasi et al. (2001)

Figure 1-4. The most common contextual factors stated across the previous reviews

Among those recent publications, the Mistiaen et al. (2016) SR of the effect of practitioner-patient communication on pain included the highest number of trials (19 RCTs and 32 quasi-RCTs). Although the outcome measure was pain through the included trials, only the summery results of eight trials were tabulated in an external review supporting information, and the results have not been quantitatively analysed. The included trials varied in quality and methodological rigour. Moreover, the communication interventions used multiple elements (i.e., procedural preparation, modifying patients' expectations, and adjunct therapies with verbal intervention). The review concluded that clinician communication with patients has a small but potentially important effect on patients' acute pain (Mistiaen et al., 2016). However, the authors claim that it is unclear what the effective components of communication are.

Just before the beginning of this research project, in 2018, the Georgopoulou et al. mixed-methods SR was published. They examined the impact of practitioner-patient communication on patient outcomes in rheumatology. However, only one out of ten studies in that review included patients with OA (39% of the study sample). All of the quantitative studies included in the SR were cross-sectional surveys. Moreover, the conditions analysed in the qualitative studies included systemic lupus erythematosus, rheumatoid arthritis, and fibromyalgia. In their detailed assessment of the methodological quality of included studies, Georgopoulou et al. (2018) showed that most of the studies (eight of ten) were of excellent quality by utilising two assessment tools depending on the study method. The SR concluded that active involvement of patients in consultations and higher levels of trust in the physician were linked to greater treatment satisfaction with fewer side effects from medications, lower disease activity, better global health, and less organ damage accrual (Georgopoulou et al., 2018).

In 2017, twenty-nine internationally recognised placebo researchers from the society for interdisciplinary placebo studies (SIPS) participated in a survey and meeting to develop recommendations about the evidence-based and ethical use of placebo and nocebo effects for clinical practice (Evers et al., 2018). First, the survey was developed based on a literature review of empirical evidence on the possible clinical application of placebo. The survey questions focused on the prescription of placebo and open-label placebo, nocebo effects and patient-clinician communication. Then, the statements that received high agreement (mean score ≥8 on a 10-point scale) were discussed with the provided written comments in the experts' meeting. Lastly, the expert consensus on the survey results and the discussion during the meeting formulated a list of recommendations. In summary, to maximise placebo effects and minimise nocebo effects, they recommended healthcare provider training in patient-clinician communication that is characterised by trust and empathy and to avoid deception (Evers et al., 2018). This recommendation appears reliable since it was based on multiple methods for gathering the data.

As reviewed above, current literature suggests a relevant clinical role and positive impact of CFs in patients experience after the clinical encounter. Mindful implementation of CEs represents a promising opportunity to enrich any well-established therapy in the healthcare setting within the ethical frame.

1.2.4 Operationalisation of the contextual enhancement

As communication is a central part of every interpersonal encounter within healthcare, medical professionals are required to learn communication skills as part of their training. However, research has shown that empathy provision was insufficient in medical school and residency personnel, which impacts on professionalism (Neumann et al., 2011). Over the last decade, several training resources have been established to foster effective communication and optimise CFs in the practitioner-patient encounter. Acknowledging the complexity of CFs properties and their multiple interacting components (i.e., range of behaviours targeted, the number of factors involved, skills required by those delivering the intervention, settings, and the flexibility in delivering the intervention), there might be pedogeological challenges in teaching CFs to medical students and professionals. Though, different institutes used different methods to facilitate contextual enhancement. Below are four examples of such training programs.

In 2015, the University of Oxford established the Oxford Empathy Programme (OxEmCare) that offers accredited training related to empathy for practitioners and managers in health and social care (OxEmCare, 2016). OxEmCare is an interdisciplinary research group that examines the effectiveness of empathic health care and influences healthcare policy and practice to support empathic care (OxEmCare, 2016). There are multiple definitions for empathy in the clinical setting.

In some OxEmCare publications, they define therapeutic empathy and how it might be attained. In brief, therapeutic empathy refers to empathy that demonstrates its therapeutic benefits (Howick et al., 2018b), and it must involve three features: understanding, communicating and acting (Howick et al., 2018a). First, understanding what an illness means to a patient is required for precise diagnosis, prognosis and decision-making. Second, communicating that understanding to avoid doubts or anxiety about whether the patient has been understood. Third, acting on the shared understanding through prescription or referral to maximise the therapeutic benefits (Howick et al., 2018a). Also, the Krznaric (2014) empathy book defined empathy as the ability to understand and share another person's perspectives and feelings and utilising that understanding and emotions to guide future actions. The emotions that people may experience in response to others' suffering include compassion, sympathy and empathy (Jeffrey, 2016). The OxEmCare web page includes valuable updated resources about empathy research findings and training.

Researchers in medicine and psychology from different organisations in the UK (i.e., University of Oxford, University of Southampton and Keele University) have developed an online training program for healthcare practitioners called "*Empathico*" (Smith et al., 2020). Empathico is an empathy and optimism project designed to enhance patient satisfaction and health outcomes for patients with OA through appropriate, effective and acceptable training of primary healthcare practitioners. This project was developed from two older projects known as "*KEPe-Warm*" and *"Empathica"*: Expectation Management for Patients with OA.

The *Empathico* project commenced in 2018, aiming to develop a brief online training to teach healthcare providers how to express empathy in their consultation and encourage patients to have positive-realistic expectations to help improve the management of OA pain. In 2019, they published the protocol of the feasibility trial for the online training package for primary care practitioners (Bishop et al., 2019). In 2020, the training program underwent acceptability testing. The development phase of Empathico is now complete and the project is now entering a feasibility trial phase (Smith et al., 2021). The online training of primary care providers on Empathico is expected to considerably improve OA patients' experience since the project development involved a rigorous person-based approach that integrates theory, evidence and primary qualitative research (Yardley et al., 2015). Also, it targets most of the CFs identified in this research project (i.e., empathy, patient expectation, positive communication, providing relevant information, and active patient involvement).

In addition, Leicester University provides empathy training as part of the foundation year teaching for medical students (Leicester, 2022). The Clinical Empathy Programme is facilitated alongside other modules and involves a series of seminars, lectures and tutorials that focus on the role of clinical empathy in medicine. The medical students are expected to use their communication and empathy skills and medical knowledge to better understand how patients experience illness and disease and provide optimal management. A SR of RCTs that assessed the effects of empathy-enhancing interventions in health education and training showed that medical students benefitted more from such training than did established doctors (SMD 0.62, 95%CI 0.38 to 0.85 versus SMD 0.33, 95%CI 0.18 to 0.47, respectively) and that longer interventions (>4 hours) were the most effective (SMD 0.57, 95%CI 0.32 to 0.82) (Winter et al., 2020). Hence, teaching medical students to be empathic doctors is an essential element of their training, and perhaps undergraduate training is the appropriate phase to learn about the importance of other CEs as well.

Moreover, Physioplus delivers a communication skills and medical interview online training program for physiotherapy clinicians and students (Fourie, 2020). The program implements a patient-centred approach using the Calgary Cambridge model (Kurtz and Silverman, 1996). The Calgary model involves a structured plan for medical consultation that integrates communication skills, information gathering, and explanation and planning. It was highly rated by the participants who undertook this self-paced course (average 4.5/5). The average duration to complete this online program is 16 to 18 hours. Furthermore, the mixed-method review by Zulman et al. (2020) recommended five practices to enhance practitioner presence and meaningful connection with patients in the clinical encounter (see Figure 1-5). Nevertheless, this model requires evaluation and validation of outcomes.

Prepare with intention.

- Familiarize yourself with the patient you are about to meet.
- Create a ritual to focus your attention before a visit.

Are you prepared for a meaningful interaction?

Listen intently and completely.

- Sit down, lean forward, and position yourself to listen.
- Don't interrupt. Your patient is your most valuable source of information.

What does your patient say when uninterrupted?

Agree on what matters most.

- Find out what your patient cares about and incorporate these priorities into the visit agenda.

What are your patient's health goals, now and in the future?

Connect with the patient's story.

- Consider the circumstances that influence your patient's health.
- Acknowledge your patient's efforts, celebrate successes.

How can you contribute positively to your patient's journey?

Explore emotional cues.

- Tune in. Notice, name, and validate your patient's emotions to become a trusted partner.

What can you learn from your patient's emotions?

Figure 1-5. Recommended practices to enhance practitioner-patient connection (Zulman et al., 2020)

1.3 Osteoarthritis

1.3.1 Overview of the nature of osteoarthritis

Osteoarthritis (OA) is the most common form of arthritis affecting middle-aged and older-adults, and a major cause of disability worldwide (Song et al., 2006, Van Dijk et al., 2009). There are several definitions for OA depending on the primary features which describe it, specifically: pathological changes (i.e., the tissues involved in the disorder); imaging changes (e.g. depicted on MRI and radiograph); physical signs (these vary according to the joint involved); and associated symptoms (particularly usage-related pain, stiffness, reduced function) (Doherty et al., 2016b). The most concise yet comprehensive definition for OA is that it is a common complex disorder of synovial joints with multiple risk factors and variable phenotypic expression (Doherty et al., 2016b). Though initially considered as a degenerative disease resulting from wear and tear that occurs with ageing and inevitably progresses, it has been observed that:

- There is a strong association between ageing and OA, but OA is not inevitably a consequence of ageing.
- OA is the inherent repair process of synovial joints.
- The site of primary insult may be any tissue in the synovial joint.
- The outcomes of OA depend on the balance between the severity and chronicity of the insult and the effectiveness of the repair process.
- There is a broad spectrum of severity of OA and variable involvement of joint tissues.

- Asymptomatic OA is especially prevalent at small joints (i.e., finger joints, lower cervical spine), but also is common in larger weight-bearing joints (i.e., knee and hip) (Doherty et al., 2016a).
- Symptomatic OA is related not only to the joint damage and repairing process but also central pain abnormalities (Akin-Akinyosoye et al., 2020).

1.3.2 Epidemiology of osteoarthritis

The estimation of OA prevalence varies depending on the population investigated, the specific joint(s) studied, and the definition of OA used in the study. There are three main parameters to describe OA in epidemiological studies: clinical, radiographic and pathological (Johnson and Hunter, 2014). Therefore, there is some difficulty in determining the exact prevalence of OA. By way of illustration, the World Health Organisation (WHO) global estimate show that symptomatic OA is prevalent in 18% of women and 10% of men over the age of 60 (WHO, 2019), while the Hospital for Special Surgery reports indicate that 15% of the world’s population have OA (HSS, 2018). In the UK, Versus Arthritis (previously Arthritis Research UK) estimated that the number of people who sought treatment for OA in 2013 reached 8.75 million adults (≥ 45 years) (ARUK, 2013), which equates to 14% of the entire UK population in that year according to the Office for National Statistics (Large, 2015).

Since OA is a chronic condition, an incident case may continue to prevail for the remainder of the patient’s life. In other words, OA patients may have to deal with OA symptoms for nearly 30 - 40 years of their life. However, some OA symptoms may improve with time, and this often occurs in hand and knee OA but to a lesser extent hip OA (Doherty et al., 2016b).

OA incidence is predicted to increase in the future mainly due to the increased prevalence and incidence of obesity and the ageing population (Zhang and Jordan, 2010). Consequently, the socio-economic burden would be enlarged if the increased incidence is not addressed as OA-related diminished quality of life, loss of productivity and considerable financial costs of care have been reported (Hubertsson et al., 2017, Rabenda et al., 2006). Although there is no clear estimate of the global economic burden of OA, worldwide, it was ranked as the sixth leading cause of years of living with disability, accounting for 3% of the overall global years of living with disability (Woolf and Pfleger, 2003).

1.3.3 **Risk factors**

OA is a complex joint condition for which many risk factors have been recognised. The susceptibility of an individual to OA increases with having multiple risk factors (Felson et al., 2000). The risk factors for OA can be classified according to their nature: local versus systemic and modifiable versus non-modifiable. Knowing the risk factors of OA may provide therapeutic opportunities for improving primary treatment outcomes that target the modifiable factors. The following section illustrates the factors as systemic factors that increase the risk of OA at any joint site and local factors that predispose certain joints to OA. Figure 1-6 depicts the predominant risk factors. Naturally, the development and progression of OA result from an interplay between various systemic and local risk factors (Kerkhof et al., 2014).

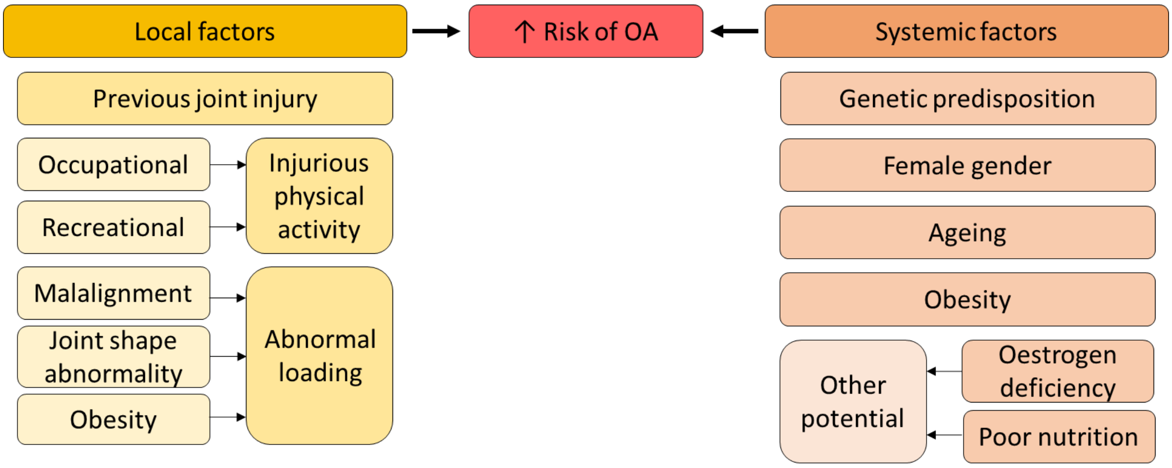


Figure 1-6. Local and systemic risk factors for OA

Systemic risk factors

Genetic predisposition profoundly determines OA development. Rare genetic single gene mutations can critically influence synovial joint morphogenesis and result in joint damage and OA in early life, whereas common polymorphisms in the general population may lead to more subtle heritable joint shape variations (Wilkinson and Zeggini, 2021). Such variations in joint shape can be measured on plain radiographs

(Solomon, 1976). These subtle variations in joint shape predispose to degenerative changes occurring in hip and knee OA (Doherty et al., 2008, Haverkamp et al., 2011). The estimated heritability of OA lies between 30% and 65%, with the risk of OA increasing with having a first degree relative affected by OA (Warner and Valdes, 2016). Nevertheless, the strength of association for genetic risk factors can vary by joint. For example, the heritability for hip OA (60%) is higher than the genetic preponderance to knee OA (45%) (Spector and MacGregor, 2004).

Additionally, ageing and female gender are recognised systemic risk factors for OA (Felson et al., 2000). Gender-specific variations in the prevalence of OA have been investigated, and they vary by age group and joint affected. Women, especially those over 55 years old, are at high risk of knee OA, but men have a significantly reduced risk of knee and hand OA and a greater risk of hip OA at younger ages (Srikanth et al., 2005). In older adults (age 70–75 years), hip OA is more common in women (Prieto-Alhambra et al., 2014), so overall, it is the one site where male and female prevalence is similar.

Obesity increases the risk of OA by two to three-fold (Blagojevic et al., 2010). The association of obesity with hip and knee OA might be attributed largely to abnormal loading on the joints (Silverwood et al., 2015), while the association with hand OA may be affected more with central obesity-related metabolic syndrome and higher circulating levels of adipokines (Jiang et al., 2016, Robinson et al., 2016). Obesity (BMI ≥ 30 kg/m^2) is a potentially modifiable factor, modest weight loss by 5 kg may improve the sign and symptoms of OA (Willims and Foulsham, 1981, Felson et al., 2000). Other potential systemic risk factors for OA include oestrogen deficiency occurring following onset of the menopause, poor nutrition and high bone mineral density, but the evidence is mixed about these factors (Felson and Zhang, 2015, Felson et al., 2000).

Local risk factors

The local factors that increase the risk of OA are predominantly joint injury, injurious physical activity (recreational or occupational), and abnormal loading on joint surfaces. Major joint trauma is one of the primary causes of OA at sites not commonly affected, such as the wrist and ankle (Felson and Zhang, 2015). A meta-analysis that included 27,326 participants with knee OA showed that the risk of knee OA significantly increased with a prior injury, and the pooled odds ratio (OR) was 2.83 (95% CI 1.91- 4.19) (Silverwood et al., 2015).

Repetitive or excessive movement may lead to OA development. A meta-analysis of 21 studies found that sports participation may increase the risk of OA in athletes, irrespective of the sport type (Risk ratio (RR)= 1.37; 95% CI 1.14 - 1.64) (Tran et al., 2016). The risk was lower in runners (RR= 0.86; 95% CI 0.53 - 1.41) and higher in soccer players (RR= 1.42; 95% CI 1.14 - 1.77) (Tran et al., 2016). This could be due to the increased risk of injury in high contact sports that contribute to OA development. Moreover, occupational movements and postures that include heavy manual work, lifting, excessive squatting or kneeling increase the risk of knee OA (Silverwood et al., 2015, Blagojevic et al., 2010).

There is a strong association between joint-level biomechanical abnormalities and OA (i.e., malalignment, excessive loading and incongruent joint surface) (Heijink et al., 2012). Joint malalignment modifies the load transmission across weight bearing joints. For example, malalignment of the knee joint (varus or valgus alignment) is a risk factor for knee OA (Tanamas et al., 2009). Indeed, the most robust hypothesis in OA pathogenesis is the adverse biomechanical factors on the joints (Aigner et al., 2015), however, this is not the only leading factor for OA. Most likely, multiple factors may contribute to the pathogenesis of OA and are responsible for the observed pathological changes.

Overall, the systemic and local risk factors act through genetic and biomechanical pathways, exerting various influences at different OA stages (Andriacchi et al., 2004) and at different joint sites (Litwic et al., 2013). Various risk factors and aetiologies contribute to OA development, such as older age, female gender, high body mass index, reduced muscle strength, metabolic disorders, and genetic predisposition, indicating that multiple underlying pathophysiological pathways may lead to similar joint destruction (Johnson and Hunter, 2014, Deveza and Loeser, 2018).

1.3.4 **Pathology**

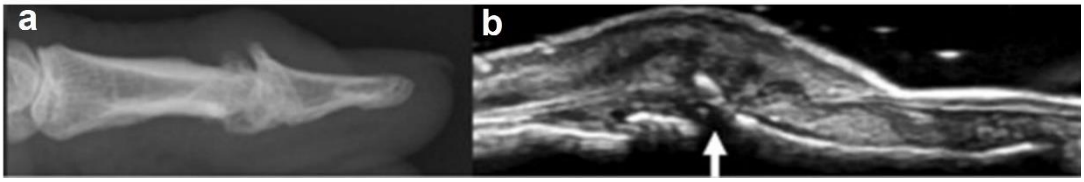
The emergence of OA predates the evolution of man. The evolutionary conservation of OA is evident from the examination of pre-hominid skeletons onwards. Osteoarthritic changes have been confirmed in a Comanchean dinosaur fossil dates as over 100 million years old (Dequeker and Luyten, 2008). Its occurrence in other animals possessing synovial joints was also detected. Also, the morphological changes of OA can be observed in human skeletons dating back to the Neolithic and Ancient Egyptian times (Dequeker and Luyten, 2008). These osteoarthritic joint changes are relatively well recognised, although the aetiologies in different species are not.

A variety of hypotheses have attempted to explain the osteoarthritis changes, including premature ageing of chondrocytes and cartilage matrix, damage to the chondrocyte's deoxyribonucleic acid, chronic mechanical overloading, pro-inflammatory cytokine production, and activation of cellular inflammatory signalling pathways (Aigner et al., 2015). The main structural features in OA are the pathological modifications that occur to the articular hyaline cartilage (fibrillation, fissures, ulceration, and full-thickness loss of the joint surface) and marginal osteophyte formation (Wyatt and Doherty, 2016, Brandt et al., 2008). Wyatt and Doherty (2016) described the pathomorphological alteration process as an initial increase in chondrocytes number, forming “clones” or “nests” of cells, and they increase their production of extracellular matrix components taking on an enlarged “hypertrophic” phenotype. Eventually, vertical fissures may develop in the cartilage, and the cartilage may lose its thickness. Such cartilage loss is focal and mainly occurs at the site of maximal load transmission across each joint. New fibrocartilage is produced at the joint margin and undergoes calcification and transition to bone to form marginal osteophyte (i.e., endochondral ossification – the same process that allows the growth of bone during development). The synovium undergoes hyperplasia, and the synoviocytes increase their production of fluid, and the outer capsule also thickens and tends to contract as if to stabilise the joint as focal cartilage loss develops (Wyatt and Doherty, 2016).

The disruption of the joint bone-cartilage interface leads to an active repair process that dynamically involves all tissues surrounding the joint. This process could be explained as ‘wear, tear and repair’ instead of just ‘wear and tear’, expressing the mechanical adaptation of the joint tissues to compensate for the initial insult and the role of inflammation in pain and progression (Birrell et al., 2011). Following an insult to the synovial joint, the metabolic activity of joint tissues increases, and new tissues production are evident (Wyatt and Doherty, 2016). In many cases, this repair process succeeds, thus leaving a joint that is abnormal structurally but is unaccompanied by pain. However, overwhelming insults and/or poor repair processes may lead to continuation of this attempted repair process and eventual “joint failure” that then commonly associates with symptoms such as pain and loss of function (Loeser et al., 2012).

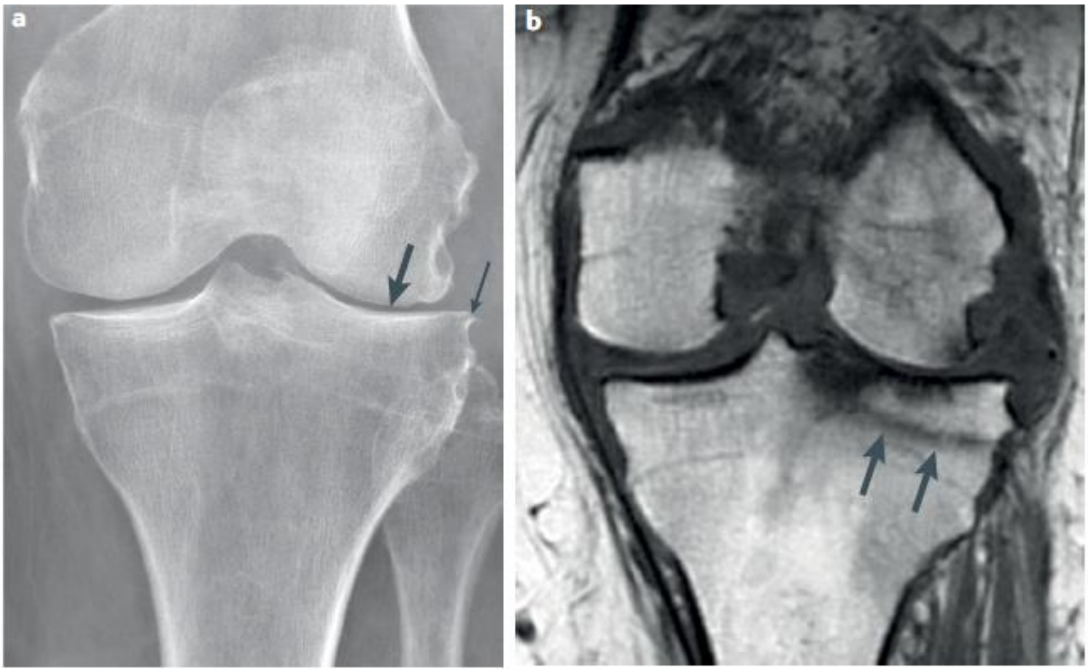
The diagnosis of OA is often based on the history and clinical examination alone, though imaging of the joint additionally may be used (Zhang et al., 2010). The most widely used imaging for assessing OA structural changes is through radiographs (X-ray), in which focal narrowing of joint spaces is an indicator of cartilage loss (Abadie et al., 2004), together with marginal osteophyte and bone contour remodelling (Doherty et al., 2016b). However, radiographs are insensitive at detecting early changes and only show definite structural changes in the bone (Chu et al., 2012).

Magnetic resonance imaging (MRI) is a useful modality for assessing the multiple joint tissue changes that occur in OA, including: focal loss of hyaline cartilage; bone marrow oedema; and ligamentous, meniscal and synovial pathologies (Phan et al., 2006). Ultrasound is an increasingly used imaging modality, alone or together with radiographs, particularly for hand OA assessment and evaluation of synovitis and soft tissue changes (Hayashi et al., 2011). It shows differences in the shape and location of osteophytes in inflammatory joint conditions (Okano et al., 2019) (see Figure 1-7). Figure 1-8 illustrates the osteoarthritic features in the knee depicted in radiograph (a) and MRI (b). The patient was experiencing severe pain on the lateral side of the knee without a history of trauma.



a | Distal interphalangeal joint radiograph. **b |** Longitudinal scan of the distal interphalangeal joint (arrow denotes osteophyte observed in hand OA nearly perpendicular to the joint space).

Figure 1-7. Radiograph and ultrasound scan of the distal interphalangeal joint (Okano et al., 2019)



a | Knee Anterior-posterior radiograph (large arrow denotes marked joint space narrowing), (thin arrow denotes osteophyte at the lateral tibial margin). **b |** Coronal T1-weighted MRI of the same knee depicts moderate lateral meniscus extrusion and lateral tibiofemoral cartilage loss (arrows show stress fracture of the lateral tibial plateau).

Figure 1-8. Radiograph and MRI of knee OA (Roemer et al., 2018)

1.3.5 **Pain in osteoarthritis**

Most people with OA do not have symptoms (Culvenor et al., 2019). However, in symptomatic OA, pain is the most frequently reported symptom. Indeed, pain is a major factor in the clinical diagnosis of OA. In a cross-sectional study of older adults with hip or knee OA, the self-reported limitations in activities were largely dependent on pain and, to a lesser extent, on the range of joint motion, muscle strength and comorbidity (Van Dijk et al., 2009). In advanced stages of OA, more severe pain may affect social activities, mood and sleep, reducing the quality of life (Neogi, 2013).

In OA, there is no single mechanism for pain formation, nor is there a single source for pain. Chronic pain is produced by either a peripheral mechanism or central mechanism, or both. OA pain is typically chronic and is enhanced by altering the central pain mechanism (Klosterhalfen et al., 2009). Nociceptive fibres are absent in cartilage but exist in the other synovial joint tissues (i.e., subchondral bone, periosteum and joint capsule with its synovial lining) as well as peri-articular sites (muscles, tendons, ligaments). These fibres send nociceptive pain signals to the spinal cord and subsequently to higher centres in the brain in response to tissue damage or potential damage of any of the joint structures as a protective mechanism (Hunter et al., 2013). Pain persistence after the resolution of the threat stimuli is considered to be a maladaptive behaviour (Neogi, 2013). However, some studies suggest that the OA pain intensity often changes and might resolve entirely at times, while structural changes stabilise (Hannan et al., 2000, Dieppe, 2004). Hence, it is important to acknowledge the OA pain is more complex than can be attributed only to peripheral nociceptive mechanisms.

Contextual aspect of pain in osteoarthritis

OA pain is a sensory and emotional experience interpreted within a psychosocial context (Walsh, 2016). The context may not only affect pain interpretation but also modulates the central processing of pain. The Oxford dictionary definition of hurt is to cause physical pain and to suffer pain (Oxford, 2021), emphasising both the physical and emotional aspects of pain. Pain-related suffering reflects the emotions concerning the physical injury that includes fear, anger, anxiety, frustration, or depression, and is affected by personality traits and demographic factors (Wade et al., 2011).

Various contextual aspects may contribute to OA pain, such as: demographic factors; comorbidities; psychological factors; social factors; and physical activity level. It has been found that some factors correlated with worsening of OA pain. For example, non-white race, medical comorbidities, anxiety, depression, lower educational achievement, lower social class, and inactivity (Juhakoski et al., 2013, Collins et al., 2014, Alschuler et al., 2013, Zeni Jr and Higginson, 2009). Reciprocally, OA pain may interfere with successful weight management behaviours in overweight patients, such as increasing physical activity and reducing caloric consumption (Rosemann et al., 2008).

There are two major contextual dimensions for OA pain: internal and external. The internal context to the patient (i.e., genes, gender, and psychological factors) and a consequence of external context (i.e., healthcare, social, and work environment) (Walsh, 2016). Examples of both contexts are demonstrated below:

Internal: The genetic contribution to pain sensitivity influences the genetic risk of clinical OA (Warner and Valdes, 2016). The variation of pain experience between people could be due to the genetic predisposition of variants related to the endogenous opioid and other pain neurotransmitters (Zubieta et al., 2001). Opioid receptor polymorphisms and catecholamine O-methyl transferase (COMT) gene might increase the sensitivities to mechanical stimuli (Bratus et al., 2014). Genetic variation might underlie the differences in emotional modulation of pain, and serotonin transporter polymorphisms might modulate the descending pain (Palit et al., 2011), which may contribute to the psychological distress associated with pain. Female gender and ageing are commonly recognised risk factors for both pain and OA (Felson et al., 2000).

Similarly, there are variations between genders in pain perception. Females tend to experience a significant increase in OA pain over the day, but males are less likely to show this pattern (Keefe et al., 2004). The level of pain reporting is also influenced by psychological factors, such as catastrophising traits and coping strategies (Bradley, 2004). A recent SR recognised that there is a potential positive effect of improving pain coping strategies in patients with knee OA (Ismail et al., 2017), however, this finding was based on reviewing four primary studies, and further research is needed to explore the psychological intervention for OA pain management.

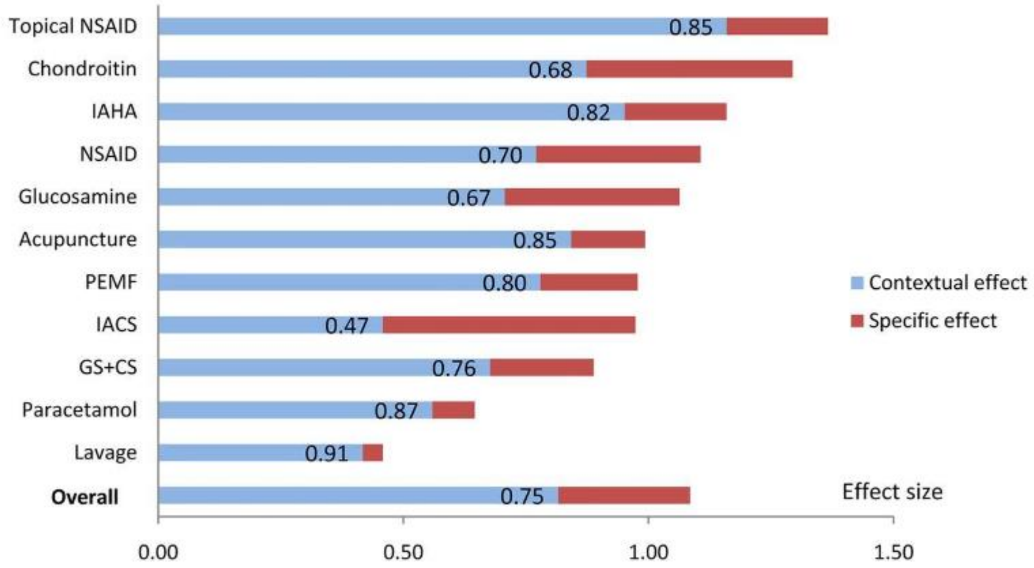
External: The external dimension of OA pain is influenced by some sociological mechanisms. The personal experiences and the external influences from social, work and healthcare environments form the individual’s beliefs about pain and its possible treatment (Walsh, 2016). Moreover, Cleveland et al. (2013) explained that the increased burden of OA pain in areas of socioeconomic deprivation might be mediated by variations in access to healthcare, greater dependence on physical ability for financial independence and other risk factors for chronic pain. Certain occupations demand physical load that increase the potential for developing OA due to strenuous or repetitive biomechanical force on the joints. A large-scale longitudinal study of labour market affiliation in Denmark found that high occupational workload was a significant predictor of hip and knee OA, and the risk increased with the increase of years engaged in the same occupation (Andersen et al., 2012).

Moreover, social support is one of the investigated determinants of health, with evidence supporting the role of social relationships in improving pain coping and reduced disability (Bartley et al., 2017). Social companionship, emotional support, and tangible assistance from the community were related to greater health-related quality of life among people with hip and knee OA. (Ethgen et al., 2004). Also, higher spousal empathy and perceived autonomy support for being active were associated with increased physical activity in patients with knee OA (Martire et al., 2013). Understanding the contextual aspects of pain can explain why not all patients with apparently the same disease severity report the same pain. Context may pose threats to successful treatment outcomes, but also it can provide opportunities to reduce OA pain.

1.3.6 Placebo effect in the management of osteoarthritis

The main reported symptoms in OA are pain, functional restriction, and reduced quality of life, which are the primary treatment focus (Doherty et al., 2016a). Management of OA begins with core non-pharmaceutical interventions to be considered in every patient with OA, such as education, exercise, and weight management if overweight or obese. Guidelines also support the consideration of other conservative treatments such as pharmacological treatments for adjunctive pain relief, physical interventions, and appliances, before considering surgery. Management decision-making should be shared between patient and practitioner, and take into account individual variations (i.e., needs, risk factors, and preference) (NICE, 2014).

One recent paper suggest that 75% of the OA treatment effect in RCTs is attributable to the CFs rather than specific effects of the treatment (Zou et al., 2016). This meta-analysis of 215 RCTs examined the overall treatment effect and the proportion attributable to contextual effect (PCE) of various treatments for OA (11 selected treatments). The overall treatment effect for pain ranged from 46% (ES=0.46, 95% CI 0.24 to 0.68) for lavage to the most considerable effect with topical non-steroidal anti-inflammatory drugs (ES=1.37, 95% CI 1.19 to 1.55). On the other hand, the PCE ranged from the smallest with the intra-articular corticosteroid (PCE=0.47, 95% CI 0.32 to 0.70) to the largest with joint lavage (PCE=0.91, 95% CI 0.60 to 1.37) (see Figure 1-9).



The horizontal bars length represents the effect size. NSAID, non-steroidal anti-inflammatory drug; IAHA, intra-articular hyaluronic acid; PEMF, pulsed-electromagnetic field therapy; IACS, intra-articular corticosteroid; CS, Chondroitin Sulphate; GS, glucosamine sulphate.

Figure 1-9. Overall treatment effect and the contribution from contextual effect and specific effect for pain in OA (Zou et al., 2016)

It should be noted that the overall measurable effects are not the summation of the active treatment effect and the placebo effect (Beecher, 1955). Instead, the placebo effect is the proportion of the total treatment effect attributed to the contextual effect. Nevertheless, the overall 75% of the treatment effect in that SR measured the treatment response from baseline, not the difference between no treatment and placebo arms (Zou et al., 2016). Additionally, Zou et al. findings might have been influenced by factors that affect PR's magnitude, such as regression to the mean, natural history of the condition and the Hawthorn effect in RCTs.

A reasonable estimate of the context effect could be generated by taking these factors into account. Krogsbøll et al. (2009) meta-analysis aimed to quantify the contribution of spontaneous recovery to the observed change from baseline in RCTs. By subtracting the 25% that Krogsbøll et al. found, which was the response rate to being ‘untreated’ (for pain precisely), the overall effect of context would be closer to 50%.

Similarly, a SR and meta-analysis of nonpharmacological therapies for knee OA pain found that a substantial portion of the total analgesic effect may be attributable to contextual effects (Chen et al., 2020). The SR included 13 acupuncture studies (1,653 participants) and 12 topical energy modality studies (i.e., TENS, Laser and ultrasound) (572 participants). The proportion attributable to contextual effect for acupuncture was 0.61 (95% CI 0.46 to 0.80) and 0.69 (95% CI 0.54 to 0.88) for topical energy modality studies (Chen et al., 2020). However, the heterogeneity between the studies was high (I^2= 85%) due to variations in the frequency of intervention administration. Several sensitivity analyses were undertaken in the SR to overcome the review caveats. Though the effect sizes remained largely unchanged in a series of sensitivity analyses that excluded studies with low trial quality, with large contributions to the overall heterogeneity, or reported exceptionally high changes in pain.

In the investigation of the placebo and nocebo effects in OA, Dieppe summarised the changes that might occur in people with OA as a result of the placebo or nocebo effect (Dieppe et al., 2016). Figure 1-10 shows the likely and unlikely changes that have been inspected in OA. An example of the various changes induced by placebo was evident in a study that compared intra-articular injection of steroids with placebo in people with painful knee OA (Hall et al., 2014). Hall et al. (2014) observed significant improvements following the placebo injection on the pain visual analogue scale (−13.4 mm SD (22.4); p=0.006), and ultrasound examination detected a reduction in synovial hypertrophy. However, the reduction in the maximal depth of synovial hypertrophy was not statistically significant following the placebo injection (−1.0 mm SD (3.7); p=0.91).

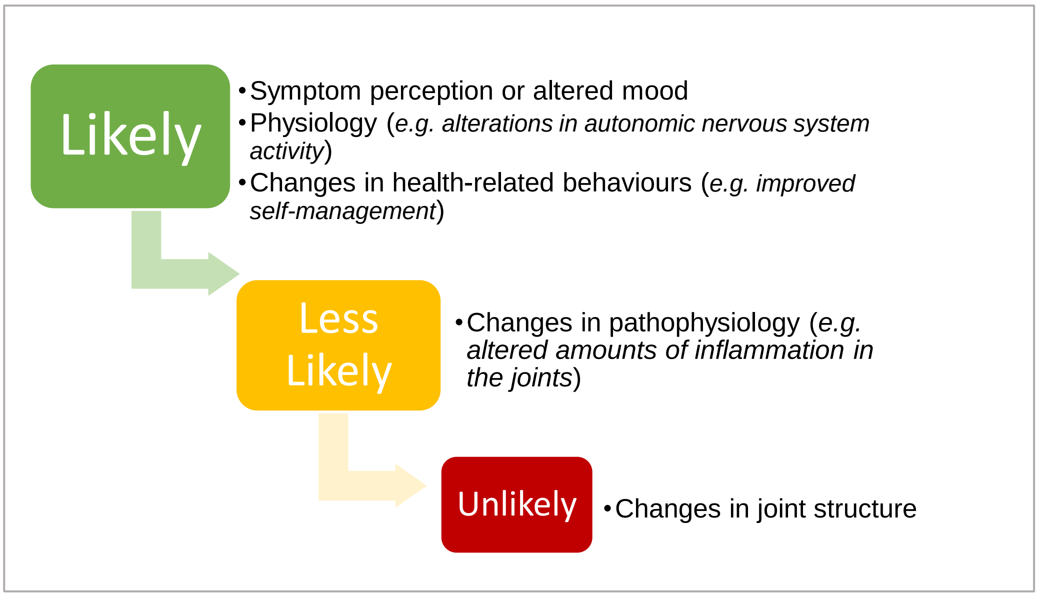


Figure 1-10. Changes in people with OA due to placebo/nocebo effects

Contextual enhancement has been acknowledged for its therapeutic effect in OA, especially for pain, stiffness, and self-reported outcomes (Zou et al., 2016, Zhang et al., 2008). In their detailed analysis of placebo effect in OA, Zhang et al. (2008) established that placebo effect is superior to non-treatment and is more effective for subjective outcomes. It is suggested that contextual optimisation should be involved in the management of OA (Abhishek and Doherty, 2013). Nevertheless, these reviews and meta-analyses investigated the placebo and the context effect of some predominant treatments for OA (i.e., pharmacological interventions and injections) except for pulsed-electromagnetic field therapy.

The placebo effect in physical therapies has not been considered in these reviews, even though it is one of the primary interventions in OA management (see Figure 1-11). This could be due to the difficulty of designing placebo treatments that are similar to the real physical therapies in all aspects, and it is almost impossible to apply the RCT ‘double-blinding’ criteria to therapists and patients.

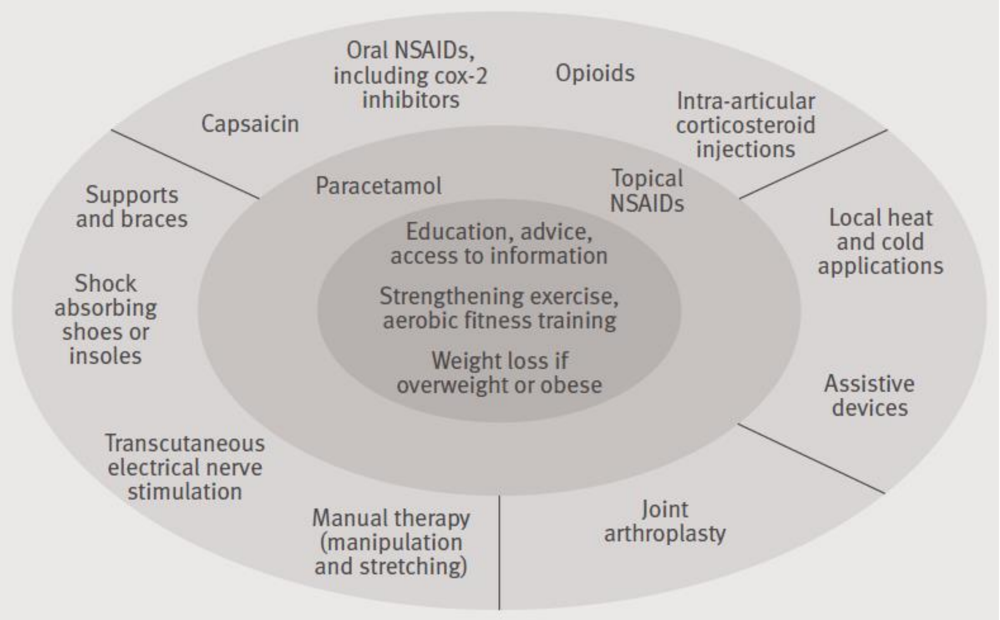


Figure 1-11. NICE guidance for OA management in adults (Conaghan et al., 2008)

Kim Bennell's RCTs on physiotherapy treatments attempt to deliver placebo control for knee and hip OA samples (Bennell et al., 2005, Bennell et al., 2014). The two RCTs fulfilled the double-blinding criteria. However, the placebo interventions did not fulfil Grünbaum's conceptualisation of placebo where placebo control should include all of the incidental features of the treatment, none of the characteristic features, and nothing more (Maddocks et al., 2016, Grünbaum, 1986). The RCTs intervention arm included exercise, manual therapy, education and advice, while the placebo arm involved sham ultrasound and application of a non-therapeutic gel.

Both knee and hip OA RCTs showed significant improvement in pain and function with physiotherapy and placebo interventions (Bennell et al., 2005, Bennell et al., 2014). Despite the use of skilled therapists and excellent adherence to treatment, the physiotherapy intervention package offered no greater benefits than regular contact with a therapist that offered a sham procedure. The authors’ explanation of findings was contributed to many factors (i.e., the natural history of OA, type of prescribed exercise, and therapist attention). The increased contextual effect on the comparator group might be due to the multiple individual sessions with an attentive therapist and the procedure that involved skin stimulation and touch.

The quality of the therapeutic relationship improves outcomes such as pain and function (Pinto et al., 2012). Bennell et al. (2014) claim that in the active intervention group, the therapists’ focus on content delivery of multiple interventions may have reduced the available time to provide patient-centred communication style (e.g., listening and providing reassurance). Thus, both groups improved in the RCTs with no significant differences between the active intervention and placebo.

CFs in physiotherapy management of osteoarthritis

Physiotherapy management of OA involves patient education and advice about their condition and about developing individualised self-management strategies, providing any necessary assistive devices and/or orthosis, and exercise (i.e., general body aerobic training and local muscle strengthening) (NICE, 2014). Furthermore, thermotherapy (i.e., the use of local cold or heat), electrotherapy and manual therapy have been recommended as adjuncts to the main management for pain due to

OA. Even though exercises for strengthening specific muscles are necessary during management of OA (Pelland et al., 2004), in their SR, Pisters et al. (2007) inferred that the positive post-treatment effects of exercise on physical function and pain in people with knee OA are not sustained in the long term (≥6 months after treatment). However, a few of the trials included in that SR reported sustained effectiveness of exercise when combined with booster sessions between the post-treatment and the follow-up periods. Accordingly, exercise and general training is not a single course of intervention, but it is a lifestyle modification that people with OA should adapt to and maintain throughout their life.

CFs could be a potential therapeutic tool to boost the outcomes in physiotherapy. However, there is currently little evidence available on the utilisation of CFs among physiotherapists. Findings from an Italian national survey of 558 physiotherapists, specialised in orthopaedic manual therapy, enquired about perspectives on using CFs in clinical practice revealed that more than 50% of participants valued the CFs' therapeutic outcomes for different health conditions (Rossettini et al., 2018c). Moreover, 52% of the physiotherapists claimed to use CFs frequently in their practice in an ethically acceptable scheme. Rossettini et al. (2018c) survey has defined a set of CFs that the participants have voted on. In 2020, Rossettini et al. reviewed context-related effects in physiotherapy interventions. Figure 1-12 shows examples of CFs in physiotherapy clinics that can influence the trajectory of outcomes towards a positive or a negative effect, depending on how the physiotherapist manages them (Rossettini et al., 2020a).

Besides, Table 1-1 depicts possible contextual enhancers in physiotherapy settings (Testa and Rossettini, 2016). Although it demonstrates promising enhancement strategies, the list was derived from a general search of the available qualitative literature. It reflected the authors' perspectives of potential enhancers, and it did not result from quantitative assessments of the effectiveness of individual CFs.

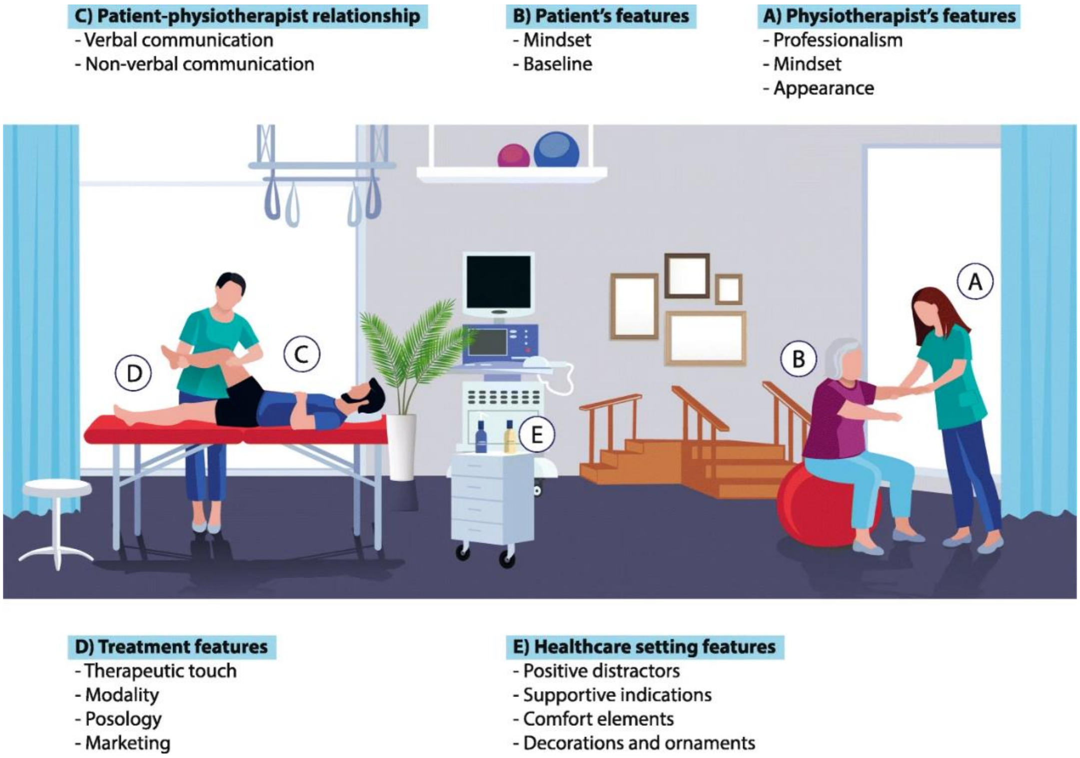


Figure 1-12. Contextual factors in clinical practice (Rossettini et al., 2020a)

Table 1-1. Strategies of contextual enhancement in physiotherapy (Testa and Rossettini, 2016)

Contextual factors	**Enhancement strategies**
Physiotherapist and patient characteristics	• Improving therapists' experience through training, positive reputation, and professionalism • Wearing professional uniform or laboratory coat • Being optimistic regarding any dysfunction and during the consultation • Providing patients with a clear explanation of their condition, diagnosis, and prognosis • Appreciating patients' opinion • Encouraging patients to ask questions and providing them with positive feedback • Considering the patient's condition, age, and gender • Inspecting patient's preferences, previous experiences, and investigating their expectations
Physiotherapist-Patient relationship characteristics	• During the clinical encounter, therapists have to be relaxed and confident • Adopting a warm and friendly behavior • Use appropriate language to express empathy and support, affirmative head nodding, eye contact, and smiling • Adopting psychosocial talks • During the treatment, use positive and reassurance messages • Adopting forward leaning and open body posture • Understanding and responding to patient's nonverbal body language expressions
Treatment characteristics	• Telling and showing the patients that treatment is applied • Using touch to prepare, assist, inform and treat patients • Implementing personalised therapies and patient-centered care • Provide the treatment by the same therapist in every session • Setting appointments with adequate session's duration, frequency, punctuality, and follow-up

Environment characteristics	• Combining positive distractors such as aromas, music, light, and temperature • Facilitating access to the physiotherapy service • Deliver the treatment in a clean and private environment • Using suitable artworks in the therapeutic environment

One of the most meaningful aspects in CEs is the consistency across all health professionals and sharing the same goals with no conflicting information to achieve successful outcomes (Kalso, 2012). In addition, the variability of treatments can influence the outcome perceived by the patient. One of the major variables in physiotherapy interventions is the extent of hands-on, hands-off therapies. Arguments about hands-on therapies were that such therapies (i.e., manual therapy) rely on placebo to maximise effectiveness (Kerry, 2019). A SR representing 4876 patients' expectations of physiotherapy interventions found that the recovery expectations are commonly associated with outcomes in musculoskeletal physiotherapy (Wassinger et al., 2022).

1.4 Study rationale

This project was driven by a promising finding of a previous meta-analysis suggesting that the majority of treatment effect in OA is attributable to contextual factors (Zou et al., 2016). Existing research recognises the essential role of these factors related to practitioner-patient communication for different health conditions (e.g. irritable bowel syndrome and rheumatological conditions) (Kelley et al., 2009a, Georgopoulou et al., 2018). The most studied medical conditions for contextual effects include pain and Parkinson's disease, in addition to the immune reactivity changes and, to a lesser extent, psychiatric disorders (Benedetti, 2014a).

Despite the increasing interest in CEs to improve patient outcomes, their detailed study in the management of musculoskeletal pain is still limited (Rossettini et al., 2018b). Moreover, research has broadly considered the CFs related to treatment characteristics (i.e., route of administration, colour, and branding) and addressed some factors related to practitioner-patient encounters (i.e., empathy and positive expectations) in the last two decades. However, the CFs that could optimise OA management have not explicitly been recognised to date. This research project will focus on identifying the CFs that are effective, amenable to change, relevant to patients with OA and health practitioners managing OA, and applicable within the medical encounter.

The European Alliance of Associations for Rheumatology (EULAR) Research Roadmap (RheumaMap) highlights the enormous burden of OA on European societies, especially the loss of productivity and health care costs. It asserts the urgent need for evidence-based policies, such as improving access to timely, high-quality health care to improve the treatment of rheumatic and musculoskeletal diseases (Taskforce, 2019).

However, there were no operational frameworks or rigorous, systematic analyses concerning CFs in OA management before the commencement of this PhD project in October 2018. Hence, this project aims to develop a primary package to optimise the management of OA that improves patient experience and perhaps eases symptoms.

This research project will deliver an impact on knowledge through contribution to the production of the CEP. It will involve a set of evidence-based CFs that can be adapted by healthcare practitioners to enhances outcomes for patients. The research report will be disseminated in open-access journals. The findings may give insight into managing other chronic pain conditions such as fibromyalgia and chronic neck and back pain.

1.4.1 Research aims and objectives

This thesis aims to develop a CEP that can be used to optimise the management of osteoarthritis.

The specific objectives of this thesis are:

[1] To identify and evaluate the current evidence for modifiable CFs that can improve clinical outcomes reported in RCTs using quantitative systematic review and meta-analysis.

[2] To explore and understand the experience and perspectives of patients and health practitioners about CFs in consultations for OA using the qualitative systematic review and meta-aggregation.

[3] To obtain views and perspectives of stakeholders' including clinicians, researchers, and public and patients on the identified CFs using an online survey and Public and Patient Involvement and Evaluation (PPI/E) meetings.

Chapter 2. General Methods

2.1 Overview

This chapter provides an overview of the CEP development and the methodology of the studies conducted in the development stage of CEP, which include a quantitative SR with conventional meta-analysis (CMA), a qualitative SR with meta-aggregation, stakeholders' involvement, and public and patient involvement and evaluation (PPI/E). Further details of each specific method are described within each chapter.

2.2 Contextual Enhancement Package (CEP)

The development of CEP goal is to optimise the management of OA. It primarily aims to improve the experience of people with OA by improving the contextual aspect of care in the clinical encounter. The CEP includes evidence-based CFs that are effective, relevant and critical to patients with OA and health practitioners managing OA, amenable to change, and applicable within the medical encounter. It will provide some behavioural and organisational guidance on key CFs to any healthcare provider treating patients with OA. Once the package is evaluated, it shall be addressed in practitioner training and integrated into clinical practice.

2.3 Medical research council framework for complex intervention development

As the CEP is a complex intervention, the 2013 revised version of the UK Medical Research Council (MRC) framework was utilised to guide the

CEP development (Craig et al., 2013). Furthermore, the research methods have been adapted to the 2021 updated MRC framework which provides a detailed guidance and thorough framework for complex interventions development and evaluation (Skivington et al., 2021b).

The term complex intervention has come to refer to any intervention with multiple interacting components or complex properties. The CEP is a notable example of complex intervention. This can be described briefly by the range of behaviours targeted, the number of factors involved, skills required by those delivering the intervention, settings, and the flexibility in delivering the intervention or its components (Skivington et al., 2021b). Therefore, such interventions need to be systematically developed based on the relevant framework.

The MRC framework aims to help researchers collaborate with stakeholders and conduct research with diverse perspectives and appropriate selection of methods. The updated framework entails a pluralistic approach and identifies four research perspectives (i.e., systems, theory-based, efficacy, and effectiveness) that overlap and could be used in conjunction (Skivington et al., 2021b). This research project had taken effectiveness and theory-based perspectives to guide the research design. Effectiveness research seeks to compare an intervention against usual care treatment, and the results inform decisions between an established and novel approach to achieve the desired outcomes. Theory-based perspective aims to understand the interplay of mechanisms and context, which might lead to the refinement of theory.

The framework assigns complex intervention research into four phases, specifically: development or identification of an intervention; feasibility testing; evaluation; and impactful implementation (Figure 2-1). Depending on the uncertainties about an intervention, the research might begin at any of the four phases. The focus of this PhD project was on the development phase only.

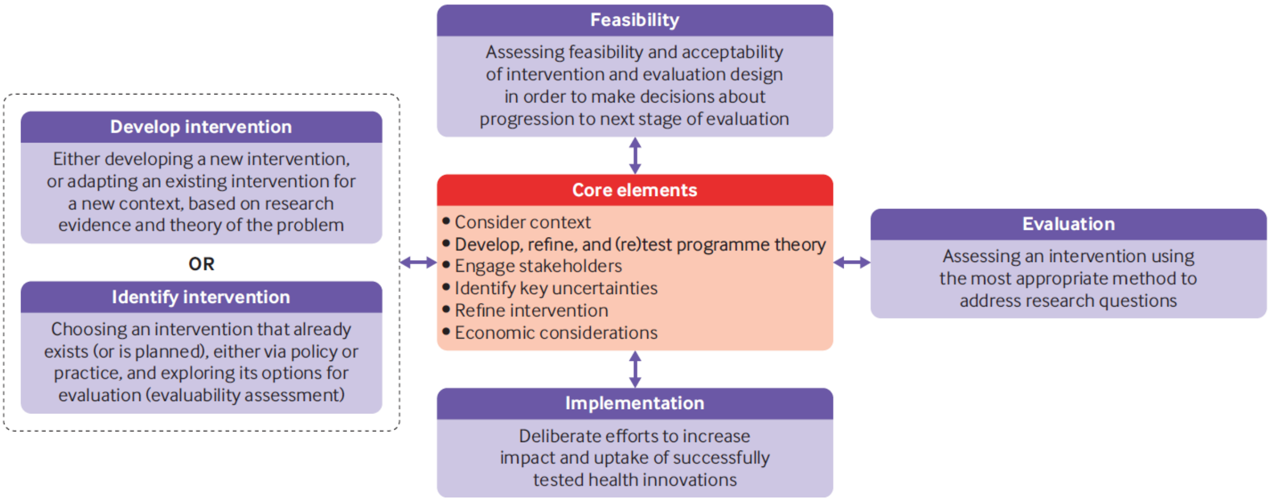


Figure 2-1. Complex intervention development and evaluation (Skivington et al., 2021)

In 2000, the MRC framework development phase involved three main elements: identifying the evidence base, identifying or developing theory, and modelling process (MRC, 2000). These elements were considered in earlier stages of designing the research project. Then, the research project was adapted to the 2021 six core elements conducted in each phase of the MRC framework, which exhibits more comprehensive details (Skivington et al., 2021a). The core elements in the development process are:

1. Consider context

The context considered in this research includes the interaction between any health professional (e.g., physiotherapist, general practitioner, rheumatologist, and nurse) and patient with OA in consultations for OA management in any healthcare setting.

2. Test a programme theory

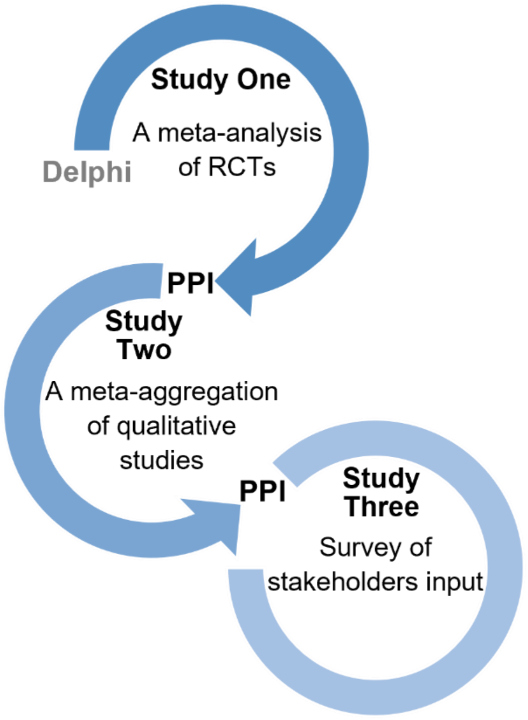
The theoretical aspect of contextual enhancers and their likely effect in osteoarthritis was explored in Chapter 1. The effectiveness of the contextual enhancers during an intervention is examined in a meta-analysis in Chapter 3.

3. Engage stakeholders

The involvement of stakeholders in the research project is described in chapter 5 and 6. The engagements were taken at multiple stages of the CEP development process.

4. Identify key uncertainties

Determination of the key uncertainties in the development of CEP informed the framing of research questions that governed the choice of research perspectives. Hence, mixed methods research design was conducted (Figure 2-2), which engaged pragmatically with the multiple uncertainties involved in CEP. Details about the chosen methods are briefly explained below. Moreover, chapter 7 discusses the research project limitations and the uncertainties that were encountered.



*Delphi study was done prior to this PhD project

Figure 2-2. Overall mixed methods research design

5. Refining the intervention

The research project involved an iterative refinement process of the modifiable contextual enhancers with transparent reporting of the rationale. The voting in the Delphi study intended to recognise the CFs in the management of chronic painful conditions. The Delphi study yielded to a generation of a list of CFs. Then, the recognised factors were refined in the meta-analysis that examined the effectiveness of those factors. Moreover, engaging potential intervention users was considered to inform refinements of the identified CFs. A stakeholders survey was conducted to refine the list considering the current research evidence and PPI/E in two stages to ensure all the above are patient-centred.

6. Comparative resources and outcome consequences

Expert opinion, research evidence, and patient preferences are the three major domains for evidence-based medicine (EBM) decision making. Each type of evidence has its strengths and weaknesses, and they are considered equally important within an “evidence-based” decision. These three resources were used in the development phase (Figure 2-3).

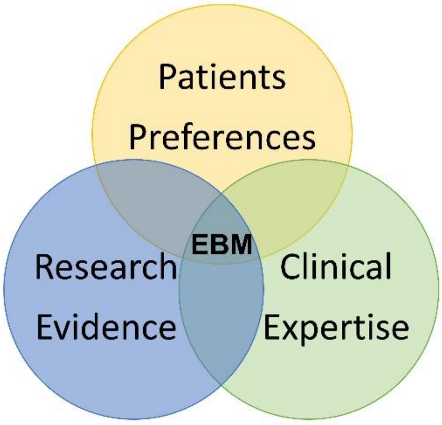


Figure 2-3. Components of Evidence-Based Medicine (EBM)

Some of the fundamental principles in developing complex interventions to improve healthcare are considering the development process as a dynamic process, understanding context, reviewing published research evidence, and using iterative development cycles with input from stakeholders throughout (O'Cathain et al., 2019). This PhD project involved five research methodologies (Figure 2-2). Brief background of these methodologies is described below.

2.4 Delphi

The Delphi exercise or study uses an anonymised individual voting procedure to obtain expert opinion consensus on a specific issue. Usually, it is conducted through questionnaires over two or more rounds in which individuals vote completely on their own via email or the internet. It decreases the effect of peer pressure in an open forum and is a cost-effective decision-making method (Okoli and Pawlowski, 2004).

The results of a previous unpublished Delphi study conducted by a previous student (R.M.) in 2016 have been utilised within this research. The purpose of the Delphi was to identify the opinions of an expert panel about contextual enhancers in management of chronic painful conditions. The results were used to guide and develop the search strategy for the SRs with agreement from his research team.

The Delphi panel was made of thirteen out of twenty invited international experts in placebo research and contextual enhancers. The Delphi was completed over two rounds. The first round was a questionnaire asking each panel member to propose minimum of five CFs they thought to be essential according to their clinical or research experiences. The propositions were then amalgamated into a list of 56 CFs. The panel members were then asked to rank these factors in the second round according to their importance in a 0-10 scale where 0 means not important at all, and 10 means extremely important. The CFs with mean ranking scores of 4 or more were accepted. Thus, Delphi assembled 16 CFs that guided the subsequent literature search for research evidence, including:

- Six practitioner factors (empathy, communication skills, professionalism, confidence, beliefs/illness perceptions, experience and knowledge)
- Three patient factors (beliefs/illness perception, active involvement, experience and expectation)

- Two practitioner-patient relation factors (holistic assessment and practitioner-patient interaction)
- Five other factors (duration of consultation, regular follow-up, environmental factors, treatment characteristics, information about the disease and management options).

The Delphi study was an essential stage for this PhD project. The experts voting on the relevant CFs for chronic pain management refined CFs in clinical settings and clarified its definition. Therefore, the Delphi results guided the search strategy in the following systematic review of CFs.

2.5 Systematic reviews

In evidence-based medicine (EBM), decisions made by healthcare professionals must be based on valid evidence. The pivotal point of the EBM paradigm with respect to research evidence is the SR, as mentioned by Stevens (2001). The Cochrane Collaboration Reviewers' handbook defines SR as a rigorous scientific approach of summarising results from a collection of original research studies and combining them into a clinically meaningful whole (Clarke and Oxman, 2000). Therefore, a SR is a secondary source of evidence, in which primary research evidence is appraised, and combined (Cook et al., 1997).

A well-conducted SR should first define a clear and clinically relevant research question. Second, a systematic search of evidence databases should be conducted in view of the research question. Third, the reliability and validity of the selected studies should be evaluated using an appropriate critical appraisal tool. Fourth, relevant data should be extracted and analysed. Finally, the SR should provide an evidence-based interpretation of the findings by referring to the selected articles, and the strengths and weaknesses of the SR should be listed (Haines et al., 2008). The primary and fundamental stage in the SR process is framing the research question. A principal goal in developing research is transforming issues facing clinicians into a research question to resolve those issues (Thabane et al., 2009). Following a re-evaluation of the available literature, the following questions were formulated:

1. Which modifiable contextual factors (CFs) have been shown to be effective in the patient-practitioner encounter?
2. From the perspective of patients with OA and healthcare professionals, how is a good consultation for OA perceived, defined and experienced?

This research project includes two systematic reviews: a SR of effectiveness and a SR of experiences or meaningfulness. Systematic reviews which utilise a quantitative method provide theoretical and statistically robust evidence. Nevertheless, such evidence may overlook the patient’s opinion and the context in which such evidence was drawn, whereas a broader picture and more comprehensive conclusions can be captured by considering quantitative and qualitative methods. Data synthesis in SRs of quantitative (numerical) data usually appears as a meta-analysis, whereas meta-synthesis is applied in SRs of qualitative (textual) data. Qualitative meta-synthesis approaches include meta-ethnography and meta-aggregation (Munn et al., 2014b).

2.5.1 **Meta-analysis**

Randomised control trials (RCTs) are one of the primary quantitative evidence sources that measure and compare two interventions using random allocation (Deeks et al., 2011). A SR of RCTs is the most trustworthy source of research evidence in the literature in evaluating the effectiveness of any intervention owing to implementation of rigorous strategies to avoid bias and random errors (Deeks et al., 2011, Abuabara et al., 2012).

The quantitative data gathered in systematically reviewing the literature are pooled statistically using a meta-analysis method. Meta-analysis could be conducted if sufficient homogeneity exists between a group of studies (i.e., population, intervention, and outcome measure). By assuming that underlying effects have a normal distribution, random-effects meta-analyses allow for some heterogeneity between the included studies (Deeks et al., 2019).

Conventional meta-analysis (CMA) combines the results from multiple primary studies and compares an active intervention and a control arm (e.g., empathy versus usual care, or positive verbal communication versus no intervention). It examines the effect size of an intervention over a control arm, which enables comparison and critical appraisal of available evidence (Munn et al., 2014b). Effect size indicates the practical significance of a research outcome (the larger the effect size, the more practical the significance). It can be categorised into large (≥0.8), medium (=0.5) or small (=0.2) according to Cohen's criteria (Nakagawa and Cuthill, 2007).

2.5.2 **Meta-aggregation**

Meta-aggregation is an integrative approach to data synthesis employed by the Joanna Briggs Institute (JBI). It was developed to mirror the Cochrane process of quantitative synthesis, while considering the contextual nature of qualitative research and its procedures (Pearson, 2004). The philosophical foundation for the JBI qualitative meta-aggregation approach is pragmatism (Hannes and Lockwood, 2011). It implies the concept of "practical usefulness", where the synthesized findings from the meta-aggregative method are usually readily usable to inform clinical or policy decision-making. Hence, this method was pragmatic in answering the research question and summarising the views on the contextual enhancers in the management of OA, in contrast to the meta-ethnography method that aims to develop explanatory theory (Noyes and Lewin, 2011).

2.6 Stakeholders and Patient and Public Involvement

Internationally, there are different labels to describe the methods of involving participants and the general public in research (i.e., users, consumers, patients, and public) (Buse et al., 2012). PPI/E is a formal method of involving patients and the public in clinical practice guideline development or implementation (Boivin et al., 2010). The involvement may be in the form of communication (communicating the research information to patients or the public), consultation (collecting information from patients or the public) or participation (the public and the patients exchange information with the stakeholders) (Rowe and Frewer, 2005). This method can be utilised at different stages from the macro-level of research development, such as selecting the topic, evidence review, and implementation to a particular target group, to the meso-level of recommendations (Boivin et al., 2010). Early engagement with patients in complex intervention research is more likely to lead to solutions in practice (Raine et al., 2016).

Stakeholders refer to the community, organisation, or individuals interested in a research, project or policy process and outcomes (Deverka et al., 2012). Meaningful engagement of appropriate stakeholders in the research would maximise the potential positive impacts of the developed intervention on policy and practice (Skivington et al., 2021b). The involvement of stakeholders in the intervention development process minimises the gap between researchers, clinicians, patients and policymakers (Forsythe et al., 2018). Moreover, studies encompassing stakeholders' input are often considered more feasible, trustworthy, and better appreciated by the public (Martinez et al., 2019).

The details of the implemented methods are explained in the subsequent specific chapters.

Chapter 3. Identifying the Contextual Enhancers in the Patient-Practitioner Encounter that have Therapeutic Effect: A Systematic Review and Meta-Analysis of Randomised Controlled Trials

3.1 Overview

This chapter presents a systematic review and meta-analysis of the literature concerned with contextual enhancers (CEs) in the practitioner-patient encounter. The evidence gained from published randomised controlled trials (RCTs) of CEs is summarised using a conventional meta-analysis (CMA).

3.1.1 Research aim

The aim of this study was to identify the modifiable contextual factors (CFs) that can improve clinical outcomes reported in published RCTs.

3.2 Methods

This SR was performed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guideline (see Appendix 2) (Moher et al., 2009).

The SR protocol was registered in PROSPERO (CRD42016052463). However, amendments to the information provided at registration were undertaken. Firstly, the primary author of the registered protocol resigned, and the same research team continued the project with Ayah Ismail as the primary author. Secondly, the sequential mixed methods submitted in the protocol was changed to a quantitative SR method.

Thirdly, the eligibility criteria of the SR were not limited to chronic painful conditions. The protocol available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42016052463

3.2.1 **Eligibility criteria**

The PICOS framework (Participants, Intervention, Comparator, Outcome, and Study design) was used to define the search terms.

Participants

The review considered studies that included adult patients (≥ 18 years) receiving treatments in any healthcare setting. Studies were excluded if the participants were healthy volunteers, a paediatric population, cancer patients, psychiatric patients, drug addicts or homeless, because social functioning in these groups is markedly different from other patient groups.

Interventions

This review considered studies that evaluated any CE that was delivered with or without a specific treatment in practitioner-patient consultation. The focus of this review was directed towards the practitioner and patient characteristics that are amenable to change, and the interaction between them. CFs related to the physical aspects of a treatment (e.g. the colour, size or shape of a tablet, route of delivery etc.) or the environment characteristics (e.g. the décor of the consulting room) were not considered because these factors have been well investigated previously (De Craen et al., 1996, Ulrich, 1993). Studies were excluded if they examined specific psychological interventions such as cognitive behavioural therapy or interventions with a theoretical base in psychology such as counselling and shared decision-making. Studies were also excluded if they involved health education.

Comparators

This review considered studies that compared the CE to no treatment, usual care, waiting list or observation group.

Outcomes

This review considered studies that included the following outcomes: disease-specific outcomes such as pain and other symptoms, and generic outcomes such as patient satisfaction and reported experience of the practitioner interaction.

Study design

Included were all randomised controlled trials (RCTs) in which at least one of the intervention arms was a contextual enhancement related to the patient-practitioner relationship. RCTs that look for CE as a predictor or modifier of outcome were excluded.

3.2.2 Information sources

A systematic search was carried out on the following five databases:

- Medical Literature Analysis and Retrieval System Online (MEDLINE)
- Excerpta Medica dataBASE (EMBASE)
- The Allied and Complementary Medicine Database (AMED)
- Psychological Information Medical (PsycINFO)
- The Cochrane (CENTRAL) library

The search dates were applied from inception up until 18th April 2019 and there was no language restriction. The reference list of all identified articles was checked for additional relevant studies. Additionally, an author-specific search for six research leaders in the field of placebo was implemented across MEDLINE, PubMed, EMBASE, PsycINFO, and Google scholar with limitation to RCTs (Appendix 3).

3.2.3 Search strategy

A comprehensive design of the search strategy was conducted and reviewed by the research supervisors. The results of a recent unpublished Delphi exercise, as well as search strategies employed in published SRs of placebo, were used as a guide to build up this review search strategy (see Appendix 4).

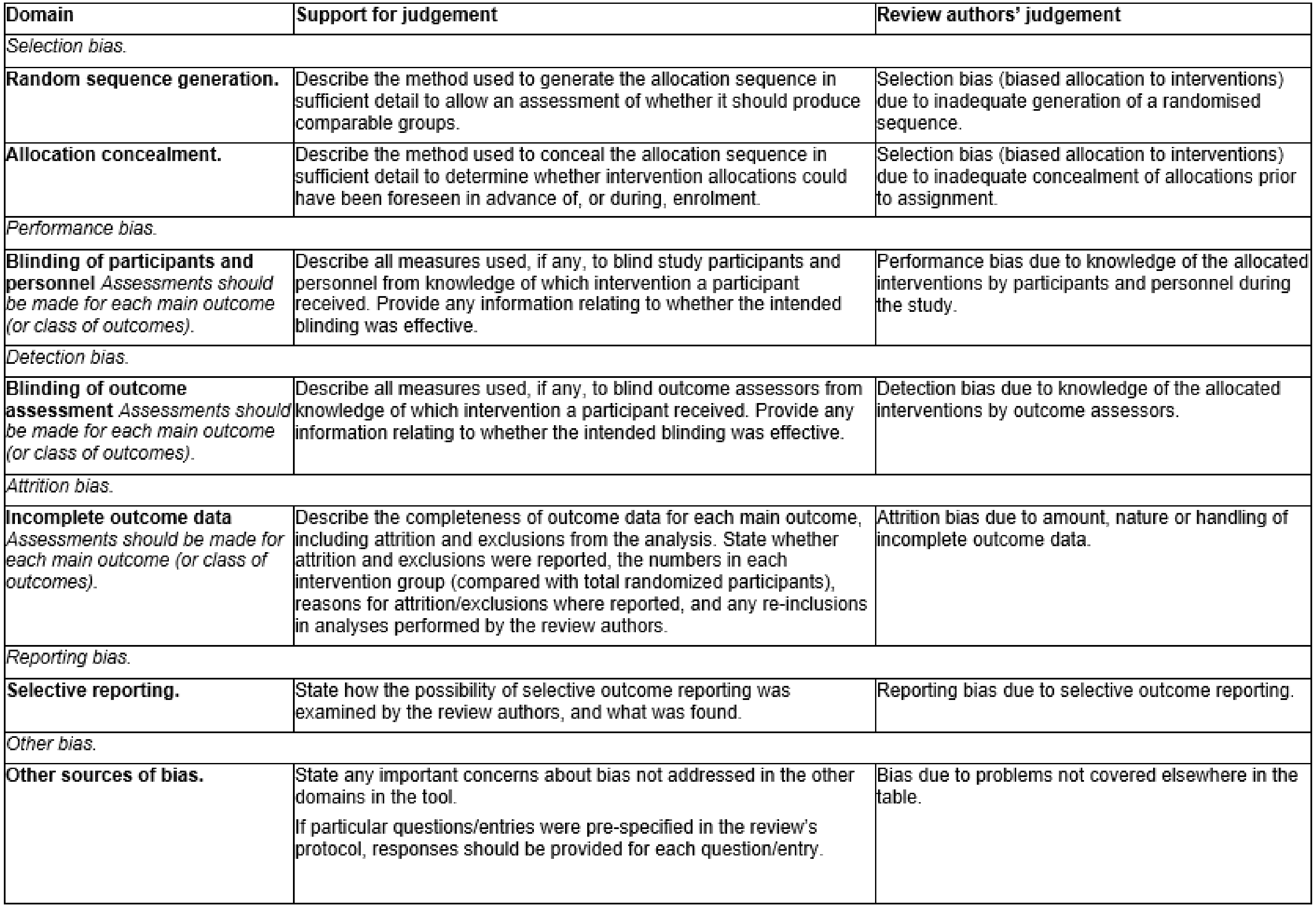
3.2.4 **Selection process**

Following the search, all identified citations were collated and uploaded into EndNote X8 and duplicates were removed. Titles and abstracts were screened against the inclusion criteria for the review. Relevant studies were retrieved, and the full text of selected citations were assessed in detail against the inclusion criteria by three independent reviewers (AI, WZ, and MH) for methodological validity and to minimise error and bias. The primary reviewer first reviewed the articles, and then the articles were reviewed by two of the PhD project supervisors independently. Reasons for exclusion of full-text studies that did not meet the inclusion criteria were recorded and reported in the SR. Any disagreements between the three reviewers were resolved by discussion with the supervision team, prior to inclusion.

3.2.5 **Risk of bias assessment**

The Cochrane risk of bias tool was used to assess the quality of the included RCTs by the primary reviewer (Table 3-1). The tool is comprised of eight questions that assess each of the domains set out by Cochrane. This quality assessment tool categorised the studies into `low risk`, `high risk`, or `unclear risk` (Higgins et al., 2011). A second reviewer (KY) with experience in SRs assessed the quality of 10% of the included studies independently, and disagreements between the assessors were resolved by discussion.

Table 3-1. The Cochrane Collaboration’s tool for assessing risk of bias (Higgins et al., 2011)



Domain	Support for judgement	Review authors’ judgement
Selection bias.		
Random sequence generation.	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.
Allocation concealment.	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
Performance bias.		
Blinding of participants and personnel *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Detection bias.		
Blinding of outcome assessment *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Detection bias due to knowledge of the allocated interventions by outcome assessors.
Attrition bias.		
Incomplete outcome data *Assessments should be made for each main outcome (or class of outcomes).*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Attrition bias due to amount, nature or handling of incomplete outcome data.
Reporting bias.		
Selective reporting.	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Reporting bias due to selective outcome reporting.
Other bias.		
Other sources of bias.	State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review’s protocol, responses should be provided for each question/entry.	Bias due to problems not covered elsewhere in the table.

3.2.6 **Data extraction process**

The JBI-form for data extraction was used for the quantitative data, and a structured database was created in Microsoft Access for data entry (Munn et al., 2014b). Several tables were used, each corresponding to a domain for data extraction. Study level data were extracted from the selected articles as follows:

1. Study characteristics:
    - Study identification details: title, author, year of publication and country
    - Study design: cluster RCT, RCT.
    - Total sample size
    - Health disorder
    - Trial settings: primary care, laboratories, or hospital wards.
2. Participant characteristics:
    - Demographics: mean age, gender
    - Number of participants
    - Educational status
3. Study intervention:
    - Study arms
    - Types of CF
    - Comparator types
4. Study outcomes:
    - Primary or secondary outcomes

- Outcome measure and unit of the assessment
- Time points for measurement
- Baseline value, endpoint value, and mean change value (i.e., standard deviation, 95%CI).

The second reviewer (KY) who carried out the quality assessment with the primary reviewer independently validated the data extraction of a random 10% of the studies that met review criteria.

Missing data

Where the required data were not available, they were calculated based on the information provided within the study (Table 3-2). If they were not calculable, the study authors were contacted. If this attempt was unsuccessful, the data were imputed using other similar studies. For example, when SD was not possible to calculate within the study due to insufficient information, it was substituted with the largest value from other studies with the same outcome. If the used outcome scale was unknown, the arithmetic mean of all SDs was used (Fu et al., 2013).

Table 3-2. Calculation of missing data (Higgins, 2011)

Calculations
SD from CI • $SD = \frac{(UpCI-LwCI)\times\sqrt{N}}{3.92}$
SD from interquartile range • $SD \cong \frac{q_3-q_1}{1.35}$
SD of the change from baseline • $SD = \sqrt{SD_{baseline}^2 + SD_{final}^2 - \left(2 \times Corr \times SD_{baseline} \times SD_{final}\right)}$
SD from standard error • $SD = SE \times \sqrt{N}$
Mean from median • $x = \frac{a+2m+b}{4}$

SD = standard deviation, CI = Confidence Interval, N =sample size, UpCI = upper confidence interval, LwCI = lower confidence interval, a = minimum value, b = maximum value, m = median, q_3 = third quartile, q_1 = first quartile, x = mean, Corr= Correlation coefficient, SE= Standard Error.

3.2.7 Assessment for publication bias

Publication bias was assessed using a funnel plot of standardised mean difference (SMD) of contextual interventions over control. A visual inspection for symmetry of SMDs in the funnel plot was undertaken. The funnel plot depicts the overall distribution of included study data, where the symmetrical distribution of data indicates an absence of publication bias (Higgins et al., 2019).

3.2.8 Synthesis methods

Microsoft Access was used to develop the database. The RCTs' results were summarised and pooled in a quantitative method (i.e., meta-analysis). Eligible trials were included in the meta-analysis if they provided enough quantitative data of the primary outcome measure (i.e., sample size distribution, mean change, standard deviation) or if the missing value could be calculated from the information provided within the study. A narrative synthesis was also conducted to report the conclusions of all studies, specifically those not pooled in the meta-analysis.

Narrative synthesis

Data were synthesised using narrative synthesis that summarises data using summary tables and structured narratives. Studies were classified according to the type of interventions, developed from theories around the aim of the intervention. The synthesis also considered the factors that might account for any differences in direction and size of effect across the included studies (Popay et al., 2006).

Meta-analysis

Meta-analysis provides a statistical aggregation of primary studies' results which has a precise estimate of the treatment effect and is more powerful than any individual trial involved (Higgins, 2011). The summary effect of this statistical aggregation indicates the magnitude and direction of the association between the intervention and outcome. Microsoft Excel and Stata software were used for the analysis and computation of the SMD.

The SMD is a point estimate of the treatment effect. To facilitate the comparison of effects of different interventions and to pool the overall effect of practitioner-patient interaction, the effect size (i.e., SMD) and the 95% confidence intervals were calculated. The mean change from baseline to end-point scores was used to calculate the effect size. Where this was not available, the endpoint mean score was used. Subgroup analysis was performed when three or more trials investigated the effects of common CF. The summary results from the meta-analysis were represented in a forest plot. The plot depicts the effect size of all included studies and the overall summary finding. Each study estimate is represented by a point estimate and the 95% confidence interval by a horizontal line.

Due to the variability of CFs interventions, heterogeneity between the studies' populations, interventions and effect sizes was anticipated.

Hence, the random-effects model was applied in pooling the SMDs from the studies using Stata software. The I^2 test was used for heterogeneity assessment between studies (Higgins and Thompson, 2002). Sensitivity analysis was conducted to exclude studies where assumptions about missing data had to be calculated (i.e., standard deviation value).

3.2.9 **Certainty assessment**

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to assess the certainty of evidence for each outcome (Balshem et al., 2011). Each outcome's quality of evidence fits into one of four categories, ranging from high to very low (Guyatt et al., 2011). The lower the quality, the more likely that further research would change the estimate and the confidence in the findings (Balshem et al., 2011). Initially, the quality rating of evidence is considered high when it is based on RCTs and low when based on observational studies. The quality is then downgraded as appropriate based on five factors (i.e., study limitations, consistency of effect, indirectness, imprecision, and publication bias) that assess the certainty in the body of evidence for each outcome (Guyatt et al., 2011).

3.3 Results

3.3.1 Study selection

A total of 3928 titles were obtained after duplicates had been removed. Abstracts of titles that appeared appropriate were examined and subsequently the full text of 63 articles were retrieved for detailed assessment. Data were extracted subsequently from 25 articles that met the inclusion criteria. The following PRISMA flow chart depicts the selection process (Figure 3-1).

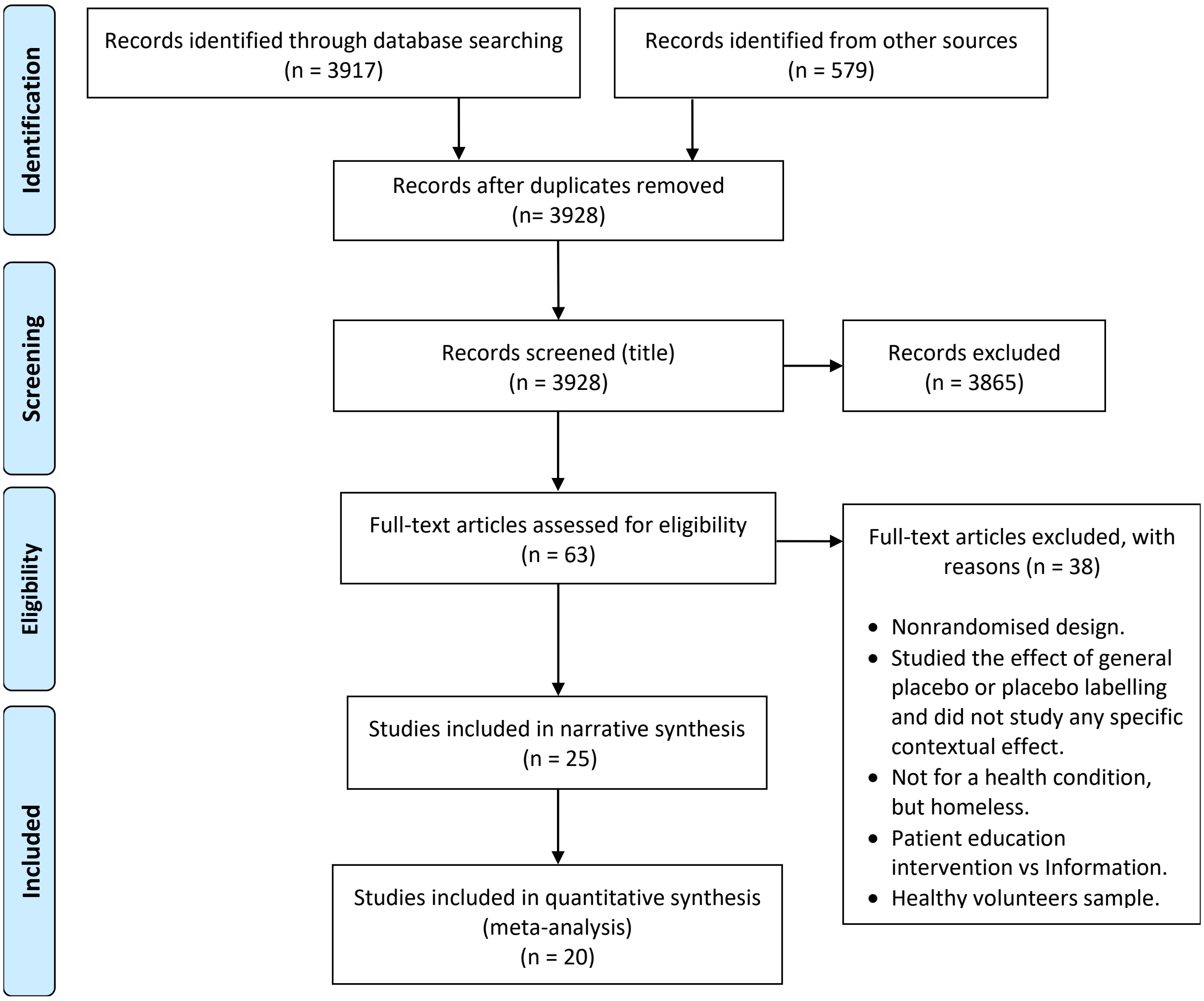


Figure 3-1. PRISMA flowchart

Excluded studies

Thirty-eight full-text articles were excluded due to the following: non-randomised design; placebo effect rather than specific contextual effect; and studies not for a health condition (e.g., in healthy volunteers). Of those with a non-randomised design, seven studies were excluded from the review because the CE (expectation) was a predictor of outcome rather than part of an intervention. Another study about the effect of health literacy was excluded for the same reason (see Appendix 5).

3.3.2 Study characteristics

Publications for 25 studies that compared a contextual intervention to usual care, or no intervention were identified from the systematic literature search. Most of the studies (88%) were published after 2000, and eight studies were conducted in the United States. English was the only language used in the included studies. Table 3-3 presents a summary of study characteristics included in the SR.

Table 3-3. Summary of included study characteristics

Study characteristics	No. of trials (%)
Publication year	
1985-1995	3 (12%)
2000-2010	11 (44%)
2010-onwards	11 (44%)
Study location	
United States	8 (32%)
United Kingdom	4 (16%)
Netherlands	4 (16%)
Sweden	3 (12%)
France	2 (8%)
Germany	2 (8%)
Australia	1 (4%)
Turkey	1 (4%)
Language	
English	25 (100%)
Blinding	
Blinding to participants	14 (56%)
Participants	
Total number	5632
Age median (range)	53.5 (29.7– 69.1)
Number of women (%)	2797 (50%)
Health disorders	
Patients attending GP	4 (16%)
Knee or hip osteoarthritis	3 (12%)
Hospitalised patients	2 (8%)
Asthma	2 (8%)
Cardiac conditions	2 (8%)
Back pain	2 (8%)
Acute pain	2 (8%)
Chronic pain	1 (4%)
Chest pain	1 (4%)
Acute tonsilitis	1 (4%)
Diabetes mellitus	1 (4%)
Irritable bowel syndrome	1 (4%)
Postoperative nausea	1 (4%)
Patients attending for musculoskeletal rehabilitation	1 (4%)
Gynaecological conditions requiring day-care surgery	1 (4%)

Participants

The total number of participants in the included studies was 5632, ranging from 25 (Pace et al., 2017) to 1262 (Krupat et al., 2004). According to the studies which reported the gender of their participants, half of them were women. The studies comprised various health conditions and disorders (Table 3-3). To describe the nature of some conditions listed in the previous table: musculoskeletal conditions treated in rehabilitation centres (one study) included rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis; patients attending in primary care (one out of four studies) had symptoms but no specified diagnosis or accompanying physical signs (i.e., headache, chest pain, sore throat, back pain); and hospitalised patients (one out of two studies) had pneumonia, pancreatitis, or diabetic complications.

Interventions

Overall, the included studies examined three interlinked CFs related to practitioner–patient interaction, specifically: empathy (6 studies); active involvement of patients by the health practitioner (7 studies); and health practitioner communication of positive messages to enhance patient expectations (12 studies). The contextual interventions were provided by different health practitioners (i.e., physicians, general practitioners, physiotherapists, nurses, and acupuncturists) in a range of settings (i.e., primary care practice, inpatients/outpatients services, rehabilitation unit, and laboratories). Moreover, each factor was delivered in different ways with different terminology. These were re-organised into three themes: empathy, patient involvement, and positive communication (Table 3-4).

Table 3-4. Characteristics of the 25 included studies

Study	Country	Condition	Mean age	No. patients	Study arms (n)	Outcome
Empathy						
Akturan et al. (2017)	Turkey	Diabetes mellitus	56.92	112	C: Usual care (55) I: BATHE interview (57)	Diabetes empowerment
Little et al. (2015)	UK	Patients attending GP	53.5	190	C: No intervention (92) I: KEPe Warm communication (98)	Patient satisfaction
Pace et al. (2017)	USA	Hospitalised patients	54.4	25	C: Usual care (12) I: BATHE intervention (13)	Patient satisfaction measure
Soltner et al. (2011)	France	Gynecological conditions requiring day-care surgery	30	68	C: Neutral anaesthesiologist behaviour (34) I: Empathic anaesthesiologist behaviour (34)	Patient satisfaction
Vangronsveld and Linton (2012)^	Sweden	Chronic back pain	48	28	C: Usual care I: Empathic consultations and validation	Pain, satisfaction
White et al. (2012)	UK	Knee or Hip osteoarthritis	66.75	221	C: Minimal empathy consultations (108) I: Empathic consultations (113)	Pain
Patient involvement						
Arnetz et al. (2004)^	Sweden	Patients attending musculoskeletal rehabilitation	-	77	C: Usual physical therapy (38) I: Patient involvement (39)	Patients rating of the quality of care
Chassany et al. (2006)	France	Knee or Hip osteoarthritis	69.1	818	C: Usual care (413) I: Prescribing and negotiation of a therapeutic contract with the patient (405)	Pain
Jellema et al. (2007)	Netherlands	Low back pain	42.7	314	C: Usual care (171) I: Minimal psychosocial strategy (143)	Functional disability
Krupat et al. (2004)	USA	Patients attending GP	56.8	1262	C: Usual care (489) I: Guided choice (773)	Patient satisfaction
Mathews et al. (2018)	USA	Hospitalised patients	62.1	60	C: Usual care (30) I: Option to add Point-of-care ultrasound (30)	Patient understanding of health problem and contributors to diagnostic process
Shively et al. (2013)	USA	Heart failure	66.15	84	C: Usual care (41) I: Usual care + patient activation (43)	Patient activation measure

Wetzels et al. (2005) ^	Netherlands	Patients attending GP	-	578	C: Usual care I: Patient involvement	Questionnaire measuring involvement
Positive communication						
de Craen et al. (2001)	Netherlands	Chronic pain	52	111	C: Neutral message (55) I: Positive message (56)	Pain
Dutt-Gupta et al. (2007) ^	Australia	Acute pain	48.3	101	C: Neutral message (49) I: Positive message (52)	Pain
Kaptchuk et al. (2008)	USA	Irritable bowel syndrome	38.3	175	C: Placebo acupuncture + limited interaction (88) I: Placebo acupuncture + augmented interaction (87)	Symptom severity
Kemeny et al. (2007)^	USA	Asthma	29.7	55	C: Neutral message I: Positive message	Calculated concentration of methacholine required to induce a 20% decrease in FEV$_1$
Knipschild and Arntz (2005)	Netherlands and Belgium	Acute pain	-	128	C: Neutral message (64) I: Positive message and explanation (64)	Pain
Lauder et al. (1995)	UK	Postoperative nausea	43.4	226	C: Neutral message (112) I: Positive message (114)	Nausea
Olsson et al. (1989)	Sweden	Acute tonsilitis	30.8	100	C: Limited interaction (50) I: Positive message (50)	Symptoms severity
Rief et al. (2017)	Germany	Disability after heart surgery	66.4	78	C: Usual care (37) I: Expectation optimisation (41)	Pain
Ronel et al. (2011)	Germany	Chest pain	64	28	C: Saline solution injection (15) I: Saline solution injection + Verbal suggestion (13)	Percentage of diameter stenosis of the index coronary artery segment; Chest pain perception
Suarez-Almazor et al. (2010)	USA	Knee osteoarthritis	64.1	455	C: Neutral expectation (229) I: High expectation (226)	Pain; Satisfaction
Thomas (1987)	UK	Patients attending GP	-	100	C: Negative message (50) I: Positive message (50)	Patient satisfaction
Wise et al. (2009)	USA	Asthma	37.8	238	C: Neutral message (118) I: Positive message (120)	Mean change in daily peak expiratory flow; Perceptions of asthma treatment

^: The studies data were not extracted as it does not provide clear results in terms of sample size distribution or outcomes reporting, n: number of participants; C: Control group; I: Intervention group; BATHE: Background, Affect, Troubles, Handling, Empathic statement; GP: General Practitioner KEPe: demonstrating Knowledge of the patient’s, Encouraging, and Physically engaging, FEV1: Forced Expiratory Volume in one second

Comparators

The intervention groups were compared against comparator groups of non-enhanced control across the studies (i.e., no intervention, neutral communication or usual care). However, the controls were different in four studies, a limited interaction group in Kaptchuk et al. (2008) and Olsson et al. (1989), a minimal empathy consultation group in White et al. (2012) and negative message group in Thomas (1987).

Outcomes

The primary outcome was extracted from all included studies. In addition, pain and satisfaction outcomes were also extracted if reported, as these were common outcomes across the included trials. These were separated into three categories:

- Ten studies reported patient experience outcomes (i.e., satisfaction, involvement, understanding, and empowerment).
- Eleven studies reported symptoms (i.e., pain, severity, and functional restriction).
- Two studies measured objective outcomes (e.g., peak expiratory flow).

Outcomes assessment end-point varied between the studies included in the meta-analysis from 60 seconds after the procedure (Ronel et al., 2011) to 52 weeks (Krupat et al., 2004, Jellema et al., 2007). Table 3-5 represents the types, categories, measures of outcomes, and end-point time for outcome measures extracted from the 20 trials that provided sufficient quantitative data.

Table 3-5. Types of outcomes

Trial	Outcome	Outcome measure	Endpoint assessment
Patient experience			
Akturan et al., 2017	Empowerment	The diabetes empowerment scale (0 -105)	26 weeks
Krupat et al., 2004	Satisfaction	Overall satisfaction (5-point scale)	52 weeks
Little et al., 2015	Satisfaction	Overall medical interview satisfaction scale (1-7)	After the consultation
Mathews et al., 2018	Understanding	Patient understanding of health problem (0 -10)	After the consultation
Pace et al., 2017	Satisfaction	Patient satisfaction measure (5-point scale)	At discharge
Shively et al., 2013	Involvement	Patient activation measure (100-point scale)	26 weeks
Soltner et al., 2011	Satisfaction	Patient satisfaction (0-100)	Immediately before anaesthesia
Suarez-Almazor et al., 2010	Satisfaction	Satisfaction with knee procedure (6- item scale)	13 weeks
Thomas K.B., 1987	Satisfaction	Patient satisfaction (%)	After the consultation
Wise et al., 2009	Perception of treatment	Perception of treatment (1-9 scale)	4 weeks
Symptoms improvement			
Chassany et al., 2006	Pain	Visual analogue scale pain scoring (0-100)	2 weeks
de Craen et al., 2001	Pain	Visual analogue scale pain scoring (0-10)	After one hour
Knipschild and Arntz, 2005	Pain	Visual analogue scale pain scoring (0-100)	2 weeks
Rief et al., 2017	Pain	Pain disability index (0-70)	26 weeks after surgery
Ronel et al., 2011	Pain	Pain perception (0-10)	After the procedure
Suarez-Almazor et al., 2010	Pain	Visual analogue scale pain scoring (0-100)	13 weeks
White et al., 2012	Pain	Visual analogue scale pain scoring (0-100)	7 days after treatment completion
Jellema et al., 2007	Functional disability	Roland-Morris functional disability questionnaire (0 - 24)	52 weeks
Kaptchuk et al., 2008	Symptoms severity	Symptom severity scale (0 -500)	3 weeks
Olsson et al., 1989	Symptoms severity	Symptoms severity (%)	2 days
Lauder et al., 1995	Nausea	Nausea score (0-10)	24 hours after operation
Objective outcomes			
Ronel et al., 2011		Percentage of diameter stenosis (% DS)	After 60 seconds
Wise et al., 2009		Peak expiratory flow (L/min)	4 weeks

3.3.3 **Risk of bias in studies**

Figure 3-2 shows results obtained with a modified version of the risk of bias tool recommended by the Cochrane Collaboration (Higgins et al., 2011). Of the 25 RCTs, 23 had low risk of bias in random sequence generation, 11 had low risk of bias in allocation concealment, 16 had high risk of bias in blinding of personnel due to the nature of the intervention, 10 had low risk of bias in blinding of outcome assessment, 18 had low risk of incomplete outcome data, and 16 had unclear risk of selective reporting bias. Detailed assessments of the risk of bias for each included study are presented in Appendix 6.

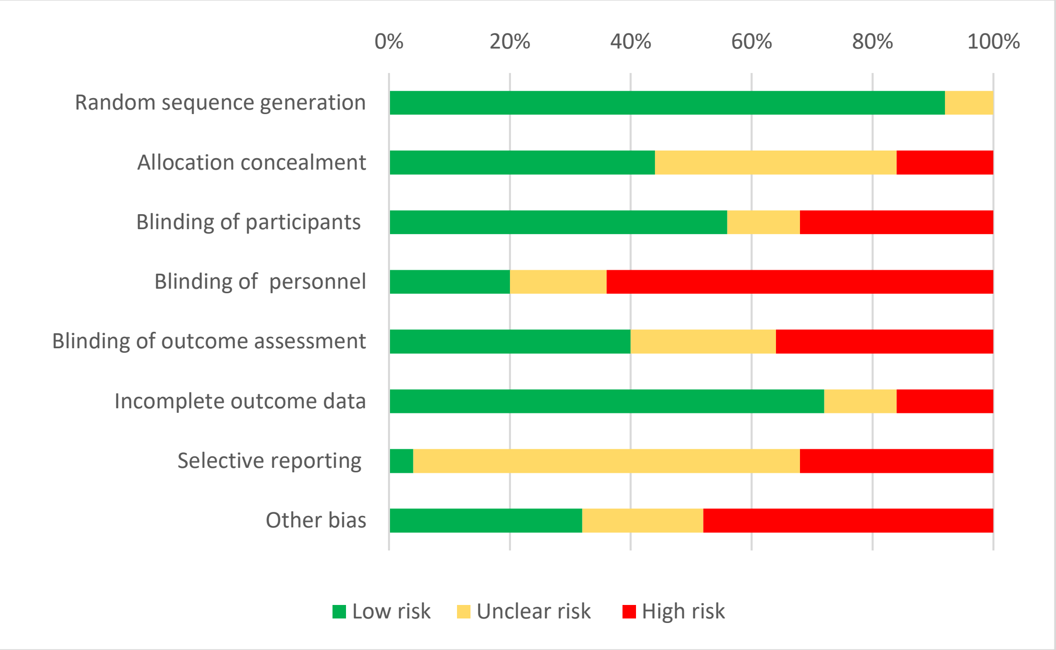


Figure 3-2. Risk of bias of all included RCTs

3.3.4 **Publication bias**

The funnel plot showed that trials with larger SMD between the two groups were more likely to be published (Figure 3-3).

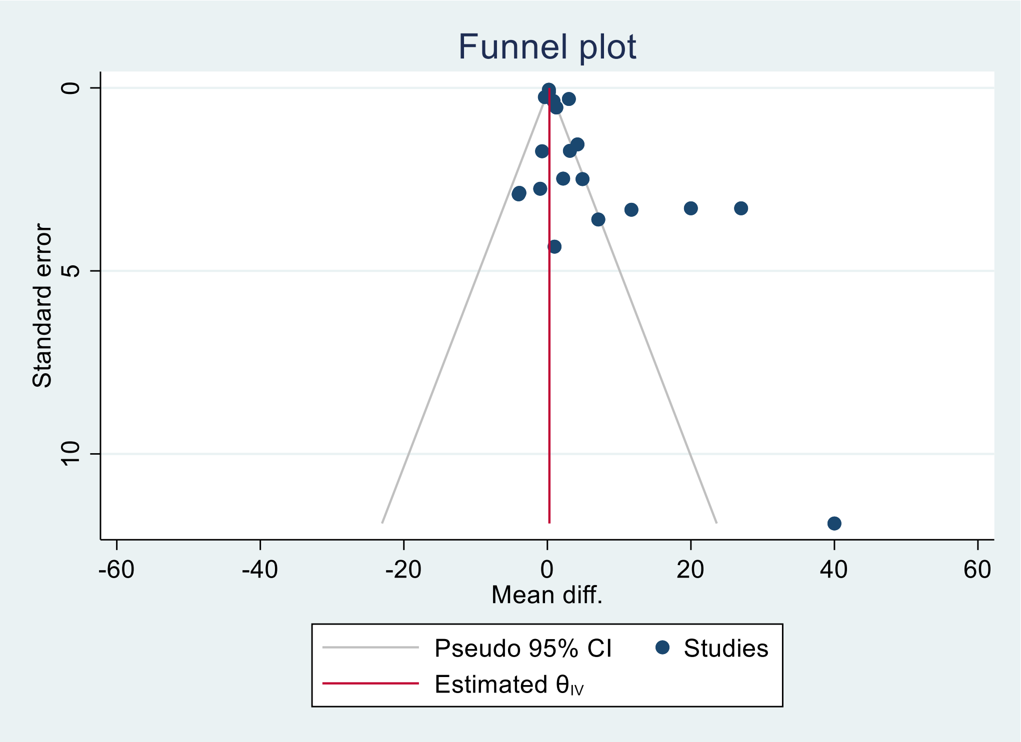


Figure 3-3. Funnel plot for the 20 RCTs

3.3.5 Results of syntheses

Narrative synthesis

Five studies out of the 25 eligible for the SR did not provide enough quantitative data for the meta-analysis. Four studies did not clearly state the sample size distribution (Arnetz et al., 2004, Wetzels et al., 2005, Kemeny et al., 2007, Vangronsveld and Linton, 2012), and one study did not explicitly report the outcomes according to the primary outcome measure (Dutt-Gupta et al., 2007). Thus, their results were only summarised narratively, as follows: Firstly, patient involvement in consultations was studied in seven trials. Five of those trials results were included in the meta-analysis and two trials did not provide enough quantitative data. Higher rating for the quality of care was found when patients were involved in establishing physical therapy goals compared to controls (Arnetz et al., 2004). Also, the logistic regression analysis shown that involvement in treatment goals setting had better physical treatment outcomes (i.e., strength and balance) compared to control. However, no relevant effects on satisfaction or involvement were found by using leaflets to enhance older patient (≥70) involvement during the GP consultation (Wetzels et al., 2005), and provided that the response rate was low (38%).

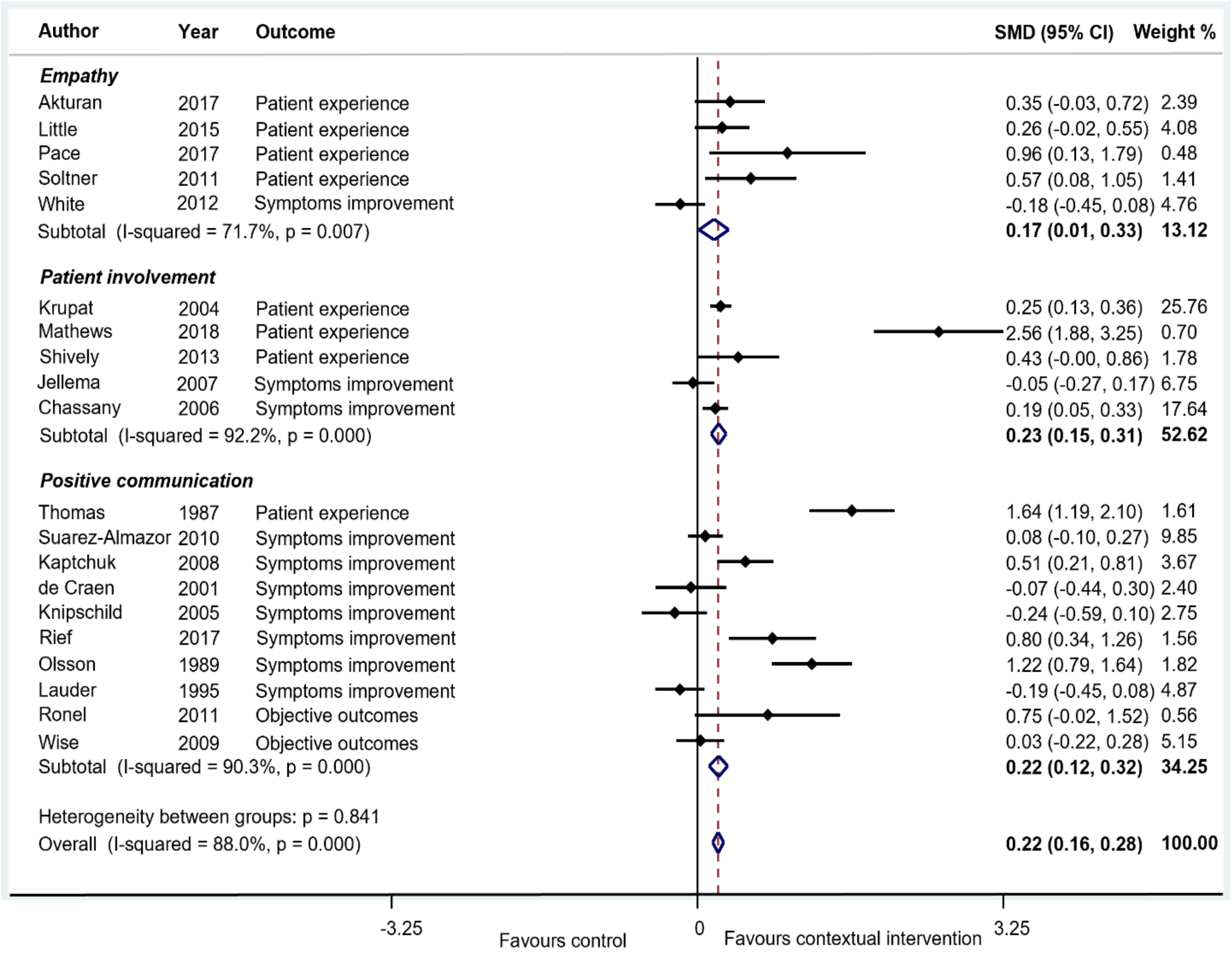
Secondly, two out of twelve trials that investigated the effect of positive messages in enhancing patient expectations were not included in the meta-analysis (Dutt-Gupta et al., 2007) and (Kemeny et al., 2007). Both studies showed an insignificant effect of enhanced expectation by positive communication. Dutt-Gupta et al. (2007) assessed the effect of two similar messages on cannulation pain in patients awaiting elective surgery within two minutes of placement. The randomisation was to receive a communication of either: ‘I am going to apply the tourniquet and insert the needle in a few moments, it is a sharp scratch, and it may sting a little’ or ‘I am going to apply the tourniquet on the arm, as I do this many people find the arm becomes heavy, numb and tingly, this allows the drip to be placed more comfortably’ (Dutt-Gupta et al., 2007). Kemeny et al. (2007) study applied a crossover design of active drug versus placebo and randomisation to two different physicians’ interactions to provide positive versus neutral messages. Although the study claims a significant positive effect of placebo on objective outcomes for patients with asthma, there was no significant difference between enhanced and neutral groups in the objective outcome levels at either the placebo or the active drug recipients ($P > 0.1$).

Finally, six studies investigated the effect of empathy interventions. All but one had adequate data for pooling (Vangronsveld and Linton, 2012). Vangronsveld and Linton (2012) studied the effect of empathy by interviewing nurses suffering from low back pain. The participants in the validation and empathy communication group were more satisfied with the interview, but there were no differences between the intervention and control groups for pain intensity at the assessment endpoints (i.e., $P = 0.937$ after one week, $P = 0.59$ after three months). Regardless of the interview type, both groups experienced less pain after the interview (*P* = <.001) (Vangronsveld and Linton, 2012).

Meta-analysis

The results from the 20 studies that provided enough quantitative data for meta-analysis were pooled using the CMA method. Of the 20 included studies, the pooled result of outcomes for contextual interventions was greater than that for outcomes for controls. The overall effect size of practitioner-patient interaction was small but statistically significant (SMD= 0.22; 95%CI 0.16, 0.28). However, the estimate was associated with a high level of inconsistency (I^2= 88%).

Figure 3-4 shows the forest plot of meta-analysis of the 20 studies sub-grouped by the identified contextual intervention. All the contextual interventions were better than control and had positive significant effects on outcomes: Empathy (SMD 0.17, 95%CI 0.01, 0.33); active involvement of patients by the health practitioner (SMD 0.23, 95%CI 0.15, 0.31); and practitioners positive communication (SMD 0.22, 95%CI 0.12, 0.32). All but one of the studies on enhanced practitioner empathy had the same (positive) effect direction (White et al., 2012). The same trend was depicted in the effect of patient involvement, with one study on the opposite effect direction (negative) (Jellema et al., 2007). The effect sizes of positive communication studies were varied. Four out of ten studies found significant improvements in the intervention group (see Figure 3-4).

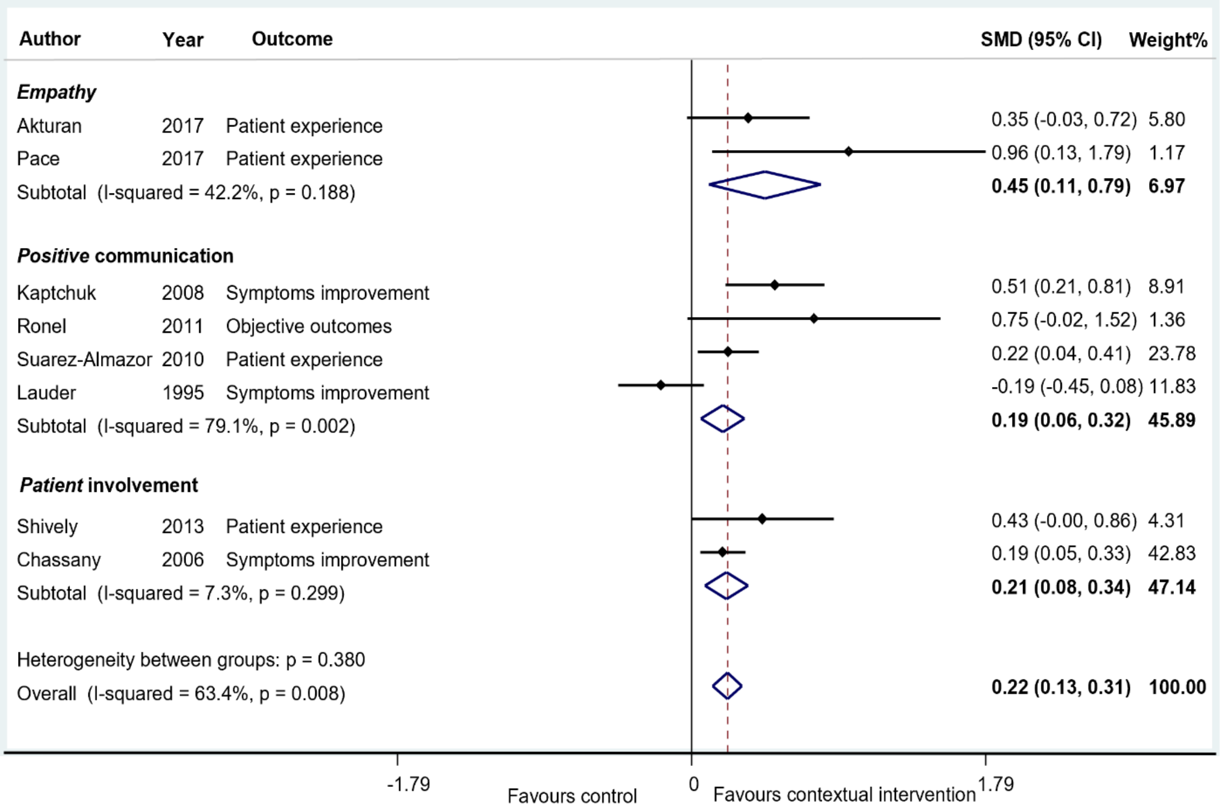


Effects are shown with 95% confidence intervals (95% CI); SMD: standardised mean difference.

Figure 3-4. Summary of contextual intervention efficacy (n= 20 studies)

Sensitivity analysis

A sensitivity-analysis of the eight studies that reported the standard deviation (SD) of mean values indicated that the overall effect size of contextual interventions was similar to the effect size of pooled results of the 20 studies (0.22; 95%CI 0.13, 0.31), with less heterogeneity between the studies (I^2= 63.4%). Empathy had a moderate effect on patient experience (0.45; 95%CI 0.11, 0.79) (Figure 3-5). Empathy became significantly better than control after excluding the trial that did not report SD, requiring an estimate derived from the other studies. However, the overall effect sizes for positive communication and patient involvement slightly decreased when pooling the studies that initially reported SDs (SMD= 0.19, SMD= 0.21, respectively).



Effects are shown with 95% confidence intervals (95% CI); SMD: standardised mean difference.

Figure 3-5. Primary studies that reported SD

In terms of outcomes, contextual interventions conferred a small but statistically significant benefit on patient experience outcomes (SMD 0.34; 95% CI 0.27, 0.42) and symptom improvement (SMD 0.12, 95% CI 0.04, 0.19). However, the effects on objective outcomes (SMD 0.10; 95% CI -0.14, 0.34) was minor and not significant (Table 3-6).

Table 3-6. Efficacy according to outcomes

Outcome	**Intervention**	**No. Studies**	**No. Patients**	**SMD (95% CI)**	***I²***
Patient experience	Empathy	4	395	**0.38 (0.18, 0.58)**	3.3%
	Patient involvement	3	1406	**0.32 (0.21, 0.42)**	95.3%
	Positive communication	3	793	**0.38 (0.24, 0.52)**	93.9%
	Overall	10	2594	**0.34 (0.27, 0.42)**	88.7%
Symptom improvement	Empathy	1	221	-0.18 (-0.45, 0.08)	0.0%
	Patient involvement	2	1132	**0.12 (0.01, 0.24)**	68.8%
	Positive communication	8	1301	**0.17 (0.06, 0.28)**	86.0%
	Overall	11	2654	**0.12 (0.04, 0.19)**	83.0%
Objective outcomes	Positive communication	2	266	0.10 (-0.14, 0.34)	66.6%

No.: number; SMD: standard mean difference, CI: confidence interval, I^2: heterogeneity.
Text in bold shows significant values. Positive SMD favours intervention group.

3.3.6 Certainty of evidence

GRADEpro GDT software was used to create the summary of findings table (GRADEpro, 2015). Table 3-7 shows the GRADE summary of findings of the contextual enhancement interventions compared to usual care for adult patients receiving treatments in any healthcare setting. The confidence in the findings was phrased as suggested in the informative statement guidance (Santesso et al., 2020). Contextual enhancement interventions may improve patients experience, but the evidence is very uncertain. The evidence suggests that contextual enhancement interventions improve symptoms slightly and may result in little to no difference in objective outcomes.

Table 3-7. GRADE summary of findings

Certainty assessment						No. Participants		SMD treatment effect (95% CI)	Certainty
No. Studies	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Usual care**	**Contextual enhancer**		
Patient experience									
10 RCTs	very serious[a]	serious[b]	not serious	not serious	none	1150	1444	SMD 0.34 SDs higher (0.27 higher to 0.42 higher)	⊕◯◯◯ Very low
Symptoms improvement									
11 RCTs	serious[c]	serious[b]	not serious	not serious	none	1343	1311	SMD 0.12 SDs higher (0.04 higher to 0.19 higher)	⊕⊕◯◯ Low
Objective outcomes									
2 RCTs	serious[d]	not serious	not serious	serious[e]	none	133	133	SMD 0.1 SDs higher (-0.14 lower to 0.34 higher)	⊕⊕◯◯ Low

CI: confidence interval; **SMD:** standardised mean difference; **SD:** standard deviation. a. All studies were at high risk of bias; b. Statistically significant heterogeneity; c. 10 studies were at high or unclear risk of bias; d. One study was at high risk of bias; e. Wide confidence interval.

3.4 Discussion

3.4.1 Key findings

This SR of RCTs has identified three CEs, namely empathy, positive communication and patient involvement, that appear to be effective for patient-centred outcomes. The effect size is small to moderate which may be used to enhance a treatment effect. The overall effect size of practitioner-patient interaction was statistically significant (SMD= 0.22; 95%CI 0.16, 0.28). This finding indicates that enhancing the CFs while delivering a treatment would increase the overall treatment effect, especially for patient-centred outcomes.

3.4.2 Findings in relation to previous literature

Based on the five dimensions of the clinical context identified by Di Blasi et al. (2001), this SR of RCTs aimed to identify the factors related to three of the dimensions (i.e. the practitioner characteristics, the patient characteristics and the interaction between the practitioner and patient) and to find additional studies that can be meta-analysed. Di Blasi et al. (2001) reported that positive verbal communication about the treatment enhances patient expectations and health outcomes (i.e., increases the speed of recovery and decreases pain).

The findings of this systematic review accord with published literature that examined CFs of practitioner-patient interaction. Howick et al. (2018b)

SR of RCTs stated that there are significant, yet small, benefits for patients having greater empathy and positive message communication from practitioners. The outcomes for that SR were classified into physical outcomes (e.g., length of hospital stay and physical function) (SMD -0.18; 95%CI -0.32, -0.05) and psychological outcomes (i.e., pain, anxiety, and patient satisfaction) (SMD -0.43; 95%CI -0.65, -0.21) (negative value indicates more effective than control). This SR chapter goes beyond just empathy and positive messages. The search strategy involved 16 CFs attained from the previous Delphi study. However, the three factors that showed to be effective from the quantitative SR were connected and similar to the two factors that Howick et al. 2018 SR examined.

Empathy is regarded as a valuable characteristic amongst healthcare providers. The findings of this SR indicated that empathy was moderately effective for improving patients' experience. Likewise, empathic behaviour has been shown to associate with greater patient satisfaction (Londhe et al., 2021), increased patient compliance (Hojat, 2009), and greater diagnostic accuracy (Hojat et al., 2003).

The relationship between patient and health provider has been considered central to the therapeutic process and viewed as an essential determinant of treatment outcome (Hall et al., 2010). The Georgopoulou et al. (2018) SR of the impact of physician-patient interaction disclosed that higher levels of active involvement of patients in medical consultations was linked to lower disease activity ($B = -0.20$; $p = 0.03$), less organ damage (OR = 0.93; 95%CI 0.91–0.94; $p < 0.0001$), better overall health ($r = 0.20$; $p < 0.05$), and greater treatment satisfaction with fewer adverse effects from the medication ($r = -0.28$; $p < 0.05$). However, the Georgopoulou et al. findings reflected the results of the primary mixed methods studies included in their review and did not include a meta-analysis of the data.

3.4.3 Limitations of the study

This SR of RCTs had several limitations in the searching process. First, the study of the practitioner-patient interaction is a complex undertaking and naming conventions, and definitions are heterogeneous. Consequently, despite a rigorous search process, some studies that would have met the eligibility criteria might have been missed. Second, the SR is restricted to publications in peer-reviewed journals and did not include unpublished studies.

Third, the search was limited to one study design (i.e., RCT). Expanding the search to other study designs could potentially identify further studies investigating CEs. Some principal contextual interventions are hard to study in an RCT design, as the randomisation and blinding criteria are hard to implement, for example, the expectations and beliefs about illness and treatment (de Craen et al., 2001). Other RCTs examined expectations of treatment as a predictor of outcome rather than an intervention (Klaus et al., 2007, Myers et al., 2008b, Vase et al., 2013).

Another limitation was the marked heterogeneity between studies due to variations in participants, health disorder and methodological characteristics (Riley et al., 2010). Moreover, the details of what the intervention involved were often absent or indefinite, so it is hard to take the findings of the SR forward to develop a CE intervention. For instance, some of the included studies' methods provided little information about the intervention implementation (Arnetz et al., 2004; Shively et al., 2013). Rosendal et al. (2013) claimed that investigations are needed to examine the effect of enhanced care when delivered per protocol to a well-defined population with functional disorders.

In addition, SD was not reported in most of the included studies. The reviewer computed the SD for the mean change values (see missing data section). A sensitivity analysis was therefore undertaken for studies that reported SD to verify the results. Finally, variable outcomes were investigated in this SR, yet little has been done for objective health outcomes. How effective CEs are for modulating disease processes remains largely unknown.

3.5 Conclusion

In conclusion, the SR of RCTs has identified three CFs, specifically empathy, positive communication and patient involvement, that are effective *per se* for patient-centred outcomes. These three CFs may be included in the CEP for further assessment. More research is needed to examine the clinical objective outcomes of these CFs and understand the influence of CFs on disease processes.

Chapter 4. Understanding and Identifying Key Contextual Factors that Influence the Practitioner-Patient Encounter in Management of Osteoarthritis: A Qualitative Systematic Review

4.1 Overview

This chapter presents a qualitative SR and meta-aggregation of the evidence related to CFs in the practitioner-patient encounter. The evidence gained from published qualitative studies of CFs was synthesised using a pragmatic meta-aggregative methodology.

4.1.1 Research aim

The aim of the study was to explore and understand the experience and perspectives of patients and health practitioners with respect to CFs in consultations for OA.

Objectives:

1. To identify the key CFs in OA consultations.
2. To identify the barriers and facilitators of delivering the key CFs.

4.2 Methods

The SR was conducted in accordance with the Joanna Briggs Institute (JBI) methodology for SRs of qualitative evidence (Lockwood et al., 2020). The JBI applies a meta-aggregative approach of qualitative evidence synthesis, drawing upon a philosophy of pragmatism (Hannes and Lockwood, 2011). For reporting this SR, the 'Enhancing

Transparency in Reporting the Synthesis of Qualitative Research' (ENTREQ) guideline was followed (Tong et al., 2012).

The SR protocol was registered in PROSPERO (CRD42020197530), available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020197530

4.2.1 Eligibility criteria

The PICo framework (Population, phenomenon of Interest, and Context) was used to define the search terms.

Population

The review considered studies that included:

(i) Any health professional (e.g., general practitioner, rheumatologist, nurse, and physiotherapist) involved in the care of adults living with OA.

(ii) Adults with OA of any synovial joint, regardless of OA severity.

Phenomena of interest

Studies that explored the experience of OA patients and health practitioners through face-to-face consultation for OA that involved any CFs related to the interaction between them were considered, including: patient's expectation, clinician's behaviour, belief, therapeutic touch, patient-centred approach, and health care setting (Rossettini et al., 2018a).

Context

This review considered studies that were conducted in the context of the practitioner-patient interaction/consultation in any healthcare setting and in any country.

Types of studies

All types of qualitative studies, including but not limited to, designs such as phenomenology, grounded theory, ethnography, action research and feminist research were considered. Studies that were retrievable in full text and in the English language were included.

4.2.2 Information sources

The databases searched included MEDLINE via Ovid, EMBASE, AMED, PsycINFO and CINAHL. In addition, reference lists of all included studies were checked for relevant studies. The search for unpublished studies included Google Scholar and digital theses (i.e., ProQuest Dissertations).

4.2.3 Search strategy

The primary reviewer A.I. developed and piloted a comprehensive search strategy to seek all available studies. The strategy was reviewed by a librarian, and a qualitative study expert, Dr Catrin Evans (C.E.). A detailed literature search was conducted between March 15 and May 18, 2020.

Each database was searched individually, then the citations from all information sources were combined. The search was not limited to any publication year (from database inception to May 2020). An example of one of the searches undertaken in MEDLINE is presented in Appendix 8.

4.2.4 **Selection process**

Following the search, all identified citations were collated and uploaded into EndNote X8 bibliographic software and duplicates were removed. Titles and abstracts were screened for assessment against the inclusion criteria for the review. Relevant studies were retrieved, and the primary reviewer assessed the full text of selected citations in detail against the inclusion criteria. The second reviewer Khalid Yaseen (K.Y.) participated in the validation of the SR stages. Fifty randomly selected citations were independently checked by K.Y. to confirm that studies met the predefined inclusion criteria. The primary reviewer then assessed the full texts of the retrieved studies. Reasons for exclusion of full-text studies that did not meet the inclusion criteria were recorded. The process is represented in the PRISMA flow diagram.

4.2.5 **Assessment of methodological quality**

The included studies were assessed for methodological quality by A.I. using the standardised critical appraisal instrument from the Joanna Briggs Institute Qualitative Assessment, Review and Appraisal Instruments (JBI-QARI) (See Appendix 9). This instrument comprises ten questions related to congruency of the research methodology with the stated philosophical perspective, research question, method, and interpretation of the results, in addition to the consolidated criteria for reporting qualitative research. Compared to other qualitative appraisal instruments, the JBI tool has been described as the most coherent in assessing original qualitative study validity (Hannes et al., 2010). The JBI-QARI addresses four types of validity, specifically: descriptive, interpretive, theoretical, and evaluative validity. Table 4-1 briefly explains the types of validity addressed in the JBI tool and which questions considered each type of validity.

Table 4-1. Types of validity addressed in the JBI-QARI tool (Hannes et al., 2010)

Types of Validity	Explanation	Questions
Evaluative validity	The extent to which a framework is applied to the object of study. Reflected in the appropriateness criterion.	1, 2, 3, 4 and 5
Descriptive validity	The extent of accuracy of reporting the descriptive information. Reflected in the criterion of investigator impact.	6 and 7
Interpretive validity	The extent of accuracy of reporting the participants viewpoint and experiences. Reflected in the criterion "believability".	8 and 9
Theoretical validity	The extent to which a theory informing a research study fits the data, thus, credible. Reflected in the "theoretical framework" criterion.	10

4.2.6 Data extraction process

Qualitative data were extracted from studies included in the review using the JBI-QARI data extraction tool (See Appendix 10). The data extraction tool comprises both study characteristics (i.e., publication year, country, population, methodology, research questions) and findings. All text under the ‘Results’ heading was checked for relevant findings. Each finding was extracted and assigned a level of credibility as per JBI guidelines. The primary reviewer had appraised the congruency between the data and the accompanying illustration. The three degrees of credibility are:

- Unequivocal (U) – findings accompanied by an illustration that is beyond a reasonable doubt.
- Credible (C) – findings accompanied by an illustration lacking clear association with it.
- Non-supported (N) – findings not supported by the data.

The data were extracted electronically and entered into an Excel spreadsheet. K.Y. assessed the quality and data extracted from a random sample of 10% of the included studies. Any disagreements between the reviewers were resolved through discussion. ≤5% disagreement was allowed, otherwise the full set of data would be double extracted. Furthermore, advice was sought from C.E. throughout the SR process.

4.2.7 Synthesis methods

According to the included studies population, two syntheses were undertaken for this SR. One synthesis focused on patients' experience with OA consultations and another synthesis focused on health practitioners' perspectives about OA management and encounters with patients. For both syntheses, findings across the papers were compared, contrasted and pooled, using the JBI-QARI meta-aggregative approach (Lockwood et al., 2015). The JBI approach meta-aggregation does not include re-interpretation or re-analysis of the primary studies. Instead, it involves categorizing the findings based on similarity in meaning and concepts. Subsequently the categories were pooled to produce a comprehensive set of synthesized findings. These statements represent the meaning of the aggregation and can provide direction for policy and practice.

4.2.8 Confidence assessment

According to the JBI manual for qualitative synthesis, this qualitative SR followed the Establishing ‘Confidence in the Output of Qualitative Research Synthesis’ (ConQual) approach to assess the confidence in the synthesised findings (Munn et al., 2014a). The ConQual score assists healthcare professionals and policymakers establish confidence or trust in research results and implement evidence-based decision-making. Two main elements define confidence: credibility and dependability (Guba and Lincoln, 1982). These elements are analogous to the validity and reliability concepts in quantitative research.

Credibility is assessed by evaluating the extent to which the findings related to each synthesised finding are unequivocal, credible, or not supported. If the constituent findings are unequivocal, the credibility rating is high. If some of the findings are credible, then the overall credibility rating of the synthesised finding is downgraded. Dependability is evaluated by assessing the answers to five of the questions on the JBI-QARI critical appraisal tool (questions numbers 2,3,4,6, and 7) that are deemed to be directly related to dependability within a study. If studies have low dependability scores, then the synthesised finding is downgraded for dependability. An overall judgement is then made on the confidence in a synthesised finding, based on the credibility and dependability ratings, with each synthesised finding assessed as having a ConQual evaluation of high, moderate, low or very low confidence (Munn et al., 2014a).

4.3 Results

4.3.1 Study inclusion

The systematic search of databases and grey literature yielded 1985 citations. From 1808 screened titles, eight were included in the meta-aggregation (Figure 4-1). Reasons for excluding studies after full text assessment are briefly outlined in the flowchart (details in Appendix 11). No studies were rejected because of concerns about methodological quality.

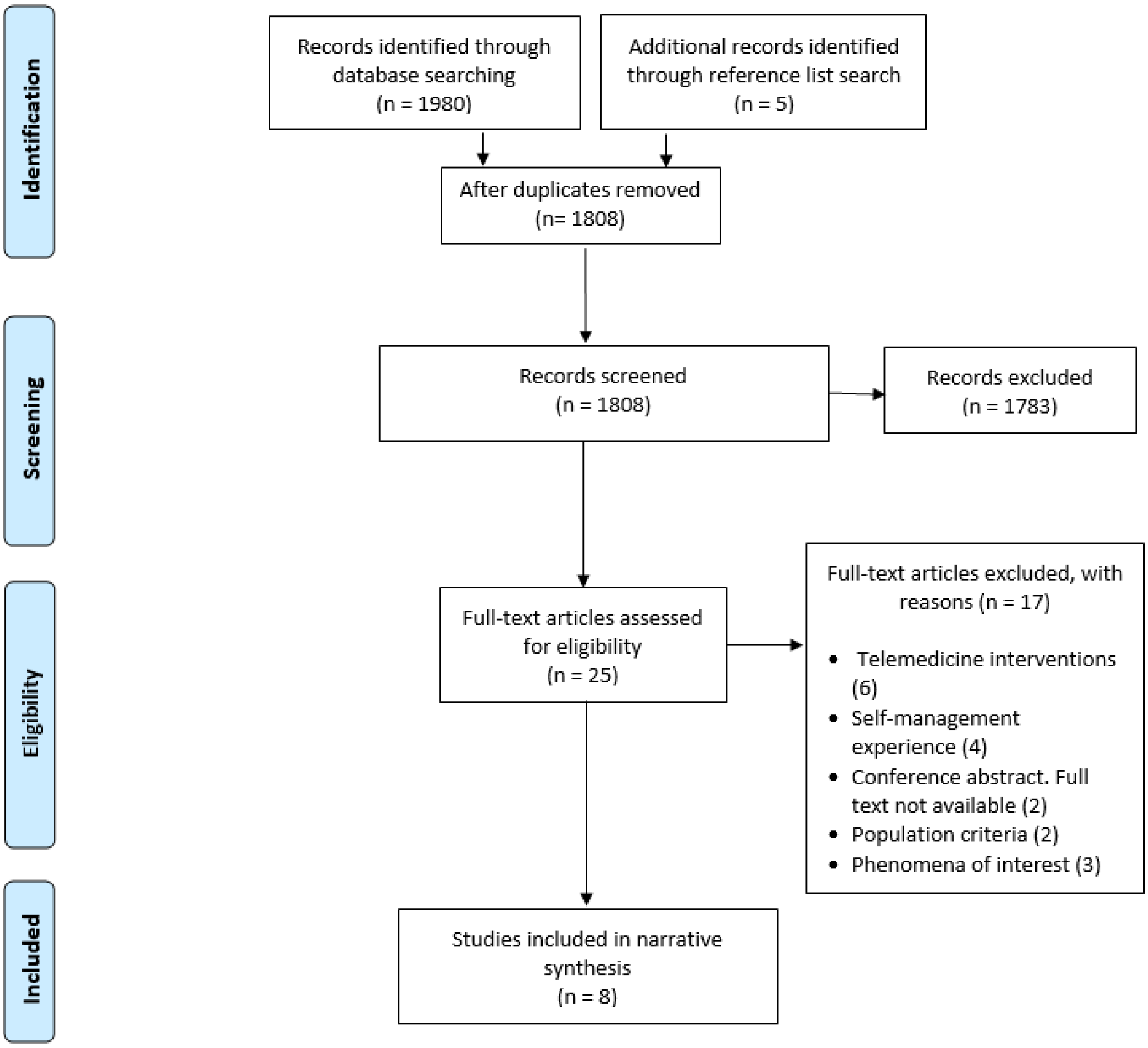


Figure 4-1. PRISMA flowchart of the study selection and inclusion process

4.3.2 **Characteristics of included studies**

The characteristics of the final eight studies included in the qualitative synthesis are summarised in Table 4-2. The publication dates ranged from 2006 to 2018. The studies were conducted in six different countries. The philosophical perspectives and research methodologies differed across the included studies. Two methods of data collection were conducted in the included studies: focus group and interview. All the interviews followed a semi-structured approach. The studies included the following groups of participants: people with OA [three studies]; health providers dealing with OA patients [two studies]; and both OA patients and health providers [three studies].

Table 4-2. Characteristics of included studies

Study	**Country**	**Method**		**Participants**	
		Interviews	**Focus group**	**OA Patients**	**Health Providers**
Alami et al. (2011)	France	●		●	●
Austine et al. (2016)	India	●			●
Baumann et al. (2007)	France		●	●	
Brembo et al. (2016)	Norway	●		●	
Egerton et al. (2018)	Australia	●			●
Mann and Gooberman-Hill (2011)	UK	●	●	●	●
Rosemann et al. (2006)	Germany	●		●	●
Ryan et al. (2013)	UK		●	●	

OA: Osteoarthritis

The aims and participants information are summarised in Table 4-3. The review included 231 patients with OA and 107 health practitioners.

Patients varied from 40 to 89 years old, and more than 50% of them were women. The majority of OA diagnosis was knee or hip OA. Patients had various experience with OA concerning the duration lived with OA and pain severity when interviewed.

The health providers' professions were general practitioners, rheumatologists, orthopaedic surgeons, nurses, physiotherapists, and occupational therapists. They had different years of experiences with OA management. The healthcare systems and settings in which health providers interact with the patients were different across the studies.

Table 4-3. Summary of study aims and participants information

Study	**Aims**	**Participants**	
		Number & roles	**Gender & age**
Alami et al	To identify the views of pts and care providers regarding the management of knee OA and to reveal potential obstacles to improving health care strategies	81 knee OA pts, 19 GPs, 6 rheumatologists, 4 orthopedic surgeons	37% female, (45–80) years
Austine et al	To assess orthopedists' perspectives on pain management in OA	15 orthopedists managing OA pain	Unknown
Baumann et al	To evaluate the expectations of OA pts in France	96 OA pts: 66% knee; 50% finger; 46% hip	81% female, (42-89) years
Brembo et al	To explore pts' emotional and informational needs across the whole care continuum for hip OA	13 hip OA pts	53% female, (59-88) years
Egerton et al	To identify key factors influencing implementation of guidelines in the primary-care setting	11 GPs managing knee OA	64% female
Mann and Gooberman-Hill	To explore the opinions of pts and health professionals about the provision of health care for people with OA and possible service improvements	16 pts with hip or knee OA 12 HPs (4 nurses, 2 GPs, 2 orthopedic surgeon, 2 PT, rheumatologist, OT)	56% female, (56-81) years
Rosemann et al	To identify health care needs of pts with OA and to reveal possible obstacles for improvements in primary care management of OA pts	20 OA pts, 20 GPs and 20 nurses	60% female, (40-78) years
Ryan et al	To explore the perceptions and experiences of people with OA and RA regarding the knowledge and skills they want health professionals to have to manage their care needs	5 OA pts and 8 RA pts	OA: 80% female, (41-64) years. RA: 75% female, (42-67) years

GPs- General practitioners, HP- Health providers, OA- Osteoarthritis, OT- Occupational Therapists, PT- Physiotherapist, pts- Patients, RA- Rheumatoid arthritis, SDM- shared decision-making.

4.3.3 Quality assessment

Table 4-4 presents the answers obtained by the ten-question-JBI appraisal tool. Overall, the included papers were of a relatively high quality. Most of the JBI-QARI checklists were fulfilled. The philosophical perspective was not clearly stated for all but one study by Alami et al (2011). The key weaknesses were that the influence of the researcher on the research was not addressed in three studies (Q7). Also, the participants' voices were not adequately represented in three studies (Q8).

Table 4-4. JBI-QARI Critical appraisal checklist

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Alami et al. (2011)	Y	Y	Y	Y	Y	Y	N	U	Y	Y
Austine et al. (2016)	U	Y	Y	Y	Y	Y	Y	U	Y	N
Baumann et al. (2007)	U	U	U	U	U	Y	N	N	U	N
Brembo et al. (2016)	U	Y	Y	Y	Y	Y	Y	Y	Y	Y
Egerton et al. (2018)	U	Y	Y	Y	Y	Y	Y	N	Y	Y
Mann and Gooberman-Hill (2011)	U	U	U	U	U	Y	Y	Y	Y	Y
Rosemann et al. (2006)	U	U	U	U	U	Y	N	N	Y	Y
Ryan et al. (2013)	U	U	U	U	U	Y	Y	Y	Y	Y

Y - Yes, N - No, U – Unclear

Q 1: Is there congruity between the stated philosophical perspective and the research methodology?

Q 2: Is there congruity between the research methodology and the research question or objectives?

Q 3: Is there congruity between the research methodology and the methods used to collect data?

Q 4: Is there congruity between the research methodology and the representation and analysis of data?

Q 5: Is there congruity between the research methodology and the interpretation of results?

Q 6: Is there a statement locating the researcher culturally or theoretically?

Q 7: Is the influence of the researcher on the research, and vice-versa, addressed?

Q 8: Are participants, and their voices, adequately represented?

Q 9: Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body?

Q 10: Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data?

4.3.4 Results of syntheses

Three out of the eight included studies had perspectives of both health providers and people with OA. Thus, the first synthesis considered the experience of people with OA extracted from six papers. The second synthesis considered health providers' perspective and experience dealing with people with OA based upon data extracted from five papers (see Table 4-2). Each finding was given an assigned level of credibility based upon the JBI credibility levels. As per JBI guidance, only unequivocal and credible findings were included in the syntheses.

Synthesis related to patients' perspectives and experiences

<u>Synthesized finding 1:</u> The key CEs from the patients' perspective were provision of *clear information, attentive and empathic healthcare providers, involvement in consultations, positive expectations, and easy access to care.* It is likely that people with OA will experience comprehensive and satisfactory management of their condition if these key CEs are implemented. This synthesised finding was derived from five categories and 36 patient findings. The constituent categories with some illustrations from primary studies are presented below. Figure 4-2 depicts a graphical representation of the combined five categories.

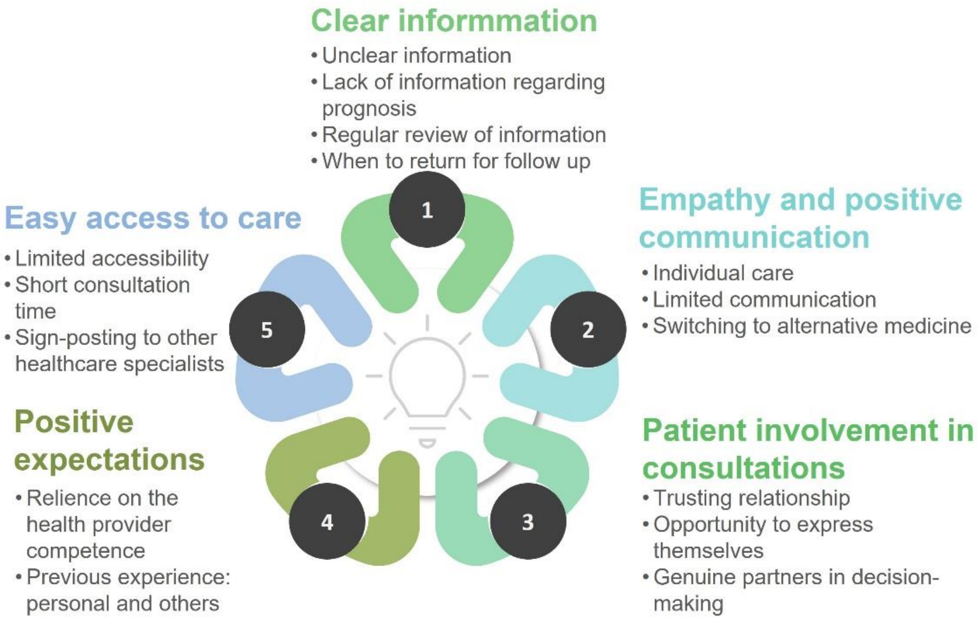


Figure 4-2. The five categories that constitute the first synthesized finding

The first category was **clear information** needed for reassurance and to boost self-confidence to manage the condition. Patients claimed that they received unclear explanations or insufficient knowledge during their consultations, and the clinicians' decisions were not always consistent. They wanted clarity and simplicity of information. Advice about exercise was given as an example of incomplete information.

> *'Concrete types of exercise or other possibilities were not mentioned, directions were mostly quite vague.'* (Rosemann et al., 2006, pg.6).

Receiving sufficient information was linked to high satisfaction. Patients felt well informed about the OA structural changes. However, in the early stages of OA, patients lack enough information about OA prognosis, making them feel insecure and less confident about managing their condition.

> *'Can it get worse again?; Am I likely to go on to worse disability?; Am I likely to become bedridden?; I am afraid of being in a trolley; ....in a little (wheel) chair; especially when you are living alone..'* (Baumann et al., 2007, pg. 407).

Self-reliance and self-management could be promoted by regular review of information, explaining the likely course of OA, and clarifying when to request the clinician's support. The findings revealed that providing relevant prognostic information would help the patients accept the diagnosis and the uncertainty about the future and promote self-confidence.

> *'I would like someone to explain to me why and how the dose should be increased when there is a flare-up, and why it is decreased afterwards. Why is it important to avoid getting too used to these drugs?'* (Baumann et al., 2007, pg. 407).

Patients argued that care was reactive rather than proactive. Some patients felt that they were left coping on their own after the radiograph had confirmed the diagnosis, and they were not sure when to return to doctors.

> *'Well, I think I was told that, at some stage you will need a hip replacement, but . . . you are a bit too young, you know, to have that done. And my doctor said, if it gets any worse come back, which I did, and then he said, if it gets any worse come back. There is nothing proactive coming from the doctor to manage that condition.'* (Mann and Gooberman-Hill., 2011, pg. 967)

The second category, **empathy and positive communication skills**, refers to the aptitude of health providers' interpersonal skills to enhance the patient encounter. Patients appreciated having an empathic and attentive doctor who can adopt a holistic approach to the patient and provide individualised care and support.

> *‘My doctor, he sorts out everything! He is really competent. He is kind and he has a real sense of humour. I do appreciate him a lot, because he is really human.’* (Alami et al., 2011, pg.3).
>
> *‘I can tell you that I have the world’s best GP! She gives me all the information I need and instructs me what to do. You should do this kind of exercises and you’ll have an X-ray and you should do this, she arranges the whole show. Everything comes into my mailbox and I check it regularly.’* (Brembo et al., 2016, pg.8).

Nevertheless, patients complained about some of the providers’ behaviour. For example, when the practitioners overuse the computer during the consultation, patients considered it a misuse of the consultation time and upsetting as it limits face-to-face interaction and expression. Moreover, they felt that some practitioners might be trivializing OA, and their complaints were not recognised.

> *‘His face is hidden by the computer. His eyes are on the computer, I can’t see the way he is looking; the consultations could almost be done over the phone.’* (Baumann et al., 2007, pg. 407).

Due to the high value placed upon positive communication and interaction with health providers, some patients preferred switching to alternative therapies where specialists are more empathic, open to discussion, spend more time with their patients, and consider patients more globally.

> *‘At first, the acupuncturist asks me how I feel, and we talk too. I felt depressed occasionally, so it is another thing we can talk about. He can do something. He considers the patient as a whole, which is a real difference with physicians like the rheumatologist who examines you, asks you three questions and has finished with you. I do think the relationship with the doctor in alternative medicine is longer, deeper and makes more sense.’* (Alami et al., 2011, pg. 5).

The third category was the **patient preference for involvement in consultations** and to be a genuine partner in the management process. Meaningful consultations for OA participants comprise a trusting relationship that allows for the patient’s participation. Patients considered themselves genuine partners in the medical decision-making process when they had an active role in the discussion and the opportunity to ask questions.

> *‘Treated as an intelligent human being … he showed me where my hip had fused together. My husband was with me, and it was a discussion between the three of us.’* (Ryan et al., 2013, pg. 810).

Nevertheless, the Baumann et al. study showed that the participants had too little opportunity to express themselves in OA consultations.

> *‘You dare not ask (for information) ’; ‘They don’t really like people asking questions’; ‘He made me feel I was being a nuisance.’* (Baumann et al., 2007, pg. 407).

The fourth category, **the influence of previous experience and expectations**, refers to how patients behave during and after consultations based on their expectations and experience. Patients’ expectations relied on health providers’ competence and experience. Some patients found it difficult to disclose their concerns to their GP, as they perceived the GP as not an expert about OA.

> *‘GPs aren’t specialists in osteoarthritis, so they.... they do what they can to refer me within the health care system, so I can’t say that I have anything to complain about in that respect… I get help for things I ask about, but I don’t really expect to receive any particular kind of information.’* (Brembo et al., 2016, pg. 8).

Moreover, positive previous experiences, either personal or others, provided hope and knowledge about possible future risks.

> *‘When you have suffered long enough, you’ll try almost anything… learning from the experiences of others I have talked to, who have had a successful hip replacement– it makes me see possibilities for myself as well.’* (Brembo et al., 2016, pg. 10).

The fifth category was **accessibility to primary healthcare professionals** and signposting to other specialists if required. Many patients discussed limited consultation time as a barrier and that GPs were generally too busy to spend enough time with each patient.

> *'The GP is just keen to get you out in order to let the next patient in… He listens to what you say, but haven't taken it seriously enough.'* (Brembo et al., 2016, pg. 8).

Moreover, they wanted to have the opportunity to consult an arthritis specialist again if they had any concerns after the consultation. Patients preferred to be sign-posted to other healthcare professionals, i.e., physiotherapy, occupational therapy or practice nurse, to receive a range of pain interventions and learn how to manage their condition efficiently.

> *'There's nobody that appears to be an expert in osteoarthritis. There are so many of us! We need not only specialist doctors, but nurses and physios as well.'* (Ryan et al., 2013, pg. 811).

Table 4-5 depicts a summary of the findings and categories for synthesized finding 1. The findings were taken directly from the primary studies that reflected the authors' expression and assigned a level of credibility.

Table 4-5. Results of first meta-aggregation of patients' findings

Findings	**Categories**	**Synthesized findings**
The physician accentuating the patient's feeling of uncertainty about OA by the patient feeling that they received unclear explanations or insufficient knowledge. (U)	Clear information is needed for reassurance and to boost self-confidence to manage the condition.	*Synthesized finding 1:* The key contextual enhancers from patients' perspective were provision of clear information, empathy and positive communication, involvement in consultations, positive expectations, and easy accessibility to care. *It is likely that people with OA will experience comprehensive and satisfactory management of their condition if these key contextual enhancers are implemented.*
They needed information that would help them accept the diagnosis and the uncertainty and doubt about the future that goes with it. (C)		
Practitioners, in turn, possessed knowledge that they could pass on to patients in order to promote self-reliance and the self-confidence required to cope with the anxieties inherent in all chronic diseases. (C)		
There is a need for more clarity, accessibility, and simplicity. (C)		
Elective patients receive standardized information prior to admission that explains what to expect and what they should do to prepare for the recovery period. (U)		
Most of the participants in this study expressed satisfaction about the information provided by the hospital staff. (U)		
Most patients expressed a strong desire for improved information about OA and its likely progression, particularly at diagnosis and in the early stages of OA, so that they could know what to expect, as well as feel confident in their management of the condition. (C)		
Seven patients described feeling left to cope on their own and that nothing was done once the radiograph had confirmed the diagnosis. One patient noted that care was reactive rather than proactive. (U)		
Others found it difficult to know when to return to the doctor. (U)		
Some felt that regular review and information about the likely course of OA would help them to make a judgment about their own need and felt that this could support self-management. Continuity of care was also considered important. (U)		
Patients noted that the clinicians' decisions or advice were not always consistent. (U)		
Regarding the cause and the pathomorphology, patients felt well informed. But in terms of the prognosis, patients were very insecure. Many patients argued that physicians were mainly focused on explaining the pathology of the disease and the treatment options such as new surgical methods, but less focused on their main fears (Pain and becoming disabled). (C)		

According to patients' statements, concrete types of exercise or other possibilities were not mentioned, directions were mostly quite vague. Receiving just a short, vague hint without a clear advice or motivation was regarded as insufficient. (C)		Cont'd: *It is likely that people with OA will experience comprehensive and satisfactory management of their condition if these key contextual enhancers are implemented.*
The feeling of being in a specific and individualised relationship with the care provider that gives the feeling that the physician is ‘‘their’’ doctor. This feeling was related to the interpersonal and communication skills of physicians and their ability to adopt a holistic approach to the patient. (U)	Empathy and positive communication skills	
Practitioners trivializing OA and having fatalistic attitudes gave patients the feeling that their complaints were not recognised. (C)		
Reasons advanced for choosing or switching to alternative therapies are to have a physician directly administer the therapy and that physicians who deliver or prescribe alternative therapies be open to discussion, have more empathy, spend more time with their patients, and consider patients more globally in their environment as compared with physicians prescribing biomedicine options. (U)		
Computers ‘steal’ time from relationships and may upset the patient by hiding the practitioners face. Facial expression and body language enhance communication. (U)		
The support provided by practitioners was considered an integral part of care provision (Trust in the GP). (C)		
One participant expressed great satisfaction with her GP, however, demonstrating the value of having an attentive GP. (U)		
The trusting relationship appeared to allow for patient cooperation and participation and for patients to be part of the medical decision-making process. (U)	Patient preference for involvement in consultations and to be a genuine partner in the management process.	
Patients also wanted to be able to ask questions of their practitioners and to see them, above all, as genuine partners. (U)		
OA patients surveyed appeared to feel that they had too little opportunity to express themselves. (C)		
The knowledge and skills required for a meaningful consultation for OA participants included the opportunity to be involved in the consultation, being listened to and having an active role in the discussion. (U)		
Some also indicated a feeling of shame attached with talking about their emergent hip pain or OA diagnosis and felt that their hip disease was lower in the hierarchy than other diagnoses, such as cancer and diabetes type 2. (U)	Influence of previous	

Most of the participants did not actively seek information during consultations. This was explained partly by the fact that they did not know what to ask specifically and because the GP was not perceived to have the necessary expertise about OA. (U)	experience and expectations.	Cont’d: *It is likely that people with OA will experience comprehensive and satisfactory management of their condition if these key contextual enhancers are implemented.*
Some found it difficult to appropriately disclose their concerns to their GP. (C)		
Learning from others’ experiences provided hope for a better future. (U)		
Others relied heavily on the experience and competence of the orthopaedic surgeon. (U)		
One participant brought up personal experiences with surgery performed earlier as grounds for deliberation about possible risks. (C)		
This feeling also stemmed from specific behaviour that conveyed the accessibility of the physician and ethical qualities such as devotion, conviction, prioritising therapeutic over financial considerations, and resoluteness in disease management. (U)	Accessibility to primary healthcare professionals and signposting to other specialists if required.	
Reasons advanced for choosing or switching to alternative therapies are to have a physician directly administer the therapy and that physicians who deliver or prescribe alternative therapies be more accessible. (U)		
Many discussed available time as a barrier. (C)		
They agreed with each other that GPs were generally too busy to spend much time discussing OA and were not specialists in arthritis. Patients expressed a desire to have access to someone with specialist knowledge of arthritis, possibly a practice nurse. (C)		
Participants said that they would like nurses and AHPs to be able to offer a range of pain interventions including medication advice, relaxation, acupuncture, and distraction. (U)		
Although none of the OA participants had received input from an occupational therapist or a nurse, they perceived that access to these professionals would enable them to receive advice on how to manage their condition. (U)		
All participants wanted access to a consultant, nurses and AHPs to manage their care. Participants felt this would provide the opportunity to consult them again if the treatment recommended was not effective. (U)		

Synthesis of the views and experiences of health providers

The meta-aggregation of health providers qualitative results yielded two synthesized findings, represented in Table 4-6 and 4-7, respectively. Two categories representing nine findings supported the second synthesized finding, and three categories from 22 findings supported the third synthesized finding. The second synthesized finding demonstrated the factors that may enhance OA management, while the last synthesized finding expressed the challenges perceived by health practitioners in OA management. The synthesized finding and categories were as follows.

<u>Synthesized finding 2:</u> Health providers acknowledged that information provision and efficient communication skills are important factors to facilitate patient engagement and provide a response to patients' expectations which likely enhance the management of OA.

The first supporting category was **the advantages of providing information** from the health providers' point of view. The information provision advantages were facilitation of provider-patient communication about the management, assistance for patients to understand their condition, managing patients' expectations, facilitation to lifestyle changes, and acceptance of self-management and treatment options.

> *'That initial education phase is actually really important and, you know, helping them to understand . . . what arthritis means, what they can do to help themselves and . . . what other things are*

> *available down the line, I think is really important.'* (Mann and Gooberman-Hill., 2011, pg. 968).

The second category, **communication skills in the consultation**, refers to the clinicians' interpersonal approach. General practitioners reflected on the importance of possessing effective communication skills. Hence, responding to patients' expectations and demands and improving their compliance with treatments.

> *'Most of a GP's life is about understanding the patient's difficulties and barriers and motivations and then acting out your advice in a way that, hopefully, helps that patient.'* (Egerton et al., 2018, pg. 5).

Table 4-6. Results of second meta-synthesis of qualitative research findings

Findings	**Categories**	**Synthesized findings**
Participants concurred that this statement holds true in clinical practice as the two-way process allows patients to understand their condition and cope accordingly. (C)	The advantages of providing information	*Synthesized finding 2*: *Health providers acknowledged that information provision and efficient communication skills are important factors to facilitate patient engagement and provide a response to patients' expectations that likely enhance the management of OA*.
Having access to customisable, printable patient resources was suggested as a facilitator to GP-patient communication about both diagnosis and management options. The resources are already available, commenting the issue is not a lack of resources but awareness of them. (C)		
Shifting patients' mind-sets to active participation in management and making lifestyle changes was reported as challenging and time consuming for GPs. (C)		
They argued that delivering a relatively positive prognosis to patients facilitated uptake of lifestyle changes. (C)		
The need for early education about OA and its likely course was emphasized since patients' expectations and illness perceptions have an important effect on their acceptance of self-management and treatment options. (C)		
The health professionals also thought patients should have the opportunity to discuss these options and be provided with more information to aid self-management at diagnosis, or soon after. (C)		
GPs' main aim was to ensure that the patient actually took the prescribed drugs. Therefore, they had mostly developed individual strategies that consisted of a balancing act of explanations for anticipated objections regarding treatment, legal requirements and belittlement. (U)		
All GPs reflected on the importance of having highly effective communication skills. (U)	Communication skills in the consultation	
When practitioners elaborate a prescription, their objectives are not restricted to solving knee OA symptoms but are also to provide a response to patients' demands and expectations, optimise compliance to treatments, and minimise risks. (C)		

Synthesized finding 3: Effective consultations are affected by an intersection of organisational challenges as well as patient and provider characteristics. Limited experience with OA of some practitioners, unrealistic patient expectations, and short consultation duration are barriers that need to be adjusted for better management. If the management was provided by clinicians who have sufficient OA knowledge and experience and address patients' expectations in their encounter, they would likely respond better to the treatment. Extending consultation duration and providing a clear follow-up plan might improve OA management. The third synthesized finding was derived from the following three categories.

The first category was **knowledge gaps and confidence to effectively manage OA.** Some participants declared that they were less confident in making a diagnosis without imaging and in providing proper exercise and weight loss advice. The skills and knowledge of motivation and facilitation of behavioural change were considered gaps for clinicians in OA consultations.

> *‘The problem is how do you actually get people to do this stuff…how do you tell them what the right thing to do is?’*
> (Egerton et al., 2018, pg. 5).

Furthermore, some GPs stated that it was challenging to distinguish between the complaints originating from chronic arthritis and those related to concomitant depressive symptoms.

The second category, **patients' expectations** from health providers' perspectives, refers to how clinicians speculate about patients' expectations concerning OA management and outcomes. Clinicians claimed that patients' expectations influence their decision considerably. They feel that patients have negative connotations associated with the label when diagnosed with OA. Moreover, they doubt the patients' willingness to make behavioural changes. Health providers got this impression from patients craving immediate pain relief, leading to poor compliance with physiotherapy and lifestyle modification. Findings from surgeon participants described patients' expectations as unrealistic such as the expectations about the surgery and returning to the functional performance that was lost a long time ago.

> *'And there are the subjectively unsatisfied: the ones who always have pain; who no longer can walk three hours hunting; who are never happy with anything and who have thought that it (surgery) would bring them back 10 years before.'* (Alami et al., 2011, pg. 8).

The third category was **short session duration and limited accessibility** to follow-up sessions. Time pressure was discussed as a major barrier in OA consultations. It impeded providing individualised exercise plans, prescribing a weight management program, and allowing patients to discuss their condition. Clinicians also highlighted that OA was often just one of a patient's complex multi-morbidity that needed more time to assess and manage.

> *'The bigger issue is, I feel I don't have enough time to really give it in a way that I'm completely satisfied with.'* (Egerton et al., 2018, pg. 5).

The effect of the follow-up system was discussed in three of the included studies. One study highlighted a loss of follow-up system in their settings (Austine et al., 2016), while absence of proactive follow-up was emphasised in another study (Mann and Gooberman-Hill, 2011). Some health providers argue that patients should initiate their follow-up when needed for efficient use of resources.

> *'I think to just get somebody up on a routine basis, and if they come up go, "Oh no well actually everything's absolutely fine," I don't think that that's a good use of a patient's time or our time. So I think it probably would be better for it to be at the patient's request.'* (Mann and Gooberman-Hill., 2011, pg. 969).

Table 4-7. Results of third meta-synthesis of qualitative research findings

Findings	**Categories**	**Synthesized findings**
Reduced confidence with making a diagnosis without imaging, despite having the knowledge that x-ray findings are not needed. (C)	Knowledge gaps and confidence to effectively manage OA	*Synthesized finding 3: Effective consultations are affected by an intersection of organisational challenges as well as patient and provider characteristics.* Limited experience with OA of some practitioners, unrealistic patients' expectations, and short consultation duration are barriers that need to be adjusted for better management. If the management was provided by clinicians who have sufficient OA knowledge and experience and address patients' expectations in their encounter, they would likely respond better to the treatment. Extending consultation duration and providing a clear follow-up plan might improve OA management.
Reduced confidence with providing suitable exercise and weight loss advice. (C)		
GPs acknowledged challenges of facilitating behaviour change and most felt they lacked skill in promoting readiness and motivation for these lifestyle treatments. (U)		
Most said they were afraid of upsetting their patients and this resulted in a temptation to avoid the discussion. (C)		
Quality of care was also thought to be adversely affected by general lack of expertise and interest in OA in the community. (C)		
Many GPs stated that they found it difficult to assess to what extent complaints originate from arthritis and what part of the complaints are due to concomitant depressive symptoms. (U)		
Most of the GPs admitted that they did not focus on increasing patients' motivation for behavioural change, but just gave general recommendations. (C)		
Practitioners identify specific but various patients’ expectations concerning surgery (patients wishing to undergo surgery as soon as possible and others wishing to avoid this treatment option). They also have concerns about patients’ unrealistic expectations about surgery such as returning to the functional performance lost a long time ago. (U)	Patients’ expectations from health providers perspectives	
Two major contributing factors are the outpatient workload and the mind-set of patients who crave immediate pain relief, resulting in poor compliance to physiotherapy and lifestyle modification. (C)		
Interviewed GPs reported patient “expectation” and “pressure” had substantial influence on their decision to order x-ray investigations. (U)		
GPs stated concerns with giving patients a knee OA diagnosis because they assumed patients would have negative connotations associated with the label. (U)		
Some expressed doubts about the patients’ willingness to make behavioural changes. (U)		
The surgeons identified an information gap prior to referral for surgery since they sometimes saw patients who they felt had unrealistic expectations of the outcome of joint replacement. (U)		

They expect tools (decision trees) to help in therapeutic decision-making by defining treatments according to patient profiles. (C)		Cont'd: Short consultation duration, unrealistic patients' expectations, and limited experience with OA of some practitioners are barriers that need to be adjusted for better management.
There also lacks a system of follow-up due to low finances and the time expenditure suffered by the patient. (C)	Short session duration and limited accessibility to follow-up sessions	
Time pressure was discussed as a major barrier. Most GPs said they felt unable to individualise weight management and develop exercise plans within the appointment time. (U)		
All interviewed GPs said that OA was often only one part of a patient's complex multi-morbidity and having time to devote to discussing OA management feels like a "luxury". (U)		
All participants expressed concerns regarding financial cost to patients when considering referral to other services. (C)		
It was thought that patients lacked proactive follow-up to support self-management. The rheumatologist thought that patients would be better served by a long-term condition model of care providing consistency over time, rather than one that consisted of episodes of care in response to symptom exacerbation. (U)		
3 health professionals also felt that routine follow-up was not the best use of their time or health care resources and that patients should initiate their own follow-up when needed. (U)		
Lack of time to give patients sufficient opportunity to discuss their condition arose in all but one of the health professional interviews. (U)		
The GPs, physiotherapist, nurse practitioner, and 1 practice nurse felt that the wait for physiotherapy was too long, and there was insufficient intervention when patients were seen. (U)		

4.3.5 Confidence in the evidence

The synthesized findings of this review were graded according to the ConQual approach. All the synthesized findings from this review had the same ConQual score (see Table 4-8). The credibility score was downgraded one level for all the synthesized findings because they were constructed from unequivocal and equivocal (credible) findings. Due to common dependability issues across the included studies, the average dependability score was 4/5. Thus, the dependability outcome remained unchanged.

Table 4-8. ConQual summary of findings

Synthesized finding	**Type of research**	**Dependability**	**Credibility**	**ConQual score**
I. It is likely that people with OA will experience comprehensive and satisfactory management of their condition if the key contextual enhancers are implemented.	Qualitative	Unchanged*	Downgrade 1 level**	Moderate
II. Health providers acknowledged that information provision and efficient communication skills are important factors which likely enhance the management of OA.	Qualitative	Unchanged*	Downgrade 1 level**	Moderate
III. Effective consultations are affected by an intersection of organisational challenges as well as patient and provider characteristics. Limited experience with OA of some practitioners, unrealistic patients' expectations, and short consultation duration are barriers that need to be adjusted for better management.	Qualitative	Unchanged*	Downgrade 1 level**	Moderate

* The average score was (4/5) for dependability.
** Downgraded one level due to a mix of unequivocal and credible findings.

4.4 Discussion

4.4.1 Summary of findings

This qualitative SR aimed to synthesise the existing evidence relating to the experience of CFs in OA consultations from the perspectives of patients and health practitioners. A comprehensive search of the literature utilising specified selection criteria resulted in a small but insightful number of included studies (n=8). The collective depth and breadth of the obtained research papers revealed several CEs. The meta-aggregative analysis produced three synthesized findings from ten categories that were developed from the 67 findings extracted from the eight studies, supported by illustrations taken directly from the primary studies.

All included papers were moderate to high quality (scores 5 –9.5) based on the JBI qualitative critical appraisal tool. However, when the ConQual criteria assessed dependability in conjunction with credibility assessment, the three synthesised findings' level of evidence was rated as moderate. This discussion section examines the synthesised findings and considers possible implications for practice and further research.

The patients’ synthesized finding provided evidence to support the importance of CEs. Patients were satisfied with consultations when the CEs were in place. Moreover, they expressed their need to have positive CFs for meaningful consultation. The CFs convey a hidden meaning, detected and actively analysed by the patient, which is essential for the perception of care and the therapeutic intervention's interpretation (Colloca and Miller, 2011a).

Synthesis of the findings related to health providers revealed barriers and facilitators of delivering the CFs in OA management. These factors emerged from different healthcare systems in six different countries, where access to care and available resources varies greatly. Despite this, common concepts were documented in the meta-aggregation process. This increases the transferability of the review’s synthesised findings.

This qualitative synthesis has recognised some CFs in the management of OA. Emotional, cognitive, social, and relational factors were all recognised as necessary within the clinical encounter. These factors were viewed from the perspectives of health providers and patients. Similar factors have been stated by both patients and health providers, specifically information, communication, session duration, and expectation. There were clear agreements about the following factors: the necessity of providing clear and relevant information; the influence of positive communication and empathy; and the need for longer consultation duration and a defined follow-up plan (see Figure 4-3).

Figure 4-3. The key contextual factors identified in the qualitative systematic review

In terms of the consultation duration factor, both patients with OA and health practitioners claim the need for longer sessions. However, in a study on the impact of patient-centred communication on patients' satisfaction with care received in German primary care practices, patients who had a consultation with a physician trained on patient-centred communication perceived that their GP spent enough time with them, and they were satisfied with their GP (Altin and Stock, 2016). It could be justified by the quality of spending the consultation time and the approach the health provider uses to communicate with patients.

The perspectives of patients and health providers on the patient expectation factor were distinct. The synthesis of patients’ perspectives revealed that patients’ expectations relied on health providers’ competence, and previous positive experiences were promising for future outcomes. However, the synthesis of health providers views indicated that the patient’s previous experiences and expectations seldom constitute a barrier to OA management that profoundly affect patients’ behaviour and practitioners’ performance. Enhancing the patient’s expectation through positive information and reassurance may significantly influence the health outcomes (Di Blasi et al., 2001). Investigating patients’ expectations is essential for clinicians treating musculoskeletal conditions. Yet, this is not routinely investigated in clinical practice (Rossettini et al., 2020b). This highlights the need for a framework that consider patients’ expectations and could be clearly implemented in clinical practice.

The review recognised another barrier to OA efficient management related to practitioners’ knowledge gaps and confidence to effectively manage OA. Health professionals need to be aware of current best practices for the management of OA to gain confidence in consultations and to improve patients’ experience.

4.4.2 **Findings in relation to previous literature**

The CFs identified in this review concur with the factors documented from previous literature. Available literature in OA and other chronic conditions supports the impact of these factors. For example, practitioner-patient alliance in physical rehabilitation had positive effects on treatment outcome (Hall et al., 2010). The alliance implies an affective bond between patient and health practitioner and patient involvement in management, i.e., agreement on goals and shared decision on interventions. Alliance was positively associated with treatment adherence in patients with multiple pathologies, symptoms relief in patients with cardiac conditions, treatment satisfaction in patients with musculoskeletal conditions, and physical function improvement in geriatric patients (Hall et al., 2010).

In addition, the CEs recognised in this review accord well with the findings of an integrative review about the qualities of a ‘good’ musculoskeletal physiotherapist from patients’ and physiotherapists’ perspectives (Kleiner et al., 2022). The integrative review methodology facilitates a more comprehensive understanding of a phenomenon by integrating experimental and non-experimental studies and theoretical literature as appropriate. Kleiner et al. (2022) integrative review included 27 qualitative and quantitative experimental studies and theoretical literature. The six identified qualities of a good physiotherapist are communicative, caring, collaborative, competent, ethical, and responsive. They described the six qualities as follows: communicative quality is the ability to communicate clear explanations and educate patients; caring quality as an empathic and understanding; collaborative quality as involving patients through dialogue and willingness to adapt to patients' needs; competent quality as being confident, knowledgeable and possessing clinical reasoning and practical skills; ethical quality as being honest, trustworthy, and practising within professional boundaries; responsive quality as listening to patients, being attentive, and communicating verbally and non-verbally.

In 2022, two further qualitative SRs examined CFs in primary care and rehabilitation to develop training tools to enhance treatment in OA and physiotherapy management of chronic pain (Vennik et al., 2022, Chapman et al., 2022). These SRs referred to the CFs as communication strategies and interaction between health providers and patients. The main differences between this chapter and the recent publication are highlighted below.

In January 2022, Vennik et al. published '*Patient and Practitioner Priorities and Concerns about Primary Healthcare Interactions for Osteoarthritis: A Meta-ethnography*'. The meta-ethnography was conducted in accordance with eMERGe Reporting Guidelines (France et al., 2019). This approach of qualitative synthesis warranted the interpretation of findings and developing of explanatory theories rather than the aggregation of primary data into a combined whole that is more than the sum of individual findings (Noyes and Lewin, 2011). As the reporting guidelines vary from the JBI's, the search strategy framework (i.e., Spider) and the quality assessment tool (i.e., CASP checklist) differed. Vennik et al. (2022) review included some of the studies in this current review in addition to other studies due to different eligibility criteria. Although the data were analysed from ethnographical perspectives, the findings were similar to the extracted categories in this chapter since the same CFs were examined. The developed conceptual model to promote a shared understanding of OA in primary care consultations involved encouraging conversation, validating the patient experience, using clear non-medical language, and sharing tailored information. Hence, Vennik et al.'s explanatory meta-ethnography complements this chapter's meta-aggregation findings, where the synthesised findings are readily usable to inform policy decision-making.

Later, in June 2022, Chaman et al. published ‘*Preferred Communication Strategies Used by Physical Therapists in Chronic Pain Rehabilitation: A Qualitative Systematic Review and Meta-Synthesis’*. Ten databases were searched in this SR. Then, the synthesis included 11 qualitative and mixed-method studies that have not been included in this current review. The quality of the studies was assessed using the CASP tool. The meta-synthesis identified eight communication themes: (1) disclosure-facilitating; (2) empathic; (3) collaborative communication; (4) rapport-building; (5) professional accountability; (6) informative; (7) meta-communication; and (8) agenda-setting (Chapman et al., 2022). Five of those themes were also identified in this chapter as key contextual factors in OA management. However, the overall quality of the available evidence from the GRADE-CERQual assessment level of confidence was moderate for four themes (i.e., 1, 2, 3 and 4) and low for four themes (i.e., 5, 6, 7 and 8).

4.4.3 Limitations of the study

Given that OA is a condition largely depending on the contextual factors in management (Zou et al., 2016), it is noteworthy that only a small number of qualitative studies were identified in the literature which investigated the perspectives of HCPs and patients regarding CFs in consultations for OA. Seven of the included studies were conducted in Western and high-income countries and it is possible that other CFs might have arisen from a similar sample in other countries. In addition, the qualitative SR was limited to studies published in the English language so some relevant studies may have been missed.

A comprehensive search strategy was created in consultation with a research librarian and an expert in qualitative research. However, because the phenomenon of ‘contextual factors’ has not been well defined and is not limited to a specific study design or health setting, it was essential to include a few interrelated factors, including patient participation, communication skills, empathy, and satisfaction. A diverse range of themes was found across the included factors, yet some relevant CEs may have been missed. Further, if the triangulation procedure had been undertaken in the extraction of findings, that would have enriched the review results and made them more valid. Instead, a second reviewer validated the extraction of 10% of the included studies.

4.4.4 Implications

The three synthesized findings from this review hold actionable recommendations for policy and practice to optimise OA management. These recommendations could also be implemented in managing other chronic musculoskeletal conditions. Further research that examines the CFs in different cultures and Eastern countries could help understand the CFs globally and possibly adjust the encounter accordingly. Also, qualitative research could investigate CFs in telemedicine and online clinical sessions as prevailing in OA management.

4.5 Conclusion

This qualitative SR explored the CFs in OA consultations from the perspectives of practitioners and patients. The findings indicated some correspondence between patients' and health providers' viewpoints about the CFs in OA management. The eight key factors were positive communication, attentive and empathic healthcare providers, patient involvement in consultations, clear and relevant information provided by the health practitioner, patient expectations concerning their outcome and the consultation experience, confidence in the health practitioner, sufficient consultation time, and easy access to consultations. The findings are in line with and add additional CEs to the previous quantitative SR to better inform the development of the CEP.

Chapter 5. Stakeholders Involvement

5.1 Overview

This chapter presents the process of seeking the opinions of stakeholders (e.g., healthcare providers (HCP), academics/researchers, policy makers, consumers/patients) on the CFs identified in this project.

5.1.1 Study aim

The stakeholders' survey aimed to obtain clinicians', researchers', and patients' views and perspectives on the eight identified CFs reported in chapters 3 and 4.

5.2 Materials and method

5.2.1 Design

The stakeholders' involvement was conducted through an online survey using Microsoft Forms software. Forms facilitated this study by offering multiple features. This Microsoft software enables anonymity of participation and supported summarisation of the results in Excel sheets. Also, Forms is user friendly with almost no risk to the privacy and security of participants.

The survey introduction presented a brief overview of the research topic and the objective. The survey included a Likert scale question that rated the importance of each of the eight CFs identified in this project. The options were: not important at all, less important, somewhat important,

important, and very important. The last question was an optional open-ended question that enquired about additional CFs related to practitioner-patient interaction which needs to be considered (see Appendix 12).

5.2.2 Ethics considerations

The School of Medicine Research Ethics Committee were consulted for ethical approval of the online stakeholders' survey. The response was that the study did not require a full research ethics review (Appendix 13).

5.2.3 Participants and settings

The online survey was emailed to a group of health practitioners and placebo researchers. The supervisors sent the online survey to a group of health practitioners through an evidence-based healthcare mailing list. The researchers were sought from the reference list of cited work in the previous chapters. Also, one of the supervisors posted the survey on the Chartered Society of Physiotherapy (CSP) website. The survey was also posted on A.I. Twitter account and retweeted by other medical researchers and physiotherapists. Additionally, the survey was emailed to the patients who had participated in the second PPI/E meeting. Apart from profession, no personal information was asked on this survey to keep the survey anonymous.

5.2.4 Data collection and analysis

The online survey was circulated between the 20th of September 2021 and the 15th of October 2021. The sample size count, the HCP professions’ proportion, and the Likert scale answers percentages were calculated for the data analysis. Moreover, thematic analysis and a summary of the open-ended narrative answers were conducted.

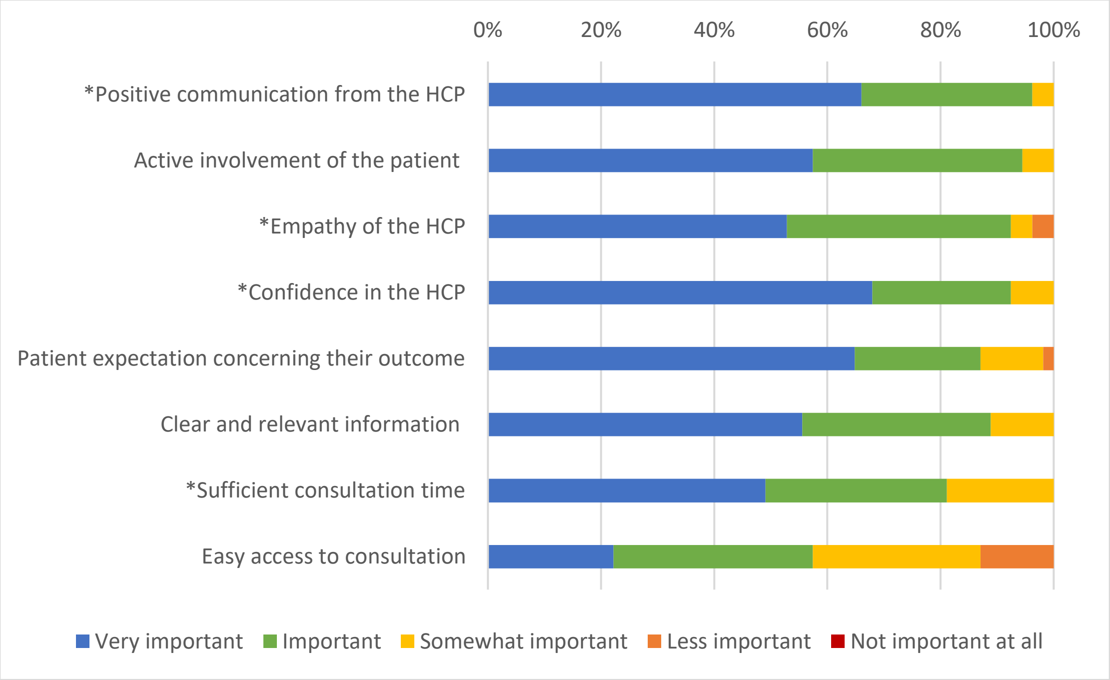
5.3 Results

5.3.1 Participant characteristics

Fifty healthcare professionals responded to the online survey (70% clinician, 14% academic and 16% academic-clinician). The HCP professions included 20 physicians, 24 physiotherapists, 5 health researchers, and one podiatrist. The physicians' specialities were general practice, rheumatology, paediatrics, psychology, and emergency medicine. In addition, the four patients who contributed to the second PPI/E meeting also completed the online survey.

5.3.2 Results of rating the eight contextual factors

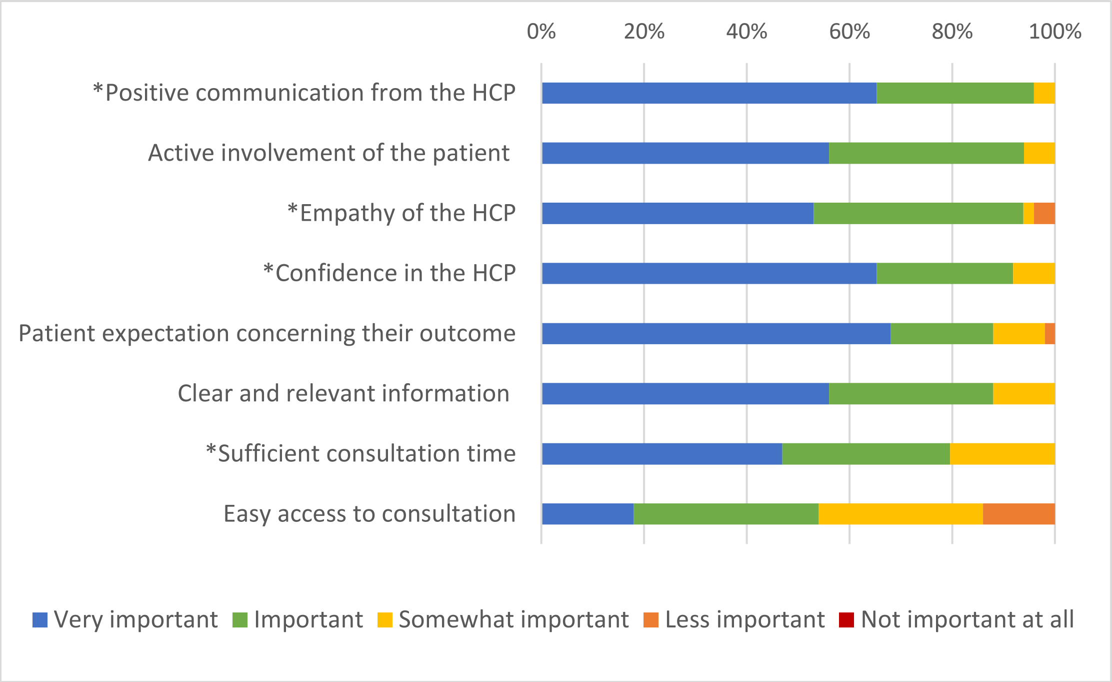
The majority of stakeholders (>57%) score on the eight factors as very important and important (see Figure 5-1). Figure 5-2 and Figure 5-3 show the rating of the healthcare providers and patients, respectively.



*: one missing response= 2%, HCP: Healthcare provider

Figure 5-1. Overall stakeholders' input on the eight contextual factors

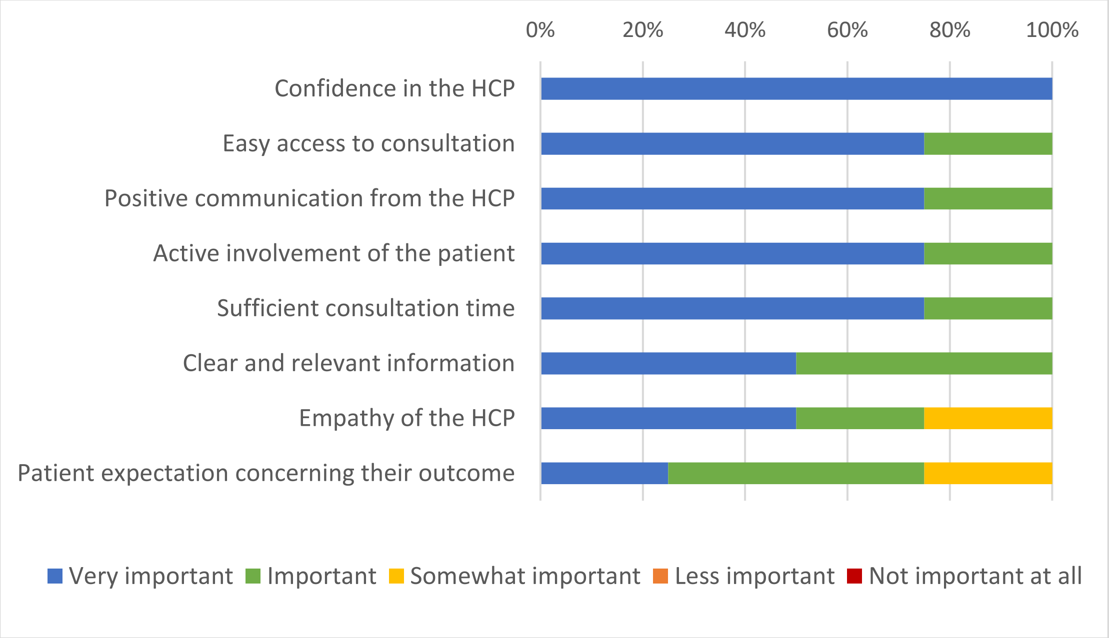
The CFs that received the highest importance rates from HCPs were positive communication from the HCP and active involvement of patients by the HCP in consultations (94%), followed by empathy of the HCP (92%). The lowest importance level was given to "easy access to consultations" (54%). A summary of the HCP answers to the Likert scale questions is presented in Figure 5-2.



*: one missing response= 2%, HCP: Healthcare provider

Figure 5-2. Healthcare provider input on the eight contextual factors

The CF that received the highest importance rates from the patients was the confidence in the HCP. Easy access to consultations, positive communication from the HCP and active involvement of patients in consultations had the same high-level of importance. A summary of the patients answers to the Likert scale questions is presented in Figure 5-3.



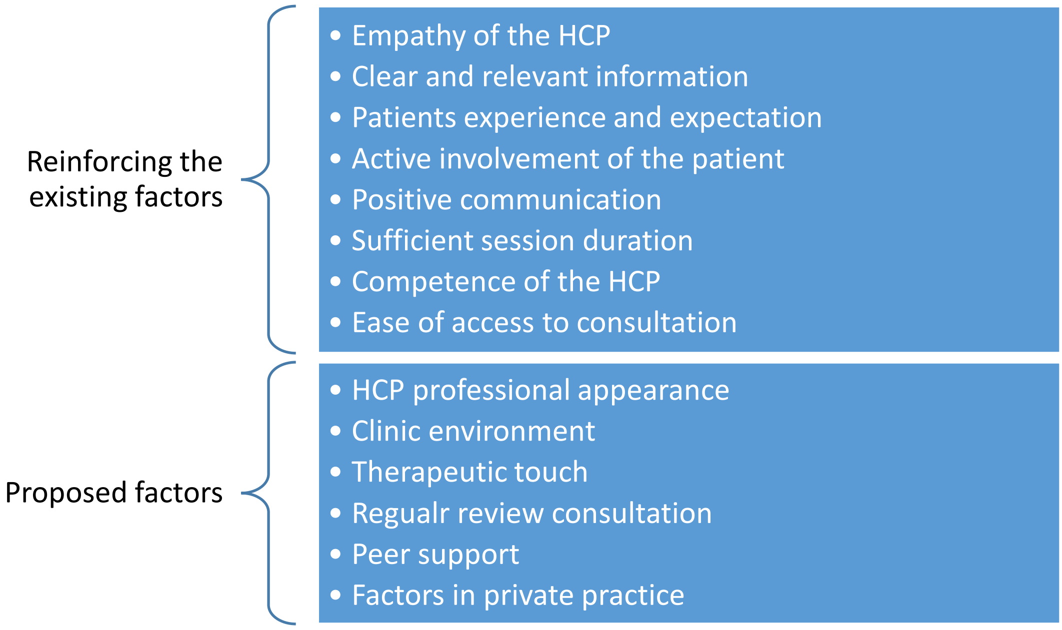
HCP: Healthcare provider

Figure 5-3. Patients input on the eight contextual factors

5.3.3 Additional contextual factors

Out of the 50 HCP respondents to the survey, 35 answered the open-ended question about any suggested additional CFs. All the patients responded to this question. Thematic analysis of answers was undertaken to identify patterns across the data. The factors added by the stakeholders were grouped under two categories, specifically “reinforcing the existing factors” and “proposed factors" (see Figure 5-4). The principal opinion from both HCP and patients was that all eight CFs are essential and to adapt the approach according to the patient's needs.

The stakeholders proposed six additional factors: the care provider’s attire and professional appearance (suggested by 4 HCPs and one patient representative); clinic environment (suggested by 4 HCPs); therapeutic touch (suggested by 3 HCPs); regular review consultation (suggested by 2 HCPs and one patient representative); social prescribing (suggested by two patients and one HCP); in addition to the factors related to private practice (provided by 4 HCPs). HCPs noted that in private practice, the cost of the consultation and the marketing to the clinic, the clinician or the treatment provided are distinct CFs.



HCP: Healthcare provider

Figure 5-4. Contextual factors suggested by the stakeholders

5.4 Discussion

5.4.1 Summary of findings

The stakeholders who participated in the survey were 50 representative HCPs and four patients with OA. The stakeholders' importance rating for each of the eight CFs was high. Both HCPs and patients with OA considered all factors essential and expanded their responses about how important these factors are in the open-ended question. However, "Easy access to consultations" received a distinct rating from HCPs and patients with OA. The patients considered this factor as very important and had stated this factor as well on the narrative question. In contrast, the HCPs rating for this factor was the least important compared to other factors (i.e., 54% important). Hence, the gap between HCPs' and patients' perspectives about the value of easy access to consultations could be improved from the HCP side. HCPs might need to consider this factor as it has been overlooked or neglected.

Moreover, the stakeholders provided valuable suggestions in the open-ended question. The six additional factors should be considered in future research. Overall, the stakeholders' input corresponds with the outcomes from the previous studies in this research project and previous research (Smith et al., 2021, Pinto et al., 2012, Kelley et al., 2014). The stakeholders' involvement in the research might have been enriched if a direct discussion with stakeholders had been conducted. However, this limitation could be outweighed by the advantage of seeking the opinions of a large sample which was accessible through the online survey. Also, the online survey may be a more convenient method for participants.

5.5 Conclusion

This chapter has provided recognition of stakeholders' views on the results of the previous chapters. Agreement was reached on the eight CFs that have a therapeutic effect. The results of the stakeholder's survey will inform the development of CEP for OA management.

Chapter 6. Public and Patients Involvement and Evaluation

6.1 Overview

Throughout the PhD project, public and patient inputs were collected as needed. This chapter presents the process of involving the public and patients in two stages of the research project. The first PPI/E meeting was held in the early stages of designing the research project, and it introduced the research project to a PPI group and obtained inputs on the conceptualisation and design of this study. The second PPI/E meeting was conducted after completing the systematic reviews of the literature to help the interpretation and progression of the project.

6.1.1 Objectives

1. To consider the relevance of the research topic to the public and patients.
2. To seek patient and public views on the importance of the identified eight CFs from their experience.

6.2 Materials and method

The PPI/E process in this research project took two forms of involvement. At the early stages of the project, in November 2019, the PPI/E focus-group discussion aimed to communicate the research information (i.e., research question and topic) to patients with OA. Whereas, at the later stage of the research, in September 2021, the public and patients exchanged information and participated by providing their opinion and input on the research outcomes.

6.2.1 Ethics considerations

The PPI/E focus-group meeting did not require any ethical application. The PPI/E group members had the freedom to choose to participate in the meetings after they received the invitation that included description of the research topic and meeting objectives. The meetings were conducted without any audio or video recording of the participants' voices. Instead, we took notes to capture their own words. The forms that the participants completed were anonymous.

6.2.2 Design

The primary researcher (A.I) discussed the objectives of each PPI/E focus-group meeting with the supervision team. Then, we contacted the translational research facilitators from the musculoskeletal (MSK) PPI patient advisory group in the Pain Centre Versus Arthritis. We provided them with information regarding the research topic and the aims of the PPI/E meetings. The participants were provided with the lay summary of the research project to be informed about the topic ahead (Appendix 14). They had an independent decision in participation in the meetings. All the participants were treated fairly and equally throughout the study.

First PPI/E meeting

A MSK PPI/E request form was completed and sent to the Pain Centre (see Appendix 15) together with the suggested date and time of the event. A translational research facilitator emailed a representative PPI/E group and invited them to the meeting. The face-to-face focus-group meeting was held on the 27th of November 2019 in A11 Clinical Sciences Building, City Hospital, Nottingham. It lasted for one hour (2-3 pm). The meeting involved a concise presentation about the research project, a discussion with the participants, and filling a short form about the relevance of the research topic (see Appendix 16). Refreshments and snacks were provided in the meeting.

Second PPI/E meeting

The MSK PPI/E patient advisory group lead had contacted a PPI group and arranged with A.I. for the second PPI/E meeting. The online focus-group meeting through Microsoft Teams was held on the 22nd of September 2021. It aimed to obtain the public and patients views on the research outcomes. The meeting lasted for an hour (10-11 am). The meeting involved an explanation of the eight CFs that have a therapeutic effect and this meeting objectives and discussion about the identified CFs. At the end of the meeting, we invited the PPI to participate in the stakeholder’s involvement survey.

6.2.3 Participants and settings

The participants were recruited from an existing PPI advisory group in the Pain Centre Versus Arthritis at the University of Nottingham.

6.2.4 Data collection and analysis

Data were collected from focus-group discussions by documenting PPI opinions. In addition, data were gained from the PPI/E answers to the form by the end of the first meeting. For analysis, average scores were calculated for numerical answers, and narrative summary and tabulation of narratives were implemented.

6.3 Results

6.3.1 Participant characteristics

Of five participants who confirmed the invitation to the first meeting, only three female participants with OA attended. Dr Michelle Hall also attended the first PPI/E meeting as an observer from the supervision team. In the second PPI/E meeting, four participants attended (3 female and one male). Two of the three ladies participated in both meetings. All participants (>50 years old) had OA and other medical conditions. In the second meeting, Professor Weiya Zhang participated and assisted in facilitating the meeting. Also, Mr Khalid helped in taking notes throughout the meeting.

6.3.2 Summary of results

First PPI/E meeting

The participants were actively engaged throughout the discussion, and some participants had prepared notes before the meeting. The overall PPI/E responses were as follows:

1. The average score for the topic importance was very important (= 10).
2. The average score for the importance of the study question to people with OA was very important (= 10).
3. The CFs that the PPI suggested in the meeting and the forms are shown in Table 5-1:

Table 6-1. The contextual factors discussed in the first PPI/E meeting

Contextual factors	***PPI statements***
Empathy and warmth	*- Empathy from the GP* *- Initial greeting, kindness, and language*
Positive communication skills (verbal and non-verbal)	*- Facing the patient and not tapping on a computer (active listening)* *- Every experienced GP should have customer service training*
Practitioner competence	*- A good examination*
Session duration	*- Time given for each patient (assessment and listening to the patient)*
Regular follow up	*- Regular follow up after the consultation* *- Follow up, to see if there is improvement or any more questions* *- NHS email contact*
Referral	*- Prescribe various activities* *- Social prescribing*

Second PPI/E meeting

The PPI/E members concurred that all eight CFs are related, and they should all be considered in the practitioner-patient encounter and tailored to each patient's needs. The additional CFs that the participants suggested were signposting to multidisciplinary management and peer support and that continuity of care is essential for a patient with a chronic condition.

6.4 Discussion

Two PPI/E meetings were conducted where participants engaged actively in discussions about the relevance of the research findings to their perceptions and experience. The first meeting confirmed the importance and relevance of the research topic to a group of OA patients. Also, the PPI suggested some CFs that were considered later in developing the search strategy for the qualitative SR. The second meeting obtained the PPI input on the CFs identified from previous reviews in the research project. The PPI supported the delivery of all the factors and suggested tailoring the factors to patient needs.

The PPI/E meetings included only a small number of participants. It was challenging to recruit a group of participants to a specific time and date. To mitigate this, we created a poll to the PPI to select the date and time for the online meeting.

6.5 Conclusion

Involving patients and the public in this research project is consistent with the increasing national and international requirement of acquiring PPI opinions during research development. The involvement in two stages of the development ensured that the research objectives had been communicated and agreed upon, to ensure the research outcomes highly relevant to the patient benefits.

Chapter 7. General Discussion

7.1 Summary of findings

By following the MRC framework for CEP development, research evidence, clinical expertise, and patient experiences were all considered. This thesis involved four research methodologies that contributed towards CEP development.

Meta-analysis of RCTs was used to identify the CFs with therapeutic effects. Meta-aggregation was used to identify the CFs that both patients and practitioners believe essential to deliver in OA clinical setting. The findings of the quantitative and qualitative systematic reviews complement each other to generate the key CFs that need to be included in the CEP. All identified CFs from the quantitative SR were also reported in the qualitative SR as relevant factors. However, the qualitative review identified more CFs than the quantitative review with a broader understanding of the context. This may be explained by the fact that qualitative studies seek to understand the social contexts and human experiences, which adds to research credible and complementary material to address in clinical practice (Hannes and Lockwood, 2011). Nevertheless, the quantitative SR confirmed the efficacy of some (three) modifiable CFs in different conditions.

The overall effect size of practitioner-patient interaction was small but statistically significant (SMD= 0.22; 95%CI 0.16, 0.28). The three CFs that were identified from the 20 trials included in the meta-analysis are empathy, patient involvement and positive communication. The qualitative review focused solely on OA and the perspectives of patients and health practitioners of CFs in the consultations. The additional factors recognised in this review were: clear and relevant information provided by the health practitioner; the confidence of the health practitioner; patient expectation concerning their outcome and the consultation experience; sufficient consultation time; and easy access to consultations.

Following these two systematic reviews, stakeholders were involved in an online survey to obtain their views on the eight identified CFs. An agreement was reached on eight modifiable CFs that could be implemented in consultations to enhance the management of OA. Also, the stakeholders suggested that different CFs can be selected for patients in an individualised manner depending on their needs. In addition, PPI/E was undertaken twice during the research project to ensure that the patients' viewpoints were considered with the research evidence, and expert knowledge in the development phase of the CEP.

This research project has provided a fair representation of research, expert practitioners, and patients' views on CFs in OA consultations. Table 7-1 shows the eight CFs that were obtained in this research project studies. All evidence supports empathy, positive communication and patient involvement, which should be implemented fully for every patient encounter. The additional five factors were supported by various research findings suggesting they should be considered in consultations. Evidence on the therapeutic effects of these factors is still controversial. However, as they are related to the other three essential factors, they need to be considered according to individual needs to maximise the CEP potential.

Table 7-1. Contextual factors result across the studies

Contextual Factors	Delphi study	Quantitative SR	Qualitative SR	Stakeholders' involvement	PPI/E
Empathy	✓	✓	✓	✓	✓
Positive communication	✓	✓	✓	✓	✓
Practitioner confidence	✓	-	✓	✓	✓
Patient expectations	✓	-	✓	✓	✓
Patient involvement	✓	✓	✓	✓	✓
Information provision	✓	-	✓	✓	✓
Sufficient consultation time	✓	-	✓	✓	✓
Easy access to consultations	-	-	✓	✓	✓

7.2 Proposed Contextual Enhancement Package

The eight key contextual factors will be incorporated into a management package suitable for implementation in clinical practice. The package will be individualised according to the context characteristics and needs of the patient (to be tested and evaluated). Table 7-2 shows the proposed CEP.

Table 7-2. Proposed Contextual Enhancement Package (CEP)

Practitioner factors	
Empathy	*Expressing empathy to the patient through:* • *Initial greeting, kindness, and warm language.* • *Active listening.* • *Communicating the understanding and validation of patient's disclosure.*
Positive communication	*Conveying positive verbal and non-verbal communication to patients*. Examples of essential non-verbal communication in clinical encounters involve appropriate eye contact and touch. Positive verbal communication may include the following elements: • Enhancing patient expectations by informing them about the purpose of prescribing the treatment and the likely success of the outcome. • Letting the patient know when they are about to receive a treatment.
Practitioner confidence	Practitioner *confidence* in consultations, which could be manifested by thorough examination, possession of sufficient knowledge about the diagnosis, and communication of individualised management plan (i.e., exercise, weight management or multidisciplinary management).
Patient factors	
Patient expectations	*Considering the patient's previous experience and expectations* through questioning, explaining, and clarifying.
Patient involvement	*Active involvement of patients in the consultation* through: • Involvement in discussion and communicating information about the procedures. • Sharing decisions about management options and planning.
Information provision	*An individualised and clear explanation of information regarding the condition*. The practitioner might also ask the patients if they have any concerns regarding their condition to provide more relevant and individualised information.
Organisational factors	
Sufficient time	*Sufficient consultation time*, which allows for a comprehensive examination, adequate information exchange, and prescribing of necessary treatment.
Easy access	*Easy access to consultations* and a clear follow-up plan.

7.3 Findings in relation to previous literature

Having discussed this project’s findings and outcomes, this section addresses the differences between this project and related research publications. Firstly, the differences between Di Blasi et al. (2001) review and this PhD project is that the latter intended to identify the factors related to three out of five context dimensions identified by Di Blasi (i.e. the practitioner characteristics, the patient characteristics and the interaction between the practitioner and patient) and to find additional studies that can be meta-analysed.

Secondly, this project commenced in late 2018. In the same year, a multidisciplinary research team from different universities across the United Kingdom commenced a project called Empathico (Smith et al., 2020). It should be noted that the two projects were concurrently running, and the author of this PhD thesis was independently conducting the project under the supervision of PhD supervisors with no intention to replicate any existing research. Empathic communication and positive messages (also referred to as optimism) are the only components of the placebo that the Empathico project considered (Smith et al., 2021). However, this PhD project goes beyond just empathy and positive messages. The search strategy of the systematic reviews involved 16 CFs attained from a placebo expert panel from the previous Delphi study.

Empathico was driven by the Pearson-Based Approach (PBA) for intervention development, in contrast to the MRC framework followed in this PhD project. Their approach entailed combining qualitative research and insights from placebo and behaviour change theory and evidence. The PBA process included two phases: planning and optimisation. In the first phase, three literature reviews were performed alongside two interviews. The reviews aimed to identify theory and evidence on the targeted behaviours and approaches to modify them. In contrast, the second phase was refining and acceptability testing, where additional interviews were conducted with patients and practitioners. Empathico prototype development was completed in the first phase, while the second phase ensured it was highly acceptable and meaningful to practitioners.

In comparing this PhD project with the Empathico planning phase, both projects involved a quantitative SR, a qualitative SR, involvement of patients and stakeholders. The differences between the SRs were discussed and highlighted in detail in the pertaining chapters. In brief, the main differences were that their quantitative SR investigated the effect of two CFs only (i.e., empathy and positive message) and the qualitative SR was conducted following different methodology (i.e., meta-ethnography) and method. The patient and stakeholder involvement objectives differed; consequently, methods and results were various (i.e., focused-group PPI meetings and online survey vs semi-structured interviews and think-aloud interviews). The logic model suggested in Empathico is based on previous literature and theory reading and formal literature review (KEPE WARM). In their recent publication, they provided a brief outline of the online intervention that comprises seven self-learning sections that conclude with a certificate awarding (Smith et al., 2021). Their findings could support the development of training materials about CEP.

7.4 Challenges and limitations

It must be acknowledged that developing a CEP for OA management is considered a complex intervention development. The CFs in the medical encounter have multiple interacting components that can impact the outcomes. These components involve skills required by those delivering the intervention, the settings, the flexibility in delivering the interventions, and the range of behaviours targeted. Therefore, the UK Medical Research Council (MRC) framework for developing and evaluating complex interventions was used to guide CEP development (Skivington et al., 2021b).

One of the first challenges in the development process was defining the concept of CFs related to the practitioner and patient. There are various concepts or interventions in the literature concerned with the interaction between the healthcare provider and the patient or person receiving care. For example, patient-centred care, shared-decision making, practitioner-patient coordination, therapeutic alliance, motivational counselling, relational empathy, psychosocial elements, and the general term interpersonal communication skills. Moreover, researchers have examined these concepts from different disciplines (i.e., medicine, psychology, and sociology). The previous Delphi exercise in this research topic assisted in narrowing down the factors and selecting relevant terms for the systematic reviews search strategy.

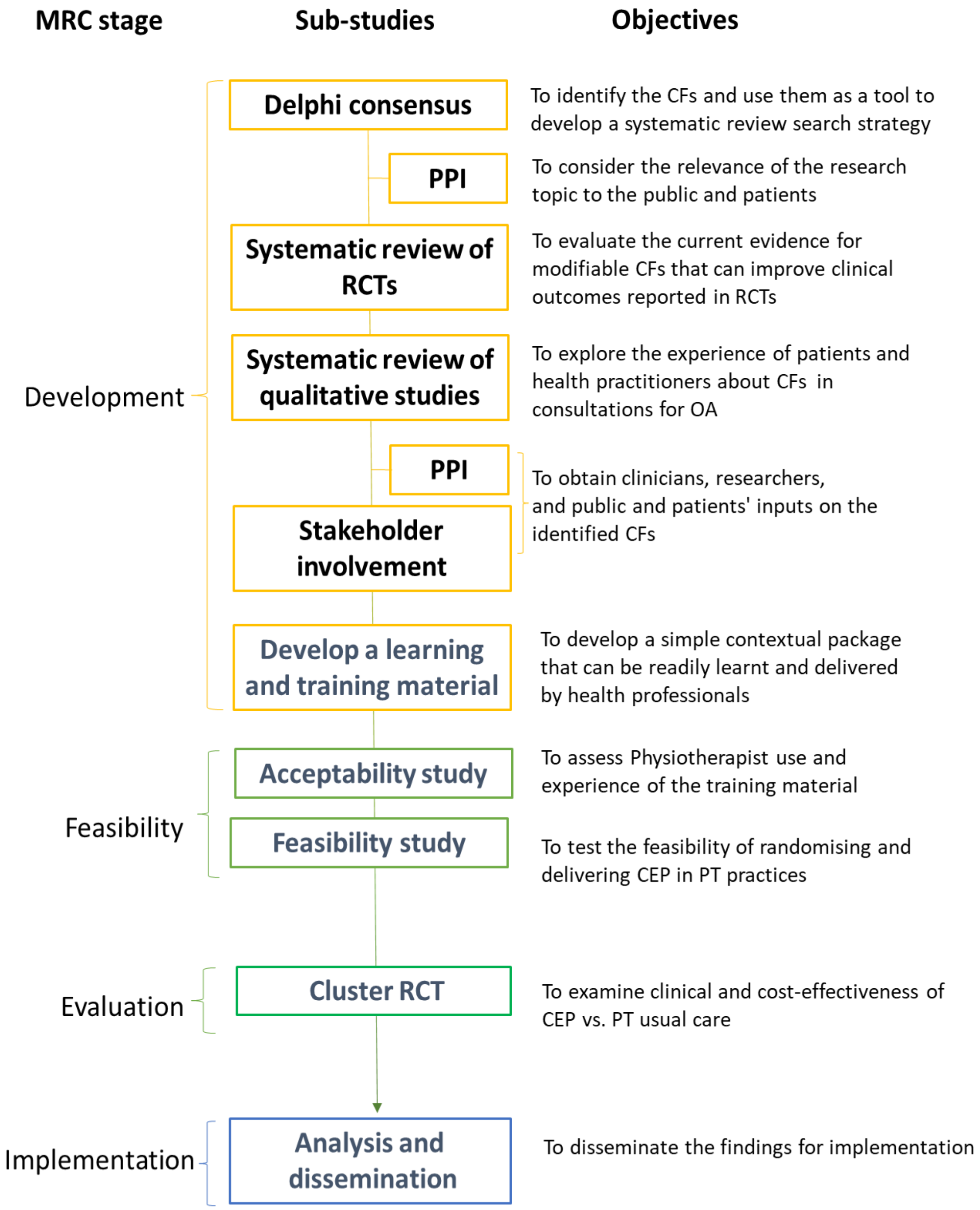
Another challenge with investigating the CFs in OA management was the limited number of RCTs that examined the effect of CFs on OA. Unlike the other studies in this project, the quantitative SR investigated the effect of CFs for all health conditions (including OA). Hence, the heterogeneity between studies was high (I^2= 88%). Other methodology-related limitations encountered were discussed in each study chapter.

This project encountered some uncertainties. Although one of the research project objectives was to identify the modifiable CFs that improve clinical outcomes, the details of some factors are unclear. The explanation of the extent of patient involvement by the health provider in the consultations has not been specified. Also, there is no specific principle for positive communication or positive messages that would undoubtedly enhance outcomes. In 2020, Howick et al. investigated the anatomy of positive messages delivered in 22 randomised trials. They grouped the components of the positive messages into five areas: making a message personal, specifying the positive outcomes, providing a rationale, drawing on associations and meanings, and encouraging supportive communication (Howick et al., 2020). Similarly, Howick et al. (2020) claimed that most of the investigated studies in their review did not adequately explain positive messages' components.

Finally, this thesis is the result of research conducted over three years that dealt with the COVID-19 pandemic and lockdown measures from the start of the second year. These challenges developed a resilient and adaptable researcher that could adjust work according to the available recourses.

7.5 Considerations for future work

Training materials and courses on the CEP must be designed and evaluated for its delivery to complete the development of CEP for OA. The available resources and existing developed contextual enhancing training programs, including some of the relevant identified factors, may guide the development of the training materials. Then, in alignment with the UK Medical Research Council (MRC) guidance for complex intervention development, the research project should proceed to the feasibility phase (Skivington et al., 2021b). The training acceptability will be assessed, and then a feasibility study shall be conducted to test the feasibility of randomising and delivering CEP in physiotherapy practices. That can be followed by an evaluation of the clinical effectiveness and cost-effectiveness of the package. Lastly, analysis of the data and subsequently dissemination for implementation in clinical practice. Figure 7-1 briefly describes a plan for future studies following the MRC stages for complex intervention development. Then, protocols for the transition from the development stage to the feasibility stage are established.



MRC, UK Medical Research Council; CF, Contextual Factor; PPI, Public and Patient Involvement; RCT, Randomised Controlled Trial; OA, Osteoarthritis; PT, Physiotherapy; CEP, Contextual Enhancement Package.

Figure 7-1. An MRC-framework plan for the contextual enhancement package for OA management

7.5.1 Development of CEP training course

Introduction

Changing clinical behaviour is fundamental for successfully delivering the Contextual Enhancement Package. A training course will be developed for practitioners to promote the delivery of the package.

Aim: To develop a training course and deliver it preliminary to a sample of physiotherapists.

Methods

Design: The course will be delivered face to face, assisted with online materials.

Participants: The course will be led by a medical educationalist and supported by IT experts and NHS trainers. Trainees will be selected from primary care in Nottinghamshire.

Course content: Introduction and outline of the CEP; presentation of the influential effect of context on patients' condition and experience; definition and explanation of the eight key CFs; and demonstration of the CFs in clinical scenarios.

Procedure: Each learning outcome and competency will be taught through relevant learning modalities using deep and active learning techniques. Knowledge will be attained via specifically designed workshops, presentations and self-directed online resources. The workshops will utilise relevant video and role-play resources with patients to facilitate practical and interpersonal communication skills.

Assessment: Trainees will be assessed and given feedback on their recorded interaction with patients. Learning outcomes and competencies will be evaluated against a consensually generated standard.

7.5.2 Feasibility stage protocol

Following the development phase of the MRC framework, the research project will proceed to the feasibility phase to determine the acceptability of the CEP from the perspective of the physiotherapists and patients with OA and to determine the feasibility of delivering CEP in a future trial. Below is a *brief study protocol for the acceptability and feasibility of delivering the CEP in clinical practice.*

Introduction

According to the MRC guidelines, several key questions must be addressed before undertaking a full trial to evaluate a complex intervention: can it be delivered (i.e., CEP); does the intervention do what we expect; which outcomes are sensitive to change; how many enhanced contextual consultations are needed to be effective (Skivington et al., 2021b, Orsmond and Cohn, 2015). Interviews with physiotherapists who attended the CEP training course will help to assess their use and experience of the training. Also, it will assist in identifying possible strategies to overcome the barriers to delivering the package.

Overall aim: To determine the acceptability of the CEP and the feasibility of delivering CEP to patients with OA in physiotherapy practices.

Specific objectives:

1. Evaluate the training package in terms of delivery format, training materials, content and application of the course materials into clinical practice.
2. Gain physiotherapists perspective on the usefulness of the CEP and identify potential barriers to delivery of the package in clinical practice.
3. Gain patient perspectives of the clinical encounter following therapist training.
4. Evaluate importance and acceptability of patient reported outcome measures.
5. Identify factors that may affect the running of a future RCT, including barriers and facilitators to recruitment and retention.
6. Assess intervention fidelity post training.
7. Assess recruitment and follow-up rates, processes and data completeness.

Methods

Design: Qualitative semi-structured interviews with therapists and patients, and observational study (i.e., video recording).

Participants: A purposive sample of ten physiotherapists treating patients with OA will be recruited from primary care in Nottinghamshire to undertake the CEP training. Physiotherapists will be chosen to present a range of age, gender, seniority and ethnicity. Up to 25 patients with OA who have been treated by the CEP-trained therapists will be invited to take part in a brief telephone interview.

Procedure: Five physiotherapy practices will be selected from Nottingham. Each practice will be asked to nominate two physiotherapists to receive the training and deliver the package. Interviews will be conducted within four weeks after training in the CEP to allow therapists to put the training into practice. Therapists' interviews will be semi-structured with questions about the experience and usefulness of the training program. The telephone interview with patients will enquire about their experiences of their care and treatment by CEP-trained therapists. Video recordings of five sessions will be conducted randomly to examine the package fidelity. Patients will complete a questionnaire measuring patient expectations and satisfaction before and after the first session (Bowling et al., 2012). The core outcome set for OA (i.e., pain, physical function and quality of life) will be collected at baseline, one week, 1, 3, and 6 months (Smith et al., 2019).

Analysis plan: The interviews will be recorded and transcribed. Data will be coded, analysed and interpreted using thematic analysis (Clarke et al., 2015) (to address objective 1-5). The video-recorded session will be assessed against a fidelity checklist for CEP delivery (to address objective 6). Using descriptive statistics, recruitment rates, the number of sessions required, the average duration of each session will be calculated (to address objective 7).

7.6 Conclusion

In conclusion, this PhD project aimed to identify key CFs in the practitioner-patient encounter to develop a contextual enhancement package in the management of OA. Following the MRC framework, this doctoral thesis contributed to the development of a person-centred, scientifically informed package that includes eight modifiable CFs. The future work includes designing a training material about these CFs, testing the feasibility of delivery, and evaluating CEP's clinical effectiveness and cost-effectiveness. It is anticipated that the CEP provision by trained general practitioners and physiotherapists in OA management will potentially improve overall treatment benefits and lead to higher patient satisfaction with their care.

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Appendices

Appendix 1 Summary of CEs reviews and consensus

no.	Review	Publication year	Authors	Included studies	Authors conclusion
	Systematic Reviews				
1	Effects of empathic and positive communication in healthcare consultations: a systematic review and meta-analysis	2018	Howick et al.	28 RCTs	The interventions bring **small improvements** to a range of psychological and physical patient conditions, improve overall patient satisfaction with care, without inducing any harm.
2	Positive messages may reduce patient pain: A meta-analysis	2017	Howick et al.	16 RCTs	Care of patients with chronic or acute pain may be enhanced when clinicians deliver **positive messages** about possible clinical outcomes.
3	The effect of patient–practitioner communication on pain: a systematic review	2016	Mistiaen et al.	19 RCTs & 32 quasi-RCTs	Different types of communication have a significant but small effect on (acute) pain. Positive suggestion may reduce pain. Emotional care studies showed no evidence of a direct effect on pain.
4	Does improving patient–practitioner communication improve clinical outcomes in patients with cardiovascular diseases? A systematic review of the evidence	2014	Schoenthaler et al.	14 RCTs & 1 case-control study	Few interventions targeting patient–practitioner communication have assessed the impact on **cardiovascular**-related clinical outcomes, limiting the ability to determine effectiveness.
5	The Influence of the Patient-Clinician Relationship on Healthcare Outcomes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials	2014	Kelley et al.	13 RCTs	Patient-clinician relationship has a small, but statistically significant effect on healthcare outcomes.
6	Effectiveness of empathy in general practice: a systematic review	2013	Derksen et al.	7 studies	only 7 studies could be used in this search, empathy in the patient–physician communication in general practice is of unquestionable importance.
7	Patient-centred communication is associated with positive therapeutic alliance: a systematic review	2012	Pinto et al.	12 studies	67 communication factors were identified (36 interaction styles, 17 verbal factors and 14 non-verbal factors).
8	Association between nonverbal communication during clinical interactions and outcomes: A systematic review and meta-analysis	2012	Henry et al.	26 observational studies	Greater clinician warmth, less nurse negativity, and **greater clinician listening** were associated with greater patient satisfaction.
9	Empathy Decline and Its Reasons: A Systematic Review of Studies With Medical Students and Residents	2011	Neumann et al.	18 studies	Empathy decline during medical school and residency compromises striving toward professionalism and may threaten health care quality.
10	Spontaneous improvement in randomised clinical trials: meta-analysis of three-armed trials comparing no treatment, placebo and active intervention	2009	Krogsbøll et al.	37 trials	Both the spontaneous improvement and the effect of placebo contribute importantly to the observed treatment effect in actively treated patients, and that the relative importance of these factors differ according to clinical condition and intervention.
11	Effect on Health-Related Outcomes of Interventions to Alter the Interaction Between Patients and Practitioners: A Systematic Review of Trials	2004	Griffin et al.	35 RCTs	Trial evidence suggests that a range of approaches can achieve changes in the practitioner-patient interaction, and some show promise in improving patient's health.
12	Physician-patient communication in the primary care office: a systematic review	2002	Beck et al.	22 studies	Existing research is limited because of lack of consensus of what to measure, conflicting findings, and relative lack of empirical studies (especially of nonverbal behaviour).
13	Influence of context effects on health outcomes: a systematic review	2001	Di Blasi et al.	25 RCTs	Physician who adopt a warm, friendly, and reassuring manner are more effective than those who keep consultations formal and do not offer reassurance.
	Narrative Reviews				
14	Enhance placebo, avoid nocebo: How contextual factors affect physiotherapy outcomes	2016	Testa and Rossettini	–	The possibility of adopting knowledgeable, expert and ethical strategies to enhance placebo and avoid nocebo offers a valuable opportunity for every PT to enrich their therapeutic toolbox.
15	Health promoting effects of the physician-patient encounter	2002	Van Dulmen and Bensing	_	The stressfulness of the medical encounter impacts on a paitent's health negatively. Yet, this negative experience can be transformed into a positive one when physician use empatheic and patient-centered communication
	Expert Consensus				
16	Implications of Placebo and Nocebo Effects for Clinical Practice: Expert Consensus	2018	Evers et al.	29 Placebo experts	The current paper forms a first step towards developing evidence- based and ethical recommendations about the implications of placebo and nocebo research for medical practice, based on the current state of evidence and the consensus of experts.

Appendix 2 PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			**Page no.**
Title	1	Identify the report as a systematic review.	78
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	ii
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	60
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	73, 78
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	79
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	81
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	81
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	82
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	82
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	84
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	86
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	82
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	85
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	87
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	86
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	88
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	88

Section and Topic	Item #	Checklist item	Location where item is reported
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	89
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	89
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	87
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	89
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	90
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	91
Study characteristics	17	Cite each included study and present its characteristics.	94-95
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	217
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	103
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	98
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	103
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	103
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	104
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	99
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	106-107
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	106
	23b	Discuss any limitations of the evidence included in the review.	110
	23c	Discuss any limitations of the review processes used.	110
	23d	Discuss implications of the results for practice, policy, and future research.	112
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	78
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	78 -79
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	78 -79

Section and Topic	Item #	Checklist item	Location where item is reported
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	x
Competing interests	26	Declare any competing interests of review authors.	N/A
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

Appendix 3 Author-specific search

Author	Country	Medline RCT	PubMed RCT	PsycINFO RCT	Embase RCT	Google Scholar (Placebo and RCT)	Relevant RCT
Daniel E Moerman	USA	0	0	0	2	7	0
Fabrizio Benedetti	Italy	39	16	0	33	14	0
George Lewis	USA	0	2	0	3	10	0
Irving Kirsch	USA	35	21	0	27	14	10
Paul Little	UK	121	107	0	139	37	2
Ted J Kaptchuk	USA	49	46	0	72	71	5

Appendix 4 Quantitative systematic review search strategy

MEDLINE (Ovid) Search conducted in April 2019

1. Placebo.ti.
2. (Placebo adj control).tw.
3. (Placebo adj effect*).tw.
4. (Placebo adj3 response*).tw.
5. Context.ti.
6. (Context* adj3 factor*).tw.
7. (Contextual adj2 theory).mp.
8. (Context* adj3 enhanc*).mp.
9. Contextual enhancer.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
10. (Healing adj3 context).mp.
11. (Therapeutic adj3 ritual*).mp.
12. Non-specific effects.mp.
13. Physician-Patient Relation*.mp.
14. exp *Physician-Patient Relations/
15. Practitioner-patient interaction.mp.
16. Nurse-Patient Relation*.mp.
17. Physician-Patient Relation*.mp.
18. Physiotherapist-Patient Relation*.mp.
19. Holistic assessment.mp.
20. Empathy/ or Empath*.mp.
21. Patient Participation/ or Patient active involvement.mp.
22. Duration of the consultation.mp.
23. Patient belief*.mp.
24. illness perception.mp.
25. (Treatment adj2 characteristic*).mp.
26. Information about the disease.mp.
27. Practitioner* Communication skill*.mp.
28. Practitioner confidence.mp.
29. Professional Practice/ or Professionalism.mp.
30. Practitioner belief*.mp.
31. Positive communication.mp.
32. Regular follow-up.mp.
33. Patient experience.mp.
34. Patient expectation*.mp.
35. (no adj treatment).ab.
36. (usual adj care).ab.

37. waiting list group.ab.
38. observation* group.ab.
39. observation* control.ab.
40. controlled clinical trial.pt.
41. randomized controlled trial.pt.
42. randomized.ab.
43. 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 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
44. 35 or 36 or 37 or 38 or 39
45. 40 or 41 or 42
46. 43 and 44 and 45

Appendix 5 Table of excluded studies (n=38)

Author	Reason for exclusion
Benedetti et al. (2003)	Three cohort studies of open versus hidden medical treatments administration
Bertisch et al. (2009)	Nonrandomised design (secondary analysis)
Bialosky and Robinson (2017)	Studied the effect of general placebo and did not study any specific contextual effect
Carvalho et al. (2016)	Studied the effect of placebo labelling and did not study any specific contextual effect
Curtis et al. (2018)	The intervention was similar to shared decision making and not related to the contextual effect
Eyssen et al. (2014)	The intervention provided is irrelevant to any contextual factor
Faasse et al. (2018)	The intervention and outcomes are irrelevant (the nocebo effect of sham capsule)
Fernandez et al. (2019)	Healthy volunteer sample
Foster et al. (2010)	Nonrandomised design
Fujimori et al. (2014)	Studying the effect of oncologist training
Hochhalter et al. (2010)	Nonrandomised design, irrelevant intervention
Hoenemeyer et al. (2018)	Studied the effect of placebo labelling and did not study any specific contextual effect
Hsieh et al. (2014)	The contextual intervention is related to environment factors (i.e., music)
Kam-Hansen et al. (2014)	Studied the effect of placebo labelling and did not study any specific contextual effect
Kaptchuk et al. (2010)	Studied the effect of placebo labelling and did not study any specific contextual effect
Kelley et al. (2009b)	Nonrandomised design (secondary analysis of clinical trial)
Kaptchuk et al. (2006)	Studied the effect of general placebo and did not study any specific contextual effect
Kerr et al. (2011)	Nonrandomised design (qualitative study)
Klaus et al. (2007)	The contextual enhancer was a predictor of outcome rather than part of an intervention
Leech et al. (2012)	The intervention is not related to any of the patient-practitioner factors
Locher et al. (2017)	Studied the effect of placebo labelling and did not study any specific contextual effect
Locher et al. (2019)	Studied the effect of placebo labelling and did not study any specific contextual effect
Lorber et al. (2007)	Healthy volunteer sample

Myers et al. (2008b)	The contextual enhancer was a predictor of outcome rather than part of an intervention
Noureldin et al. (2012)	The contextual enhancer was a predictor of outcome rather than part of an intervention
Pariente et al. (2005)	No contextual elements examined
Petersen et al. (2014)	Nonrandomised design (Each patient went through three test days)
Petersen et al. (2012)	Nonrandomised design (Each patient went through three different sessions)
Phillips (2006)	A dissertation (not peer reviewed), and not a randomised trial
Razavi et al. (2003)	Healthy volunteer sample
Redelmeier et al. (1995)	Not for a health condition, but homeless
Rosen et al. (2016)	Healthy volunteer sample
Siemonsma et al. (2013)	Studied the effect of a defined psychological approach
Szilágyi et al. (2007)	Studied the effect of psychologists training in providing a specific psychological intervention
van Osch et al. (2017)	Healthy volunteer sample
Vase et al. (2013)	The contextual enhancer was a predictor of outcome rather than part of an intervention
Verheul et al. (2010)	Healthy volunteer sample
Zhou et al. (2018)	Studied the effect of placebo labelling and did not study any specific contextual effect

Appendix 6 Risk of bias in studies

Author	Selection bias		Performance bias		Detection bias	Attrition bias	Repoerting bias	Other bias
	Random sequence generation	Allocation concealment	Blinding of participants	Blinding of personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	
Akturan et al.	✓	!	✗	✗	✗	✓	!	!
Arnetz et al.	!	✗	✗	✗	✗	✗	✗	✗
Chassany et al.	✓	!	✗	✗	✗	✓	!	✗
de Craen et al.	✓	✓	✓	✓	!	✓	!	✓
Dutt-Gupta et al.	✓	✓	✓	✓	!	✓	!	✗
Jellema et al.	✓	!	✗	✗	✗	!	!	✗
Kaptchuk et al.	✓	✓	✓	!	✓	✓	!	✓
Kemeny et al.	✓	✗	✓	✓	✓	✓	✗	✗
Knipschild and Arntz	✓	✗	✓	✗	✓	✓	✗	✗
Krupat et al.	✓	✗	✗	✗	✗	✗	!	!
Lauder et al.	✓	!	✓	!	✓	✗	✗	✗
Little et al.	!	✓	✗	✗	✗	✓	✗	!
Mathews et al.	✓	!	!	✗	✗	✓	!	✓
Olsson et al.	✓	!	✓	!	✓	✓	!	✗
Pace et al.	✓	!	✗	✗	✓	✓	!	✓
Rief et al.	✓	✓	✓	✓	✓	✓	✓	✓
Ronel et al.	✓	✓	✓	!	✓	!	!	✓
Shively et al.	✓	!	✗	✗	✗	✓	!	✓
Soltner et al.	✓	!	✓	✗	!	✓	✗	✗
Suarez-Almazor et al.	✓	✓	✓	✗	✓	✓	!	✓
Thomas K.B.	✓	!	✓	✗	✓	✓	!	✗
Vangronsveld and Linton	✓	✓	✓	✓	!	!	✗	✗
Wetzels et al.	✓	✓	!	✗	!	✗	✗	✗
White et al.	✓	✓	✓	✗	✗	✓	!	!
Wise et al.	✓	✓	!	✗	!	✓	!	!

Key: low risk of bias ; high risk of bias; Unclear risk of bias
✓ ✗ !

Appendix 7 Forest plots of subgroup analysis based on outcomes

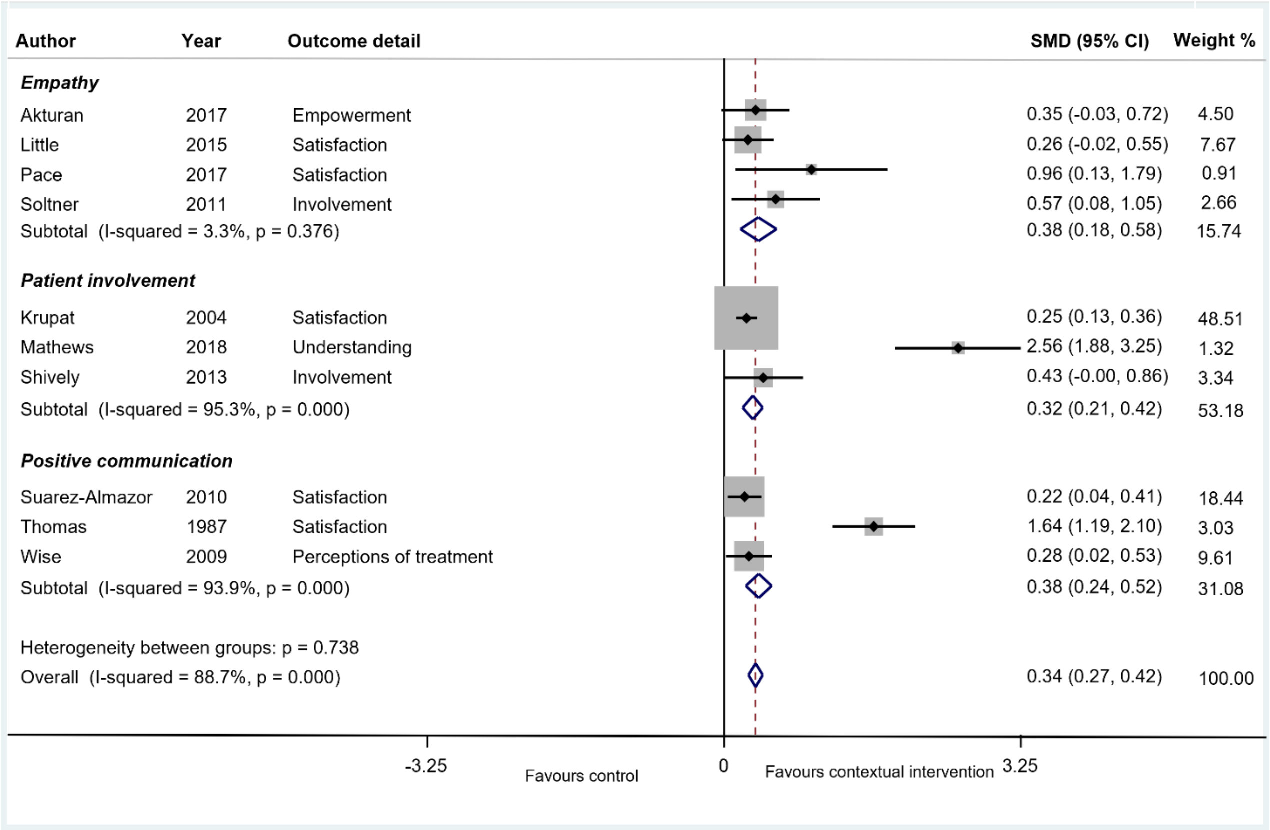


Figure 1. Efficacy of contextual interventions on overall patient experience in the ten studies reporting this

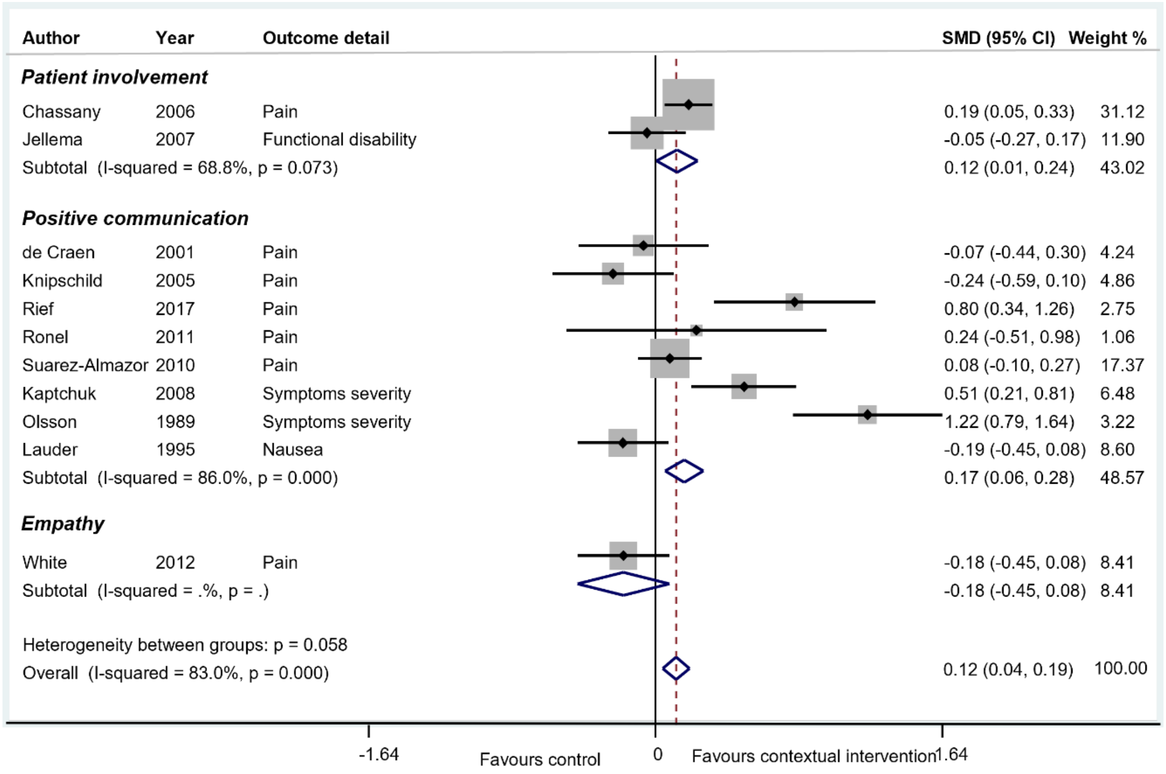


Figure 2. Efficacy of contextual interventions on symptom improvement in the eleven studies reporting this

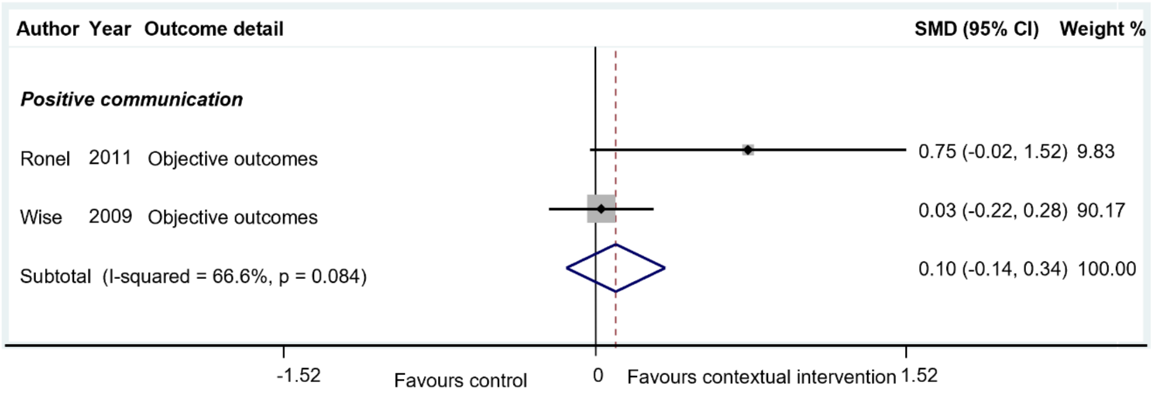


Figure 3. Efficacy of positive communication on objective outcomes in the two studies reporting this

Appendix 8 Qualitative systematic review search strategy

MEDLINE (Ovid) Search conducted in May 2020

1. exp Health Personnel/

2. (Health adj3 profession*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

3. (Health adj3 practitioner$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

4. (General adj3 practitioner$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

5. exp General Practitioners/

6. doctor$.mp.

7. exp Physicians/

8. nurs*.mp.

9. rheumatolog*.mp.

10. exp Rheumatologists/

11. physiotherap*.mp.

12. exp Physical Therapists/

13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12

14. osteoarthriti*.mp.

15. exp Osteoarthritis/

16. 14 or 15

17. exp "Referral and Consultation"/

18. consultation$.mp.

19. Face-to-face.mp.

20. exp Physician-Patient Relations/

21. physician-patient relation$.mp.

22. Practitioner-patient interaction$.mp.

23. Context* enhance*.mp.

24. Context* factor*.mp.

25. (Context* adj2 factor*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

26. (Context* adj2 effect$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

27. Context* theor*.mp.

28. exp Placebo Effect/

29. (Therapeutic adj2 ritual$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

30. (Healing adj2 context).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

31. Non-specific effect$.mp.

32. exp Empathy/

33. Empath*.mp.

34. Communication skill*.mp.

35. (consultation adj2 duration).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

36. exp Professionalism/

37. exp Patient Participation/

38. Patient involvement.mp.

39. exp Illness Behavior/

40. exp "Attitude of Health Personnel"/

41. exp Attitude to Health/

42. exp Communication/

43. exp Emotions/

44. exp Personal Satisfaction/

45. exp Self Concept/

46. Experience*.mp.

47. Perspective*.mp.

48. Expectation*.mp.

49. 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 or 36 or 37 or 38

50. 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48

51. 49 or 50

52. Clinic$.mp.

53. exp Outpatient Clinics, Hospital/

54. exp Pain Clinics/

55. exp Hospitals/

56. (primary adj2 care).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

57. exp Primary Health Care/

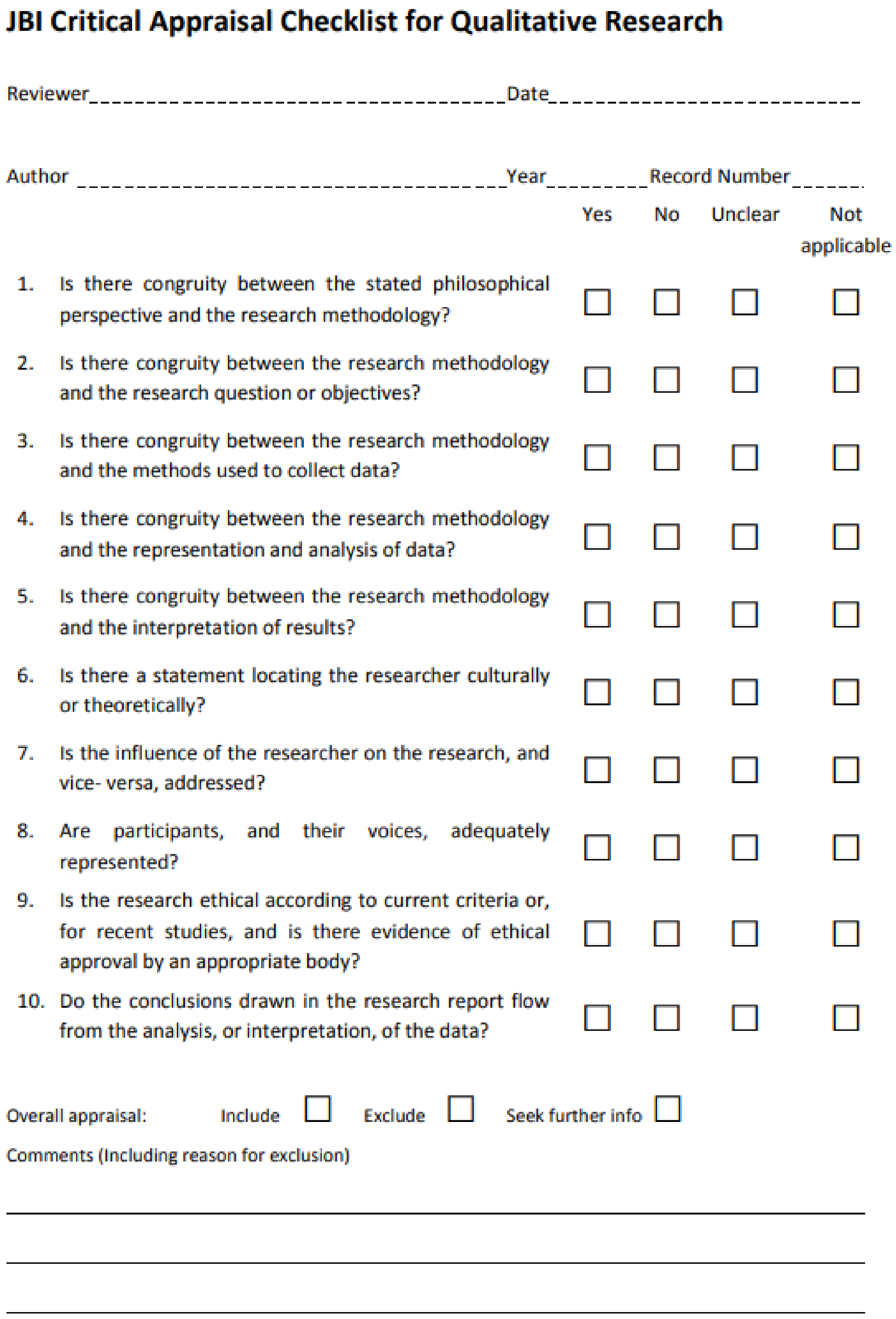
58. exp Outpatients/

59. 52 or 53 or 54 or 55 or 56 or 57 or 58

60. 13 and 16 and 51 and 59

61. Limit 60 to "qualitative (best balance of sensitivity and specificity)"

Appendix 9 JBI Critical Appraisal for Qualitative Research



JBI Critical Appraisal Checklist for Qualitative Research

Reviewer____________________________________Date___________________________

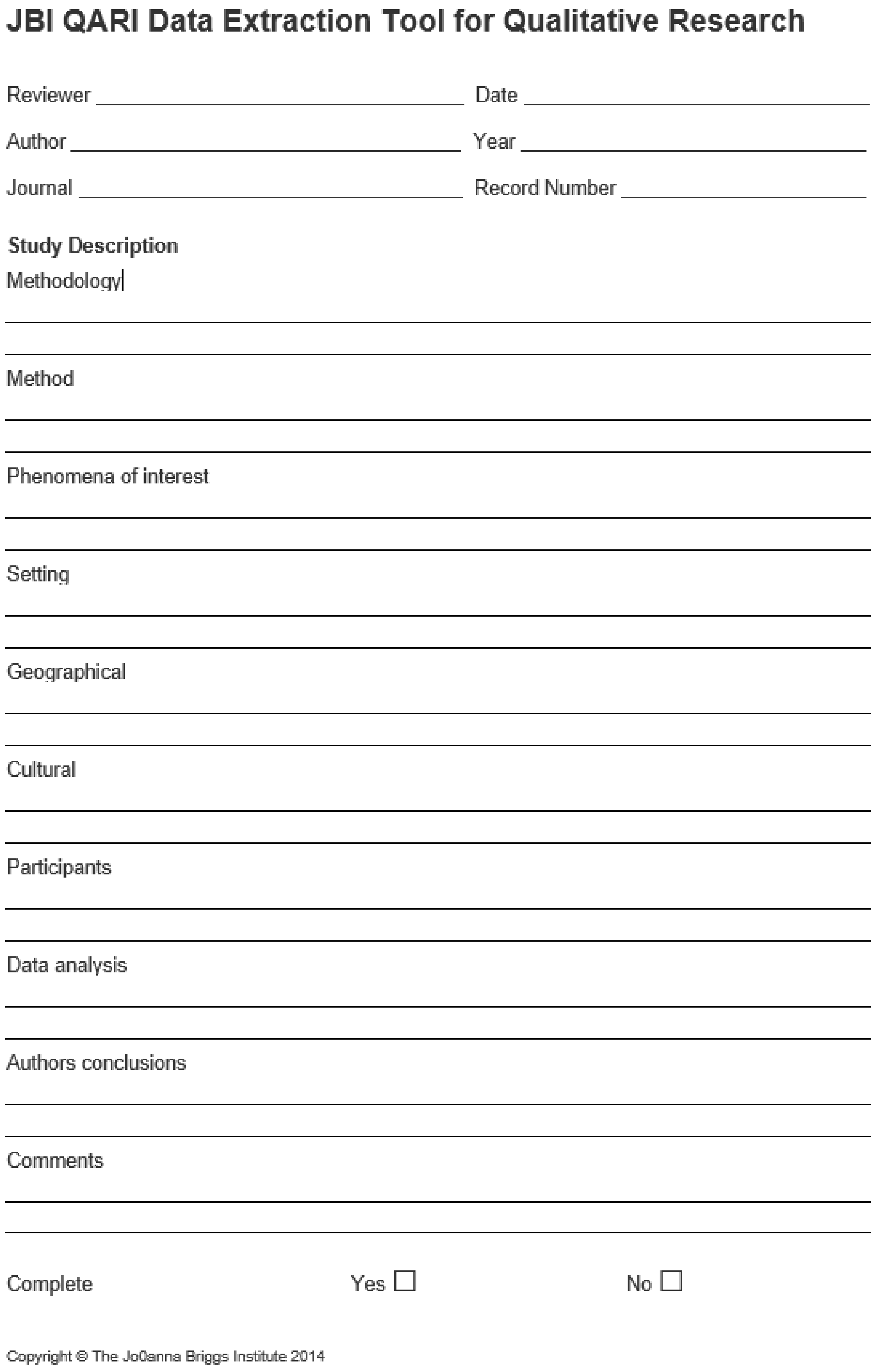
Author _____________________________________Year_________Record Number______

		Yes	No	Unclear	Not applicable
1.	Is there congruity between the stated philosophical perspective and the research methodology?	☐	☐	☐	☐
2.	Is there congruity between the research methodology and the research question or objectives?	☐	☐	☐	☐
3.	Is there congruity between the research methodology and the methods used to collect data?	☐	☐	☐	☐
4.	Is there congruity between the research methodology and the representation and analysis of data?	☐	☐	☐	☐
5.	Is there congruity between the research methodology and the interpretation of results?	☐	☐	☐	☐
6.	Is there a statement locating the researcher culturally or theoretically?	☐	☐	☐	☐
7.	Is the influence of the researcher on the research, and vice- versa, addressed?	☐	☐	☐	☐
8.	Are participants, and their voices, adequately represented?	☐	☐	☐	☐
9.	Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body?	☐	☐	☐	☐
10.	Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Comments (Including reason for exclusion)

Appendix 10 JBI Qualitative data extraction tool



JBI QARI Data Extraction Tool for Qualitative Research

Reviewer ______________________ Date ______________________

Author ______________________ Year ______________________

Journal ______________________ Record Number ______________________

Study Description

Methodology ______________________

Method ______________________

Phenomena of interest ______________________

Setting ______________________

Geographical ______________________

Cultural ______________________

Participants ______________________

Data analysis ______________________

Authors conclusions ______________________

Comments ______________________

Complete Yes ☐ No ☐

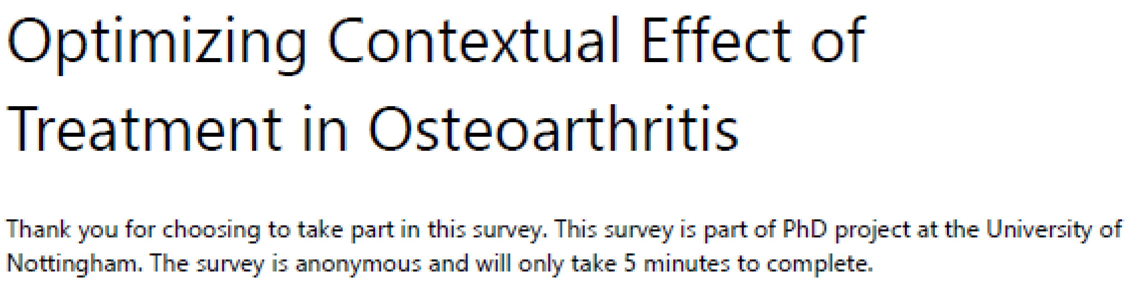
Findings	Illustration form Publication (page number)	Evidence		
		Unequivocal	Credible	Unsupported

Extraction of findings complete Yes ☐ No ☐

Appendix 11 Table of exclude studies (n=17)

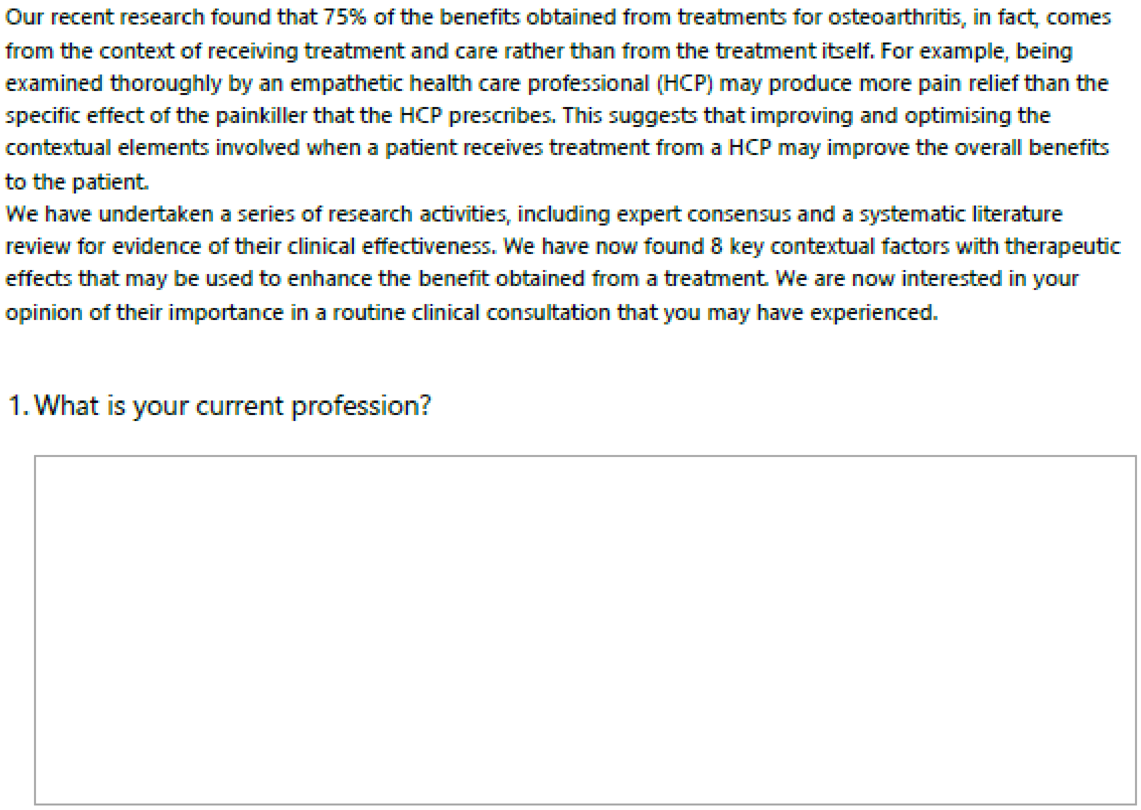
Studies	Reason for exclusion
(Egerton et al., 2017)	Telemedicine interventions
(Kulcsar et al., 2016)	Telemedicine interventions
(Lawford et al., 2018)	Telemedicine interventions
(Lawford et al., 2019)	Telemedicine interventions
(Rostom et al., 2018)	Telemedicine interventions
(Cronstrom et al., 2019)	Telemedicine interventions
(Cuperus et al., 2013)	Self-management experience. Does not include any interaction with health practitioners
(Carmona-Terés et al., 2017)	Self-management experience
(Darlow et al., 2018)	Self-management experience
(Yu et al., 2016)	Self-management experience
(Thomas et al., 2013)	Population criteria does not match the inclusion criteria
(Hausmann et al., 2011)	Population criteria does not match the inclusion criteria
(Ackerman et al., 2016)	Phenomena of interest does not match the inclusion criteria
(Brembo et al., 2020)	Phenomena of interest does not match the inclusion criteria
(Jones et al., 2013)	Phenomena of interest does not match the inclusion criteria
(Bunzli et al., 2019)	Conference abstract. Full text was not available
(Bartlett et al., 2019)	Conference abstract. Full text was not available

Appendix 12 The online survey



Optimizing Contextual Effect of Treatment in Osteoarthritis

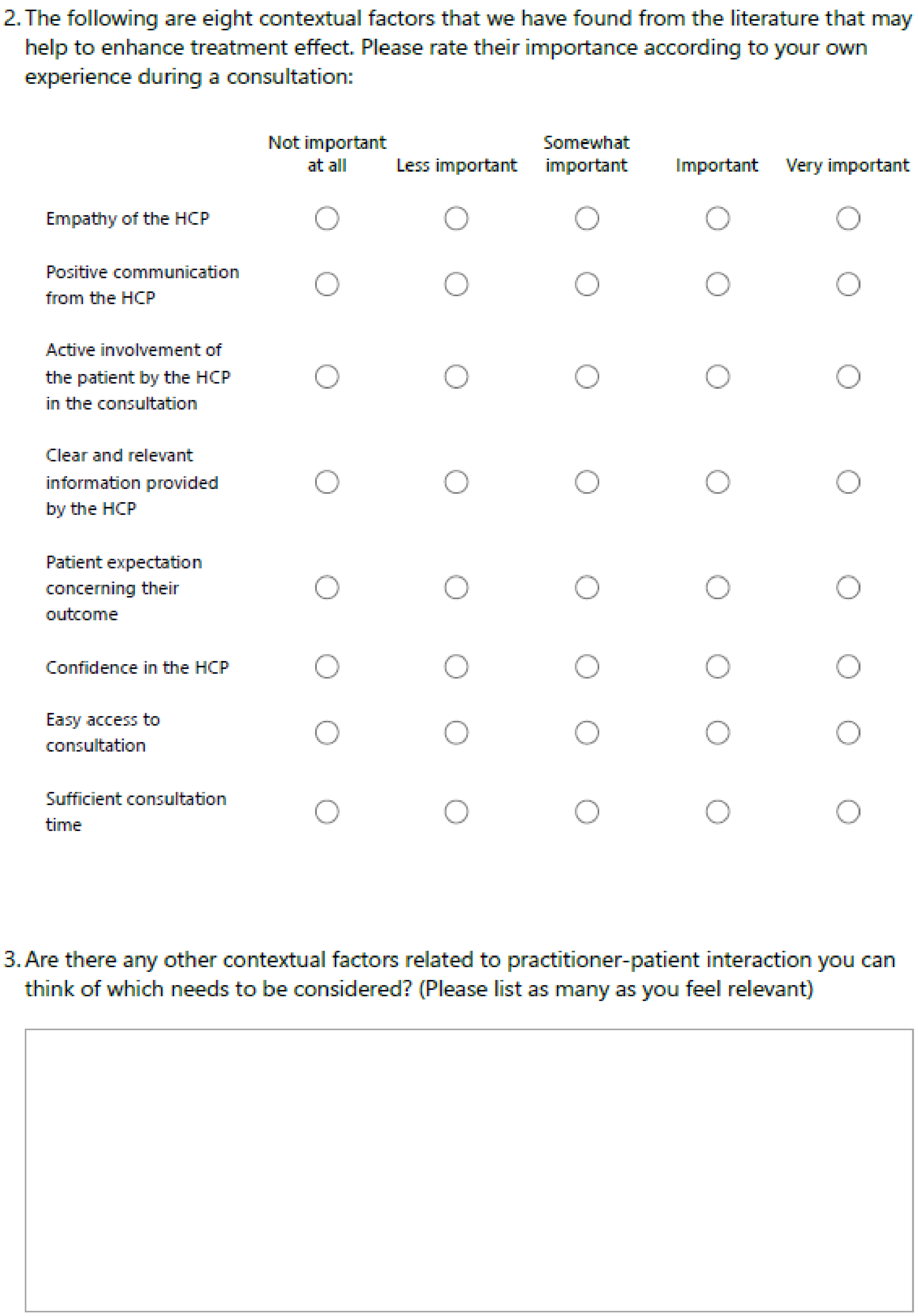
Thank you for choosing to take part in this survey. This survey is part of PhD project at the University of Nottingham. The survey is anonymous and will only take 5 minutes to complete.



Our recent research found that 75% of the benefits obtained from treatments for osteoarthritis, in fact, comes from the context of receiving treatment and care rather than from the treatment itself. For example, being examined thoroughly by an empathetic health care professional (HCP) may produce more pain relief than the specific effect of the painkiller that the HCP prescribes. This suggests that improving and optimising the contextual elements involved when a patient receives treatment from a HCP may improve the overall benefits to the patient.

We have undertaken a series of research activities, including expert consensus and a systematic literature review for evidence of their clinical effectiveness. We have now found 8 key contextual factors with therapeutic effects that may be used to enhance the benefit obtained from a treatment. We are now interested in your opinion of their importance in a routine clinical consultation that you may have experienced.

1. What is your current profession?



2. The following are eight contextual factors that we have found from the literature that may help to enhance treatment effect. Please rate their importance according to your own experience during a consultation:

	Not important at all	Less important	Somewhat important	Important	Very important
Empathy of the HCP	○	○	○	○	○
Positive communication from the HCP	○	○	○	○	○
Active involvement of the patient by the HCP in the consultation	○	○	○	○	○
Clear and relevant information provided by the HCP	○	○	○	○	○
Patient expectation concerning their outcome	○	○	○	○	○
Confidence in the HCP	○	○	○	○	○
Easy access to consultation	○	○	○	○	○
Sufficient consultation time	○	○	○	○	○

3. Are there any other contextual factors related to practitioner-patient interaction you can think of which needs to be considered? (Please list as many as you feel relevant)

Appendix 13 Ethics application

University of Nottingham
UK | CHINA | MALAYSIA

Faculty of Medicine & Health Sciences
Research Ethics Committee
Faculty Hub
Room E41, E Floor, Medical School
Queen's Medical Centre Campus
Nottingham University Hospitals
Nottingham, NG7 2UH
Email: FMHS-ResearchEthics@nottingham.ac.uk

23 July 2021

Ayah Ismail
PhD Student
c/o Weiya Zhang, Professor of Epidemiology
Pain Centre Versus Arthritis, Rheumatology
School of Medicine
Clinical Sciences Building
Nottingham University Hospitals
City Hospital Campus
Hucknall Road
Nottingham, NG5 1PB

Dear Ms Ismail

Ethics Reference No: FMHS 312-0721 – please always quote
Study Title: Optimizing Contextual Factors in the Practitioner-Patient Encounter in the Management of Osteoarthritis.
Chief Investigator/Supervisors: Weiya Zhang, Professor of Epidemiology, Michael Doherty, Professor of Clinical Rheumatology & Epidemiology, School of Medicine, Dr Michelle Hall, Assistant Professor, Arthritis Research UK Pain Centre/Physiotherapy and Rehabilitation, School of Health Sciences.
Lead Investigators/student: Ayah Ismail, PhD School of Medicine

Thank you for your recent query about your proposed stakeholder and PPI involvement study as part of your PhD.

Based on the information provided the proposed anonymous online survey does not require full research ethics review because it is seeking expert opinion to inform for the design and focus of your research.

Yours sincerely

Dr John Williams, Associate Professor in Anaesthesia and Pain Medicine
Chair, Faculty of Medicine & Health Sciences Research Ethics Committee

Appendix 14 Lay summaries

A. The summary used for the first PPI/E meeting

Enhancing contextual effect of treatment in osteoarthritis

Ayah Ismail (Physiotherapy), Weiya Zhang (Evidence Based Medicine), Michael Doherty (Rheumatology) Michelle Hall (Physiotherapy).

Summary

About 2.5 million people in the UK have painful osteoarthritis and 1 million consult their GPs each year. The yearly cost to the NHS is £1 billion. The burden of the disease keeps rising due to aging, increasing obesity and lack of effective treatment. More than 53 treatments have been developed of which half are drugs with limited benefits but potential serious side effects.

Our recent research found that 75% of the benefits obtained from treatments for osteoarthritis in fact comes from the context of receiving a treatment and care, rather than from the specific effect of the treatment itself (for example, the chemical effect of a pain-killing tablet). This suggests that improving and optimising the contextual elements involved when a patient receives a treatment from a health professional (e.g., receiving full information, being examined thoroughly, not being hurried, being offered the opportunity to ask questions) may improve the overall benefits to the patient. This programme aims to identify key contextual factors that can be delivered by every doctor to enhance the treatment effect.

We will undertake a literature search for studies in osteoarthritis and other chronic conditions to identify key contextual factors that have therapeutic effects. We will develop a contextual enhancement package (CEP) using a panel of experts consisting of GPs, other healthcare professionals and patients. We will develop training materials and guidance on how to deliver the package. A qualified physiotherapist will subsequently test whether the package can be delivered in the first instance to 10 to 15 people with osteoarthritis while she trains them with strengthening exercise – a strongly recommended treatment for osteoarthritis. The success of the delivery and acceptability of the package will be evaluated.

The results of this study will be used to inform further studies where people with osteoarthritis will be exposed to CEP, exercise, CEP plus exercise and neither. This will allow us to examine the effect alone for each treatment and the interaction between CEP and exercise therapy. The CEP will then be applied into clinical practice to improve the treatment benefits of patients in the future.

B. The updated summary used for the second PPI/E meeting

Optimising contextual effect of treatment in osteoarthritis

About 2.5 million people in the UK have painful osteoarthritis, and 1 million consult their GPs each year. The yearly cost to the NHS is £1 billion. The burden of the disease keeps rising due to ageing, increasing obesity and lack of a curative treatment. More than 50 treatments have been developed, of which half are drugs with limited benefits and potentially serious side-effects.

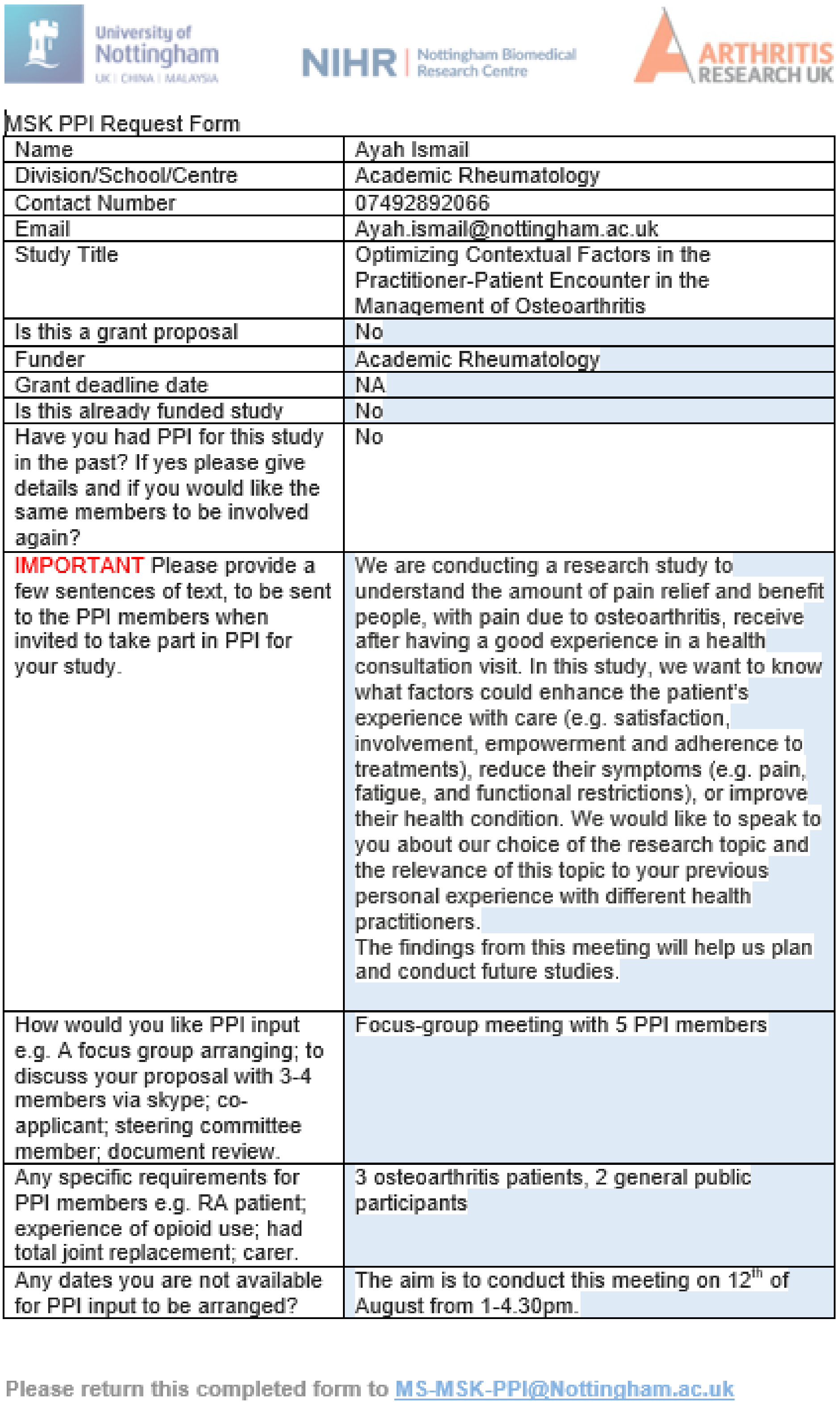
Our recent research found that 75% of the benefits obtained from treatments for osteoarthritis, in fact, comes from the context of receiving treatment and care rather than from the treatment itself (for example, the chemical effect of a pain-killing tablet). This suggests that improving and optimising the contextual elements involved when a patient receives treatment from a health professional (e.g., receiving full information and being examined thoroughly, not being hurried) may improve the overall benefits to the patient. This project aims to identify key contextual factors that every doctor can deliver to enhance the treatment effect.

We have undertaken a series of research activities, from expert consensus for potential contextual factors, to systematic literature reviews for research evidence on their clinical effectiveness. We have now found 8 key contextual factors with therapeutic effect that may be used to enhance the benefit obtained from a treatment.

1. Empathy of the Health Practitioner
2. Positive communication from the Health Practitioner
3. Active involvement of the patient by the practitioner in consultation
4. Clear and relevant information provided by the Health Practitioner
5. Patient expectation concerning their outcome and the consultation experience
6. Confidence of Health Practitioner
7. Easy access to consultations
8. Sufficient consultation time

We are now interested in your opinion of their importance in a routine clinical consultation that you may have experienced.

Appendix 15 MSK PPI/E request form



University of Nottingham
UK | CHINA | MALAYSIA

NIHR | Nottingham Biomedical Research Centre

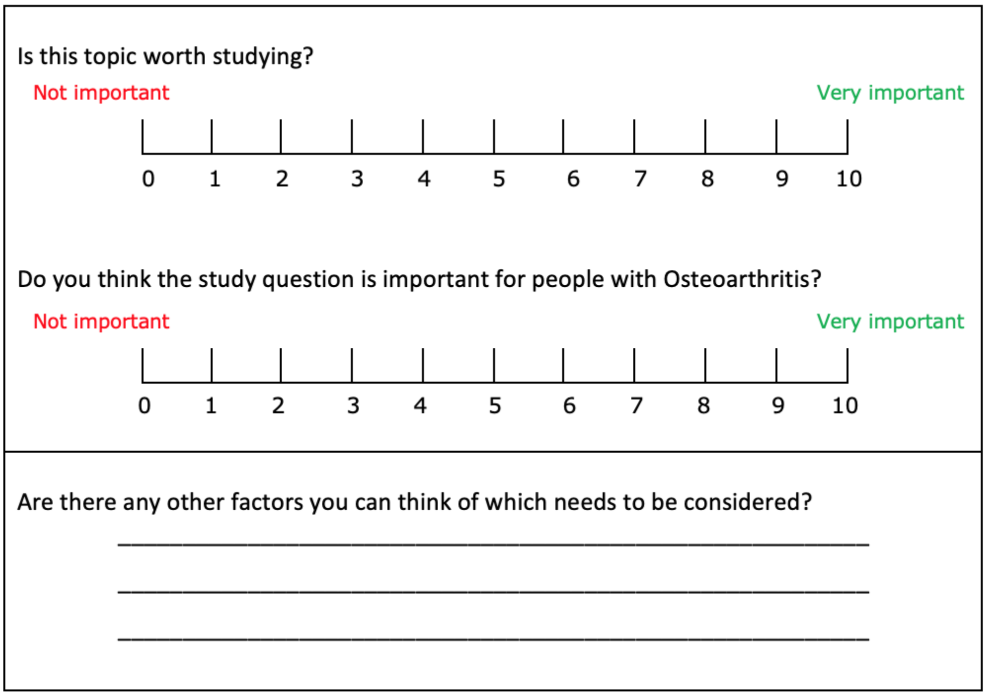
ARTHRITIS RESEARCH UK

MSK PPI Request Form

Name	Ayah Ismail
Division/School/Centre	Academic Rheumatology
Contact Number	07492892066
Email	Ayah.ismail@nottingham.ac.uk
Study Title	Optimizing Contextual Factors in the Practitioner-Patient Encounter in the Management of Osteoarthritis
Is this a grant proposal	No
Funder	Academic Rheumatology
Grant deadline date	NA
Is this already funded study	No
Have you had PPI for this study in the past? If yes please give details and if you would like the same members to be involved again?	No
IMPORTANT Please provide a few sentences of text, to be sent to the PPI members when invited to take part in PPI for your study.	We are conducting a research study to understand the amount of pain relief and benefit people, with pain due to osteoarthritis, receive after having a good experience in a health consultation visit. In this study, we want to know what factors could enhance the patient's experience with care (e.g. satisfaction, involvement, empowerment and adherence to treatments), reduce their symptoms (e.g. pain, fatigue, and functional restrictions), or improve their health condition. We would like to speak to you about our choice of the research topic and the relevance of this topic to your previous personal experience with different health practitioners. The findings from this meeting will help us plan and conduct future studies.
How would you like PPI input e.g. A focus group arranging; to discuss your proposal with 3-4 members via skype; co-applicant; steering committee member; document review.	Focus-group meeting with 5 PPI members
Any specific requirements for PPI members e.g. RA patient; experience of opioid use; had total joint replacement; carer.	3 osteoarthritis patients, 2 general public participants
Any dates you are not available for PPI input to be arranged?	The aim is to conduct this meeting on 12th of August from 1-4.30pm.

Please return this completed form to MS-MSK-PPI@Nottingham.ac.uk

Appendix 16 PPI/E form



Is this topic worth studying?

Not important　　　　Very important

0　1　2　3　4　5　6　7　8　9　10

Do you think the study question is important for people with Osteoarthritis?

Not important　　　　Very important

0　1　2　3　4　5　6　7　8　9　10

Are there any other factors you can think of which needs to be considered?

____

____

____