

EVALUATION OF NEUROTTEXT  
AS A MEMORY AID FOR  
PEOPLE WITH MULTIPLE SCLEROSIS

**Rachel Goodwin BSc. MSc.**

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



# Abstract

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**Objectives:** Memory problems are reported in 40-60% of people with multiple sclerosis (MS), they can affect independence in activities of daily living and may limit their ability to benefit from rehabilitation. There was some evidence to support the use of NeuroPage, a memory aid service, in people with neurological conditions, but there were methodological limitations. The aim of this study was to evaluate the effectiveness of the NeuroPage service for people with MS who have memory problems.

**Systematic Review:** A systematic review on external memory aids for people with MS was performed. Eight studies were included; one study reported a treatment effect on subjective memory functioning; one on mood. No effect was demonstrated on objective memory functioning or quality of life. It was concluded that the evidence was insufficient, and high quality trials were needed.

**Methods:** A multicentre, single-blind randomised controlled crossover trial design was employed. People with MS and self-reported memory problems were recruited into the trial, following referral from MS services. The intervention was 'NeuroText', a service that sends reminder messages to people's mobile phones at pre-arranged times via the existing NeuroPage system. In the control condition participants received non-memory texts, containing items of interest, such as news headlines. Outcome measures were completed using postal questionnaires. t-tests were employed to compare intervention and control conditions. Semi-structured feedback interviews were performed with 25 participants.

**Results:** Of the 106 people referred 38 took part. They were aged 28 to 72 (mean=48, S.D.=11) and 10 were men. No significant differences between NeuroText and control were detected on the Everyday Memory Questionnaire ( $t = 0.84$ ,  $p = 0.41$ ). The number of daily diary items forgotten in the NeuroText condition was significantly less than in the control (9% vs. 31%;  $t = -2.8$ ,  $p = 0.01$ ).

Reported psychological distress in the NeuroText condition was also less than control ( $t=-3.83$ ,  $p=0.001$ ). Seven themes were identified from participant feedback.

**Conclusions:** NeuroText appears to help people with MS to achieve their everyday tasks and improve mood, however these improvements were not reflected on the questionnaire measure of the frequency of memory problems in everyday life.



# Preface

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All research documented in this thesis was funded by the MS Society on a PhD Studentship grant, award number 971/12. The author completed the research and thesis between March 2013 and February 2016. Findings of the research have been disseminated by the author in one peer-reviewed publication; and at multiple conferences, some listed below.

Goodwin, R., Lincoln, N., das Nair, R., & Bateman, A. (2015). *Evaluation of NeuroText as a memory aid for people with multiple sclerosis*. Oral presentation at MS Frontiers, London, UK.

Goodwin, R., Lincoln, N., das Nair, R., & Bateman, A. (2015). *Evaluation of NeuroText as a memory aid for people with multiple sclerosis*. Poster presentation at the Division of Neuropsychology (DoN) Annual Conference, London, UK.

Goodwin, R., Lincoln, N., das Nair, R., & Bateman, A. (2014). *External memory aids for memory problems in people with multiple sclerosis: A systematic review*. Oral presentation at The NR-SIG World Federation for NeuroRehabilitation (WFNR) Conference, Limassol, Cyprus.

Goodwin, R., Lincoln, N., das Nair, R., & Bateman, A. (2014). *Evaluation of NeuroText for people with multiple sclerosis*. Poster presentation at the The NR-SIG World Federation for NeuroRehabilitation (WFNR) Conference, Limassol, Cyprus.

Goodwin, R., Lincoln, N., das Nair, R., & Bateman, A. (2014). *External memory aids for memory problems in people with multiple sclerosis: A systematic review*. Oral presentation at Rehabilitation in MS (RIMS) Conference, Brighton, UK.

Goodwin, R., Lincoln, N., das Nair, R., & Bateman, A. (2014). *External memory aids for memory problems in people with multiple sclerosis: A systematic review*. Poster

presentation at the Society for Research in Rehabilitation (SRR) Conference,  
Glasgow, UK.

# Acknowledgements

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Many people have contributed to the production of this thesis. Firstly, I would like to thank all of the participants who offered up their time and energy to take part in this research, and their families and carers for assisting. I am grateful to the MS Society for funding this research, and to the many clinicians and research nurses for aiding recruitment.

Thank you to my fantastic supervisors, Nadina Lincoln, Roshan das Nair and Andrew Bateman. You have provided unique, continuous support, and have helped me grow as a researcher. I am also indebted to the administrative team at the Division of Rehabilitation and Ageing, Shirley Thomas, the Eastern NIHR CRN and Jacqui Mhizha-Murira. I am grateful to the team at the Oliver Zangwill Centre for assisting with transcription and handling outcome data, as well as boosting my morale when needed.

Finally, thank you to Daniel, Mum, Dad and Matthew, for your encouragement and patience throughout.



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# **1 Background**

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## **1.1 Chapter Overview**

This chapter will describe the context in which the research has taken place. It will begin by explaining what multiple sclerosis (MS) is, how it impacts the central nervous system, and affects cognition. Memory as a construct will be investigated, followed by the effect of MS on memory function, and what this means for the individual. How to measure memory, and factors that should be considered when interpreting the findings, will be discussed. The rehabilitation of memory problems will be introduced, with a particular focus on assistive technology, followed by the rationale for the study.

## **1.2 Multiple Sclerosis**

### **1.2.1 What is Multiple Sclerosis?**

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating and degenerative disease of the central nervous system (CNS). Research published in 2014 estimated that there are approximately 127,000 people with MS in the UK, and 6,000 people newly diagnosed each year (I. Mackenzie, Morant, Bloomfield, MacDonald, & O'riordan, 2014). MS is the most common non-traumatic neurological cause of disability of young and middle-aged adults, and the economic effects of the disease are noticeable (Barten, Allington, Procacci, & Rivey, 2010; Rao, 1990). The precise aetiology of MS remains unknown; however it is generally accepted that MS results from an interaction between genetic predisposition and environmental factors (Grant, 2009). MS mostly affects the female sex, with a male/female ratio of 0.5 (World Health Organization, 2008). People with MS typically develop symptoms in their late 20s, experiencing visual and sensory disturbances, limb weakness, gait problems, and bladder and bowel symptoms (National Clinical Guideline Centre, 2014). Partial recovery may occur initially, but over time people develop progressive

disability. During the course of MS, a wide range of functional impairments and disabilities can develop, resulting in a significant impact on the quality of life of people with MS and their families.

MS is most commonly classified into four subtypes reported by Lublin and Reingold (1996), based on the temporal profile. Relapsing-remitting MS (RR) is the most common form; affecting 85% of all people diagnosed (Multiple Sclerosis Society, 2010). RR is characterized by relapses followed by full or partial recovery of impaired functions, with a stable course and lack of progression between relapses. A relapse is defined as an episode of neurological symptoms that lasts at least 24 hours and happens at least 30 days after any previous episode began (W. McDonald et al., 2001). People often make a good recovery from a relapse, with complete remission, however around half of all relapses may leave some lingering problems (Vercellino et al., 2009). Most people with relapsing remitting MS eventually develop secondary progressive MS, around 65% develop it after 15 years (Koch, Uyttenboogaart, Van Harten, & De Keyser, 2008). Secondary progressive is characterised by a steady worsening of symptoms over time with occasional relapses and minor remissions (Grant, 2009). A smaller proportion, 10-15% of individuals suffer from Primary progressive MS, which has a continuous and gradual worsening of MS symptoms with no distinct relapses or remission of symptoms. Benign MS is characterised by little disease activity, and is reported to affect up to 10-15% of people with MS (Mohr & Cox, 2001).

### **1.2.2 How does MS affect the Central Nervous System?**

MS is a progressive disease of the CNS that is characterised by widespread lesions, or plaques, in the brain and spinal cord (Chiaravalloti & DeLuca, 2008). MS is an autoimmune disease, caused by dysregulation of the immune system, with the formation of immune cells specifically activated against CNS components (Nocentini, Caltagirone, & Tedeschi, 2012). The main feature of this disease is an inflammatory process resulting in the loss of the myelin sheath and subsequent axonal degeneration, culminating in chronic multifocal sclerotic plaques. This

process occurs preferentially in the white matter surrounding the ventricles, corpus callosum, optic nerves, brainstem, cerebellum and spinal cord (Grant, 2009). MS lesions predominately affect white matter, but lesions also appear in grey-white matter junctions and grey matter (Kidd et al., 1999). The precise cause of inflammation is not yet fully understood, but an autoimmune response directed against CNS antigens is suspected (Nocentini et al., 2012). Due to the widespread development of plaques, MS results in a broad range of symptoms, including motor, cognitive and neuropsychiatric problems (Chiaravalloti & DeLuca, 2008).

#### ***1.2.2.1 How does MS affect cognition?***

Cognitive symptoms can include problems with attention, memory, learning and planning. Cognitive symptoms affect up to 60% of people with MS (E. M. Rosti-Otajärvi & Hamalainen, 2011), and because the disease is progressive, the lifetime prevalence is higher than 60% (Mohr & Cox, 2001). Studies into the symptoms in different types of MS have not shown clear differences in cognitive symptoms (D. Miller & Leary, 2007). Cognitive dysfunction seen in people with MS is heterogeneous and occurs independently of physical disability (Cobble, 1992; Rosti-Otajärvi & Hämäläinen, 2014). Overt dementia is rare in people with MS, and the more common clinical presentation is one of specific and subtle cognitive deficits (Fischer, 2001). Cognitive variability was demonstrated by Rao, Hammeke, McQuillen, Khatri, and Lloyd (1984), who studied memory disturbances in people with MS and found that their memory performance was highly variable, when compared to healthy controls. Rao et al. (1984) suggested this was due to the variable distribution of plaques in the CNS in the people with MS. The degree of cognitive impairment evident in individuals with MS appears to be unrelated to their neurological disability status or disease duration (Maurelli et al., 1992; Rao et al., 1991).

Neuropsychological studies have found common cognitive deficits in MS, despite the considerable variability in cognitive dysfunction seen in people with MS (Rao, 1990, 1996). Intelligence, basic attention and basic verbal skills are commonly intact

in people with MS (Nocentini et al., 2012). Memory, executive dysfunction and learning dysfunction are considered the most common MS-related impairments; as is slowed information processing speed, which is thought to underlie cognitive problems observed in MS (Bravin, Kinsella, Ong, & Vowels, 2000; Larner, 2013; Rosti-Otajärvi & Hämäläinen, 2014). Complex attention skills, visual-spatial learning; visual perception and language impairments can also occur (Fischer, 2001; Mohr & Cox, 2001).

## **1.3 Memory problems and MS**

### **1.3.1 Memory Systems**

Memory impairment is one of the most common sequelae of brain injury or disease. Many different patterns of impairment arise from brain damage, and this is reflected by the now well-established fact that memory is not a unitary concept or function (Evans, 2004). The most important conceptual division is between short term or working memory, and long-term memory. Working memory stores information temporarily for a matter of seconds, whereas long-term memory is a permanent repository of memory for knowledge or events that are acquired in the past, i.e. from a few minutes to 50 years ago.

Working memory, as described in the Baddeley and Hitch (1974) multicomponent model, is thought to involve three components: the phonological loop holds verbal information for a few seconds or whilst it is being rehearsed; the visuospatial sketchpad holds non-verbal material in the same way; and the central executive is the attentional controller, modulating the interface between the long-term store and the two slave systems. It has since been suggested that a good account of the central executive might be provided by the supervisory attentional system for executive functioning, proposed by Norman and Shallice (1986).

Long-term memory has also been broken down into conceptual divisions at three levels. The main division is between verbal and non-verbal material, which appears



to result from hemispheric asymmetry within the brain, where the left is more concerned with verbal processing and the right with non-verbal information (Evans, 2004). The second division is between declarative (explicit) and non-declarative (implicit) systems (Squire, 1992). Non-declarative memory system allows us to learn procedures without conscious awareness, functioning by the gradual acquisition of learning over time (Poldrack et al., 2001). The different forms of implicit learning include procedural learning, such as motor skills or habits; priming; and classical conditioning. The declarative learning system represents knowledge and includes conscious information about an individual's life, such as facts and events. Tulving (1972) documented the third conceptual division of declarative memory into semantic and episodic memory systems. Semantic memory stores facts of the world, including word meanings, objects, people and encyclopaedic facts. Semantic knowledge is therefore independent of context, and is gathered through multiple exposure or rehearsal of the material. Whereas episodic memory refers to context-dependent information, such as autobiographical events or information linked to a particular time or place, e.g. remembering what you did yesterday.

Recent models focus on the processes involved in memory formation, to enable researchers to examine how component processes could be manipulated to enhance or restore memory functions (Skeel & Edwards, 2001). Skeel & Edwards (2001) proposed a simple taxonomy of functional memory processes: encoding describes the unconscious or effortful processes by which information or motor skills are initially organised and processed for immediate or later recall; consolidation refers to mostly unconscious processes by which memories are converted from temporary, active processing to permanent storage; retrieval is effortful or passive process where previously learned material or skills are recalled. Once information is stored, if it is to be used, it must be retrieved. The two principle methods of retrieval are recall and recognition (Baddeley, 2004). Recognition occurs when you may not be able to bring to mind the thing you are trying to remember, but instantly recognise when you see it. Recall involves the recollection of something in the absence of the thing to be remembered.

### **1.3.2 Prospective memory**

Prospective memory, remembering to do things in the future, is distinct from retrospective memory, and is one of the most practically important uses for memory. Prospective memory processes allow us to plan future behaviours and act on these at the appropriate time (Baddeley, 2004). Ellis (1996) used the term 'realising delayed intentions', for these tasks. There are several types of prospective memory, with the most important distinction being between time-based and event-based tasks (Einstein & McDaniel, 1990). Time-based tasks involve remembering to perform a given action at a given time (e.g. phone a friend at 6pm). Event-based tasks involve remembering to perform an action in the appropriate circumstance (e.g. buy milk when you walk past the shop). Time-based tasks are considered to be more difficult than event-based tasks, because the association aspect in event-based tasks may function as a cue (Einstein, McDaniel, Richardson, Guynn, & Cunfer, 1995).

Prospective memory could be deemed a misleading term, because it requires the coordinated integration of planning skills (setting the intention), attention and memory (recognising it is time to do the intended action, remembering what the action is, and then remembering it has been carried out) (Evans, 2004). Therefore it has been postulated that prospective memory functioning relies on attention and executive functioning (Dagenais et al., 2016; Fish, Manly, Kopelman, & Morris, 2015; Glisky, 1996), as well as retrospective memory functioning, as you need to recall the intention to be carried out (Rendell, Jensen, & Henry, 2007). The separate stages or processes involved in prospective memory have been described by many authors, such as Sohlberg and Mateer (2001) who suggest that to successfully perform the prospective memory task, the person must plan the behaviour; keep the steps required to accomplish this in mind; recall the task; and take action. The most recent conceptual model was presented by Zogg, Woods, Saucedo, Wiebe, and Simoni (2012), and contains five components: intention formation, where the individual forms or encodes the intention linked to a cue (time or event related); retention interval, is the typical time delay between intention formation and execution, monitoring of the environment for task-related cues occur; cue

detection and intention retrieval, requires the individual to detect and recognise the relevant cue and self-initiate retrieval of appropriate intention; intention recall, successful retrieval of the intention from retrospective memory; intention execution.

### **1.3.3 Memory problems experienced in MS**

Approximately 40-60% of people with MS have memory problems (Rao et al., 1993). Investigations into memory impairment in MS have largely focused on retrospective memory (Bravin et al., 2000), and there is considerable evidence that MS is associated with impaired retrospective memory (Rendell et al., 2007). Thornton and Raz (1997) concluded that MS is associated with significant impairment on all three types of retrospective memory: short-term, long-term and working memory. Long-term memory is one of the most consistently impaired cognitive functions in MS, occurring in 40-65% of patients (Rao et al., 1993). Recall in both verbal and non-verbal categories are reported as affected by MS (Grafman, Rao, & Litvan, 1990; Larner, 2013; Mohr & Cox, 2001). Although retrieval of verbal information is the problem that most commonly interferes with memory function, impairments can occur across all domains, including problems with encoding and storage (Mohr & Cox, 2001). Recognition memory and implicit learning appear to remain intact (Brassington & Marsh, 1998).

Originally it was thought that the MS-related memory impairment resulted from a difficulty in retrieval processes, however recent research indicates that the primary problem is in the learning of information (DeLuca, Barbieri-Berger, & Johnson, 1994; Thornton, Raz, & Tucker, 2002). This deficit in learning new information results in poor decision-making abilities, and appears to affect prospective memory abilities (Nagy et al., 2006; Rendell et al., 2007). Slow processing speed, susceptibility to interference, executive dysfunction and perceptual deficits have been associated with the poor learning abilities seen in people with MS (Chiaravalloti & DeLuca, 2008).

Specific types of memory impairments, such as autobiographical and prospective memory impairment, have also been reported in people with MS (Ernst et al., 2013; Rendell et al., 2007). People with MS often complain of forgetfulness related to prospective memory, such as forgetting to take their medications, rather than retrospective memory, and these memory failures greatly affect their daily living (Dagenais et al., 2016; Demers et al., 2011). Prospective memory in people with MS has not been examined to the same extent as retrospective memory (Bravin et al., 2000), but the evidence for prospective memory impairment in people with MS is mounting (A. Miller, Basso, Candilis, Combs, & Woods, 2014). Given the evidence for retrospective memory impairment in MS, it is logical that people with MS would also have deficits in prospective memory. This is because prospective memory tasks involve a retrospective component (McDaniel & Einstein, 1992). Research has found that people with MS had prospective memory problems (i.e. the implementation of delayed intentions), as well as the retrospective memory deficits (i.e. remembering what needs to be done) associated with poor prospective memory performance (Dagenais et al., 2016; Kardiasmenos, Clawson, Wilken, & Wallin, 2008; Rendell et al., 2007).

#### **1.3.4 Impact of memory problems**

Memory problems are persistent, frustrating both to patients and carers, and are debilitating and difficult to treat (Williamson, Scott, & Adams, 1996). Cognitive deficits may have both physical and mental effects, leading to symptoms of fatigue (DeLuca, 2005), and severe cognitive impairment presents a major barrier to rehabilitation programmes because individuals may be unable to retain advice (Thomas, Thomas, Hillier, Galvin, & Baker, 2006). Many people with MS report feeling more restricted by cognitive impairments than by limited mobility (Amato, Zipoli, & Portaccio, 2006), and there is considerable evidence indicating that their quality of life is decreased (Grima et al., 2000).

Cognitive impairment in MS is often a hidden condition, which brings difficulties for people with MS in terms of everyday functioning, which contributes to depression,

anxiety, distress and fatigue (Gilchrist & Creed, 1994; Sá, 2008). Depression is a common co-morbidity in people with MS, with a lifetime prevalence of around 50%, which is three times that of the general population; and higher than that of other groups of chronic diseases (Bruce & Arnett, 2004; Feinstein, 2011; Feinstein, O'Connor, Gray, & Feinstein, 1999; Minden & Schiffer, 1990; Thomas et al., 2006). Despite the high rate of memory problems and depression seen in people with MS, relatively little is known about how the two symptoms relate to each other. Depression may worsen cognitive functioning and cognitive dysfunction may induce depression (Sá, 2008). Furthermore, the cause of the higher prevalence of depression in people with MS is unclear. Explanations include the view that depression could be a psychological reaction to having a chronic debilitating disease (Koch et al., 2014). For example, the perceived intrusiveness of MS on daily activities is related to depression and adjustment (Devins et al., 1996), as is loss of social role functioning (Pakenham, 1999).

Cognitive impairments may also negatively interfere with daily functioning (Engel, Greim, & Zettl, 2007; Langdon & Thompson, 1996), participation in social activities (Thomas et al., 2006) and employment status (A. O'Brien, Chiaravalloti, Goverover, & DeLuca, 2008; Rao et al., 1991). Cognitive deficits detrimentally affect many aspects of daily life, such as the ability to run a household and perform self-care tasks, including medical adherence (Gulick, 1998). The safety of the person with memory deficits can also be compromised, making them vulnerable in the home and work. Therefore cognitively impaired people with MS are more socially isolated and have greater need for personal assistance in the home than MS patients with only physical activities (Rao et al., 1991). Prospective memory plays an important role in independent functioning, and is crucial for activities of daily life, health needs and social relations (McDaniel, Einstein, & Rendell, 2008), and Salthouse, Berish, and Siedlecki (2004) claim that prospective memory is a more important determinant of the ability to live independently than retrospective memory. Therefore failures of prospective memory are embarrassing, risky to the individual, and hamper their ability to function independently.

Cognitive deficits are one of a few disease manifestations predictive of vocational status (Benedict et al., 2005). 40-80% of people with MS are unemployed, and cognitive impairment is a large contributor to this high rate (Grønning, Hannisdal, & Mellgren, 1990; Rao et al., 1991). Impairment in memory, executive dysfunction and poor information processing skills, have been blamed for this difficulty in maintaining employment (Beatty, Blanco, Wilbanks, Paul, & Hames, 1995; Parmenter, Shucard, & Shucard, 2007). The onset of MS typically occurs in young adulthood, when individuals are most active and productive in many aspects of their lives, and therefore MS leads to the loss of gainful employment for many (Beatty et al., 1995). The loss of employment, along with informal care, accounts for up to 60% of the cost of MS, due to the loss of earnings for both the patient and the carer (Whetten-Goldstein, Sloan, Goldstein, & Kulas, 1998). Therefore impairments in memory can have a detrimental effect on the psychological wellbeing of people and others around them (Skeel & Edwards, 2001), and have significant long-term effects for patient, their families and communities.

### **1.3.5 Assessment of Memory**

Assessment of memory problems is necessary in order to understand the nature of the deficits, and to inform rehabilitation practice as well as to evaluate the outcome of intervention (Mohr & Cox, 2001). Memory assessment should ideally be carried out immediately before the start of the rehabilitation programme, and should be planned, carried out and interpreted in the wider context of the individual person (Bradley, Kapur, & Evans, 2005).

Instruments that assess multiple domains of memory can be employed, as well as those looking specifically at components of memory. Additionally the latter can be in the form of formal clinician-led assessments requiring the client to perform certain tasks, or they can be self-report measures completed by the clients themselves or significant others. This distinction can be termed respectively as 'objective' and 'subjective' reports of memory.

The primary advantage of administering batteries of tests is that they include a variety of memory tasks (Lezak, 2004). Comprehensive batteries of memory are frequently employed in rehabilitation settings, such as, Wechsler Memory Scales (Wechsler, 1997) or Rivermead Behavioural Memory Test (Wilson, Cockburn, & Baddeley, 1985). Other tests focus on specific modalities of memory, e.g. verbal or visual memory; types, e.g. autobiographical, or prospective memory; components of memory, e.g. working memory; or processes, e.g. encoding, recall or recognition.

Self-report measures provide invaluable information regarding a person's memory functioning, and highlight their own perception of the level at which they are functioning and the impact on their everyday life (Godfrey, Partridge, Knight, & Bishara, 1993). Inconsistencies between subjective and objective tests are commonly reported (Goverover et al., 2005). This inconsistency is likely because everyday memory problems reported in subjective measures are not necessarily solely caused by "memory" deficits. Therefore it is suggested the two types of measures assess different constructs (G. Cohen, 1989).

#### ***1.3.5.1 Factors affecting performance on memory measures***

Memory performance can be affected by other cognitive, emotional and behavioural functions (Bradley et al., 2005). Measured memory problems could actually be the result of attention and information processing deficits, or executive dysfunction (Howieson & Lezak, 1995). Therefore it is vital to measure attention and executive functioning, alongside broad measures of memory.

NICE guidelines state that anxiety, depression, difficulty sleeping and fatigue can impact on cognitive problems (National Clinical Guidelines Centre, 2014). Up to 60% of people with MS have depression (Minden & Schiffer, 1991). Early studies consistently failed to find any clear relation between depression and cognitive impairment in MS (Siegert & Abernethy, 2005). However recent literature suggests that depression may exacerbate cognitive dysfunction (Chiaravalloti & DeLuca, 2008; Feinstein, 2006). Some studies demonstrated that depression has a

detrimental impact on particular aspects of cognitive capacity, namely information processing speed, working memory, learning and executive functioning (Arnett, Higginson, Voss, Bender, et al., 1999; Douglas R Denney, Sworowski, & Lynch, 2005; Gilchrist & Creed, 1994; Siegert & Abernethy, 2005; Thornton & Raz, 1997). Additionally depression may decrease the accuracy of patient-reported cognitive impairment (Julian, Merluzzi, & Mohr, 2007). Therefore it is common practice to assess mood symptoms alongside neuropsychological tests (Sá, 2008).

Fatigue is one of the most common symptoms in MS, being reported in over 90% of patients (Schapiro, 2002). Fatigue is believed to influence performance on memory tasks, and Bryant, Chiaravalloti, and DeLuca (2004) found that individuals with MS showed a decline in performance on a working memory task when they were fatigued. Additionally, recent research has found that pain may degrade ability to remember new intentions and suggests that pain is associated with prospective memory dysfunction in people with MS (A. Miller et al., 2014). Age is another factor known to have an effect on memory tests (Chiulli, Haaland, Larue, & Garry, 1995; Savage & Gouvier, 1992). Therefore these factors should be considered when interpreting performance on memory measures.

## **1.4 Cognitive rehabilitation for people with MS**

### **1.4.1 Memory rehabilitation**

Neuropsychological rehabilitation involves teaching compensatory strategies, using aids, supporting patient's awareness and teaching coping strategies to patients and their significant others (Rosti-Otajärvi & Hämäläinen, 2014). The ultimate aim of neuropsychological rehabilitation is to alleviate the impact of the memory impairment and consequently improve everyday functioning (Evans, 2004).

There are two main neuropsychological approaches to memory rehabilitation: restitution and compensation (Evans, 2006; Sohlberg & Mateer, 1989). Restitution techniques typically involve repetitive practice training, which aims to target a



person's underlying memory impairment (M. O'Brien, das Nair, & Lincoln, 2013). Compensatory approaches differ from restitution, in that they do not attempt to promote recovery of function, and instead focus on maximising a person's functional abilities (Sullivan, Dehoux, & Buchanan, 1989). Therefore compensatory techniques involve teaching people with memory problems to bypass problems by employing external and internal memory aids (Wilson, 2000).

The majority of published memory rehabilitation studies favour the use of compensatory strategies over restitution approaches, as there is a distinct lack of evidence for the effectiveness of restitution (Glisky, Schacter, & Tulving, 1986; Robertson, 1999; Wilson, Evans, Emslie, & Malinek, 1997). Cognitive problems associated with MS are not expected to follow a natural course of recovery, as might be seen in people with acquired brain injury (ABI); MS is more likely to result in progressive deterioration of function. Therefore, restitution approaches may lead to initial therapeutic gains, which are then lost by the progressive loss of cognitive function; and hence compensatory strategies are preferable. Additionally compensatory approaches are usually goal-directed, individualised, and linked to function (Simmons-Mackie & Damico, 1997), whereas restitution techniques often have limited generalizability to real world function.

Compensatory approaches can take multiple forms: internal memory aids, such as enhanced learning and mnemonics; environmental modification; and external aids. Enhanced learning places emphasis on making the most of any residual learning capacity, by paying more attention to the information to be remembered, and making sure you're not distracted by the environment. Additionally more time should be spent on encoding and repetition of the information needed to remember, using spaced and varied repetition (expanded rehearsal). Errorless learning is another technique that focuses on preventing people from making errors in their learning process (Wilson, Baddeley, Evans, & Shiel, 1994). Instead of trial and error, information is presented in such a way to avoid or significantly reduce mistakes (Wilson, 2002). PQRS and Mind Maps are techniques useful for people who are returning to formal education, as they are means of enhancing the

meaningfulness and memorability of information to be learnt (Buzan & Buzan, 2000; Robinson, 1970). One mnemonics technique is the method of loci, where a route around a familiar place or journey with specific location is pre-learned. Each item to be remembered is then associated with locations on the route. Method of loci is best used when learning a list, and takes considerable practice. A simpler and more commonly used mnemonic strategy is mental retracing, where you retrace your steps in order to remember where you've left something or what you've done. Environmental modification aims to reduce the memory demands placed upon a person. This can be achieved by using signposts, labels or colour-coding to aid orientation to the environment; as well as keeping objects in a particular place; or using orientation boards.

By far the most commonly used strategy for supporting memory is the use of external aids. External aids used in a compensatory fashion are generally viewed as a means to reduce the cognitive load and enable successful completion of a task (Linden, Hawley, Blackwood, Evans, & Anderson, 2014). Evans, Wilson, Needham, and Brentnall (2003) found that nearly 70% of people with a memory impairment used a calendar, notebook or diary. External memory aids do not aim to improve 'memory', but focus on reducing functional problems, by means of recording and accessing information externally (Teasell et al., 2007). Examples of external memory aids include paper-based systems such as calendars, diaries, Filofaxes. Another form of aid is a dosset box, which comprises multiple sections for storing daily medication doses, particularly helpful for people with complicated medication regimes.

However, for a person with a memory impairment the process of learning to use an external memory aid is not straightforward, and support is needed (Evans, 2004). Many barriers exist that prohibit the uptake of compensatory memory strategies, such as people believing they will "make their memory worse", feeling of dependency, or feeling embarrassed or stupid about using them (Baldwin, Powell, & Lorenc, 2011; Evald, 2015; Wilson & Watson, 1996). Therefore these factors need to

be considered when implementing compensatory aids with people with memory problems.

#### ***1.4.1.1 Assistive technology for memory problems***

There is a rapidly growing market of technological memory aids, for example timers, PDAs, smartphones, voice recorders, watches with alarms and paging devices (Dewar, Kopelman, Kapur, & Wilson, 2014). Everyday memory problems seen in both neurological and general populations are commonly prospective memory difficulties (Fish, Wilson, & Manly, 2010), and technological memory aids commonly focus on alleviating prospective memory problems (Linden et al., 2014). An aid could be used to hold information concerning intended actions, such as a reminder to take medication, which would be considered a meta-knowledge reminder. Additionally the content of a reminder could include monitoring information, e.g. medication needs to be refilled, or out-put monitoring such as, “have you refilled your medication”. People with memory problems have an inherent difficulty in developing rehabilitation strategies, because by definition patients will have difficulty remembering to apply compensatory techniques that they have been taught. Technological aids are gaining in popularity because they counteract this problem, as users do not have to remember to use the device (Lannin et al., 2014; Wilson et al., 1997). Johnson, Bamer, Yorkston, and Amtmann (2009) administered a survey to over 1,000 people with MS and found that approximately half of them used electronic memory aids.

Assistive technology for memory problems comes in a variety of forms, including electronic organisers, pagers, mobile phones, web-based scheduling and voice recorders (Linden et al., 2014). People with autobiographical memory deficits can be supported by SenseCam, which passively records images throughout the day, to act as a pictorial memory aid later (Hodges, Berry, & Wood, 2011). Voice recorders are an electronic memory aid that can replay messages at the time and date specified by the user, (Van den Broek, Downes, Johnson, Dayus, & Hilton, 2000). Portable electronic organisers (PDA) were an early form of assistive technology

used to aid memory function. PDAs have been shown to be beneficial to people with traumatic brain injury (TBI) (Dowds et al., 2011; Gillette & DePompei, 2004), and specifically for prospective memory (Waldron, Grimson, Carton, & Blanco-Campal, 2012). Additionally alarms can be used as electronic memory aids to prompt people into action. However, cueing devices alert the individual that there is something they need to do, but the lack of content means those individuals often cannot remember what that task is, and therefore lack functional practicality (McKerracher, Powell, & Oyebode, 2005; Zencius, Wesolowski, Krankowski, & Burke, 1991).

Much of the research on electronic memory aids has focussed on NeuroPage (Wilson, Emslie, Quirk, & Evans, 2001; Wilson, Emslie, Quirk, Evans, & Watson, 2005; Wilson et al., 1997), which is an alpha-numeric paging system that provides audio/vibration alerts (Hersh & Treadgold, 1994). NeuroPage now also sends SMS text messages to mobile phones, as well as pagers. Reminders are externally programmed, and therefore NeuroPage does not require training or learning to be used effectively (Kapur, Glisky, & Wilson, 2004). Evidence shows NeuroPage assists people with memory and planning problems following ABI, in achieving everyday target behaviours, relative to baseline (Baldwin & Powell, 2015; Dewar et al., 2014). NeuroPage has been examined for use in participants with TBI, CVA, encephalitis, children and adolescents (Emslie, Wilson, Quirk, Evans, & Watson, 2007; Fish, Manly, Emslie, Evans, & Wilson, 2008; Wilson, 2009; Wilson, Emslie, Quirk, et al., 2005). Fish et al. (2008) found that NeuroPage was effective in compensating for everyday memory and planning problems in a mixed ABI sample, and found that both TBI and CVA groups had short-term benefits. The TBI group had greater maintenance of pager-related benefits associated with increased executive functioning, whilst CVA group performance returned to baseline.

The use of Google Calendar as a cost-effective electronic memory aid has been investigated in people with ABI. At the time, Google offered a free of charge service that sent out pre-programmed timed text reminders directly to client's mobile phone. Google calendar was found to be more effective than paper-based aids in

supporting prospective intentions (A. McDonald et al., 2011), and reducing the forgetting of target behaviours (Baldwin & Powell, 2015). Mobile phones and smartphones are ubiquitous in the general population, and are therefore increasingly attractive for use as memory aids. Additionally mobile phones are highly portable, socially acceptable and cost effective (Dewar et al., 2014). Early mobile phone studies evaluated the impact of SMS text message reminders to act as a memory prompt for everyday tasks, planning and organisation skills (Stapleton, Adams, & Atterton, 2007; Wade & Troy, 2001). Smartphone technology has created a PDA-style memory aid within our mobile phones. The reminder functions on smartphones have been found to improve compliance in healthcare settings (Prasad & Anand, 2012), and everyday more “apps” are becoming available, including reminder functions that can even remind you to do a specific task when you arrive at a certain location. However, despite this advance of technology, people with moderate-severe cognitive impairments still need to be trained in how to use them as an effective memory aid (Svoboda, Richards, Leach, & Mertens, 2012). The NeuroPage experience showed that its effectiveness depended on first establishing what is important for the user, programming accordingly, and ensuring that the person actually uses the system (Baddeley, Eysenck, & Anderson, 2014).

#### **1.4.2 Effectiveness of memory rehabilitation for people with MS**

The effects of neuropsychological rehabilitation in people with MS have not been as widely studied as they have in acquired brain injury, where the advantages have been more extensively evaluated (Rosti-Otajärvi & Hämäläinen, 2014). Although the findings from individual studies appear promising, reviews of memory rehabilitation in people with MS have indicated that the effectiveness of memory rehabilitation programmes is far from conclusive (Carr, das Nair, Schwartz, & Lincoln, 2014).

A recent Cochrane review by das Nair, Ferguson, Stark, and Lincoln (2012) evaluated the effectiveness of memory rehabilitation for people with MS. Eight studies were included in the review, 4 studies included teaching in the use of internal and external memory aids; 3 studies employed computerised memory and

attention retraining packages; and one study used story memory technique, the use of imagery and story generation. das Nair et al. (2012) concluded that there was no evidence to support the effectiveness of memory rehabilitation for people with MS. The authors stated that the findings were probably due to the limited quality of some of the primary studies in the literature and concluded that robust RCTs, with high quality methodologies and reporting, were needed. However, a qualitative meta-synthesis of group-based memory rehabilitation for people with long-term neurological conditions found that programmes had a positive impact on daily life. Changes were seen in personal, inter-personal and professional spheres, and therefore the programme gave positive outcomes (das Nair, Martin, & Sinclair, 2015). Similar findings were reported in an individual qualitative study evaluating memory rehabilitation for people with neurological disabilities (das Nair & Lincoln, 2013).

External memory aids are the most effective and widely used intervention for rehabilitation of memory impairments (Sohlberg, 2005; Sohlberg et al., 2007). In a review on the effectiveness of cognitive rehabilitation for ABI, Cicerone et al. (2011) indicated there was evidence to support training using internal and external aids for people with mild memory impairments. Cicerone et al. (2011) also recommended that people with moderate to severe memory problems should receive training in the use of external compensatory strategies, linked to functional activities. This notion is supported by McKerracher et al. (2005), who stated that internal mnemonics such as visual imagery, tend not to be maintained or translatable to real-life problems, especially in people with severe memory problems. Individual studies in MS report that people who received compensatory memory rehabilitation reported significantly less emotional distress than those who received restitution (Martin, Lincoln, & das Nair, 2014). However, a recent study compared the restitution and compensatory approaches in a group trial with people with MS, and found there was no difference in outcomes measuring self-reported memory problems, mood or activities of daily living (M. O'Brien et al., 2013).

## **1.5 Rationale for current study**

Therefore the literature suggests that memory impairment is a major factor in determining the quality of life of people with MS. The majority of research on electronic memory aids has been on people with ABI, and there is an evidence-base for their effectiveness in supporting everyday memory functioning (Charters, Gillett, & Simpson, 2015). There is some suggestion that compensatory strategies, such as memory aids, could be effective in reducing everyday memory problems in people with MS. However the quality of research in this area, and cognitive rehabilitation in general, is poor. Therefore the next chapter documents a systematic review on the effectiveness of external memory aids for people with MS.

NeuroPage has the most evidence of effectiveness of any assistive technology, and the most compelling evidence regarding rehabilitation of prospective memory comes from studies using automated reminders for specific activities (Fish et al., 2010; Wilson et al., 2001). Although there are increasingly sophisticated developments in assistive technology, such as smart phones and mobile phones, there is often little effort to assess their usefulness (Baddeley et al., 2014). Martin-Saez, Deakins, Winson, Watson, and Wilson (2011) reviewed NeuroPage, considering more recent available technology, e.g. smartphones, and concluded that the service continued to have a role within cognitive rehabilitation. However, no studies have explicitly studied the effectiveness of NeuroPage for people with MS, and they have all compared the intervention to usual care, and so it is not understood which element of the intervention is most useful. Furthermore, the impact of NeuroPage on non-memory aspects of daily life such as mood, have not yet been evaluated; nor has qualitative research been undertaken on NeuroPage to date. Systematic reviews, such as A. O'Brien et al. (2008), have stated that future research should use empirically supported cognitive rehabilitation protocols and replicate interventions that have shown effectiveness in other neurological populations who commonly exhibit cognitive impairments. Therefore this study evaluated the effectiveness of the well-established NeuroPage, for people with MS.

In response to the request for more methodologically robust trials (das Nair et al., 2012), this study employed a randomised controlled crossover design, comparing the intervention to an active control. The trial was designed to evaluate feasibility, and the active control was intended to explore whether alerting is sufficient, or whether the reminder content is necessary for benefit. The literature suggests that attention and executive functioning impact on memory performance, and so these abilities were measured at baseline. Furthermore mood, everyday functioning and quality of life are impacted by memory problems, and so these were assessed as outcome measures, alongside everyday memory performance. Subjective outcome measures were employed, to capture the impact of the intervention on everyday functioning, rather than memory performance on objective measures. Additionally, outcome measures used were those frequently employed in memory rehabilitation studies, in order to facilitate future meta-analysis of pooled data in systematic reviews. Finally, the effectiveness of memory rehabilitation has been largely based on randomised controlled trials and has been inconclusive, however patient reports based on qualitative studies have been more positive. Therefore following trial completion, participants were invited to take part in feedback interviews to gather their perspectives.

### **1.5.1 Aims and objectives of the study**

- Evaluate whether people with MS who used NeuroText memory text messages show reduced subjective reports of memory problems in daily life in comparison with social text messages
- Evaluate whether people with MS who used NeuroText memory text messages show increased attainment of personally identified target behaviours in comparison with social text messages
- Evaluate whether people with MS who used NeuroText memory text messages show improved mood and quality of life compared with social text messages.



## **2 Systematic Review: External memory aids for memory problems in people with multiple sclerosis**

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### **2.1 Abstract**

#### **2.1.1 Background**

Approximately 40-60% of people with Multiple Sclerosis (MS) have memory problems, which are persistent and impact on their everyday functioning, mood and ability to respond to rehabilitation. Evidence supports the use of external memory aids in other patient groups, such as people with stroke and brain injury. There is some suggestion that external memory aids may be effective in reducing everyday memory problems in people with MS, however previous reviews on MS have only included randomised controlled trials. Therefore this review included research that employed other methodologies.

#### **2.1.2 Objectives**

The aim was to assess the efficacy of external memory aids for people with MS for improving memory functioning, mood, quality of life and coping strategies.

#### **2.1.3 Search methods**

A systematic search was performed on seven electronic databases.

#### **2.1.4 Selection criteria**

Intervention studies with at least 75% people with MS were included. Interventions included in this review involved training in the use of external memory aids, e.g. diaries, and personal digital assistants. Studies involving general cognitive rehabilitation programmes were included, providing they explicitly covered external memory aids.

### **2.1.5 Data collection and analysis**

Primary outcome measures were subjective reports of memory functioning and secondary outcome measures were objective measures of memory functioning, mood, quality of life and coping strategies. Two 10-point scales were used to rate the quality of included studies: the SCED scale for single case experimental design studies, and the PEDRO scale for group.

### **2.1.6 Main results**

Nine studies involving 540 participants with MS were included. The interventions varied from general cognitive rehabilitation programmes to specific training on a personal digital assistant. One single case experimental design (mean = 8 on SCED scale) and eight group studies (mean = 5 on the PEDro scale) were included; six of which were randomised trials. One study reported a significant effect of treatment on subjective reports of memory functioning, and two reported a significant effect on mood. Two studies reported a beneficial effect on the use of coping strategies. No significant effect of intervention was found on objective measures of memory or quality of life.

### **2.1.7 Author's conclusions**

Only one study evaluated programmes solely focusing on the use of external memory aids. The majority of studies involved comprehensive cognitive rehabilitation programmes, and thus were aimed at tackling a range of cognitive deficits. The methodological quality of included studies was poor. In conclusion, there is insufficient evidence to support or refute the effectiveness of external memory aids for improving memory function in people with MS.

## **2.2 Background**

### **2.2.1 Description of condition**

Multiple Sclerosis (MS) is a neurodegenerative disease characterised by a wide range symptoms that may include visual, motor and cognitive impairments (Gentry, 2008). Cognitive impairments, such as dysfunction in attention, executive abilities and memory, are common in people with MS, with estimates of prevalence varying from 43% to 72% (Prosiegel & Michael, 1993). Memory problems are a common cognitive complaint, with approximately 40-60% people with MS living with memory difficulties (Rao, 1995). These can be debilitating, persistent and frustrating both to patients and carers (Williamson et al., 1996).

Impairments in cognitive functioning are related to low mood (Gilchrist & Creed, 1994), and have the potential to affect independence in activities of daily living (Langdon & Thompson, 1996). Severe cognitive impairment presents a major barrier to rehabilitation, because individuals may be unable to retain advice or have difficulty acquiring new skills (Thomas et al., 2006). The safety of people with memory deficits can also be compromised, making them vulnerable in the home (e.g. forgetting to turn the oven off) and at work (e.g. forgetting deadlines). Impairments in memory can have a detrimental effect on the psychological wellbeing of people and others around them (Skeel & Edwards, 2001), and have significant long-term effects on a person's work and social life (Amato, Zipoli, & Portaccio, 2008).

### **2.2.2 Description of intervention**

Cognitive rehabilitation is a process whereby people with neurological trauma and clinicians work together as a team to remediate or alleviate the resulting cognitive deficits (Wilson & Watson, 1996). Cognitive rehabilitation aids the development of functional independence and adjustment of individuals with brain damage (Robertson, 1993). Memory rehabilitation plays a large part in the management of

people with memory problems and is administered as part of a comprehensive programme or as an independent intervention (das Nair & Lincoln, 2012).

Cognitive rehabilitation literature is divided on what strategies work best for people with cognitive impairment (das Nair et al., 2012). Restoration focuses on improving a specific cognitive function, potentially forcing a damaged neural circuit to work through regeneration. Compensation focuses on teaching people to adapt to the presence of a cognitive impairment, probably employing other undamaged circuits to perform a task (H. Cohen, 1999). Restitution approaches typically involve retraining exercises. Compensation is achieved through teaching people to use internal strategies such as mnemonics, or external strategies e.g. environmental adaptation or external memory aids. Wilson (2009) claimed there is insufficient evidence for recovery of memory function after the spontaneous recovery period and therefore promoted the use of compensatory strategies. Traditionally memory rehabilitation has focussed on teaching people to use compensatory strategies. These include applying/ using internal aids, such as mental imagery, mnemonics and rehearsal; or external memory aids, such as diaries, lists and notice boards. These aids aim to help people with memory impairments remember and recall information in their daily lives. Recently technology has enabled the use of paging systems (Wilson et al., 2001), mobile phones and palmtop devices to reduce prospective memory problems.

Cicerone et al. (2005) conducted a narrative review and reported cognitive rehabilitation to be beneficial for treating cognitive deficits following brain damage. The updated review (Cicerone et al., 2011) recommended the use of external compensatory devices for people with memory problems following traumatic brain injury (TBI) or stroke; while another review (de Joode, van Heugten, Verhey, & van Boxtel, 2010) found assistive technology, such as personal digital assistants (PDA) reduced prospective memory problems after acquired brain injury (ABI). A more recent systematic review (Jamieson, Cullen, McGee-Lennon, Brewster, & Evans, 2014) performed a meta-analysis including seven group studies and concluded that there was strong evidence for the efficacy of prospective memory prompting

devices for people with ABI or degenerative diseases. This suggested that prosthetic technology improves the performance of everyday tasks requiring memory. Jamieson et al. (2014) only reviewed one study that included people with MS and concluded that there was a specific need for the investigation of technology for people with degenerative diseases.

Recommendations for the provision of cognitive rehabilitation for people with MS have largely been based on single case experimental designs and controlled clinical trials (CCT). A systematic review, (A. O'Brien et al., 2008), concluded there was insufficient evidence to support or refute the effectiveness of memory rehabilitation for people with MS, due to small sample sizes, inadequate randomisation and blinding procedures and impairment-level outcome measures. In a Cochrane review of Neuropsychological Rehabilitation for MS, Rosti-Otajärvi and Hämäläinen (2014) found that cognitive training improved memory span and working memory, and when combined with other neuropsychological methods also improved delayed memory. However, the authors concluded that the overall quality of included studies was relatively poor due to methodological limitations and the heterogeneity of interventions and outcome measures. Other Cochrane reviews, such as das Nair et al. (2012) and Thomas et al. (2006), also stated that the literature base examining the effectiveness of memory rehabilitation for people with MS is weak and of poor quality, and concluded there is no evidence to support or refute the effectiveness of memory rehabilitation. Furthermore, it is unclear which elements of memory rehabilitation are most effective, for example, training, mnemonics or external memory aids. das Nair et al. (2012) concluded that more research is required to determine whether memory rehabilitation for people with MS is effective in reducing memory problems.

An expert panel underscored the need for cognitive rehabilitation interventions for people with MS and recommended the use of compensatory devices (Multiple Sclerosis Society, 2006). Additionally research has shown that there is a high frequency of spontaneous utilisation of strategies to deal with cognitive difficulties in people with MS, with the most common being the use of external memory aids

(Sullivan, Edgley, & Dehoux, 1990). There is insufficient evidence to support the use of compensation strategies for memory problems in people with MS (das Nair et al., 2012). Compensatory strategies for memory impairment have been more widely examined in people with stroke or TBI. Wilson et al. (2001) examined an external memory aid, NeuroPage, which sends specific reminders regarding important tasks to patients' individual pagers or mobile phones. NeuroPage was found to significantly reduce failures of memory in people with brain injury (Wilson et al., 2001), and improvements were maintained at follow-up. A recent study further supports the use of external memory aids, finding that occupational therapy training in the use of a handheld computer improved ABI patients' daily memory function more than standard rehabilitation, (Lannin et al., 2014).

### **2.2.3 Why is it important to do this review**

There is some suggestion that external memory aids may be effective in reducing everyday memory problems in people with MS (das Nair & Lincoln, 2012). A recent Cochrane review (das Nair et al., 2012) investigated the evidence base for memory rehabilitation for people with MS. However, most of the literature on memory aids did not employ RCT designs, and so was not included in the Cochrane reviews. A systematic review of external memory aids for cognitive problems in a clinical population of mixed aetiologies (Gillespie, Best, & O'Neill, 2012) highlighted that most studies have been qualitative or single subject designs. Therefore the present systematic review evaluated research that employed other quantitative methodologies, such as quasi-experimental designs and single case experimental designs, as well as RCTs. This review supplements Jamieson et al.'s (2014) findings by evaluating the effectiveness of all types of external memory aids not just technological; specifically for people with MS; and included comprehensive cognitive rehabilitation programmes, providing the use of memory aids was included.

## **2.3 Objectives**

The objectives were to test the following two hypotheses:

1. People with multiple sclerosis who received training in the use of external memory aids showed better outcomes in their subjective report of memory functions than those given other types of interventions or usual care or a placebo control.
2. People with multiple sclerosis who received training on the use of external memory aids had better objective memory performance, mood and quality of life than those given other types of interventions or usual care or a placebo control.

## **2.4 Methods**

### **2.4.1 Criteria for considering studies for this review**

#### ***2.4.1.1 Type of studies***

Studies evaluating the effectiveness of interventions were considered for review. Therefore, randomised controlled trials (RCTs); controlled clinical trials; before and after designs and single case experimental designs (SCED) were included. A study was deemed to be a RCT on the basis that the individuals followed in the trial were definitely or probably assigned prospectively to one of two (or more) alternative forms of health care using random allocation (Higgins & Green, 2013). Single case experimental design studies were distinguished from descriptive case reports by the inclusion of a control condition either through multiple baseline measures or a separate control measure that allowed the causal impact of the treatment efficacy to be inferred, as in reversal/withdrawal (A-B-A) designs (Tate et al., 2008). AB design SCEDs were also considered. Studies were included with any type of control group (i.e. care as usual, standard care, placebo, waiting list, other rehabilitation or intervention).

#### ***2.4.1.2 Type of participants***

Studies in this review were limited to people with MS, regardless of clinical course or length of time since diagnosis. Therefore studies that included participants whose memory impairments resulted from TBI, stroke, brain tumour or any other brain damage were excluded. In studies with mixed aetiology samples, studies were included if the sample consisted of 75% or more MS participants or a subgroup of MS participants could be identified for which separate data were available. Memory impairments were not defined in advance and it was assumed that people receiving training on the use of external memory aids had memory impairments. Studies were included if participants were 18 years or over, or if separate data were available for those over 18 years.

#### ***2.4.1.3 Types of interventions***

Interventions included in this review involved the use of, or training in the use of, external memory aids, defined as any external means of compensating for a memory deficit, e.g. diaries, PDAs, electronic calendars. Studies involving general cognitive rehabilitation programmes covering other aspects of cognition, such as executive function or visual perception; or other forms of memory rehabilitation, such as training on internal strategies, were included provided they explicitly provided training on the use of external memory aids. Studies were considered to involve an intervention if the training took place over more than a single session. Thus, single session experiments were not included. Pharmacological interventions were not included. Where studies had active control groups, it was checked that these groups contained no memory content, to allow pure comparison with the treatment group.



#### **2.4.1.4 Types of outcomes**

##### Primary outcomes

The primary outcome was measures that directly assessed the degree of subjective memory problems in everyday life. If more than one outcome measure was used to measure this construct, the following hierarchy was used:

Everyday Memory Questionnaire (EMQ) (Sunderland, Harris, & Gleave, 1984); Cognitive Failures Questionnaire (Broadbent, Cooper, FitzGerald, & Parkes, 1982); Subjective Memory Questionnaire (Davis, Cockburn, Wade, & Smith, 1995); Memory Functioning Questionnaire (Gilewski, Zelinski, & Schaie, 1990). This was based on the degree to which the measure focussed on memory and the psychometric properties.

##### Secondary outcomes

Secondary outcomes were measures of objective memory; mood; quality of life and coping strategies for memory problems. If more than one outcome measure was used to measure each construct, the following hierarchies were used:

- i) Performance on memory tests such as, Wechsler Memory Scale (Wechsler, 1997) or newer versions of this test; The Cambridge Prospective Memory Test (Wilson, Emslie, Foley, et al., 2005); Doors and People Memory Test (Baddeley, Emslie, & Nimmo-Smith, 1994); Rivermead Behavioural Memory Test (RBMT) (Wilson et al., 1985) or newer version of this test.
- ii) Mood, such as the General Health Questionnaire (GHQ) (Goldberg, 1992); Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983); Beck Depression Inventory (BDI) (Beck, Ward, & Mendelson, 1961); State-Trait Anxiety Inventory (Spielberger, 1983).
- iii) Quality of life, such as MS Quality of Life Inventory (LaRocca et al., 1996); MS Impact Scale (Hobart, Lamping, Fitzpatrick, Riazi, & Thompson, 2001); the Short Form (SF-36) (Ware & Kosinski, 2001); EuroQoL (Brooks, 1996).

iv) Coping strategies for memory problems, such as the Adaptation to Memory Difficulties Outcome Questionnaire (AMEDO) (Chouliara, 2013); Memory Aids Questionnaire (MAQ) (Wilson & Moffat, 1984); The Strategy Subscale of the Multifactorial Memory Questionnaire (MMQ-Strategy) (Troyer & Rich, 2002); Internal & External Memory Aids Questionnaire (das Nair & Lincoln, 2012); Cognitive Strategies Questionnaire (CSQ) (Shevil & Finlayson, 2010); PDA Checklist (Gentry, 2008).

Hierarchies were established by considering the relevance of each measure to each construct and psychometric properties in people with MS. MS specific measures were placed above generic measures. General measures of constructs were placed above specific measures. If no psychometric properties were available, the hierarchy was decided through discussion between authors.

## **2.4.2 Search methods for identification of studies**

The following electronic databases were searched and all potential studies were identified by the reviewer (RAG).

### ***2.4.2.1 Electronic searches***

1. Cochrane Central Register of Controlled (CENTRAL) (The Cochrane Library, latest issue)
2. MEDLINE (1966 to August 2014)
3. EMBASE (1980 to August 2014)
4. Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1982 to August 2014)
5. PsycInfo (1980 to August 2014)
6. Web of Science (January 1981 to August 2014)
7. Psycbite (2004 to August 2014)

The search strategy used and modified for all databases can be found in Appendix 1.

#### **2.4.2.2 Searching other resources**

Citation tracking of primary study articles was employed and the reference lists of identified papers were searched for further relevant studies. Journals covering relevant topics were identified and the contents of new volumes were hand searched. Grey literature was accessed by searching GreyNet (<http://www.greynet.org/>), Mednar (<http://mednar.com/>). The first four pages of results on Google Scholar were searched, with date restricted from 2010-present, (<http://scholar.google.co.uk/>); along with websites relevant to the topic area, such as MS Society (<http://mssociety.org.uk/>) and MS Trust (<http://MSTrust.org.uk/>). These websites were searched using combinations of the following search terms: memory (memory; cognition; remember; remembering; recall; plan; planning); multiple sclerosis (multiple sclerosis; MS); external aids (memory aids; external aids; reminder systems; assistive technology; paging).

### **2.4.3 Data collection and analysis**

#### **2.4.3.1 Selection of studies**

The review primary author (RAG) developed the search strategy, following consultation with a university librarian and using guidance from relevant past reviews. She reviewed abstracts of studies identified by this strategy to identify those appearing pertinent and systematically excluded studies that did not fit the inclusion criteria: 1. Less than 75% participants with MS; 2. Study design did not evaluate the effectiveness of an intervention; 3. Did not include use of external memory aids in intervention. After this initial search, duplicate papers were filtered out using endnote software (<http://endnote.com>).

The studies that met the criteria were then subject to a full text review, using the inclusion criteria again to select studies. Authors were contacted if clarification was needed in order to reach the decision of whether or not their study fitted the inclusion criteria, e.g. if it was unclear whether training on external memory aids was provided. Authors were also contacted to retrieve MS subgroup data, where published data sets were of mixed aetiology (less than 75% participants with MS).

#### ***2.4.3.2 Data extraction, management and assessment of risk of bias***

The methodological quality of each of the selected studies was assessed using the PEDro or SCED scales (Maher, Sherrington, Herbert, Moseley, & Elkins, 2003; Tate et al., 2008). The main measures of trial quality were whether random allocation had been concealed and whether outcomes were conducted blind to group allocation (Maher et al., 2003). The inclusion of non-RCTs in this review meant that some studies did not have randomisation and blinding procedures, and these were considered as lower quality.

Data for the review were extracted using a pre-prepared data extraction form that included the following items:

Date, country and clinical setting of the study

Sample size (percentage of people with MS)

Numbers lost to follow up, at specific time points, by group

Adequacy of matching at baseline between groups

Inclusion and exclusion criteria

Method of diagnosing MS and memory problem

Description of intervention and control, including duration, frequency, intensity, setting, and individual or group

Demographic characteristics of participants (age, gender, years since diagnosis, type of MS, years of education)

Outcomes measured, whether primary or secondary and when they were recorded

Random sequence generation

Allocation concealment

Blinding of participants and personnel

Blinding of outcome assessment

Intention to treat analysis used

Incomplete data

Selective reporting

Other sources of bias

Results for each outcome

Sample size justification

Reliability, validity and standardisation of new primary outcome measures

Appropriate analytical techniques applied, measures of variability, probability value

Key conclusions from authors

These characteristics were judged on the basis of information provided in the reports of the studies. Risk was assessed as being low, high or unclear if the information available was insufficient to make this judgement, on the basis of the following criteria: random sequence generation; allocation concealment; blinding; incomplete outcome data; selective reporting. Two 10-point scales were used to assess methodological quality: the PEDro Scale (Maher et al., 2003) was used to rate the group studies and the SCED scale (Tate et al., 2008) was used for single case experimental design studies. Previous research has established that there is good inter-rater reliability for both scales (Maher et al., 2003; Tate et al., 2008).

Broadening the inclusion criteria to non-RCT designs meant that studies without control groups were included for evaluation in the review. Therefore it was decided that performing a meta-analysis on the data would be inappropriate and inconsistent with the aims of the study.

## **2.5 Results**

### **2.5.1 Description of studies**

#### ***2.5.1.1 Results of the search***

The search strategy identified 1,171 results for review. Appendix 2 provides a flowchart demonstrating the search process.

### **2.5.1.2 Excluded studies**

In total 1,110 studies were excluded on the basis of the criteria. During title and abstract screening, 1,093 papers were excluded. Of these 792 studies were excluded because they did not evaluate the effectiveness of an intervention; 57 because the sample did not include people with MS; and 244 did not instruct participants in the use of external memory aids. Fifty-two duplicates were removed, leaving 26 studies.

Of the 26 studies that received full text review, 17 were excluded. These excluded studies are summarised in Table 1. Five studies were excluded as they did not evaluate the effectiveness of an intervention (Beer & Kesselring, 2009; das Nair et al., 2012; Johnson et al., 2009; Kesselring, 2004; E. M. Rosti-Otajarvi & Hamalainen, 2011); eleven studies did not instruct participants on the use of external memory aids (Allen, Goldstein, Heyman, & Rondinelli, 1998; Allen, Longmore, & Goldstein, 1995; Brissart, Leroy, & Debouverie, 2010; Brissart, Leroy, Morele, Baumann, & Debouverie, 2011; Brissart et al., 2013; Gich et al., 2011; Kardiasmenos et al., 2008; Mantynen et al., 2014; Ramio et al., 2010; Solari et al., 2004; Topcular et al., 2010); and one study was not yet published and data were not yet available from the author (Ben Ari, Hertzman, Mosberg-Galili, & Hellmann, 2012).

Table 1: Characteristics of excluded studies

| Study                                      | Reason for exclusion  |
|--|---|
| Allen et al. (1995)                        | Did not use external memory aids  |
| Allen et al. (1998)                        | Did not use external memory aids  |
| Beer and Kesselring (2009)                 | Did not evaluate the effectiveness of an intervention                               |
| Ben Ari et al. (2012)                      | Conference abstract; full article not published yet; data not available from author |
| Brissart et al. (2010)                     | Did not use external memory aids  |
| Brissart et al. (2011)                     | Did not use external memory aids  |
| Brissart et al. (2013)                     | Did not use external memory aids  |
| das Nair et al. (2012)                     | Did not evaluate the effectiveness of an intervention                               |
| Gich et al. (2011)                         | Did not use external memory aids  |
| Johnson et al. (2009)                      | Did not evaluate the effectiveness of an intervention                               |
| Kardiasmenos et al. (2008)                 | Did not use external memory aids  |
| Kesselring (2004)                          | Did not evaluate the effectiveness of an intervention                               |
| Mantynen et al. (2014)                     | Did not use external memory aids  |
| Ramio et al. (2010)                        | Did not use external memory aids  |
| E. M. Rosti-Otajarvi and Hamalainen (2011) | Did not evaluate the effectiveness of an intervention                               |
| Solari et al. (2004)                       | Did not use external memory aids  |
| Topcular et al. (2010)                     | Did not use external memory aids  |

### **2.5.1.3 Included studies**

The remaining 9 studies, were included in the review, and are detailed in Table 2.

Nine studies, including 540 participants with MS, met the inclusion criteria for this review (Carr et al., 2014; das Nair & Lincoln, 2012; Gentry, 2008; Jonsson, Korfitzen, Heltberg, Ravnborg, & Byskovottosen, 1993; Lincoln, Dent, & Harding, 2003; Lincoln et al., 2002; Shevil & Finlayson, 2010; Stuifbergen et al., 2012; Tesar, Bandion, & Baumhackl, 2005).

Six studies were from Europe (UK, Denmark, Austria) and three from the USA. Eight studies were conducted in community settings and one was conducted in a rehabilitation hospital.



Table 2: Characteristics of Included Studies

| Study                 | Methods  | Participants   | Interventions   | Outcomes  | Notes  |
|-----------------------|--|--|---|---|--|
| Carr et al.<br>(2014) | Single blind RCT,<br>randomisation by<br>independent<br>researcher,<br>computer<br>generated random<br>number sequence | n=48 with MS<br>Randomised (A:24 B:24)<br>Intention to treat analysis used<br>Mean age: 54.3<br>Education years: 14.6 years<br>Groups comparable on all<br>variables | Groups:<br>A: Group memory rehabilitation, ten<br>1.5 hour sessions. Combination of<br>restitution and compensation<br>strategies.<br>B: Waiting list control | Significant difference<br>between groups on GHQ-<br>28 at 8 months.<br>Non-significant<br>differences between<br>groups, on EMQ or MS-<br>Impact Scale at 4 or 8<br>months, or GHQ-28 at 4<br>months. | Analysis used in<br>this review: A vs.<br>B. |

|                             |   |  |  |   |                                       |
|-----------------------------|---|--|--|---|---------------------------------------|
| das Nair and Lincoln (2012) | Single blind RCT, randomisation by off-site independent randomisation centre, computer generated random number sequence | n=39 with MS<br>Randomised (A:12 B:17 C:10)<br>Intention to treat analysis used<br>Mean age: 47.2 years<br>Education years: 14.1 years<br>Groups comparable on all variables | Groups:<br>A: Compensation – how to use external memory aids and taught about internal memory aids<br>B: Restitution - taught about internal memory aids, exercises on encoding and retrieval strategies, attention retraining<br>C: Attention placebo – self-help group, relaxation techniques<br>10 sessions, 90 minutes | Non-significant differences across compensation and control group post-treatment, on EMQ, RBMT-E, GHQ or Internal and External Memory Aids Questionnaire. | Analysis used in this review: A vs. C |
| Gentry (2008)               | Before and after group design   | n=21<br>Intention to treat analysis not used<br>Median age: 50 years<br>Median time since diagnosis: 14 years  | A: Pretraining, usual care (8 weeks)<br>B: Individual format intervention training: PDA installation and demonstration of calendar and alarm usage; enter feature tasks. (3 weeks, 4 visits: 2x90 minutes, 2x60 minutes)<br>C: Post-training, can contact administrator for questions (8 weeks)                            | Non-significant change over time on the RBMT-E  | None                                  |

|                          |  |   |   |  |   |
|--------------------------|--|---|---|--|---|
| Jonsson et al.<br>(1993) | Closed envelope<br>randomisation<br>(RCT)  | n=40 with MS (E:20; C:20)<br>hospital in-pts (16 + 16<br>completed)<br>Intention to treat analysis not<br>used<br>Mean age: 44.5 (SD: 8.3)<br>Education: 11.5 (SD: 2.5)<br>Gender: 19F, 21M<br>Groups comparable on all<br>variables, except visuo-spatial<br>memory and visual perception<br>(E group more impaired) | Individual goal-directed treatment<br>E: Compensation (internal and<br>external memory aids), substitution,<br>direct training and<br>neuropsychotherapy<br>C: Attention placebo – discussion and<br>games<br>1-1.5hours 3 times a week; mean 17.2<br>hours | Short term effects: E<br>significantly effected<br>performance on BDI<br>Long term effects: E had a<br>significant effect on visuo-<br>spatial and memory; C had<br>significant effect on BDI<br>(more depressed at<br>second follow-up) | None  |
| Lincoln et al.<br>(2002) | Single blind RCT;<br>independent<br>phone<br>randomisation<br>Computer<br>generated<br>numbers | n=240<br>Randomised (A:82; B:79; C:79)<br>Completed (A:77; B:71; C:73)<br>Intention to treat analysis used<br>Mean age: 43 years<br>Age left education: 16 years<br>Groups comparable on all<br>baseline variables  | Individual treatment<br>A: Only baseline assessment with no<br>feedback<br>B: Detailed cognitive assessment with<br>feedback<br>C: Detailed cognitive assessment with<br>feedback and training on internal and<br>external memory aids.                     | No significant differences<br>between groups on EMQ,<br>GHQ, SF-36 or MAQ at<br>follow-up 1 or 2 for<br>patient or relative data   | Analysis used in<br>this review: A vs.<br>C |

|                                   |  |  |  |  |   |
|-----------------------------------|--|--|--|--|---|
| Lincoln et al.<br>(2003)          | Single Case<br>Experimental<br>Design: AB Design | n=29<br>Mean age: 43 years<br>Age left education: 16 years   | Individual treatment<br>A: Baseline<br>B: Detailed cognitive assessment with<br>feedback and training on internal and<br>external memory aids. | Significant reduction in<br>the frequency of memory<br>problems per week from<br>baseline to intervention<br>on diaries.                                       | Diaries were<br>completed daily,<br>reporting any<br>cognitive<br>difficulties that<br>interfered with<br>daily life. |
| Shevil and<br>Finlayson<br>(2010) | Before and after<br>group design                 | n=41<br>Intention to treat analysis not<br>used<br>Mean age: 52.4 years<br>Time since diagnosis 13 years | Group format<br>Problem solving techniques, taught<br>internal and external strategies and<br>application.<br>5 session, (2 hours, weekly)     | Significant change over<br>time on CSQ in<br>effectiveness of strategies<br>used, no significant effect<br>in number of strategies<br>used. Effect size small. | None  |

|                           |  |  |  |  |      |
|---------------------------|--|--|--|--|------|
| Stuifbergen et al. (2012) | Single blind RCT; random number sequence and sealed envelope | n=63<br>Randomised (E:36; C:27)<br>Completed (E:33; C:25)<br>Intention to treat analysis used<br>Age: 51-60 years (44% of sample); 36-50 years (43% of sample); 20-35 years (13% sample)<br>Groups comparable on all baseline variables except DKEFS (C group scored higher) | Group format<br>8 sessions (2 hour sessions once a week)<br>E: Training on use of compensatory strategies including external memory aids; computer assisted cognitive training programme (home based practice 45 minutes 3 times a week)<br>C: Wait list control | Significant interaction effect of group and time between baseline and follow-up on MMQ-Strategy. | None |
| Tesar et al. (2005)       | Simple random sampling with independent allocation           | n=19 (E:10; C:9)<br>Mean age: 46 years<br>Intention to treat analysis not used<br>Groups comparable on baseline variables  | Group treatment<br>E: 12 one hour session in 4 weeks<br>Neuropsychological training programme; computer based direct functional training on compensatory strategies: internal and external memory supports.<br>C: Rehabilitation only (OT, PT, ST etc.)          | No significant group x time effects on BDI, VLT or NVLT.   | None |

Note: Tests used: EMQ: Everyday Memory Questionnaire; GHQ: General Health Questionnaire; RMBT-E: Rivermead Behavioural Memory Test – Extended; BDI: Beck Depression Inventory; SF-36: Short Form; MAQ: Memory Aids Questionnaire; CSQ: Cognitive Strategies Questionnaire; DKEFS: Delis-Kaplan Executive Function System;

MMQ-Strategy: Strategy Subscale of the Multifactorial Memory Questionnaire; VLT: Verbal Learning Test; NVLT: Non-verbal Learning Test. Other abbreviations: E: Experimental; C: Control.

### Types of design

Six studies were RCTs (Carr et al., 2014; das Nair & Lincoln, 2012; Jonsson et al., 1993; Lincoln et al., 2002; Stuifbergen et al., 2012; Tesar et al., 2005). Two studies employed before and after group designs (Gentry, 2008; Shevil & Finlayson, 2010), and one study was a single case experimental design (SCED) (Lincoln et al., 2003). Within the RCTs, the method of generating the randomisation schedule was mentioned in all but one study (Tesar et al., 2005). Independent randomisation was reported in three studies (Carr et al., 2014; das Nair & Lincoln, 2012; Lincoln et al., 2002) and two studies used a closed envelope system (Jonsson et al., 1993; Stuifbergen et al., 2012). Outcomes were assessed by an individual blind to group allocation in five RCTs but not by Tesar et al. (2005). The SCED (Lincoln et al., 2003) employed an AB design (where A=baseline and B=intervention) for 29 participants within the treatment group of the randomised controlled trial (Lincoln et al., 2002).

### Types of participants

The diagnosis of participants was based on the Poser criteria (Poser et al., 1983) in four studies (das Nair & Lincoln, 2012; Lincoln et al., 2002; Lincoln, et al., 2003; Tesar et al., 2005); the Jonsson et al. (1993) study used the Schumacher criteria (Schumacher et al., 1965) and four studies relied on self-reported diagnoses (Carr et al., 2014; Gentry, 2008; Shevil & Finlayson, 2010; Stuifbergen et al., 2012). Seven studies had mixed types of MS [relapsing remitting MS (RRMS), primary progressive MS (PPMS) and secondary progressive MS (SPMS)] (Carr et al., 2014; Gentry, 2008; Lincoln et al., 2002; Lincoln et al., 2003; Jonsson et al., 1993); and [RRMS and SPMS] (das Nair & Lincoln, 2012; Tesar et al., 2005). The subtypes of MS were not described by Shevil and Finlayson, (2010) or Stuifbergen et al. (2012). The sample size in the studies varied from 19 (Tesar et al., 2005) to 240 (Lincoln et al., 2002); the number of participants receiving active treatment similarly varied from 10 (Tesar et al., 2005) to 82 (Lincoln et al., 2002). The majority of participants were in their mid to late 40s, with mean ages ranging from 42.1 years (Lincoln et al., 2002) to 54.3 years (Carr et al., 2014). Eight studies reported there to be a higher percentage of women than men in their samples, with percentage of women

ranging from 88% (Stuifbergen et al., 2012) to 47% (Jonsson et al., 1993). Time since diagnosis ranged from a mean of 9 years (Tesar et al., 2005) to 15 years (Jonsson et al., 1993); and years of education varied from a mean of 11.5 years (Jonsson et al., 1993) to the majority having BSc or postgraduate education (Stuifbergen et al., 2012). In the six studies comparing performance between groups, four studies had groups comparable at baseline on all variables (Carr et al., 2014; das Nair & Lincoln, 2012; Lincoln et al., 2002; Tesar et al., 2005); the remaining two studies were comparable on all baseline variables except visuo-spatial and visual perception (Jonsson et al., 1993) and executive function (Stuifbergen et al., 2012).

### Types of interventions

Four studies employed individual treatment (Gentry, 2008; Jonsson et al., 1993; Lincoln et al., 2002; Lincoln et al., 2003) and five studies used group interventions (Carr et al., 2014; das Nair & Lincoln, 2012; Shevil & Finlayson, 2010; Stuifbergen et al., 2012; Tesar et al., 2005). Two studies ran three-group comparisons (das Nair & Lincoln, 2012; Lincoln et al., 2002) and three studies employed two-group comparisons (treatment vs. control) (Carr et al., 2014; Stuifbergen et al., 2012; Tesar et al., 2005). Two studies evaluated the performance of one group: before treatment and immediately after treatment (Gentry, 2008); before treatment; after post-training period and at follow-up (Shevil & Finlayson, 2010). One study evaluated performance at multiple time points at baseline and at multiple time points during intervention (Lincoln et al., 2003). Most programmes were three (Gentry, 2008) to ten weeks (Carr et al., 2014; das Nair & Lincoln, 2012) long. Two individual treatment studies specified that the time period was a maximum of six months post-assessment (Lincoln et al., 2002; Lincoln et al., 2003). Sessions were between one hour (Tesar et al., 2005) and two hours (Shevil & Finlayson, 2010; Stuifbergen et al., 2012), and participants met 1-3 times a week in all studies, except two where it depended on the needs of the participant (Lincoln et al., 2002; Lincoln et al., 2003). Eight studies employed comprehensive cognitive or memory rehabilitation programmes, which all included teaching participants how to use external memory aids, as well as internal memory strategies. Of these eight studies,



five (Carr et al., 2014; das Nair & Lincoln, 2012; Jonsson et al., 1993; Stuifbergen et al., 2012; Tesar et al., 2005) ran programmes that also included cognitive training, such as computerised functional training and attention retraining. One study also included a 'neuropsychotherapy' component (Jonsson et al., 1993), and one study provided psycho-education (Shevil & Finlayson, 2010). Six studies (Jonsson et al., 1993; Lincoln et al., 2002; Lincoln et al., 2003; Shevil & Finlayson, 2010; Stuifbergen et al., 2012; Tesar et al., 2005) were cognitive rehabilitation programmes, which were not specific to memory rehabilitation, therefore the amount of time dedicated to memory rehabilitation, let alone external memory aids, is unknown. The study by Gentry (2008) was the only one with the content solely confined to teaching participants how to use external memory aids. This study involved the installation of PDA software and demonstration of how to use calendar and alarm functions on a PDA, followed by a post-training period where administrative support was available if needed.

#### ***2.5.1.4 Risk of bias in included studies***

The risk of bias in the nine included studies was mixed, with high risk of detection bias associated with the lack of blinding in one group study (Tesar et al., 2005), and two group studies at high risk of selection, detection and performance bias associated with the lack of a control group, and therefore absence of randomisation, allocation and blinding procedures (Gentry, 2008; Shevil & Finlayson, 2010). The risk of bias in the SCED (Lincoln et al., 2003) was considered to be generally low, but with some risk of observer bias and bias in determining the treatment efficacy due to it being AB design. The risk of bias was deemed to be unclear in five studies, due to lack of information when reporting the methods used for random sequence generation (Jonsson et al., 1993; Stuifbergen et al., 2012; Tesar et al., 2005), blinding (Jonsson et al., 1993) and how incomplete data were handled (Gentry, 2008; Shevil & Finlayson, 2010; Tesar et al., 2005).

The methodological quality of group studies, using the PEDro scale (Maher et al., 2003) are summarised in Table 3, and single case experimental designs, using the

SCED scale (Tate et al., 2008) in Table 4. Group studies received a mean score of 5 (S.D.= 2.51; Range = 2-8) out of a possible 10. The SCED scored 8 out of a possible 10.



Table 3: Risk of bias table for group studies, using the PEDro scale (Maher et al., 2003)

| Criteria met on PEDro scale   | Carr et al.<br>(2014) | das Nair and<br>Lincoln (2012) | Gentry (2008) | Jonsson et<br>al. (1993) | Lincoln et<br>al. (2002) | Shevil and<br>Finlayson (2010) | Stuifbergen et<br>al. (2012) | Tesar et al.<br>(2005) |
|---|-----------------------|--------------------------------|---------------|--------------------------|--------------------------|--------------------------------|------------------------------|------------------------|
| Subjects were randomly<br>allocated into groups                       | Y                     | Y                              | N             | N                        | Y                        | N                              | Y                            | N                      |
| Allocation was concealed  | Y                     | Y                              | N             | Y                        | Y                        | N                              | Y                            | Y                      |
| Groups matched at baseline  | Y                     | Y                              | N             | Y                        | Y                        | N                              | Y                            | Y                      |
| Blinding of all subjects  | N                     | N                              | N             | N                        | N                        | N                              | N                            | N                      |
| Blinding of all therapists who<br>administered therapy                | N                     | N                              | N             | N                        | N                        | N                              | N                            | N                      |
| Blinding of all assessors   | Y                     | Y                              | N             | N                        | Y                        | N                              | Y                            | N                      |
| Key outcome obtained from<br>more than 85% subjects                   | N                     | Y                              | Y             | N                        | Y                        | Y                              | Y                            | N                      |
| Subjects received intended<br>condition or intention to treat<br>used | Y                     | Y                              | N             | N                        | N                        | N                              | N                            | N                      |
| Between-group statistical<br>comparisons reported                     | Y                     | Y                              | N             | Y                        | Y                        | N                              | Y                            | Y                      |
| Point measures and measures<br>for variability provided               | Y                     | Y                              | Y             | N                        | Y                        | Y                              | Y                            | Y                      |
| TOTAL   | 7                     | 8                              | 2             | 3                        | 7                        | 2                              | 7                            | 4                      |

Table 4: Risk of bias table for single participant designs on the SCED scale (Tate et al., 2008)

| Criteria met on the SCED scale                                   | Lincoln et al. (2003) |
|--|-----------------------|
| Target behaviours – precise and repeatable measures              | Y                     |
| 3 phases, study is A-B-A or multiple baseline                    | N                     |
| Baseline (pre-treatment). Sufficient sampling                    | Y                     |
| Treatment phase. Sufficient sampling                             | Y                     |
| Raw data points recorded   | Y                     |
| Inter-rater reliability was established for at least one measure | N                     |
| Independence of assessors  | Y                     |
| Statistical analysis   | Y                     |
| Replication either across subjects, therapists or settings       | Y                     |
| Evidence for generalisation                                      | Y                     |
| TOTAL  | 8                     |

#### Random sequence generation in group studies

Three group studies were judged to have a low risk of selection bias on the basis of having adequate random sequence generation, using a computerised random number generator by an independent agency or researcher (Carr et al., 2014; das Nair & Lincoln, 2012; Lincoln et al., 2002). Three studies were unclear in their explanation of random sequence generation, and thus the risk of bias was unclear (Jonsson et al., 1993; Stuifbergen et al., 2012; Tesar et al., 2005). Two studies had no control group and therefore there was a high risk of selection bias (Gentry, 2008; Shevil & Finlayson, 2010).

#### Allocation in group studies

Six group studies were judged as having a low risk of selection bias on the basis of adequate group allocation concealment using a computerised random number generator by an independent unit (Carr et al., 2014; das Nair & Lincoln, 2012; Lincoln et al., 2002), having a separate member of staff, not involved with the study to complete allocation (Tesar et al., 2005), or using a closed envelope system (Jonsson et al., 1993; Stuifbergen et al., 2012). Two studies had no control group and therefore there was a high risk of selection bias (Gentry, 2008; Shevil & Finlayson, 2010).

#### Blinding in group studies

Four group studies were single blind (Carr et al., 2014; das Nair & Lincoln, 2012; Lincoln et al., 2002; Stuifbergen et al., 2012), indicating a low risk of performance and detection bias. Three studies had a high risk of bias (Gentry, 2008; Shevil & Finlayson, 2010; Tesar et al., 2005) as they had no blinding procedures, and Jonsson et al. (1993) provided an unclear description of the blinding procedures employed.

#### Incomplete outcome data in group studies

Four group studies addressed incomplete data, indicating a low risk of attrition bias. In one study (das Nair & Lincoln, 2012), list-wise deletion was utilised and baseline

data were imputed for missing follow-up data. In another study (Lincoln et al., 2002), analysis covered just those who completed outcomes, however it also included those who did not get the intervention as planned in an intention to treat analysis. One study (Stuifbergen et al., 2012), replaced missing values with the last observation value carried forward if the participant did not complete later measurements, or imputed if an intermediate value was missing. In another study (Carr et al., 2014), if missed items occurred for less than 10% of questions in a questionnaire, the missing item was replaced with the mean for the questionnaire. The four remaining studies did not address incomplete data: two studies did not use intention-to-treat analysis after reporting dropouts (Gentry, 2008; Shevil & Finlayson, 2010) and two studies provided no explanation of how drop out data were dealt with (Jonsson et al., 1993; Tesar et al., 2005), thus the risk of bias is unclear.

#### Selective reporting in group studies

There was no selective reporting in any of the nine studies, indicating a low risk of reporting bias

#### Risk of bias in SCED

The risk of bias in the one SCED study was generally low (Lincoln et al., 2003). The measure of target behaviours was specified and the variability in behaviour was established through sufficient sampling during baseline and treatment phase. Verification of treatment efficacy was demonstrated using statistical analysis and generalisation was assured through replication across subjects and transfer to beyond target behaviours. However there was a high risk of bias in determining treatment efficacy as an AB design was used. There was also a high risk of observer bias, as inter-rater reliability was not established for measures.

## **2.5.2 Effects of interventions**

Parametric and nonparametric statistical analyses were used to compare groups. Significance testing was reported in all studies, however the appropriate measures of variability were not.

### ***2.5.2.1 Outcome 1: Subjective Memory Measures***

Four studies (Carr et al., 2014; das Nair & Lincoln, 2012; Lincoln et al., 2002; Lincoln et al., 2003) used subjective measures of participants' memory functioning. Three studies used the EMQ (Sunderland et al., 1984) (Carr et al., 2014; das Nair & Lincoln, 2012; Lincoln et al., 2002) and one study used diaries to record specific instances of memory difficulties that interfered with daily life (Lincoln et al., 2003). One study (Lincoln et al., 2003) found a significant effect of treatment on subjective memory functioning, demonstrated by a significant reduction ( $p < 0.01$ ) in the frequency of reported memory problems per week from baseline to intervention. Subgroup analysis of MS participants from das Nair and Lincoln, (2012) detected no significant effect of treatment; Carr et al. (2014) and Lincoln et al. (2002) found no significant treatment effect.

### ***2.5.2.2 Outcome 2: Objective Memory Measures***

Two studies (das Nair & Lincoln, 2012; Gentry, 2008) included objective measures of memory; both used the RBMT-E (Wilson et al., 1985). Subgroup analysis of MS participants from das Nair and Lincoln (2012) showed no significant effect of treatment; Gentry (2008) also found no significant long-term effect.

### ***2.5.2.3 Outcome 3: Mood***

Five studies (Carr et al., 2014; das Nair & Lincoln, 2012; Jonsson et al., 1993; Lincoln et al., 2002; Tesar et al., 2005) included measures of participants' mood. All measured mood both immediately after treatment and long-term. Three of these studies used the GHQ (Goldberg, 1992) (Carr et al., 2014; das Nair & Lincoln, 2012; Lincoln et al., 2002) and two used the BDI (Beck et al., 1987) (Jonsson et al., 1993;



Tesar et al., 2005). A significant effect of intervention was found at long-term follow up in one study (Carr et al., 2014). Jonsson et al. (1993) found a significant effect of treatment on mood, however it was due to the control group worsening in mood over time.

#### ***2.5.2.4 Outcome 4: Quality of Life***

Two studies included a measure of quality of life (Carr et al., 2014; Lincoln et al., 2002), using the MS Impact Scale (Hobart et al., 2001) (Carr et al., 2014), and the SF-36 (Ware & Kosinski, 2001) (Lincoln et al., 2002). No effect of treatment on quality of life was found either immediately or long-term.

#### ***2.5.2.5 Outcome 5: Coping strategies for memory problems***

Four studies (das Nair & Lincoln, 2012; Lincoln et al., 2002; Shevil & Finlayson, 2010; Stuifbergen et al., 2012) used measures of coping strategies for memory problems. One study (Shevil & Finlayson, 2010) found a significant treatment effect ( $p < 0.05$ ) on the effectiveness of strategies used on the CSQ, but no significant effect on the number of strategies used. One study (Stuifbergen et al., 2012) detected a significant treatment effect ( $p < 0.01$ ) on the use of compensatory strategies on the MMQ-Strategy (Troyer & Rick, 2002). No significant treatment effect on coping strategies was reported in two studies (das Nair & Lincoln, 2012; Lincoln et al., 2002) on the Internal and External Memory Aids Questionnaire (das Nair & Lincoln, 2012) and the Memory Aids Questionnaire (MAQ) (Wilson & Moffat, 1984) (Lincoln et al., 2002).

## **2.6 Discussion**

### **2.6.1 Summary of main results**

Despite evidence demonstrating the existence of memory problems in people with MS and the associated everyday problems, literature examining the effectiveness of external memory aids on alleviating memory problems in people with MS remains weak. This review included a variety of study designs, in an attempt to collate all available evidence to evaluate whether people with MS who received training on the use of external memory aids showed better outcomes in their memory functions, mood and quality of life, than those who did not. Broadening the inclusion criteria to non-RCT designs meant that studies without control groups were included for evaluation. However, few additional studies were identified that were not included in previous reviews confined to RCTs.

Nine studies were included in this review; six studies were RCTs; two employed before and after group designs; and one was a SCED. One study specifically evaluated an external memory aid; the others were either memory rehabilitation or cognitive rehabilitation studies that included a component attending to external memory aids. These studies were published between 1993 and 2014 and the majority were of poor quality; lacking detailed description of the randomisation procedures, blinding and dealing with incomplete outcome data. Although the one SCED (Lincoln et al., 2003) scored 8 out of 10 for methodological quality, the mean for group studies was only 5 out of 10. Only five of the included studies evaluated participant outcomes using ecologically valid memory measures (Carr et al., 2014; das Nair & Lincoln, 2012; Gentry, 2008; Lincoln et al., 2002; Lincoln et al., 2003); five studies included measures of participants' mood, and only two assessed quality of life.

The evidence for the effectiveness of teaching people with MS to use external memory aids to improve everyday memory functioning was limited, with only one study reporting an improvement on a subjective memory measure (Lincoln et al., 2003), and none demonstrating benefits on objective measures of memory.

However it should be noted that only four studies employed subjective memory measures, and only two used objective memory measures. Five studies assessed participants' mood, though only two studies reported positive results following intervention (Carr et al., 2014; Jonsson et al., 1993), and no studies reported an effect on quality of life. Five studies assessed the use of coping strategies for memory problems, with two reporting beneficial effects of treatment (Shevil & Finlayson, 2010; Stuifbergen et al., 2012).

There are several limitations of this review that need to be considered. Despite systematically searching seven electronic databases it is possible that not all relevant studies were identified. Studies, particularly SCEDs may have been published in journals that were not searched by the databases, or may not have been identified with the search strategy used. Due to the nature of memory problems affecting many areas of life, it is possible that some relevant articles did not use words applied in the search strategy. For example if an article were named 'problems at work', it would not have been included. Selection was also performed by only one author, which reduces the likelihood that errors are detected, compared to employing a review team. Another issue that should be considered is the change in the way SCEDs are classified. This review classifies SCEDs using the SCED scale (Tate et al., 2008), which included AB designs, such as the Lincoln et al. (2003) study. A revised classification system has since been developed, the RoBiNT Scale (Tate et al., 2013) which states that AB designs should not be classified as SCEDS due to the inability to determine cause and effect, with the absence of ABA reversal or multiple baseline designs. Therefore it should be noted that the included SCED (Lincoln et al., 2003) does not provide staggered baselines to support determining the impact of the intervention.

This review evaluated the evidence for the use of external memory aids for people with MS, however only one study provided data on participants that had solely received dedicated training in the use of external memory aids. The majority of studies involved comprehensive cognitive rehabilitation programmes, and thus were aimed at tackling a range of cognitive deficits. Therefore it is difficult to

deduce how much time was spent on memory rehabilitation in general, let alone external memory aids specifically. Consequently, the results of this review suggested that there was no evidence to support or refute the effectiveness of external memory aids on subjective or objective reports of memory function.

### **2.6.2 Quality of the evidence**

The literature base investigating the effectiveness of external memory aids for people with MS is poor. Only six RCTs were identified, of these five were single blind, although it should be noted that the Jonsson et al. (1993) paper stated that blinding was problematic as patients could easily unmask their allocation in conversation. Due to the nature of the studies considered, it was unlikely that those giving the intervention could be blind to group allocation. Masking the participants to the group allocation was also not likely to be possible. Eight of the nine studies were published after the publication of the CONSORT statement (Moher, Schulz, & Altman, 2003), however these guidelines were not followed in the majority of included studies. The randomisation protocol was unclear in three studies (Jonsson et al., 1993; Stuifbergen et al., 2012; Tesar et al., 2005). All RCTs appeared to have adequate allocation concealment. Inclusion and exclusion criteria were generally defined well and all described the flow of participants through the study. The description of interventions and control conditions were inadequate in the majority of studies and the choice of outcome measures used was extremely poor, with only four studies employing ecologically valid memory measures. Feedback from participants was only obtained in one study (Tesar et al., 2005); responses to this questionnaire were positive.

### **2.6.3 Potential biases in the review process**

Two of the review authors were lead investigators in four included studies (Carr et al., 2014; das Nair & Lincoln, 2012; Lincoln et al., 2002; Lincoln et al., 2003).

#### **2.6.4 Agreement and disagreement with other studies or reviews**

This review adds to the recent Cochrane review on memory rehabilitation for people with MS (das Nair et al., 2012) by including five extra studies: two studies published since the review and three non-RCT designs. This review also evaluated only the treatment compared to control conditions in two previously included studies (das Nair & Lincoln, 2012; Lincoln et al., 2002). When conducting this review there was the assumption that broadening the criteria to include non-RCTs would yield results that had been excluded from previous Cochrane reviews. However only two before and after designs and one SCED were identified. Our findings complement the das Nair et al. (2012) and Rosti-Otajärvi and Hämäläinen (2014) Cochrane reviews, which both concluded that there was no evidence to suggest that memory rehabilitation was more effective than a control. This review supports the opinion from both previous reviews that studies evaluating the effectiveness of memory rehabilitation are of poor quality. This review also complements the findings of the Thomas et al. (2006) Cochrane review on psychological interventions for MS, showing that interventions designed to help people with cognitive impairments were inconclusive. Although this review does not support the conclusions of recent reviews of neuropsychological rehabilitation (Cicerone et al., 2011; de Joode et al., 2010) in their recommendations of the use of compensatory aids for people experiencing memory problems, it does support a recent review (Jamieson et al., 2014) that concluded there is still a specific need for investigations of technology for people with degenerative diseases.

## **2.7 Conclusions**

### **2.7.1 Implications for practice**

People with MS frequently report problems with their memory in everyday life. Training in the use of external memory aids is offered to some people during memory rehabilitation programmes, however their effectiveness has not been determined. Studies with people with other types of brain damage, such as TBI, have provided some evidence for the effectiveness of external memory aids. This

review, however, examined the literature for people with MS and found no evidence to support or refute that external memory aids improved everyday memory function, mood or quality of life. One problem with small RCTs is that they do not take into account intra-group variability, which is assumed to be controlled through the randomisation process. This is the case for fully-powered RCTs, but not small ones. Therefore, clinicians are encouraged to use single case experimental design methodology to evaluate the effectiveness of any interventions they are providing in clinical practice for memory problems with people with MS.

### **2.7.2 Implication for research**

The evidence base for the effectiveness of external memory aids for people with MS was poor, both quantitatively and qualitatively. Only six RCTs were identified and the majority of these had small sample sizes. In addition there were only two studies using other experimental designs, such as CCTs, before and after group designs, and single case experimental designs. These studies failed to use appropriate ecologically valid outcome measures necessary to establish generalisation of benefits in practice. Most of the studies failed to follow the CONSORT guidelines (Moher et al., 2003), thus limiting the ability to evaluate the accuracy of their findings. Therefore it is suggested that more high quality research is necessary to provide conclusive evidence as to whether external memory aids are effective at reducing memory problems for people with MS.

## **3 Methods**

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### **3.1 Chapter Overview**

This chapter summarises the methodology of a crossover RCT study including approval process, recruitment and design. The baseline and outcome measures used are described, as is the feedback interview process. Data collection and choice of analyses are explained.

### **3.2 Approvals**

Ethical approval was granted by the NRES Committee East Midlands – Northampton, reference number 13/EM/0324. The study was accepted for inclusion on the National Institute for Health Research Clinical Research Network (NIHR CRN) Portfolio and allocated to the Nervous System Disorders Speciality Group. Research and Design (R&D) approvals were granted by Nottingham University Hospitals NHS Trust; Nottinghamshire Healthcare NHS Trust; Cambridge University Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust and Peterborough and Stamford Hospitals NHS Foundation Trust. See Appendices 3 & 4 for approval letters.

### **3.3 Study Design**

The study was a multicentre feasibility and phase II efficacy study of a complex intervention. The study was conducted between November 2013 and October 2015, and took place across 5 NHS trusts in Nottinghamshire and Cambridgeshire. A single blind, crossover randomised controlled trial (RCT) was used to ascertain whether the use of memory reminders using NeuroText was effective in reducing everyday memory problems, and improving mood and quality of life in people with memory problems acquired through MS. Treatment efficacy was determined by comparing treatment and an attention control condition on a range of measures.

In addition, there was a qualitative component in which interviews were conducted with participants to capture participants' perspectives and experiences. The interviews sought to gather information from the participants on perceived benefits or drawbacks of the NeuroText messages.

## **3.4 Participants**

### **3.4.1 Inclusion criteria**

Participants were included if they:

1. had a diagnosis of multiple sclerosis (including relapsing, remitting, secondary progressive, primary progressive and benign), as determined by the referring clinician
2. had self-reported memory problems, defined as a score more than 20 on the participant version of the frequency scale of the Everyday Memory Questionnaire (EMQ)(Sunderland et al., 1984); to ensure that participants had everyday memory problems and were therefore representative of those who could receive this intervention in clinical practice. This cut-off was determined from a rehabilitation study (ReMIND)(das Nair & Lincoln, 2012) as 1 S.D. below the total mean and higher to include those with self-reported memory problems
3. were able to read and respond to potential requested messages independently, as determined by self-report
4. were aged 18 years or older, to allow consent
5. were more than 12 months since diagnosis, to allow time to adapt to diagnosis, as determined by self-report
6. gave informed consent

### **3.4.2 Exclusion criteria**

Participants were excluded if they:



1. had cognitive, visual or motor impairment, such that they were unable to use a pager or mobile phone, as determined by self-report
2. had another concurrent neurological diagnosis, e.g. epilepsy, to ensure that the memory problem was due to MS, as determined by self-report
3. had a concurrent severe medical/psychiatric diagnosis, to ensure they were likely to engage in treatment, as determined by self-report
4. were concurrently taking part in other psychological research studies, to ensure any changes in outcomes were not impacted by other interventions, as determined by self-report
5. people who did not understand English, as no translation service was available

### **3.4.3 Recruitment**

Participants were recruited from various MS services across Nottinghamshire and Cambridgeshire. Referrals were made through Nottingham University Hospitals NHS Trust from MS Clinics and CLRN research nurses; Nottinghamshire Healthcare NHS Trust from a community rehabilitation team; Cambridge University Hospitals NHS Foundation Trust from MS nurse clinics; Cambridgeshire Community Services NHS Trust from community MS nurses and Peterborough and Stamford Hospitals NHS Foundation Trust from Neurology outpatient clinics and MS nurses. Some participants were self-referred through charity event.

Services were provided with details of the study, and asked to forward this information to potential participants.

- i) For all participants recruited before 1<sup>st</sup> September 2014:

Potential participants were approached by a member of their clinical care team, explaining what was involved in the trial, and given an invitation to study letter (version 1), participant information sheet (PIS), consent forms, the EMQ, and a stamped addressed envelope. See appendix 5 for these documents.

After reading the Participant Information sheet, potential participants and a relative or carer completed the consent forms, the EMQ and contact details form (pg.2 of invitation to study letter) and returned in the envelope, if they wished to take part in the study.

Upon receipt of the above, the eligibility of the potential participant was checked using the completed EMQ. If potential participants scored above 20, participants were invited to continue into the study. The researcher contacted the potential participants by telephone, using the details provided on the contact details form. The researcher confirmed that the potential participant had received and read the PIS and offered a chance for them to ask any questions about the study. A date was organised to set up a visit for baseline assessment.

ii) For all participants recruited from 1<sup>st</sup> September 2014:

- Potential participants were approached by a member of their clinical care team, explaining what was involved in the trial, and given an invitation to study letter (version 2) see Appendix 6, participant information sheet (PIS), consent forms, and a stamped addressed envelope.
- If the potential participant was interested in taking part in the study they could choose to either complete the contact details form (pg. 2 of invitation to study letter) and send it themselves, or their clinician offered to complete the form and send it to the researcher for them. Due to the nature of the potential participants' memory problems they were liable to forget to complete and send the form, and therefore clinicians could aid their recruitment by offering this service. After reading the Participant Information sheet, potential participants and a relative or carer read and completed the consent forms.

The contact details form requested permission that the researcher could contact the potential participant by telephone regarding taking part in the research, and ask them questions about their memory. Upon receipt of the contact details form the researcher contacted potential participants by telephone, using the details provided. The researcher confirmed that the potential participant had received and read the PIS and completed and offered a chance for them to ask any questions about the study. The researcher then checked the eligibility of the potential participant by administering the EMQ. If potential participants scored above 20, participants were invited to continue into the study, and a date was organised to set up a visit for baseline assessment.

At the beginning of the baseline visit the researcher discussed the study and explained that entry to the study was voluntary and that their treatment and care would not be affected by their decision. It was also explained that they could withdraw at any time but attempts would be made to avoid this occurrence. In the event of their withdrawal it was explained that their data collected so far could not be erased and we would seek consent to use the data in the final analyses where appropriate. The participant had the opportunity to ask any questions about the study.

The researcher then checked that participants had signed their consent forms, and the researcher countersigned them. Baseline assessment then began.

For those who did not meet the inclusion criteria on the EMQ, e.g. scoring below 20, the researcher explained that they were not eligible to take part in the trial, and so they would not be invited to continue.

### **3.5 Group allocation**

Random allocation on a 1:1 ratio was carried out by an independent research assistant, using a web-based randomisation number generator, prepared in

advance of the study. The independent research assistant in the Division of Rehabilitation and Ageing (University of Nottingham), was blind to the participants recruited and held the randomisation schedule. Once participants were recruited and had completed baseline assessment, the researcher contacted the independent research assistant by email and provided initials and date of birth of the participant. The independent research assistant holding the randomisation schedule then disclosed group allocation of the participant. This ensured allocation concealment from those recruiting participants. Participants were randomly allocated to either the intervention condition first (group 1) or control condition first (group 2). Due to the nature of the intervention, both researcher and participants were aware of which group they had been allocated to.

### **3.6 Intervention**

During the intervention phase, participants received NeuroText memory text messages for 2 months.

NeuroText is a service that simply sends reminder messages to people's mobile phones or pager. These messages are tailor made and sent at pre-arranged times to prompt people to do the things they would otherwise forget to do. During the baseline home visit, participants identified problems such as 'I forget to lock the back door' or 'I forget to take my medication' and agreed on reminders that would be helpful, which they then received by text at their chosen times and frequency. Only messages requested or agreed by participants were selected for transmission. Participants also chose the wording of the messages and were free to modify these as necessary during the trial. An example NeuroText timetable can be found in Appendix 7.

NeuroText runs through the existing NeuroPage service at the Oliver Zangwill Centre for Neuropsychological Rehabilitation (OZC) in Ely, UK. The Neuropage service is owned by Cambridgeshire Community Services NHS Trust. Throughout the trial the intervention was named 'NeuroText' for clarity, in light of the increasing

use of texts on mobile phones, and the decreasing use of pagers. The intervention was run by the researcher, who had been given training in the use of NeuroPage. The lists of reminders were entered onto the computer at OZC by the researcher, and then the computer automatically sent out the messages at the correct time and dates. The procedures for the intervention are well established and have been used in previous trials (Wilson et al., 2001; Wilson et al., 1997).

Those who wished to receive the messages to a pager rather than their mobile phone were given a demonstration by the researcher. Participants using a pager needed to provide details of their address and the addresses of anywhere they are likely to be using the service (e.g. work), to the Neuropage service to ensure network coverage. They also needed to provide a contact number in the case of any service issues.

Two days after the start of intervention participants were contacted by the researcher by text to check that the NeuroText messages were coming through, and that they were happy with them. The NeuroText messages were programmed to run for 2 months using the rota agreed during the baseline home visit, unless participant requested any modifications, which were put in place upon receipt.

Any other rehabilitation, e.g. occupational therapy or physiotherapy, continued as usual for all patients. Any medication, including MS modifying drugs and antidepressants were prescribed as usual for all patients.

### **3.7 Control**

During the control phase, participants received non-memory text messages for 2 months.

The control condition was a text messages containing non-memory content, from RSS feeds participants were interested in, e.g. headlines on sports, current affairs, or entertainment news, or quotes. During the baseline home visit, participants

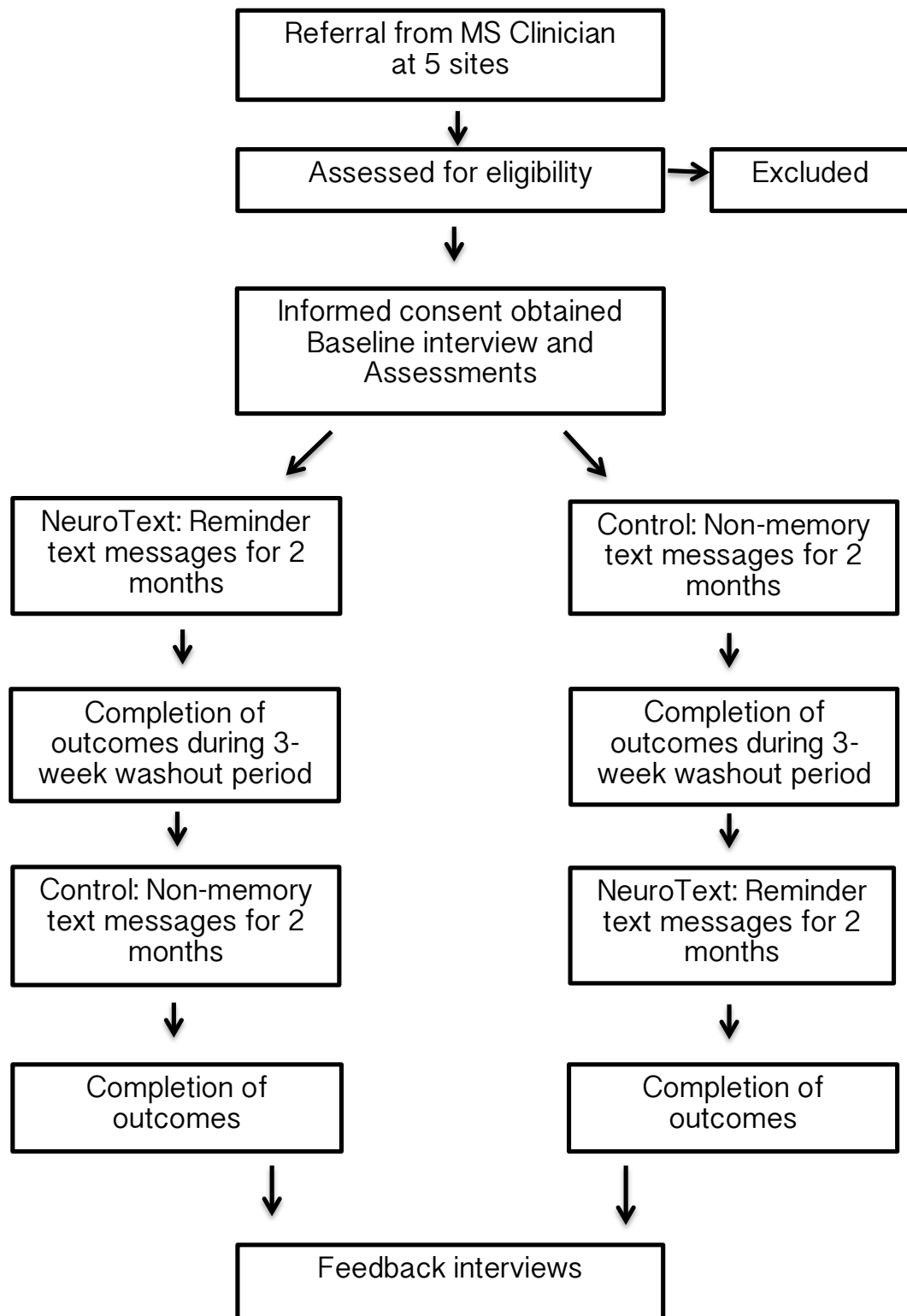
identified the type of non-memory messages they would be happy to receive e.g. football and current affairs. Participants were free to modify these during the trial. It was explained that the non-memory messages would be transmitted at the same times and frequency as the NeuroText messages, unless requested otherwise. Links of chosen RSS feeds were programmed into the NeuroPage computer at OZC, and posts from allocated RSS feeds were automatically sent out at the correct time and dates. An example control timetable can be found in Appendix 8.

Two days after the start of the control condition participants were contacted by the researcher by text to check the control messages were coming through, and that they were happy with them. The control messages were programmed to run for 2 months, using the rota agreed during baseline visit, unless participant requested any modifications, which were put in place upon receipt.

Any other rehabilitation, e.g. occupational therapy or physiotherapy, continued as usual for all patients. Any medication, including MS modifying drugs and antidepressants were prescribed as usual for all patients.

### 3.8 Flowchart

Figure 1: Participant flow through the study



### 3.9 Baseline Assessments

Baseline assessment was completed at a place convenient for the participant. This process was carried out over 1-3 sessions, according to patient choice and ability. For example, if a patient had fatigue on an assessment day they may have wished to spread that session over two visits, rather than one.

Following the consent procedures detailed above, participants were offered a choice of receiving text messages to provided pagers or participants' mobile phones. Participants and their relatives or carers were asked to describe a typical week to elicit problems that they needed help with and identify target reminders. Participants could also look over a list of common reminders to see if they thought any of them would be useful. In addition, suitable control messages were identified through discussion with the participant. Rotas were drawn up for both conditions. The outline schedule can be found in Appendix 9.

Self-reported demographic information and details of type of MS and years since diagnosis were recorded on the Demographic Record Form, which can be found in Appendix 10. In some cases demographic categories were collapsed to provide more concise categorisation: Responses in the "Partnership" category endorsing "Separated but still legally married or civil partnership; divorced or legally dissolved civil partnership; widowed or surviving partner from civil partnership" were categorised as "No longer married or in civil partnership". In the open ended "Beliefs" section responses were collapsed e.g. "Christian" and "Catholic" were grouped together as "Christian"; "Agnostic" and "None" were grouped as "None"; and "Spiritual", "Humanist", "Jehovah Witness" were grouped as "Other". "Years since relapse" data was only provided by those participants who reported experiencing relapses.



A baseline cognitive assessment was conducted to document the nature of the memory impairment and to record factors that may be related to treatment response.

### **3.9.1 Rationale for tools selected**

#### ***3.9.1.1 Everyday Memory Questionnaire***

The Everyday Memory Questionnaire (EMQ)(Sunderland, Harris, & Baddeley, 1983) is a self-rating scale, designed to assess memory functioning in everyday life (Tate, 2010). The questionnaire consists of 28 items, each describing everyday activities, which may involve memory failure. A 5-point scale was used: 0 (once or less in the last month); 1 (more than once a month but less than once a week); 2 (about once a week); 3 (more than once a week but less than once a day); 4 (once or more a day) (Lincoln et al., 2002). Items of the EMQ sample a range of potential memory failures in everyday situations, seemingly covering episodic memory for verbal and visuospatial material, procedural memory, and prospective memory, e.g. “completely forgetting to do things you said you would do, and things you planned to do”. Informant and self-report versions are available, which contain the same items, but are phrased as appropriate. The self-report version of the EMQ was used at baseline as a screening measure.

The EMQ was developed as a subjective measure of memory failure in everyday life (Sunderland et al., 1983). Sunderland and colleagues constructed the EMQ in response to clinical needs, questioning the ecological validity of laboratory-based memory tests to evaluate the effectiveness of therapy programmes for memory disorders (Tate, 2010). The list of items were assembled to include a wide range of memory failures; that would be the types of error that the majority of subjects had the opportunity to make in their daily lives, and would include cognitive difficulties (Sunderland et al., 1983). Some of the items might not normally be classed as memory failures, but a memory failure could be the root of the problem, for example, ‘finding a television story difficult to follow’. The EMQ was initially developed for use with survivors of head injury and has since been refined with

both non-clinical and clinical samples, including people with MS (Lincoln, et al., 2002; Richardson, 1996; Richardson & Chan, 1995). The original questionnaire consisted of 35 items, which was reduced to the more commonly used 28-item version to increase validity and facilitate self-administration, (Sunderland et al., 1984). The response scale has also been changed over time, from relative frequencies ('sometimes') with a 9-point scale, to absolute values (e.g. 'about once a week') on a 5-point scale (Tinson & Lincoln, 1987).

The EMQ has good face validity, assesses real-life situations and is used in clinical practice (das Nair & Lincoln, 2012). Concurrent validity was demonstrated between the EMQ and a similar rating of everyday memory, the Subjective Memory Questionnaire (Goldstein & Polkey, 1992). Concurrent validity of the EMQ has also been established when examined with Wechsler Memory Scale (WMS)(Wechsler, 1945) and Rivermead Behavioural Memory Test (RBMT)(Efklides et al., 2002; Wilson et al., 1985). Efklides et al. (2002) also reported internal consistency indices of  $\alpha=.889$ . Several factor analyses have been performed on the EMQ, including one using a non-clinical population that found the 28-item EMQ to consistently differentiate between two systems of memory and attention, with some differentiation of visual and verbal systems (Royle & Lincoln, 2008).

### ***3.9.1.2 Doors & People***

The Doors and People Test (Baddeley et al., 1994) is a broadly based test of long-term memory. This battery of four tests yields a single age-scaled overall score which can be 'unpacked' to give individual measures of visual and verbal memory, recall and recognition and forgetting, allowing the tester to assess patterns of deficit (Evans, Wilson, & Emslie, 1996). The test uses learning of names and shapes, over a series of repeated trials. The recognition tasks use the forced choice technique, where participants have to choose a target from three distractors, which eliminates problems with response bias that can affect tests using a yes-no format (Evans, 2004). The Doors test examines visual recognition; the stimuli have been

carefully designed to minimize any verbal mediation, as the distractor items are similar in most of the gross characteristics of the target (Evans, 2004).

The Doors and People test provides an analytic overview of long-term explicit memory, and is designed for use both as a clinical and research tool. The test was designed principally to provide an improved measure of nonverbal episodic memory that would be acceptable to a wide range of subjects (Bradley & Kapur, 2004). The developers wished to provide a test that was easy to administer, unstressful to the patient, and could be performed on a wide range of subjects. They also wished to abolish floor and ceiling effects and provide material with high face validity.

Ecological validity is suggested through the justification of use of test materials, i.e. names are used as forgetting names could be an everyday memory problem. Face validity is assumed as material is chosen to be purely verbal or visual, i.e. doors are hard to verbally encode and names allow minimal visual encoding. The Doors and People has a theoretical basis focusing on the fractioning of memory, and thus has content validity. The sensitivity of the test to detect memory impairment has been demonstrated in people with early stage Alzheimer's disease (Greene, Baddeley, & Hodges, 1996); and there is evidence of the test's ability to differentiate between modality specific memory impairments (Morris, Abrahams, Baddeley, & Polkey, 1995).

One benefit of using the Doors and People with people with MS, who commonly experience fatigue, is that it is relatively short in length compared to other memory batteries, and usually well tolerated due to the mixture of stimuli. The amount and complexity of drawing and writing required is low, which makes it suitable for people with MS, who often have impaired motor skills.

In the case that participants scored a raw score lower than that referred to in the normative tables, the scaled score was given as 1 point below the minimum scaled score value in the table.

### **3.9.1.3 Hayling & Brixton**

The Hayling and Brixton tests (Burgess & Shallice, 1997) are measures of executive functions (EF), specifically behavioural regulation. The Hayling Test evaluates initiation speed and response suppression, and the Brixton Test is a rule detection and rule following task. During the Hayling test participants have to complete 30 sentences from which the last word was omitted. In the first half (initiation condition) they complete the sentences with a word that makes sense. In the second half (inhibition condition), participants have to provide a word that makes no sense in the context of the sentence (e.g. London is a very busy 'banana') (Gurd, Kischka, & Marshall, 2010). This section yields two scores, an error score and a measure of response speed. In addition all three scores can be combined into an overall score. The Brixton test is a nonverbal task of set attainment and rule detection. Participants are shown a 56-page stimulus book. All pages contain 10 circles in two rows of five. Only one circle is filled in on each page and the participant has to predict where the next filled circle will be on the next page, based on previous pages (Gurd et al., 2010). The test does not require verbal responses, as the patient points to the position. The score is the number of errors made. Both tasks are easy to administer and are well tolerated by patients.

The Hayling and Brixton tests were developed to be sensitive to symptoms of executive disturbance. The Brixton test was based on the Wisconsin Card Sorting Task (WCST) (Milner, 1963). However in contrast to the WCST, the rule that is currently in operation cannot be triggered by any perceptually salient aspect of the stimuli (Strauss, Sherman, & Spreen, 2006). Significant judgement is required for assigning Hayling responses to particular categories. A study by Andrés and Van der Linden (2000) assessed interrater reliability and found that two raters agreed on 76.5% of 1425 responses. Studies evaluating the relationship between performance on the Hayling and Brixton tests found that the correlation was low (Bielak, Mansueti, Strauss, & Dixon, 2006; de Frias, Dixon, & Strauss, 2006). Therefore, it is thought that the two tests most likely measure different cognitive processes. This

notion is supported by multiple studies, showing dissociations (Burgess & Shallice, 1994; Temple & Sanfilippo, 2003).

Performance on the Hayling is impaired in a variety of conditions thought to disrupt EF, including Alzheimer's disease and Parkinson's disease (Bouquet, Bonnaud, & Gil, 2003; Collette, Van der Linden, Delrue, & Salmon, 2002). There is some evidence of ecological validity. In patients with schizophrenia, social impulsivity symptoms are moderately linked to performance on the Hayling sentence completion task (Chan, Chen, Cheung, & Cheung, 2004). The Brixton test is related to other measures of executive function. Marczewski, de Linden, and Laroie (2001) found moderately strong correlations between the Brixton and Tower of London Tests in patients with schizophrenia (Strauss et al., 2006). Impaired performance on the Brixton test has also been reported in disorders thought to compromise EF, such as schizophrenia (Marczewski et al., 2001).

The benefit of using the Hayling and Brixton tests with people with MS, who commonly experience fatigue, is that is relatively short compared to EF batteries.

#### ***3.9.1.4 Test of Everyday Attention***

The Test of Everyday Attention (TEA) (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994) is a battery of eight tasks intended to measure attentional processes in adults. Age-scaled scores are derived for each subtest; therefore the TEA can be used analytically to identify patterns of deficit. The test is presented as a pretend trip to Philadelphia, during which the participant performs a series of tasks appropriate to the context (Strauss et al., 2006).

Selective attention is tested in three subtasks: Map Search, Telephone Search and Elevator counting with distraction. On the Map search task participants search for symbols on a map amongst distractors for two minutes. Telephone Search task requires participants to circle key symbols while searching entries in a simulated telephone directory, amongst distractors. Elevator Counting with distraction (ECD)

asks participants to count the low tones and ignore the high tones. ECD also tests working memory.

Sustained attention is measured in three subtasks: Elevator Counting, Telephone Search while Counting and Lottery. On the Elevator Counting task participants are instructed to pretend they are in an elevator where the floor-indicator is broken. To establish what floor they are on they must count a series of tape-presented tones. During Telephone Search while Counting (TSC) participants must again search in the telephone directory while simultaneously counting strings of tones. TSC also measures divided attention when compared to Telephone Search performance. Lottery asks participants to listen to a tape with a series of consecutive letter and numbers, and write down letters that precede the target '55', which occur infrequently in this 10 minute long test.

Attentional switching is assessed in two subtasks: Visual Elevator and Elevator Counting with Reversal. Visual Elevator is self-paced and requires participants to count up and down when specific signals (arrows) are presented amongst stimuli (elevator doors). Elevator Counting with Reversal (ECR) uses the same paradigm as Visual Elevator but presents stimuli aurally rather than visually, presented at a fixed speed. ECR also tests working memory.

The TEA is one of the few tests based on an established theory of attention (Bate, Mathias, & Crawford, 2001), the attentional model of Posner and Petersen (1989). This proposes three attentional systems: orientation, vigilance and selection. A factor analysis on the performance of the normative reference group on the TEA revealed three factors that correspond closely to three attention concepts (Evans et al., 1996). Thus the TEA has high construct validity. TEA subtests have been shown to significantly correlate with many other tests of attention and EF, such as Trails, Digits Backward, Stroop, Word Fluency, Modified Six Elements Text and PASAT (Bate et al., 2001; Chan, Hoosain, & Lee, 2002). The reliability of all TEA subtests is good, with the exception of Telephone Search while Counting. The validity of the TEA has been studied in stroke patients, patients with Alzheimer's disease and

head-injured patients and can be judged satisfactory (Evans et al., 1996; Gurd et al., 2010). Overall the TEA appears to be useful in discriminating patients with cognitive deficits from controls, (Strauss et al., 2006).

The TEA was developed with the intention of creating a clinically valid tool of high ecological validity. The TEA is acceptable to patients, and has high face validity (Evans et al., 1996). Robertson et al. (1994) examined relationships between TEA subtests and measures of functional status in stroke patients and found the Map Search and Elevator Counting subtests were moderately correlated with two measures of activities of daily living. It was noted that other conventional measures of attention did not correlate consistently with these functional measures. In another study Elevator Counting with Distraction exhibited a high correlation with functional status, in a MS sample (Higginson, Arnett, & Voss, 2000).

In the case that participants scored a raw score lower than that referred to in the normative tables, the scaled score was given as 1 point below the minimum scaled score value in the table.

### **3.10 Outcome assessments**

At the end of each condition participants and their carers or relatives were asked to fill out the outcome measures. The researcher posted the questionnaires two days prior to the end of the participant's condition. A pre-paid addressed envelope was enclosed. A copy of the participant questionnaire can be found in Appendix 11.

- i) For all participants recruited before 1<sup>st</sup> September 2014:
  - Two weeks were granted for outcome measure completion between conditions. These two weeks also served as a washout period between conditions.
- ii) For all participants recruited from 1<sup>st</sup> September 2014:

- Three weeks were granted for outcome measure completion between conditions. These three weeks also served as a washout period between conditions.

Additionally, for the final two weeks of each condition, participants were asked to fill out daily diaries, in which they recorded the frequency of forgetting the tasks they received reminders for. The researcher posted the daily diary 4 days prior to their start date. A pre-paid addressed envelope was enclosed. Two days into expected daily diary completion, the participant is sent a text by the researcher checking that they have received the daily diary and that they were completing it without concern. An example of a daily diary is shown in Appendix 12.

The researcher sent a follow-up text 2 weeks after each condition ended if completed questionnaires had not yet been received. If participants self-reported that they were unable to complete the questionnaires, help was offered by the researcher to administer the primary outcome measure (EMQ frequency) over the phone. After that point no further action was taken.

### **3.10.1 Rationale for assessments selected**

#### **3.10.1.1 *Everyday Memory Questionnaire***

See section 3.9.1.1 above for details of the EMQ. The participant version of the EMQ-28 was the primary outcome measure. The self-report and informant (relative or carer) versions were used as outcome measures. A lower total score on the EMQ (participant and relative) indicates lower frequency of reported memory problems. Studies which have included subjective reports of memory completed by significant others have found that carers report higher frequency of problems than patients (Beatty & Monson, 1996; McIntosh - Michaelis et al., 1991). Therefore inclusion of the informant version provides an alternative perspective of memory problems faced.



Importance of memory problems were also rated in addition to frequency of problems, in the form of a saliency scale (K. Mackenzie, 2014). The importance scale was added to include the reporting of how much importance a person might place on a particular symptom. The authors suggested the addition had potential to add clinically useful information to the measure while remaining relatively short (Mackenzie, 2014).

### **3.10.1.2      *General Health Questionnaire***

The General Health Questionnaire (GHQ)(Goldberg & Williams, 1988) is a self-administered questionnaire, measuring common mental health problems of depression, anxiety, somatic symptoms and social withdrawal. GHQ-30 has 30 items and uses a 4-point Likert scale. A lower total score on GHQ indicates fewer reported mood problems.

The GHQ was developed as a 60-item screening tool to detect those likely to have or be at risk of developing psychiatric disorders. The 30-item version is easy to complete and was chosen because of time considerations. This shortened version of the GHQ was balanced for overall agreement set and had items endorsed by 'physically ill' respondents removed (Goldberg & Williams, 1988). There are multiple ways to score the GHQ, but using the 4-point Likert scale (0-1-2-3) provides a wider and smoother score distribution (Goldberg & Williams, 1988), and is therefore more sensitive to change. The 30-item version does not have questions about suicide which makes it better than GHQ-28 for postal administration.

The GHQ has been translated into 38 different languages, testament to the validity and reliability of the questionnaire (Jackson, 2007). The GHQ-30 is the version that has been most widely validated, with the median value for sensitivity across diagnosis-specific coefficients being 81%, and 21 of 29 studies yielded values within 10% of this figure (Goldberg & Williams, 1988). Sensitivity for detecting major depression was the highest, at 88% (Goldberg & Williams, 1988). Factor analyses of

the GHQ-30 indicate an impressive degree of consistency of the factor structure, and the identification of five distinct factors corresponding to anxiety, feelings of incompetence, depression, difficulty in coping and social dysfunction (Huppert, Walters, Day, & Elliott, 1989).

#### **3.10.1.3      EQ-5D**

The EQ-5D is a standardised measure of health status developed by the EuroQol Group in order to provide a simple generic measure of health for clinical and economic appraisal (The EuroQol Group, 1990). The EQ-5D consists of a 'descriptive system' comprising the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. A visual analogue scale follows where participants are asked to record their health on a vertical scale where endpoints are labelled 'Best imaginable health state' and 'worst imaginable health state'. On the EQ-5D-3L each dimension has 3 levels: no problem, some problems, extreme problems. A lower score on each item (1-5) indicates better quality of life; and a higher score on the Visual Analogue Scale indicates better quality of life. Cumulative scoring is not used on the EQ-5D. 'Health states' can be referred to in terms of a 5-digit code, for example 11111 would indicate no problems on any of the 5 dimensions. Additionally health states can be converted into a single summary index.

The National Institute for Health and Care Excellence (NICE) recommends the EQ-5D (NICE, 2008), and it is validated in many different patient populations. Construct validity has been demonstrated in a study of people with dementia (Aguirre, Kang, Hoare, Edwards, & Orrell, 2016).

#### **3.10.1.4      *Adaptation to Memory Difficulties Outcome Questionnaire***

The Adaptation to Memory Difficulties Outcome questionnaire (AMEDO)(Chouliara, 2013) is a brief and simple measure tailored to the characteristics and needs of neurologically impaired adults. The AMEDO consists of 2 parts: Part A asks questions about how participants cope with their memory problems, ranked on a 4-

point Likert scale; Part B includes checklists of memory aids used, followed by questions relating to how participants use them, ranked on a 4-point Likert scale, for example “Using external memory aids is part of my everyday life”. A higher score on AMEDO part A indicates better coping strategies for memory problems; higher scores on Parts B1 and B2 indicate better use of external and internal aids respectively.

The AMEDO was designed as an outcome measure specific to the effects of memory rehabilitation, to complement memory batteries and established generic measures (Chouliara, 2013). It was developed as a response to qualitative feedback from a rehabilitation programme (ReMIND)(das Nair & Lincoln, 2012). Participants in the ReMIND study reported improvements in domains that were not covered by existing questionnaires assessing the outcome of memory rehabilitation in people with neurological disabilities. During development of the AMEDO, the criteria of face validity, response distribution and construct validity were applied. Principal component analysis indicated that the questionnaire captured most of the content areas it was designed to cover, and construct validity was assumed (Chouliara, 2013). Part A of the questionnaire comprises of three components: memory knowledge; control; and emotional adjustment. These factors were confirmed by evaluation of item-convergent validity and high internal consistency estimates for all subscales were found.

#### **3.10.1.5      *Daily diary***

The daily diary is a self-defined outcome measure relating to participants’ everyday memory problems, and has been used in previous studies evaluating NeuroPage (Fish et al., 2008; Wilson et al., 2001; Wilson et al., 1997).

A daily diary was devised for each participant based on the earlier discussions at baseline assessment, relating to current everyday memory failures and the reminders they wished to receive during the intervention condition. For example, if participants wished to receive reminders to take their medication, the daily diary

would ask how many times they forgot to take their medication each day. For each participant the content of the daily diary was the same in both conditions, as non-memory messages were transmitted at the same times and frequency as the NeuroText messages, unless requested otherwise.

### **3.11 Feedback Interviews**

All participants were contacted by the researcher at least two months after trial completion and invited to take part in a feedback interview. Two attempts were made at contact by telephone. If participants agreed to take part, they were informed that it would be audio recorded, in order to record their views in their words.

Semi-structured interviews were conducted to capture participants' perspectives and experiences, and to inform further improvements of the programme. This interview was used to gather supplementary information from the participants on the perceived benefits (what they felt worked well/what they liked) or draw-backs (what did not go well/what did not like) of the NeuroText messages, and potential improvements. They were also asked about the perceived effects of the control messages, and potential improvements. The interview schedule was based on the one used in the ReMemBrIn trial (das Nair, Lincoln, & Ftizsimmons, 2015). Questions were open-ended, with the aim of eliciting as much information as possible about peoples' experiences of the intervention. The semi-structured interview schedule is detailed in Appendix 13.

Interviews were conducted over the telephone. This was due to the flexible nature of organising a phone call with participants at their preferred time, compared to the impracticality of organising geographically-spread home visits, when these short interviews could be done equally well over the phone. Interviews were audio recorded.

### **3.12 Data collection and entry**

Baseline data were anonymised, scored and entered into a password protected database by the researcher. Personal participant details, e.g. name, address and date of birth were entered into a separate password protected database by the researcher.

#### **3.12.1 RCT Outcomes**

Outcome measures were scored and entered into a password protected database by a person blind to the study and response. They were blind to group allocation and did not have any contact with study participants. Outcome measures were marked with ID numbers by the researcher prior to being posted to participants, to ensure blinding. The researcher performed 10% accuracy checking.

#### **3.12.2 Feedback interviews**

Interviews were digitally recorded using WebEx for the health sector teleconferencing services, to ensure secure recording. Interviews were recorded by the researcher and transcribed verbatim by two independent researchers. Transcriptions were checked by the researcher for accuracy.

### **3.13 Data analyses**

Statistical analyses were carried out by the researcher, using IBM SPSS Statistics version 22.0.

#### **3.13.1 Baseline**

The demographic characteristics were separated first into groups (1 and 2), and then into continuous and categorical variables. Categorical variables were reported using percentages, and continuous reporting the mean, standard deviation and range of the groups. The distribution of baseline data was assessed for normality by checking whether the value of the skewness statistic was greater than twice the value of its standard error (Coolican, 2014). Where the skew was twice the standard

error, non-parametric procedures were applied, otherwise the mean, standard deviation and range were reported for all measures. If the majority of variables included in the analyses were of normal distribution parametric statistics were employed. Participants were randomly allocated to the two groups, so any differences between groups were due to chance; therefore a statistical test to determine whether differences were due to chance was not employed.

### **3.13.2 Feasibility**

The number of referrals and recruitments from each NHS trust were reported, and the percentages of converted referrals were calculated. Reasons for exclusions and dropouts were described. The number and percentage of outcome measures returned were calculated, as were the completion rates of individual scales, e.g. EMQ.

The frequency and types of intervention and control messages requested by participants were calculated.

### **3.13.3 Effectiveness of intervention**

The distribution of outcome data was assessed for normality by checking whether the value of the skewness statistic was greater than twice the value of its standard error (Coolican, 2014). Where the skew was twice the standard error, non-parametric procedures were applied, otherwise the mean, standard deviation and range were reported for all measures.

Intention-to-treat analysis was used throughout the trial, such that an estimate of likely health benefits of the intervention in clinical practice may be provided. Therefore all data was categorised as the group in which participants were randomised into. The study was an AB/BA crossover, therefore group 1 received NeuroText first, control second; group 2 received control first, NeuroText second.

There are many ways to approach the analysis of crossover trials. The analysis of crossover trials should take advantage of the within-participants design and use a form of paired analysis (Elbourne et al., 2002). Therefore within-group comparisons were employed. For all outcome measures, scores from both groups 1 and 2 were combined to get a dataset for performance after the NeuroText condition, and control condition. Therefore the NeuroText data was collated using scores (Group 1 condition 1 + Group 2 condition 2); and control was calculated using (Group 1 condition 2 + Group 2 condition 1). Grouping the scores from each condition (NeuroText and control), regardless of which order they received conditions, increases the sample size, and therefore the power.

The appropriate analysis of data from an AB/BA trial is a paired t-test (Higgins & Green, 2013). Paired-samples t-tests (Senn, 2002) were employed, to compare combined performance after the NeuroText and control conditions. A significant difference in performance between conditions was determined as  $p < 0.05$ . Effect sizes were also estimated using Cohen's  $d$ , by calculating mean difference divided by standard deviation of difference (Cohen, 1988; Field, 2013). Effect size was classified as follows: 0.2 small; 0.5 moderate; 0.8 large.

When employing within-subject analyses on data from an AB/BA trial, additional checks for carryover or period effects should be performed, (Higgins & Green, 2013). This is to ensure that there was no "carryover" of effects from the first condition into the second; and that the order in which condition were received had no impact on participant outcomes. Carryover effects were tested by comparing the sum of values over both conditions, between groups 1 and 2 (Jones & Kenward, 2014). Period effects were tested by comparing the difference between NeuroText and control condition scores, between groups 1 and 2 (Jones & Kenward, 2014). The data was checked for carryover and period effects using independent t-tests.

In addition, a within-subject analysis was also performed using change data on the EMQ-participant frequency subscale. Change data was calculated using the combined data at three time-points: baseline [B], after condition 1 [T1], and after

condition 2 [T2], to enable comparison between change with NeuroText and change with control for each participant. Therefore change with NeuroText was calculated as (Group 1 T1-B) + (Group 2 T2-T1). Change with control was calculated as (Group 1 T2-T1) + (Group 2 T1-B). A paired/related-samples t-test was employed to compare the two sets of data. A significant difference in performance between conditions was determined as  $p < 0.05$ .

#### **3.13.3.1      *Sample size estimation***

A feasibility analysis was performed, as no previous trials of this nature were identified, and therefore there was no previous data on rates of consent, number who completed treatment, or outcome assessments. In order to determine the sample size, a 12-point difference on the Everyday Memory Questionnaire was identified as clinically important during the ReMemBrIn Trial (das Nair, Lincoln, et al., 2015), and a sigma value of 16.4 was identified from Carr et al. (2014). Calculating the sample size using these values equated to a required sample size of 30 in each group ( $\alpha = 0.05$ ). Therefore, considering a 10% allowance for dropouts, at least 66 participants were planned to be recruited in this study.

Post-hoc sample size estimation was calculated, to advise for a future full-powered RCT.

#### **3.13.4      *Feedback interviews***

Data were obtained using the semi-structured feedback interviews, and the transcripts were coded and analysed thematically. NVivo 10 for Windows was used to store and organise the data.

Thematic analysis was initially considered because it is a flexible approach, and not bound to any theoretical position (Braun & Clarke, 2006). However, the purpose of the interviews was to examine participant feedback on their experience of taking part in the trial, and to provide suggestions for improvement. The semi-structured interview schedule was designed specifically to capture these key questions.



Therefore it was anticipated that the data would cover similar, specific topics in response to the interview questions, and it was deemed that framework analysis (FA) would therefore be a more appropriate method.

FA is becoming an increasingly popular approach to the management and analysis of qualitative data in health research, and is most commonly used for the thematic analysis of semi-structured interview transcripts (Gale, Heath, Cameron, Rashid, & Redwood, 2013). FA sits closely with thematic analysis in its approach, identifying commonalities and differences in the data, then focusing on the relationships between different parts of the data, to cluster into themes (Gale et al., 2013). FA also is not aligned to a particular epistemological or theoretical approach. The defining feature of FA is the matrix output of rows (cases), columns (codes) and cells of summarised data, which provide structure into which the researcher can systematically reduce the data, to analyse it by case or code (Ritchie, Lewis, Nicholls, & Ormston, 2013). This layout allows the researcher to perform in-depth analyses of themes across the dataset, whilst retaining the context of participants' views. Furthermore FA allows the researcher to maintain an effective and transparent audit trail, as management and analysis take place simultaneously (Smith & Firth, 2011). An example of the framework matrix used in this study can be found in Appendix 14.

The procedure for FA described by Gale et al. (2013) was followed. Gale et al. (2013) outline seven stages of FA: (i) transcription, where audio recording is transcribed verbatim; (ii) familiarisation with the interview, by re-listening or re-reading transcripts and noting impressions; (iii) coding, carefully reading transcripts line-by-line and paraphrasing important passages and labelling with codes; (iv) developing a working analytical framework, codes were grouped together into clearly defined categories over several iterations; (v) applying the analytical framework, indexing transcripts using categories and codes; (vi) charting data into the framework matrix, a spreadsheet is used to generate a matrix and data are charted onto the matrix; (vii) interpreting the data, characteristics of data and connections between categories are identified to form themes and sub-themes.

Themes were defined as important aspects of data that broadly related to the interview questions, and were representative of patterned responses within the data set, and that appeared with some frequency (Braun & Clarke, 2006). The degree of frequency was not predefined. Themes identified were coded and analysed at a semantic/explicit level. A mixture of deductive and inductive coding was employed in this study, where some codes were pre-defined in line with the interview questions. However inductive coding also occurred, to include unexpected perspectives (Gale et al., 2013). In our write up, we opted not to 'count' the number of times a construct or theme was endorsed by participants, because we felt that this would suggest a level of accuracy, which such an analysis does not purport to do. Instead, we chose to describe the endorsement in general terms, such as, 'several participants' or 'a few...'

Saturation was assumed when the emergence of new themes stopped and code definitions were stable (Guest, Bunce, & Johnson, 2006). Saturation was assessed and agreed by two researchers, and data collection in the form of interviews was stopped.

FA was carried out by the researcher, under the supervision of an experienced qualitative researcher, to ensure quality. Multiple iterations of the framework matrix were co-reviewed, to confirm themes and sub-themes were valid.

## 4 Quantitative Results

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### 4.1 Chapter Overview

This chapter will begin by describing the demographic characteristics and baseline performance of the sample. Recruitment rates, return of outcome measures and attrition will be reported. The content of the intervention will be discussed, and the outcomes of the intervention and control will be compared.

### 4.2 Feasibility Study

#### 4.2.1 Description of the sample

One-hundred-and-seven people were referred to the trial and of these 103 were assessed for eligibility; 4 people could not be reached for assessment using the contact details provided by the referrers. 53 people were excluded. Of those excluded, 8 people did not score above the cut-off on the EMQ, 4 had a severe motor or cognitive impairment and 41 did not want to take part and so did not give consent. Figure 2 shows the flow of participants through the trial.

Fifty people were recruited to the feasibility trial. 25 people were randomised into group 1 to receive NeuroText first then control; 25 in group 2 to receive control first then NeuroText. The demographic characteristics of the participants are described in tables 5 and 6.

Table 5: Demographic characteristics of participants on continuous variables

|                          | Group 1 |       |       |       | Group 2 |       |       |       |
|--------------------------|---------|-------|-------|-------|---------|-------|-------|-------|
|                          | n       | Mean  | SD    | Range | n       | Mean  | SD    | Range |
| Age                      | 25      | 50.96 | 11.96 | 28-72 | 25      | 48.12 | 10.31 | 30-72 |
| Years since diagnosis    | 25      | 11.86 | 8.97  | 1-37  | 25      | 10.30 | 9.48  | 1-33  |
| Years since last relapse | 14      | 1.29  | 1.54  | 0-6   | 19      | 2.26  | 2.28  | 0-9   |

Table 6: Demographic characteristics of participants on categorical variables

|                            |  | Group 1 |    | Group 2 |    |
|----------------------------|--|---------|----|---------|----|
|                            |  | n       | %  | n       | %  |
| Gender                     | Men  | 11      | 44 | 7       | 28 |
|                            | Women  | 14      | 56 | 18      | 72 |
| Type of multiple sclerosis | Primary progressive  | 7       | 28 | 3       | 12 |
|                            | Secondary progressive  | 7       | 28 | 6       | 24 |
|                            | Relapsing remitting  | 9       | 36 | 15      | 60 |
|                            | Benign   | 1       | 4  | 0       | 0  |
|                            | Missing  | 1       | 4  | 1       | 4  |
| NHS Trust                  | Nottingham University Hospitals                                | 7       | 28 | 13      | 58 |
|                            | Nottingham CityCare Partnership                                | 3       | 12 | 4       | 16 |
|                            | Cambridge University Hospitals                                 | 2       | 8  | 1       | 4  |
|                            | Cambridgeshire Community Services                              | 8       | 32 | 4       | 16 |
|                            | Peterborough & Stamford Hospitals                              | 5       | 20 | 3       | 12 |
| Education                  | 1-4 GCSEs or NVQ L1  | 2       | 8  | 3       | 12 |
|                            | 5+ GCSEs or NVQ L2   | 10      | 40 | 6       | 24 |
|                            | 2+ A Levels or NVQ L3  | 1       | 4  | 5       | 20 |
|                            | Degree or Higher degree  | 8       | 32 | 7       | 28 |
|                            | Professional Qualification                                     | 1       | 4  | 0       | 0  |
|                            | Vocational qualifications                                      | 3       | 12 | 4       | 16 |
| Occupation                 | Higher managerial, administrative and professional occupations | 2       | 8  | 3       | 12 |
|                            | Intermediate occupations                                       | 2       | 8  | 2       | 8  |
|                            | Routine and manual occupations                                 | 0       | 0  | 1       | 4  |
|                            | Never worked and long-term unemployed                          | 0       | 0  | 4       | 16 |
|                            | Disability retirement/ retirement                              | 21      | 84 | 15      | 60 |
| Occupation Type            | Full time  | 3       | 12 | 2       | 8  |
|                            | Part Time  | 1       | 4  | 7       | 28 |
|                            | Unemployed   | 21      | 84 | 16      | 64 |
| Partnership                | Never married or civil partnership                             | 2       | 8  | 3       | 12 |
|                            | Married or civil partnership                                   | 19      | 76 | 17      | 68 |
|                            | No longer married or civil partnership                         | 4       | 16 | 5       | 20 |
| Ethnicity                  | White  | 23      | 92 | 24      | 96 |

|         |                                       |    |    |    |    |
|---------|---------------------------------------|----|----|----|----|
|         | Mixed/Multiple ethnic groups          | 0  | 0  | 1  | 4  |
|         | Black/African/Caribbean/Black British | 2  | 8  | 0  | 0  |
| Beliefs | Christian                             | 8  | 32 | 15 | 60 |
|         | Other                                 | 2  | 8  | 1  | 4  |
|         | None                                  | 15 | 60 | 9  | 36 |

Group 1 and group 2 are comparable for the majority of demographic characteristics. Group 2 had a higher percentage of women; people with relapsing remitting MS; and participants from Nottingham University Hospitals NHS Trust, compared to group 1. Group 1 had a higher percentage of people with primary progressive MS; participants from Cambridgeshire Community Services NHS Trust; unemployed/retired people; and people with no beliefs.

#### 4.2.2 Baseline characteristics

The distribution of scores on baseline measures were checked to determine whether they had normal distributions. The majority of measures had normal distribution and so parametric statistics are reported in table 7. Skew values for each subtest are reported in Appendix 15.

Table 7: Distribution of scores on baseline measures

|                        | Group 1 |      |      |       | Group 2 |      |      |       |
|------------------------|---------|------|------|-------|---------|------|------|-------|
|                        | n       | Mean | SD   | Range | n       | Mean | SD   | Range |
| EMQ Total Score        | 25      | 49.9 | 16.2 | 21-86 | 25      | 52.0 | 17.8 | 21-98 |
| Doors & People Test    |         |      |      |       |         |      |      |       |
| People                 | 25      | 7.7  | 3.2  | 1-13  | 25      | 6.8  | 3.4  | 1-13  |
| Doors                  | 24      | 7.6  | 3.8  | 1-14  | 25      | 6.0  | 3.1  | 1-11  |
| Shapes                 | 24      | 8.6  | 4.8  | 0-16  | 25      | 8.3  | 3.7  | 0-14  |
| Names                  | 24      | 8.1  | 4.4  | 0-15  | 25      | 10.3 | 4.4  | 1-16  |
| Overall Score          | 24      | 7.6  | 4.2  | 0-15  | 25      | 9.0  | 8.3  | 0-36  |
| Combined visual memory | 24      | 8.1  | 3.9  | 2-15  | 25      | 6.7  | 3.4  | 2-13  |
| Combined verbal memory | 24      | 7.7  | 3.8  | 2-14  | 25      | 8.3  | 3.9  | 14    |

|                                    |    |     |     |      |    |      |     |      |
|------------------------------------|----|-----|-----|------|----|------|-----|------|
| Combined recall                    | 24 | 8.1 | 3.8 | 2-14 | 25 | 7.1  | 3.6 | 2-14 |
| Combined recognition               | 24 | 7.8 | 4.1 | 2-14 | 25 | 7.9  | 3.9 | 2-14 |
| Verbal forgetting                  | 24 | 8.8 | 3.1 | 3-13 | 25 | 10.1 | 2.5 | 5-14 |
| Visual forgetting                  | 24 | 9.9 | 1.8 | 6-12 | 25 | 9.2  | 2.8 | 2-12 |
| Hayling & Brixton                  |    |     |     |      |    |      |     |      |
| Hayling error                      | 25 | 5.4 | 2.3 | 1-8  | 25 | 5.3  | 2.1 | 1-8  |
| Hayling overall                    | 25 | 4.7 | 1.8 | 1-7  | 25 | 5.0  | 1.6 | 1-7  |
| Brixton                            | 25 | 4.8 | 2.4 | 1-10 | 25 | 5.0  | 2.2 | 1-9  |
| Test of Everyday Attention         |    |     |     |      |    |      |     |      |
| Map search 1                       | 22 | 7.2 | 3.3 | 0-12 | 25 | 6.5  | 3.4 | 0-12 |
| Map search 2                       | 22 | 6.7 | 3.2 | 0-11 | 25 | 6.2  | 3.4 | 0-13 |
| Elevator counting                  | 25 | 6.6 | 0.6 | 5-7  | 25 | 6.9  | 0.4 | 6-7  |
| Elevator counting with distraction | 25 | 9.4 | 2.9 | 5-13 | 24 | 10.3 | 2.3 | 6-13 |
| Visual elevator 1                  | 23 | 8.7 | 3.2 | 3-15 | 24 | 9.3  | 2.9 | 3-14 |
| Visual elevator 2                  | 22 | 7.8 | 3.5 | 0-13 | 24 | 8.0  | 3.1 | 0-15 |
| Elevator counting with reversal    | 20 | 9.6 | 3.6 | 5-18 | 22 | 9.4  | 3.5 | 2-15 |
| Telephone search                   | 23 | 7.5 | 3.2 | 0-12 | 25 | 7.7  | 3.4 | 0-15 |
| Telephone search while counting    | 23 | 8.0 | 3.5 | 0-15 | 25 | 8.2  | 3.7 | 0-15 |
| Lottery                            | 25 | 8.0 | 3.8 | 1-13 | 24 | 8.9  | 3.7 | 1-13 |

Note: Tests used: EMQ: Everyday Memory Questionnaire

All Hayling & Brixton scores had non-normal distributions, and so non-parametric statistics are reported in table 8.

Table 8: Distribution of scores on Hayling & Brixton tests at baseline

|                 | Group 1 |        |         | Group 2 |      |         |
|-----------------|---------|--------|---------|---------|------|---------|
|                 | n       | Median | I.Q.R.  | n       | Mean | I.Q.R.  |
| Hayling Error   | 25      | 6      | 4.5-6   | 25      | 6    | 4.5-6   |
| Hayling Overall | 25      | 6      | 3.5-6   | 25      | 6    | 4-6     |
| Brixton         | 25      | 5      | 2.5-6.5 | 25      | 6    | 3.5-6.5 |

The two groups were comparable across all baseline measures. Scores on the Doors & People subtests were in the low-average to average memory ability range. Performance on the Hayling & Brixton tests in both groups showed average executive functioning. Overall scores on the Test of Everyday Attention were low-average in attention for both groups. Participants scored in the average range for the Elevator counting with distraction (ECD) subtest measuring selective attention, and Elevator counting with reversal (ECR), which measures attention switching.

### 4.2.3 Feasibility measures

#### 4.2.3.1 Recruitment

One hundred and seven people were referred from MS Clinicians. Table 9 shows referral and inclusion to study figures for each of the NHS trusts.

Table 9: Referral and inclusion figures by Trust

| NHS Trust                         | Number of referrals | Number of participants included in study | Percentage of referrals included (%) |
|-----------------------------------|---------------------|--|--------------------------------------|
| Nottingham University Hospitals   | 31                  | 20                                       | 65                                   |
| Nottingham CityCare Partnership   | 13                  | 7  | 54                                   |
| Cambridge University Hospitals    | 3                   | 3  | 100                                  |
| Cambridgeshire Community Services | 42                  | 12                                       | 29                                   |
| Peterborough & Stamford Hospitals | 18                  | 8  | 44                                   |
| Total                             | 107                 | 50                                       | 47                                   |

The majority of referrals were made from Cambridgeshire Community Services NHS Trust, however they had the lowest conversion rate for inclusion in the study.

Cambridge University Hospitals NHS Trust had 100% conversion rate, but referred the lowest number of potential participants. Nottingham University Hospitals NHS Trust had the highest number of included participants in the study.

#### **4.2.3.2 Return of Outcome measures**

The number of each of the outcome questionnaires returned after first and second conditions are detailed below in table 10. Figure 2 also demonstrates outcome measure return.

Table 10: Return of outcome questionnaires

|                  | Outcomes                        | Group 1 | Group 2 |
|------------------|---------------------------------|---------|---------|
| First Condition  | Questionnaire participant n (%) | 21 (84) | 19 (83) |
|                  | Questionnaire relative n (%)    | 17 (68) | 12 (52) |
|                  | Daily Diary n (%)               | 19 (76) | 15 (65) |
| Second Condition | Questionnaire participant n (%) | 17 (71) | 14 (61) |
|                  | Questionnaire relative n (%)    | 15 (63) | 10 (43) |
|                  | Daily Diary n (%)               | 13 (54) | 11 (48) |

Group 1 had a slightly higher return rate than group 2 across all outcome measures and conditions. Return rates decreased from condition 1 to condition 2.

Table 11 provides a breakdown of completion rates for individual outcome measures within the booklets.

Table 11: Completion of individual sections of outcome measures

|                 | Outcomes                        | Group 1 | Group 2 |
|-----------------|---------------------------------|---------|---------|
| First Condition | EMQ Frequency participant n(%)  | 21 (84) | 18 (78) |
|                 | EMQ Importance participant n(%) | 18 (72) | 15 (65) |
|                 | GHQ n(%)                        | 19 (76) | 16 (70) |
|                 | AMEDO Part A n(%)               | 19(76)  | 15 (65) |
|                 | EQ5d n(%)                       | 19(76)  | 15 (65) |
|                 | EQ5d VAS n(%)                   | 18 (72) | 14 (61) |



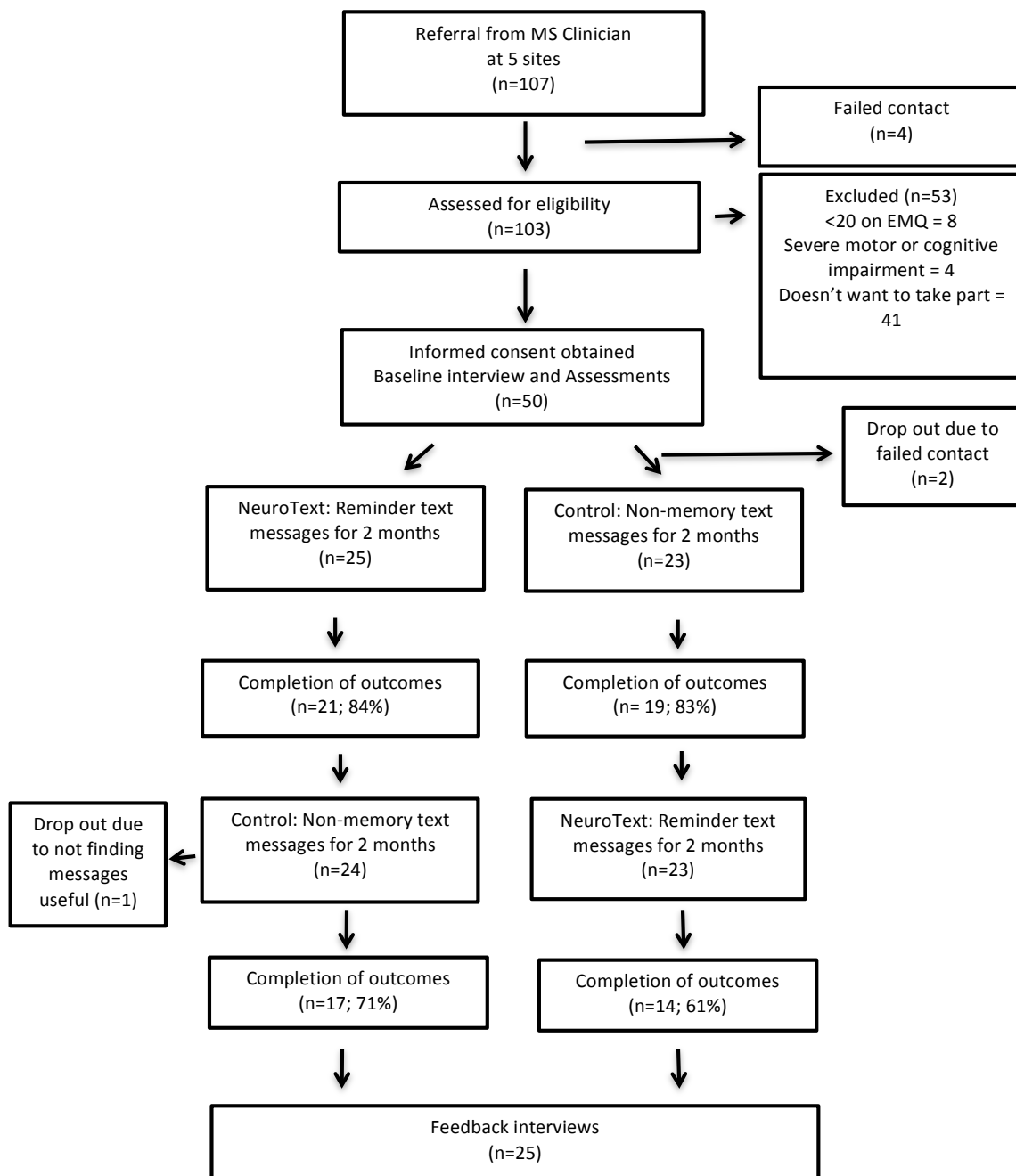
|                  |                                 |         |         |
|------------------|---------------------------------|---------|---------|
|                  | EMQ relative n(%)               | 17 (68) | 11 (48) |
| Second Condition | EMQ Frequency participant n(%)  | 17 (71) | 14 (61) |
|                  | EMQ Importance participant n(%) | 16 (67) | 13 (57) |
|                  | GHQ n(%)                        | 16 (67) | 13 (57) |
|                  | AMEDO Part A n(%)               | 16 (67) | 13 (57) |
|                  | EQ5d n(%)                       | 16 (67) | 13 (57) |
|                  | EQ5d VAS n(%)                   | 15 (63) | 13 (57) |
|                  | EMQ relative n(%)               | 14 (58) | 9 (39)  |

Note: Tests used: EMQ: Everyday Memory Questionnaire; GHQ: General Health Questionnaire; AMEDO: Adaptation to Memory Difficulties Outcomes Questionnaire.

The completion rates of individual outcome measures were similar to those of the overall outcome returns. Group 1 had a higher completion rate than group 2, and completion rates decreased over time.

Five participants requested phone assistance after their first condition, 2 in group 1 and 3 in group 2; two after their second condition, 1 from each group.

Figure 2: Flow of participants through the feasibility study



#### **4.2.3.3 Attrition**

Two participants were considered dropouts due to the researcher not being able to contact them after they had consented into the study. Technological problems at the beginning of the trial meant that ten participants did not receive the control as planned. Therefore, the trial was temporarily halted and the technological difficulties were resolved. Additionally adjustments to the protocol were implemented to boost recruitment and outcome return, and then the trial was restarted with these changes in place, as agreed by the ethics committee. See Appendix 16 for the approval letter.

Therefore, outcomes analysis was conducted on 38 participants who were recruited after problems with delivery of control condition were rectified, and in line with the new protocol.

### **4.3 Randomised controlled trial**

#### **4.3.1 Description of the sample**

After restarting the trial 38 people were included, 17 participants randomised into group 1 and received NeuroText first then control; 21 were in group 2 and received control first then NeuroText.

The demographic characteristics of the participants are described in tables 12 and 13.

Table 12: Demographic characteristics of participants on continuous variables

|                          | Group 1 |      |      |       | Group 2 |      |     |       |
|--------------------------|---------|------|------|-------|---------|------|-----|-------|
|                          | n       | Mean | SD   | Range | n       | Mean | SD  | Range |
| Age                      | 17      | 48.8 | 12.9 | 28-72 | 21      | 46.7 | 9.7 | 30-65 |
| Years since diagnosis    | 17      | 10.6 | 9.8  | 1-37  | 21      | 9.7  | 9.4 | 1-33  |
| Years since last relapse | 11      | 1.4  | 1.7  | 0-6   | 17      | 2.1  | 2.3 | 0-9   |

Table 13: Demographic characteristics of participants on categorical variables

|                            |  | Group 1 |     | Group 2 |     |
|----------------------------|--|---------|-----|---------|-----|
|                            |  | n       | %   | n       | %   |
| Gender                     | Men  | 6       | 35  | 4       | 19  |
|                            | Women  | 11      | 65  | 17      | 81  |
| Type of multiple sclerosis | Primary progressive  | 3       | 18  | 1       | 5   |
|                            | Secondary progressive  | 5       | 29  | 5       | 24  |
|                            | Relapsing remitting  | 8       | 47  | 14      | 66  |
|                            | Benign   | 1       | 6   | 0       | 0   |
|                            | Missing  | 0       | 0   | 1       | 5   |
| NHS Trust                  | Nottingham University Hospitals                                | 6       | 35  | 13      | 62  |
|                            | Nottingham CityCare Partnership                                | 2       | 12  | 1       | 5   |
|                            | Cambridge University Hospitals                                 | 1       | 6   | 1       | 5   |
|                            | Cambridgeshire Community Services                              | 3       | 18  | 3       | 14  |
|                            | Peterborough & Stamford Hospitals                              | 5       | 29  | 3       | 14  |
| Education                  | 1-4 GCSEs or NVQ L1  | 2       | 12  | 2       | 9   |
|                            | 5+ GCSEs or NVQ L2   | 6       | 35  | 6       | 29  |
|                            | 2+ A Levels or NVQ L3  | 1       | 6   | 3       | 14  |
|                            | Degree or Higher degree  | 5       | 29  | 6       | 29  |
|                            | Vocational qualifications                                      | 3       | 18  | 4       | 19  |
| Occupation                 | Higher managerial, administrative and professional occupations | 2       | 12  | 3       | 14  |
|                            | Intermediate occupations                                       | 2       | 12  | 2       | 10  |
|                            | Routine and manual occupations                                 | 0       | 0   | 1       | 5   |
|                            | Never worked and long-term unemployed                          | 0       | 0   | 3       | 14  |
|                            | Disability retirement/ retirement                              | 13      | 76  | 12      | 57  |
| Occupation Type            | Full time  | 3       | 18  | 2       | 9   |
|                            | Part Time  | 1       | 6   | 6       | 29  |
|                            | Unemployed   | 13      | 76  | 13      | 62  |
| Partnership                | Never married or civil partnership                             | 2       | 12  | 2       | 10  |
|                            | Married or civil partnership                                   | 13      | 76  | 15      | 71  |
|                            | No longer married or civil partnership                         | 2       | 12  | 4       | 19  |
| Ethnicity                  | White  | 17      | 100 | 21      | 100 |
| Beliefs                    | Christian  | 4       | 23  | 12      | 57  |
|                            | Other  | 1       | 6   | 1       | 5   |

|  |      |    |    |   |    |
|--|------|----|----|---|----|
|  | None | 12 | 71 | 8 | 38 |
|--|------|----|----|---|----|

Group 1 and group 2 were comparable for the majority of demographic characteristics. Group 2 had a higher percentage of females; people with relapsing remitting MS; and participants from Nottingham University Hospitals NHS Trust, compared to group 1. Group 1 had a higher percentage of people with primary progressive MS; participants from Peterborough & Stamford Hospitals NHS Trust; unemployed/retired people; and people with no beliefs.

#### 4.3.2 Baseline characteristics

The distribution of scores on baseline measures were checked to determine whether they had normal distributions. The majority of measures had normal distribution and so parametric statistics are reported in table 14. Skew values for each subtest are reported in Appendix 17.

Table 14: Distribution of scores on baseline measures

|                        | Group 1 |      |      |       | Group 2 |      |      |       |
|------------------------|---------|------|------|-------|---------|------|------|-------|
|                        | n       | Mean | SD   | Range | n       | Mean | SD   | Range |
| EMQ Total Score        | 17      | 51.6 | 17.8 | 32-86 | 21      | 53.3 | 18.2 | 21-99 |
| Doors & People Test    |         |      |      |       |         |      |      |       |
| People                 | 17      | 7.8  | 3.6  | 1-13  | 21      | 7.3  | 3.5  | 1-13  |
| Doors                  | 17      | 7.3  | 4.3  | 1-14  | 21      | 6.4  | 2.9  | 1-11  |
| Shapes                 | 17      | 9.0  | 5.3  | 0-16  | 21      | 8.8  | 3.7  | 0-14  |
| Names                  | 17      | 7.4  | 4.5  | 0-15  | 21      | 10.4 | 4.1  | 1-16  |
| Overall Score          | 17      | 7.7  | 4.6  | 0-15  | 21      | 8.9  | 7.6  | 0-36  |
| Combined visual memory | 17      | 8.3  | 4.5  | 2-15  | 21      | 7.4  | 3.3  | 2-13  |
| Combined verbal memory | 17      | 7.4  | 4.0  | 2-14  | 21      | 8.7  | 3.9  | 2-14  |
| Combined recall        | 17      | 8.4  | 4.1  | 2-14  | 21      | 7.9  | 3.5  | 2-14  |
| Combined recognition   | 17      | 7.4  | 4.4  | 2-14  | 21      | 8.2  | 3.8  | 2-14  |
| Verbal forgetting      | 17      | 8.8  | 2.8  | 4-13  | 21      | 10.1 | 2.4  | 5-13  |
| Visual forgetting      | 17      | 9.9  | 1.6  | 6-11  | 21      | 9.2  | 2.9  | 2-12  |

| Hayling & Brixton                  |    |      |     |      |    |      |     |      |
|------------------------------------|----|------|-----|------|----|------|-----|------|
| Hayling error                      | 17 | 5.8  | 2.0 | 1-8  | 21 | 5.6  | 1.8 | 1-8  |
| Hayling overall                    | 17 | 5.0  | 1.7 | 1-7  | 21 | 5.1  | 1.4 | 1-6  |
| Brixton                            | 17 | 5.2  | 2.7 | 1-10 | 21 | 5.1  | 2.3 | 1-9  |
| Test of Everyday Attention         |    |      |     |      |    |      |     |      |
| Map search 1                       | 15 | 7.1  | 3.4 | 0-12 | 21 | 7.0  | 3.4 | 0-12 |
| Map search 2                       | 15 | 6.9  | 3.0 | 0-11 | 21 | 6.5  | 3.4 | 0-13 |
| Elevator counting                  | 17 | 6.5  | 0.7 | 5-7  | 21 | 6.9  | 0.4 | 6-7  |
| Elevator counting with distraction | 17 | 9.2  | 3.0 | 5-13 | 21 | 10.6 | 2.3 | 6-13 |
| Visual elevator 1                  | 16 | 8.8  | 3.6 | 3-15 | 20 | 9.9  | 2.4 | 5-14 |
| Visual elevator 2                  | 16 | 7.8  | 4.0 | 0-13 | 20 | 8.3  | 2.8 | 2-15 |
| Elevator counting with reversal    | 13 | 10.9 | 3.7 | 5-18 | 19 | 9.6  | 3.7 | 2-15 |
| Telephone search                   | 16 | 7.6  | 3.5 | 0-12 | 21 | 8.1  | 3.4 | 0-15 |
| Telephone search while counting    | 16 | 8.2  | 3.7 | 0-15 | 21 | 8.6  | 3.6 | 0-15 |
| Lottery                            | 17 | 7.8  | 4.1 | 1-13 | 20 | 9.6  | 3.3 | 4-13 |

Note: Tests used: EMQ: Everyday Memory Questionnaire.

All Hayling scores had non-normal distributions, and so non-parametric statistics are reported in table 15.

Table 15: Distribution of scores on Hayling & Brixton tests at baseline

|                 | Group 1 |        |        | Group 2 |      |        |
|-----------------|---------|--------|--------|---------|------|--------|
|                 | n       | Median | I.Q.R. | n       | Mean | I.Q.R. |
| Hayling Error   | 17      | 6      | 6-7    | 21      | 6    | 5-6.5  |
| Hayling Overall | 17      | 6      | 3.5-6  | 21      | 6    | 4-6    |

The two groups were comparable across all baseline measures. Scores on the Doors & People subtests were in the low-average to average memory ability range. Performance on the Hayling & Brixton tests in both groups showed average executive functioning. Overall scores on the Test of Everyday Attention were low-average in attention for both groups. Participants scored in the average range for

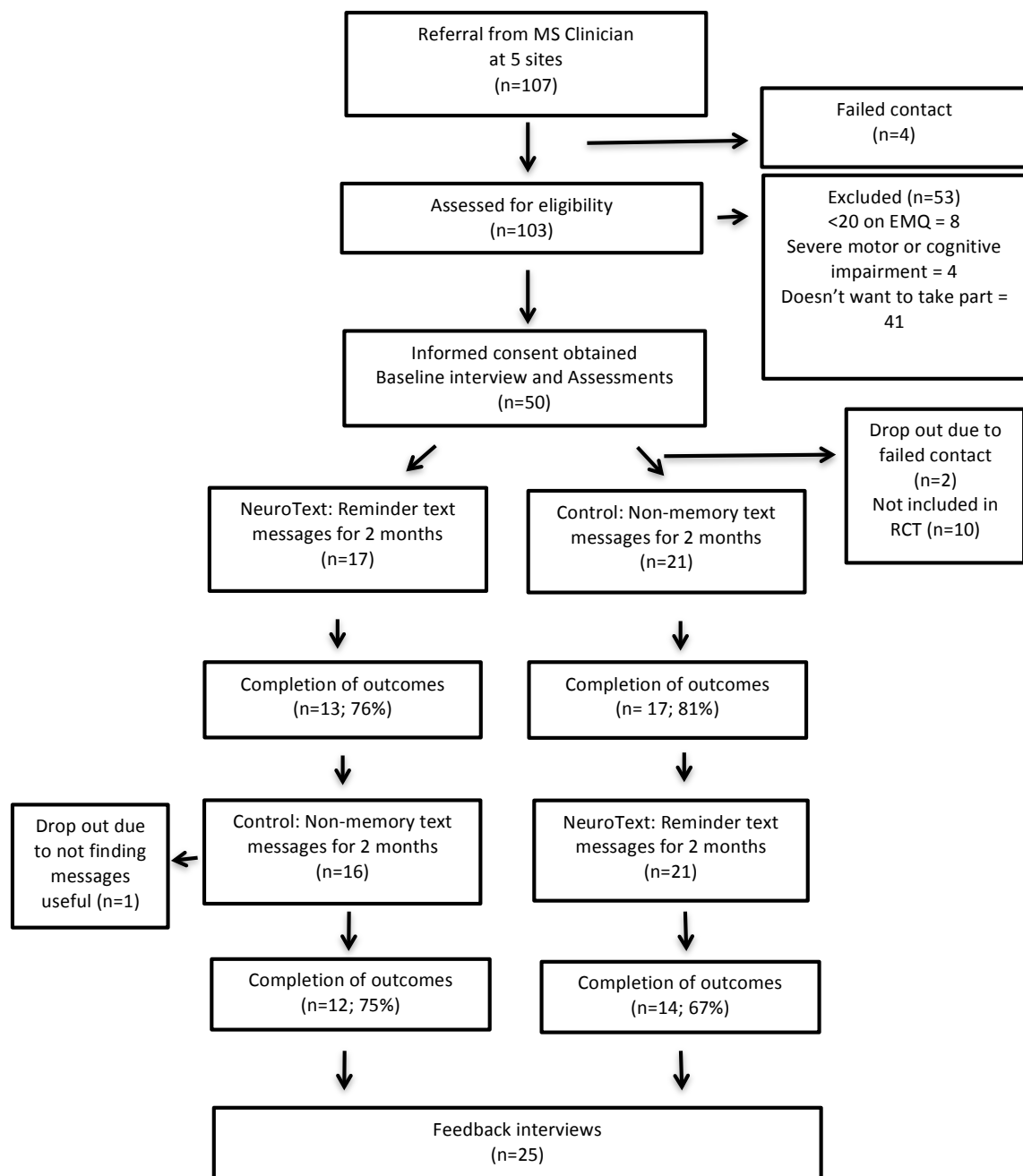
the Elevator counting with distraction (ECD) subtest measuring selective attention; and Elevator counting with reversal (ECR), which measures attention switching.

### **4.3.3 Participant Flow**

All 38 participants received the intervention and control as planned. No participants dropped out part way through intervention phase. One participant withdrew part way through the control condition. Figure 3 demonstrates the flow of participants through the study.



Figure 3: Flow of participants through the RCT



#### 4.3.4 Content of Intervention

A total of 885 reminder messages per week were requested in the NeuroText conditions, and 788 control messages. The frequency and type of reminders were evaluated in table 16 below.

Table 16: Most frequently requested text messages

|   | Group 1                  | Group 2                  |
|---|--------------------------|--------------------------|
| NeuroText Condition:<br>Requested content (%) | Medication (36)          | Medication (47)          |
|   | Toilet (10)              | Today is (11)            |
|   | Drink (8)                | Check calendar/diary (8) |
|   | Eat meal (7)             | Charge phone (6)         |
|   | Check calendar/diary (6) | Eat meal (4)             |
|   | Today is (4)             | Prepare food (3)         |
| Control Condition:<br>Requested content (%)   | Current affairs (68)     | Current affairs (51)     |
|   | Sports news (15)         | Specific news (36)       |
|   | Specific news (13)       | Sports news (13)         |
|   | Quotes (4)               |                          |

NeuroText messages regarding medication were the most commonly requested reminder in the NeuroText condition. Reminders for the day of the week; check the calendar/diary and eat meal were also frequently requested in the NeuroText condition. Messages requesting current affairs headlines were the most frequently requested in the control condition.

#### 4.3.5 Outcomes of RCT

The distribution of scores on the outcome questionnaires were checked to determine whether they had normal distributions. The majority of subscales had normal distribution and so parametric statistics are reported in table 17. Skew values for each measure are reported in Appendix 18.



Group 1= (NeuroText, Control); Group 2= (Control, NeuroText)

Table 17: RCT outcome data

| Measure                      | Group  | NeuroText |      |      |        | Control |      |      |        | Combined NeuroText |      |      |        | Combined Control |      |      |        |
|------------------------------|--------|-----------|------|------|--------|---------|------|------|--------|--------------------|------|------|--------|------------------|------|------|--------|
|                              |        | n         | Mean | SD   | Range  | n       | Mean | SD   | Range  | n                  | Mean | SD   | Range  | n                | Mean | SD   | Range  |
| EMQ-p<br>Frequency<br>total  | Group1 | 13        | 44.4 | 22.7 | 12-75  | 12      | 36.1 | 21.0 | 4-76   | 27                 | 40.3 | 22.9 | 1-83   | 29               | 40.7 | 21.3 | 4-90   |
|                              | Group2 | 14        | 36.4 | 23.2 | 1-83   | 17      | 44.0 | 21.5 | 7-90   |                    |      |      |        |                  |      |      |        |
| EMQ-p<br>Importance<br>total | Group1 | 11        | 70.9 | 17.4 | 35-98  | 11      | 71.8 | 16.3 | 51-104 | 24                 | 73.5 | 17.0 | 35-100 | 25               | 71.4 | 16.7 | 36-104 |
|                              | Group2 | 13        | 75.6 | 17.1 | 37-100 | 14      | 76.4 | 17.3 | 36-99  |                    |      |      |        |                  |      |      |        |
| GHQ total                    | Group1 | 11        | 37.1 | 9.5  | 24-61  | 11      | 44.6 | 18.4 | 22-77  | 24                 | 31.9 | 12.6 | 8-61   | 26               | 39.7 | 16.2 | 21-77  |
|                              | Group2 | 13        | 27.5 | 13.5 | 8-55   | 15      | 36.1 | 13.9 | 21-68  |                    |      |      |        |                  |      |      |        |
| AMEDO Part<br>A total        | Group  | 11        | 37.1 | 8.9  | 19-48  | 11      | 39.2 | 8.3  | 25-51  | 24                 | 38.5 | 7.9  | 19-52  | 25               | 38.5 | 6.7  | 25-51  |
|                              | Group2 | 13        | 39.7 | 7.1  | 28-52  | 14      | 38.0 | 5.5  | 32-51  |                    |      |      |        |                  |      |      |        |
| AMEDO Part<br>B1             | Group1 | 11        | 13.8 | 2.7  | 10-16  | 11      | 14.1 | 2.6  | 8-16   | 24                 | 14.2 | 2.7  | 9-20   | 25               | 13.7 | 3.2  | 3-16   |
|                              | Group2 | 13        | 14.5 | 3.0  | 9-20   | 14      | 13.4 | 3.6  | 3-16   |                    |      |      |        |                  |      |      |        |
| AMEDO Part<br>B2             | Group1 | 10        | 12.6 | 3.3  | 6-16   | 10      | 12.6 | 3.7  | 4-16   | 22                 | 11.2 | 3.7  | 4-16   | 21               | 12.2 | 3.7  | 4-16   |
|                              | Group2 | 12        | 10.1 | 3.7  | 4-16   | 11      | 11.8 | 3.9  | 4-16   |                    |      |      |        |                  |      |      |        |
| EQ5d 1                       | Group1 | 11        | 2.2  | 0.4  | 2-3    | 10      | 2.1  | 0.3  | 2-3    | 24                 | 2.0  | 0.4  | 1-3    | 24               | 1.9  | 0.5  | 1-3    |
|                              | Group2 | 13        | 1.9  | 0.3  | 1-2    | 14      | 1.7  | 0.5  | 1-2    |                    |      |      |        |                  |      |      |        |
| EQ5d 2                       | Group1 | 11        | 1.7  | 0.5  | 1-2    | 11      | 2.0  | 0.6  | 1-3    | 24                 | 1.6  | 0.5  | 1-2    | 25               | 1.6  | 0.6  | 1-3    |
|                              | Group2 | 13        | 1.5  | 0.5  | 1-2    | 14      | 1.4  | 0.5  | 1-2    |                    |      |      |        |                  |      |      |        |

| Measure                      | Group  | NeuroText |      |      |        | Control |      |      |       | Combined NeuroText |      |      |        | Combined Control |      |      |       |
|------------------------------|--------|-----------|------|------|--------|---------|------|------|-------|--------------------|------|------|--------|------------------|------|------|-------|
|                              |        | n         | Mean | SD   | Range  | n       | Mean | SD   | Range | n                  | Mean | SD   | Range  | n                | Mean | SD   | Range |
| EQ5d 3                       | Group1 | 11        | 2.2  | 0.4  | 2-3    | 11      | 2.3  | 0.8  | 1-3   | 24                 | 2.0  | 0.4  | 1-3    | 25               | 2.0  | 0.7  | 1-3   |
|                              | Group2 | 13        | 1.9  | 0.3  | 1-2    | 14      | 1.7  | 0.5  | 1-2   |                    |      |      |        |                  |      |      |       |
| EQ5d 4                       | Group1 | 11        | 2.5  | 0.5  | 2-3    | 11      | 2.7  | 0.5  | 2-3   | 24                 | 2.3  | 0.6  | 1-3    | 25               | 2.2  | 0.7  | 1-3   |
|                              | Group2 | 13        | 2.1  | 0.6  | 1-3    | 14      | 1.9  | 0.5  | 1-3   |                    |      |      |        |                  |      |      |       |
| EQ5d 5                       | Group1 | 11        | 1.8  | 0.6  | 1-3    | 11      | 2.0  | 0.6  | 1-3   | 24                 | 1.6  | 0.6  | 1-3    | 25               | 1.8  | 0.6  | 1-3   |
|                              | Group2 | 13        | 1.5  | 0.5  | 1-2    | 14      | 1.6  | 0.5  | 1-2   |                    |      |      |        |                  |      |      |       |
| EQ5d VAS                     | Group1 | 10        | 42.5 | 24.3 | 17-86  | 10      | 32.9 | 21.5 | 9-80  | 23                 | 53.2 | 26.4 | 14-100 | 24               | 44.5 | 22.5 | 9-92  |
|                              | Group2 | 13        | 61.5 | 25.7 | 14-100 | 14      | 52.8 | 19.9 | 22-92 |                    |      |      |        |                  |      |      |       |
| EMQ-r<br>Frequency<br>total  | Group1 | 11        | 37.6 | 21.2 | 0-70   | 9       | 30.0 | 16.3 | 1-56  | 20                 | 35.0 | 19.7 | 0-71   | 20               | 33.2 | 18.9 | 1-91  |
|                              | Group2 | 9         | 31.7 | 18.4 | 6-71   | 11      | 35.8 | 21.3 | 15-91 |                    |      |      |        |                  |      |      |       |
| EMQ-r<br>Importance<br>total | Group1 | 11        | 68.6 | 20.9 | 30-93  | 9       | 66.8 | 17.0 | 37-97 | 20                 | 70.5 | 17.0 | 30-93  | 20               | 63.4 | 17.2 | 31-97 |
|                              | Group2 | 9         | 72.7 | 11.3 | 57-87  | 11      | 60.6 | 17.6 | 31-81 |                    |      |      |        |                  |      |      |       |
| Daily Diary                  | Group1 | 14        | 14.1 | 16.3 | 0-53   | 9       | 15.1 | 12.6 | 0-37  | 20                 | 8.8  | 9.9  | 0-53   | 20               | 30.0 | 33.9 | 0-100 |
|                              | Group2 | 11        | 8.0  | 9.4  | 0-30   | 14      | 39.5 | 37.7 | 0-100 |                    |      |      |        |                  |      |      |       |

Note: Tests used: EMQ-p: Everyday Memory Questionnaire participant-rated; GHQ: General Health Questionnaire; AMEDO: Adaptation to Memory Difficulties Outcomes Questionnaire; EMQ-r: Everyday Memory Questionnaire relative-rated. Daily diary scores were % target behaviours forgotten.



Paired-samples t-tests were employed to compare outcome scores in the NeuroText and control conditions. These results are displayed in table 18.

Table 18: Comparison between combined treatment and control

| Measure                | t     | df | p      | Cohen's d |
|------------------------|-------|----|--------|-----------|
| EMQ-p Frequency total  | 0.12  | 24 | 0.90   | 0.02      |
| EMQ-p Importance total | -0.85 | 20 | 0.41   | -0.15     |
| GHQ total              | -3.83 | 20 | 0.001* | -0.84     |
| AMEDO Part A total     | 0.23  | 20 | 0.82   | 0.05      |
| AMEDO Part B1          | 1.11  | 20 | 0.28   | 0.24      |
| AMEDO Part B2          | -1.92 | 17 | 0.07   | -0.45     |
| EQ5d 1                 | 1.83  | 19 | 0.08   | 0.41      |
| EQ5d 2                 | -0.44 | 20 | 0.67   | -0.10     |
| EQ5d 3                 | 0.33  | 20 | 0.75   | 0.07      |
| EQ5d 4                 | 0.44  | 20 | 0.67   | 0.10      |
| EQ5d 5                 | -2.17 | 20 | 0.04*  | -0.47     |
| EQ5d VAS               | 2.03  | 19 | 0.06   | 0.45      |
| EMQ-r Frequency total  | -1.66 | 16 | 0.12   | -0.40     |
| EMQ-r Importance total | 0.84  | 16 | 0.41   | 0.20      |
| Daily Diary            | -2.88 | 19 | 0.01*  | -0.64     |

\*treatment effect

Note: Tests used: EMQ-p: Everyday Memory Questionnaire participant-rated; GHQ: General Health Questionnaire; AMEDO: Adaptation to Memory Difficulties Outcomes Questionnaire; EMQ-r: Everyday Memory Questionnaire relative-rated. Daily diary scores were % target behaviours forgotten.

Significant differences ( $p < 0.05$ ) were found on the GHQ, EQ5d question regarding anxiety & depression, and the daily diary. Therefore while receiving NeuroText participants' had less psychological distress and a lower frequency of forgetting everyday target behaviours, compared to control. There were no significant differences between the treatment and control on measures of general everyday memory problems rated by participants or significant other; adaptation to memory difficulties; and quality of life questions regarding perceived health status, mobility, self-care, usual activities and pain.

Effect sizes were calculated using Cohen's d. A large effect size was found for scores on the GHQ, and moderate effect size for the daily diary; AMEDO internal memory aids subscale; EQ5d anxiety & depression question and EQ5d VAS of health.

GHQ and daily diary scores from the first and second conditions are portrayed for both groups in figures 4 and 5, respectively.

Figure 4: Mean total scores on the GHQ

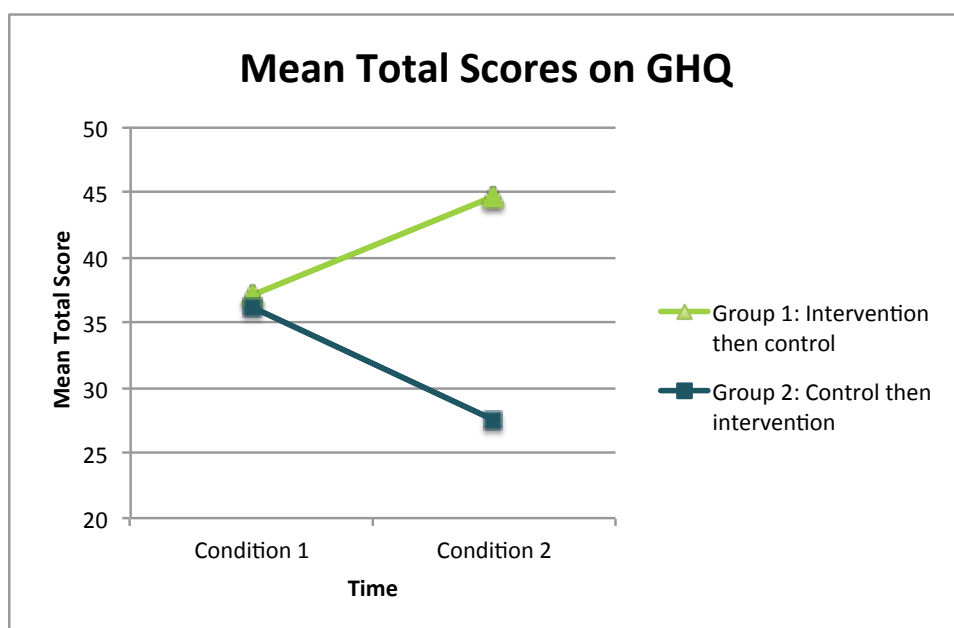
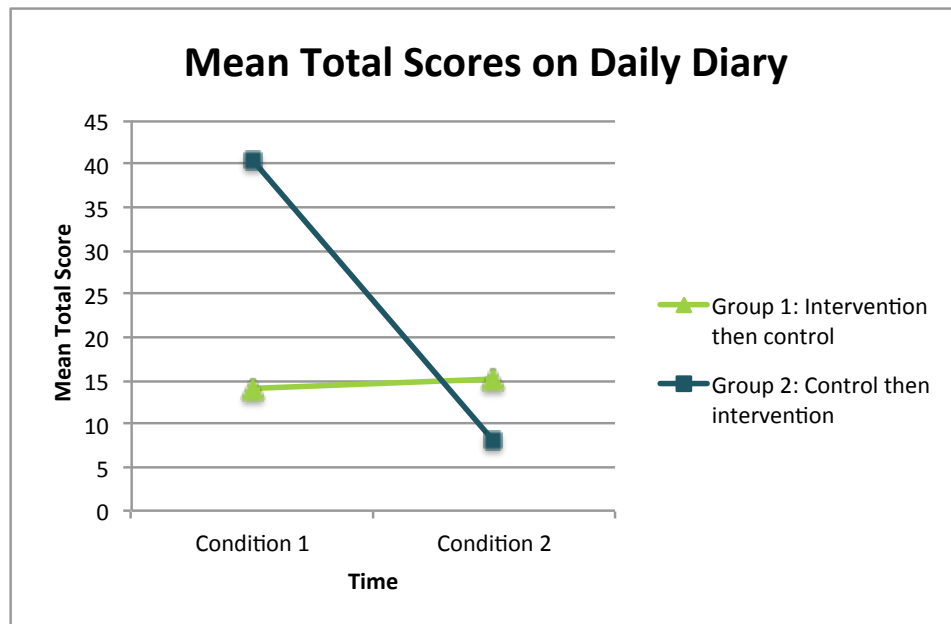




Figure 5: Mean total scores on the daily diary



The data was checked for carryover and period effects using independent t-tests, and results are reported in table 19. There was a significant period effect for scores on the daily diary ( $p < 0.05$ ).



Table 19: Carryover and period effects checks using independent t-tests

|                                 |         | Test for carryover effect |       |    |        | Test for period effect       |       |    |       |
|---------------------------------|---------|---------------------------|-------|----|--------|------------------------------|-------|----|-------|
| Measure                         | Group   | Sum of both condition     | t     | df | p      | Difference between condition | t     | df | p     |
| EMQ Frequency participant total | Group 1 | 81.6                      | -0.23 | 23 | 0.82   | 7.4                          | -1.62 | 23 | 0.12  |
|                                 | Group 2 | 77.8                      |       |    |        | -4.9                         |       |    |       |
| EMQ Importance total            | Group 1 | 144.7                     | 0.51  | 19 | 0.62   | -2.7                         | 0.13  | 19 | 0.99  |
|                                 | Group 2 | 152.1                     |       |    |        | -2.6                         |       |    |       |
| GHQ total                       | Group 1 | 83.3                      | -1.71 | 19 | 0.10   | -6.7                         | -0.51 | 19 | 0.62  |
|                                 | Group 2 | 62.5                      |       |    |        | -8.8                         |       |    |       |
| AMEDO Part A total              | Group 1 | 77.2                      | -0.13 | 19 | 0.90   | -2.8                         | 2.31  | 19 | 0.03* |
|                                 | Group 2 | 76.4                      |       |    |        | 2.6                          |       |    |       |
| AMEDO Part B1                   | Group1  | 27.8                      | -0.22 | 19 | 0.83   | 0.4                          | 0.51  | 19 | 0.62  |
|                                 | Group2  | 27.3                      |       |    |        | 1.3                          |       |    |       |
| AMEDO Part B2                   | Group1  | 26.0                      | -1.58 | 16 | 0.14   | -1.8                         | 0.44  | 16 | 0.67  |
|                                 | Group2  | 21.7                      |       |    |        | -1.1                         |       |    |       |
| EQ5d 1                          | Group1  | 4.4                       | -2.25 | 18 | 0.04*  | 0.1                          | 0.24  | 18 | 0.81  |
|                                 | Group2  | 3.7                       |       |    |        | 0.2                          |       |    |       |
| EQ5d 2                          | Group1  | 3.6                       | -1.53 | 19 | 0.14   | -0.2                         | 1.43  | 19 | 0.17  |
|                                 | Group2  | 2.9                       |       |    |        | 0.1                          |       |    |       |
| EQ5d 3                          | Group1  | 4.4                       | -2.12 | 19 | 0.047* | 0.0                          | 0.28  | 19 | 0.79  |
|                                 | Group2  | 3.8                       |       |    |        | 0.1                          |       |    |       |
| EQ5d 4                          | Group1  | 5.2                       | -2.73 | 19 | 0.01*  | -0.1                         | 1.29  | 19 | 0.21  |

|                        |         |       |       |    |       |       |       |    |        |
|------------------------|---------|-------|-------|----|-------|-------|-------|----|--------|
|                        | Group2  | 4.0   |       |    |       | 0.2   |       |    |        |
| EQ5d 5                 | Group1  | 3.7   | -1.26 | 19 | 0.22  | -0.1  | -0.78 | 19 | 0.45   |
|                        | Group2  | 3.1   |       |    |       | -0.3  |       |    |        |
| EQ5d VAS               | Group 1 | 66.8  | 2.34  | 18 | 0.03* | 6.3   | 0.51  | 18 | 0.62   |
|                        | Group 2 | 108.8 |       |    |       | 11.0  |       |    |        |
| EMQ-r Frequency total  | Group1  | 60.4  | 0.60  | 15 | 0.56  | -0.1  | -1.59 | 15 | 0.13   |
|                        | Group2  | 71.2  |       |    |       | -7.9  |       |    |        |
| EMQ-r Importance total | Group1  | 132.0 | 0.63  | 15 | 0.54  | 0.3   | 0.72  | 15 | 0.48   |
|                        | Group2  | 139.8 |       |    |       | 5.6   |       |    |        |
| Daily Diary            | Group1  | 24.8  | 1.57  | 18 | 0.13  | -5.4  | -2.13 | 18 | 0.047* |
|                        | Group2  | 51.6  |       |    |       | -35.6 |       |    |        |

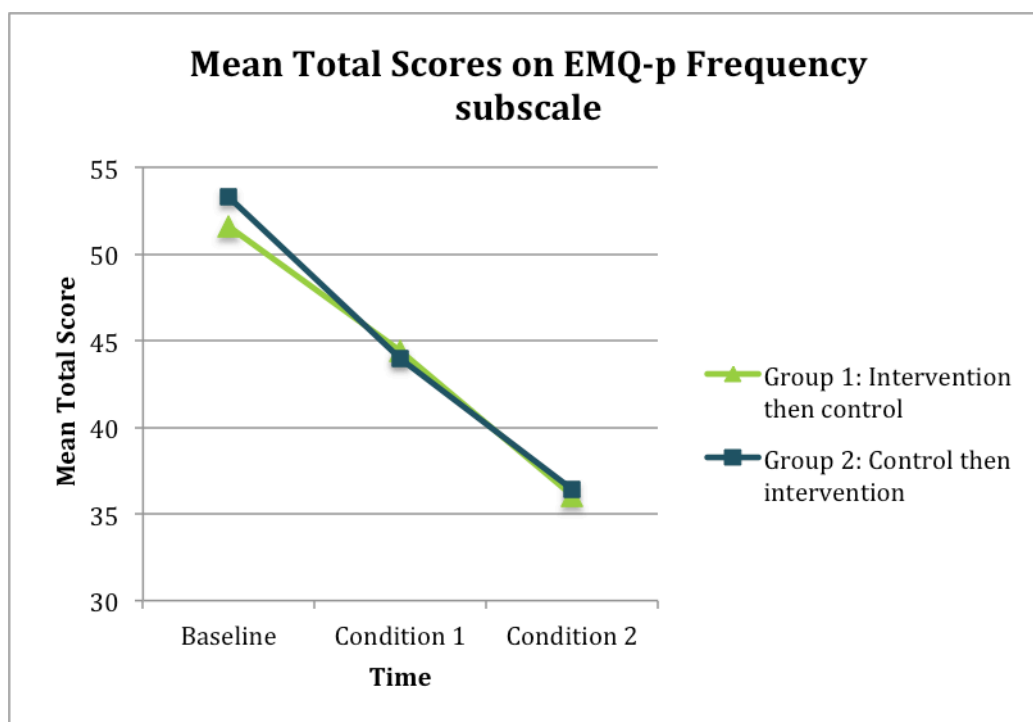
\*carryover/period effect

Note: Tests used: EMQ-p: Everyday Memory Questionnaire participant-rated; GHQ: General Health Questionnaire; AMEDO: Adaptation to Memory Difficulties Outcomes Questionnaire; EMQ-r: Everyday Memory Questionnaire relative-rated. Daily diary scores were % target behaviours forgotten.



EMQ-p frequency subscale scores are demonstrated graphically across the three time-points in figure 6.

Figure 6: Mean total scores on the EMQ participant frequency subscale



Change scores were calculated using baseline, NeuroText and control scores on the EMQ frequency subscale. Change scores are demonstrated in table 20.

Table 20: EMQ participant frequency total change scores

|                       | Mean | S.D. | Range  | t    | df | p    | Cohen's d |
|-----------------------|------|------|--------|------|----|------|-----------|
| Change with treatment | -4.6 | 16.8 | -48-43 | 0.84 | 24 | 0.41 | 0.17      |
| Change with control   | -8.9 | 16.4 | -47-22 |      |    |      |           |

There was no significance difference between change with treatment and change with control on the frequency of general everyday memory questions.

#### **4.3.6 Sample size and power**

Using the GHQ dataset from this trial, the estimated sample size needed for full powered future trial is 54 participants per group. Therefore, considering a 10% allowance for dropouts, 119 participants would need to be recruited. Alternatively using the Daily Diary dataset from this trial, the estimated sample size needed for full powered future trial is 17 participants per group. Therefore, considering a 10% allowance for dropouts, 37 participants would need to be recruited. These estimations were calculated using the Sealed Envelope Ltd. website (2012).





## 5 Qualitative Results

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### 5.1 Chapter Summary

This chapter describes the demographic characteristics of the participants that took part in the feedback interviews. The foci, themes, and sub-themes are explored and supported by participant quotes.

### 5.2 Feedback interviews

Feedback interviews were carried out with 25 participants, and their demographic characteristics are presented in table 21 below. All participants agreed to the interview being audio recorded.

Table 21: Demographic characteristics of participants in feedback interviews

| ID | First group allocation | Age | Sex    | MS Type               | Years since diagnosis | Ethnicity                              |
|----|------------------------|-----|--------|-----------------------|-----------------------|--|
| 1  | NeuroText              | 62  | Male   | Primary Progressive   | 4                     | White British                          |
| 3  | NeuroText              | 60  | Male   | Secondary Progressive | 5                     | White British                          |
| 4  | NeuroText              | 50  | Male   | Secondary Progressive | 23                    | Black/African/Caribbean /Black British |
| 7  | Control                | 72  | Male   | Primary Progressive   | 10                    | White British                          |
| 8  | NeuroText              | 52  | Female | Unsure                | 16                    | White British                          |
| 9  | NeuroText              | 67  | Male   | Primary Progressive   | 16                    | White British                          |
| 10 | NeuroText              | 61  | Female | Primary Progressive   | 19                    | White British                          |
| 11 | NeuroText              | 40  | Male   | Primary Progressive   | 19                    | Black/African/Caribbean /Black British |
| 12 | NeuroText              | 52  | Female | Relapsing Remitting   | 15                    | White British                          |
| 14 | Control                | 32  | Female | Relapsing Remitting   | 1                     | White British                          |
| 15 | NeuroText              | 67  | Male   | Secondary Progressive | 21                    | White British                          |
| 16 | Control                | 53  | Female | Relapsing Remitting   | 3                     | White British                          |
| 17 | Control                | 65  | Female | Secondary Progressive | 33                    | White British                          |
| 19 | Control                | 49  | Male   | Relapsing Remitting   | 9                     | White British                          |
| 20 | NeuroText              | 50  | Male   | Primary Progressive   | 2                     | White British                          |
| 21 | Control                | 55  | Male   | Secondary Progressive | 31                    | White British                          |
| 22 | NeuroText              | 42  | Male   | Primary Progressive   | 4                     | White British                          |
| 23 | Control                | 36  | Female | Relapsing Remitting   | 5                     | White British                          |
| 26 | Control                | 30  | Female | Relapsing Remitting   | 5                     | White British                          |
| 27 | Control                | 34  | Female | Relapsing Remitting   | 10                    | White British                          |
| 29 | Control                | 46  | Female | Unsure                | 1                     | White British                          |

|    |           |    |        |                     |    |               |
|----|-----------|----|--------|---------------------|----|---------------|
| 30 | Control   | 47 | Female | Relapsing Remitting | 2  | White British |
| 31 | NeuroText | 38 | Female | Relapsing Remitting | 1  | White British |
| 32 | Control   | 47 | Female | Relapsing Remitting | 8  | White British |
| 33 | NeuroText | 56 | Female | Relapsing Remitting | 13 | White British |

Themes were grouped by 3 foci: NeuroText messages, Control messages and Overall experience of participating in study. Seven major themes were identified: (i) perceived usefulness of NeuroText, (ii) NeuroText ending, (iii) potential improvements to NeuroText, (iv) potential usefulness of control, (v) control not useful, (vi) positive experience of study, (vii) a few concerns with participation. Foci, themes and sub-themes are summarised in figure 7.

Figure 7: Theme summary

| Foci   | Themes                            | Sub-themes                          |
|--|-----------------------------------|-------------------------------------|
| NeuroText messages                           | Perceived usefulness of NeuroText | Memory related improvements         |
|  |                                   | Improved ability to manage mood     |
|  |                                   | Improved fatigue management         |
|  | NeuroText ending                  | Benefit remained                    |
|  |                                   | Stopped achieving target behaviours |
|  |                                   | Concerns                            |
| Control messages                             | Potential usefulness of control   | Mostly nothing                      |
|  |                                   | Tailored adjustments                |
|  |                                   |                                     |
|  | Control not useful                | Acting as a prompt                  |
|  |                                   | "Gave me a lift"                    |
|  |                                   | Encouraged engagement               |
| Overall experience of participating in study | Positive experience of study      | No purpose                          |
|  |                                   | Irritating                          |
|  | A few concerns with participation | Distracting                         |
|  |                                   | Confusing                           |
|  |                                   |                                     |
| Overall experience of participating in study | Positive experience of study      | Participation                       |
|  |                                   | Enjoyed assessment                  |
|  | A few concerns with participation | Finding out impairment              |
|  |                                   | Commitment                          |
|  |                                   | No benefit                          |

Themes are explored below with excerpts from the transcripts, which highlight the participants' experiences.

## 5.2 Reminder messages

### 5.2.1 Perceived usefulness of NeuroText

#### 5.2.1.1 *Memory-related improvements*

The most highly endorsed notion throughout the feedback interviews was that receiving the NeuroText reminder messages helped participants achieve their everyday target behaviours, which they would have normally forgotten to do, such as, attending appointments, turning the oven off, or taking out the bins.

“They were good because when I got them I put the bins out because I remembered... I usually forget that I’ve got a full bin and I’d have like black bags and stuff and I have to wait another week for them to come again, it helped me, thinking ‘Oh yes, I’ve got the text to put the bins out’, things like that. That was useful.” (ID 27)

Many participants found the reminder messages helpful because it meant they adhered to their medicine regimes, which made their physical condition more stable.

“Yes, well yes and as I say it just meant that the reminders were about reminding me to take tablets at a certain time, it just meant that I didn’t miss those tablets, it just made my sort of condition more stable.” (ID 22)

“‘Take your medication’, ‘Pick the child up from school’. Yeah it was great. I haven’t missed any of my injections... they saved me missing my injection. I think I missed it once in the whole time and I usually miss it a lot. I didn’t miss any medication. Yeah.” (ID 23)

In all these instances, the participants report a direct connection between the content of the text message (e.g., ‘take your medication’) and there is some indication of the timing of the action to be completed (e.g., ‘...when I got them I put the bins out...’). After receiving the NeuroText reminder messages for a while, some participants, however, reported that the process of receiving the messages was

acting as a prompt. When the “beep” of a message came through, they would observe the time and anticipate the content of the message.

“They were very repetitive, but that was kind of good because that, sometimes I would think ‘Oh, I know what that is, I’ve got to do this’. So, they did work. They did work extremely well.” (ID 29)

“When it was half past seven, or eight o’clock, the texts would come through, I think it was eight o’clock and I would think, even with that little ‘beep’ ‘I’ve got to check the diary! I’ve got to check the diary, you know?’” (ID 31)

In fact, some participants did not even feel the need to read the reminder message, because the previous repetition of the messages meant that they knew what they had to do when the message came through.

“Well it got to a stage where I wasn’t even looking at the reminders as they came in to remind me to do a particular thing, it was almost like well, what time is it, well that reminder will be for... so it was almost jogging my memory, I didn’t actually, necessarily need to read the reminder...because I knew roughly what the reminder would be about.’ (ID 22)

As mentioned, some text messages prompted a reactive response from the participants, e.g., taking medications when prompted. However, for some participants, the reminder messages appeared to get them into a routine.

“To start with it was unusual, but then every time a text came through, I know what it was going to say, because I got used to the times and everything of what it was going to say and it, yeah the times, the dates... It’s brilliant, I tell you.” (ID 9)

Again, there is a suggestion that this action was in response to the prompt, not necessarily the content (‘I know what it was going to say’), but there is a sense of routine formation here (‘I got used to the times...’). Interestingly, some participants started anticipating when the message would come through, and even perform the

behaviour just before receiving the message. This response was most commonly seen with regard to taking medication.

“It was a nice surprise because I’d forgot all about it. Some mornings I’d err, some mornings I’d remember it was coming and if I’d remembered, I would take the medication before it comes and I would think ‘Yes, I took it, thank you.’” (ID 19)

“What I found was that the text would go off and I would think ‘Oh I need to take my tablets’, just about the same time, so I got into a habit of knowing the times I should be taking them.” (ID 33)

The fact that participants were achieving their target behaviours, and had more of a daily routine, enabled the participants to feel more organised and focussed on what they needed to do.

“Well, it generally just helped me get a lot better organised than I had previously been and focussed me a bit better on, yeah I did have problems from time to time for different varied reasons and when I know I’m going to have a problem or I think I might be having a problem I can take action to lessen the impact of it... just keep me focussed on you know sort of doing what I knew I had to do but often wouldn’t, you know if you’re just left to your own devices and you think you know right I must check my to do list you would just procrastinate all day long and wouldn’t get it done.” (ID 3)

Participants reported that the reminders made their day more structured, which allowed them to plan ahead.

“Yeah, it was fine, it was absolutely, it was okay, it was helping to sort of structure the day a little bit better, so it worked very well.” (ID 22)

“Well they were good because it gives you time to plan ahead sort of thing and know that you’ve either got to get there and arrange whatever you need to do, you know if you have looking ahead, you know that you have some warning, sort of thing.” (ID 33)

Furthermore, in association with their improved planning abilities, participants reported spontaneously employing other memory strategies into their everyday life during the study, including external memory aids. Using aids such as, calendars for appointments and creating lists, allowed participants to enhance the benefit they experienced from the reminder messages.

“I do tend to write things down, like when I go shopping I do write my list and actually remember to take it...And I write things, everything is on the calendar and I do check the calendar every day to see what’s going on, even in advance if it’s written in the calendar, like dental appointments, hospital appointments, children’s things like school lunches, it’s all written on the calendar and I do look at the calendar in the mornings to see what I’m doing to make sure I don’t forget to do anything. So yeah it has been a great.” (ID 10)

“It was great. It was really, really it really helped me, encouraged me to check the diary... we went and got a magnetic calendar to put on the fridge, so it’s in my face, all the appointments, like I’ve got the doctor’s next week, then I’m going to Wales next Friday...but I need this in my face and I go to the fridge every day so...” (ID 31)

One participant also reported using internal strategies, such as consciously increasing concentration.

“Yes, but it was helping me concentrate, let’s say that for some unknown reason I needed a pencil and some additional medication so getting back to the analogy that I’m going from the living room into the kitchen... there should be two things, I was trying things in my head that when I was actually holding on to my Zimmer I was putting two fingers together so I’d got to remember I was going in for two things, not one, so that sort of thing again sort of helped me.” (ID 7)

A portion of participants disclosed that prior to the trial they had often forgotten what day of the week it was. Therefore they found that reminders saying, e.g.

“Good morning, today is Tuesday”, gave them something to refer back to and oriented them to the day and place in the week.

“That was nice because I didn’t have to um search around for... because sometimes I really have no idea, so that was nice. I knew it was Wednesday and in my mind I kind of knew what I had to do that day... Because it is like waking up and not knowing where you are in time, rather than geographically. Um it is easier if you wake up and immediately, or soon you know exactly what date it is, you know what you have got to do that day and you know.” (ID 8)

“Yeah the day and the date, was always handy... Yeah because as you probably realised when you’re on holiday it’s impossible, it’s really hard remember what day it is anyway, you have nothing to refer back to and that’s always the, I always think it’s a Friday, I think that’s wishful thinking.” (ID 12)

Knowing what day of the week it was meant that participants knew what they needed to do, or where they were supposed to be.

“Because I could tell what day it was and know what was happening. When the children were going to college or school or whatever. I could work that out when I knew what day it was... Normally I usually phone my mother up on a Sunday and if I didn’t know it was Sunday then I would never phone her, she kept going ‘Oh, that because you know what day it is’.” (ID 30)

#### ***5.2.1.2 Improved ability to manage mood***

A large proportion of participants reported that they were coping better as a result of the reminder messages. The fact that participants were not forgetting things made them feel less anxious and frustrated.

“I knew it was Wednesday and in my mind I kind of knew what I had to do that day. Um, because I do regular things, I go to the MS Centre twice a week and so it was nice to know that I was on track and I

wasn't forgetting things... It makes you feel less anxious about things...yes. That is the best I can describe it I'm afraid." (ID 8)

Not forgetting things meant that participants were being kinder to themselves; they stopped accusing themselves of having a 'bad memory', or being useless.

"I didn't constantly feel like I've got a bad memory. You know, I didn't get annoyed at myself, if I hadn't done this or I hadn't done that and yeah... It stops the frustration I suppose... I'm quite a positive person, but just sometimes it's frustrating and embarrassing having to feel, not low, but I suppose you just feel a bit 'Oh!' because you try, I always give myself, I give 100%, so when my 100% was nowhere near good enough to even do simple tasks, it feels quite frustrating... It helped me physically and mentally, it made me feel not quite so useless and forgetful and frustrated." (ID 23)

Furthermore, participants felt reassured that they were not going to forget any important appointments, or arrangements with other people. Often the reminders gave participants a chance to acknowledge that they had already remembered an intended action, but perhaps more poignantly, the reminders acted as a reliable safety net for those times when they would have otherwise forgotten.

"Oh just much better knowing that you can rely on it and it'll come through and you then go and take, or whatever the reminder was about. It definitely, definitely was helpful... Um, I think knowing that you can, that it's something that you don't have to remember. Cos without it, there is no shadow of a doubt, I wouldn't remember. So it's like your, it's a crutch really and you know you can rely on it 'cos it's always going to come through." (ID 32)

This meant that the participants felt like they were more in control of their life and more secure in their organisational abilities, because they were remembering what they needed to, and knew what was happening.

"It was good because it was useful to me that I knew in my own mind, what was coming up and what I needed to do... Yes, it made



me feel that I was probably more in control of things because... that I'd remembered what was going to happen. I remembered what I should be doing." (ID 15)

"[Made me feel] in control. I know it sounds daft, but it's a little thing, but because I remember to check, you know it's like 'Wow! Check me out!'" (ID 16)

"A bit more in control. Even though someone else was telling me to do it, yeah, it was definitely more control, but it wasn't a constant reminder that I'd forgotten something or that I'd not done something... Yeah, it made me feel a bit better within myself because, yeah more in control and not constantly forgetting things." (ID 23)

Not having to worry about forgetting important things at work or home meant that participants felt less stressed.

"It's a lot more positive so, you feel less stressed about work, so you don't have to worry about writing stuff down all the time... It just allowed me to kind of focus my thoughts on other sort of random, non-routine tasks...just helped alleviate some stress about not having to worry about particular tasks or had I done a particular task or had I remembered to take tablets or whatever at the required time." (ID 22)

"You're then less stressed about, you know, it's just something you can cross off your list because you know you are going to get a reminder. So you know, I've never got to worry about it. I know that's always going to come through and you're less stressed cos you know that it's going to stop you from, from forgetting something like your meds, which are really important." (ID 32)

Additionally, the reminders alleviated stress by reducing the amount of time wasting, where participants previously would have to backtrack because they had forgotten to do something significant.

“So it must have saved me miles and miles of going into town and coming home and forgetting that I needed to go into town, cause I’d get a text at the end which would say ‘Do you need anything from town?’ and I thought ‘Oh yes I do’ and it was great... They saved me a lot of money with fuel. They saved me time, they saved me rushing.”  
(ID 23)

#### ***5.2.1.3 Improved fatigue management***

As mentioned before, participants reported how the reminders led to an improved ability to plan and organise their days. They also talked about how their energy levels would quickly deteriorate, and how the reminders helped them to pace themselves better, and plan their schedule accordingly. Therefore this enabled them to more effectively self-manage their fatigue.

“The fatal thing with MS is you know when you feel quite good you tend to do too much and over tire yourself and everything goes to rack and ruin very quickly if you’re not careful and that can last for a few days, so now I am much more careful about committing to what I do in terms of physical things and mental activities, so that I’m sort of getting enough... pacing myself generally a lot better.” (ID 3)

“Well it was useful in the amount I’ve got my motivation that turns around to me and says I’ve got this, this and this to do and then I’ve got my actual energy levels which unfortunately the two do not equal each other so I have to make some conscious decisions ‘what am I going to do and what am I going to sort of leave out’ so it was drawing me to think what actually I should do and it was re-emphasizing my to do list, was something that I must pay attention to so it was definitely helping me.” (ID 7)

“I do like to know what I’ve go ahead of me, so that I can try and plan my energy levels accordingly. Um and know if I’ve got time to stop off and get a pint of milk, or whatever, rather than running round or just sitting down on the sofa and then sometimes I find I am not able to get up again, whereas if I keep sort of wandering a little bit in the house, I know I’ve, I am alright to go out if I need to... But with my MS, if I sit down, sometimes that’s it. I sit down and that’s it for the day, so it’s helpful to have a mental image or plan of what I need to do.” (ID 8)

## **5.2.2 NeuroText ending**

### ***5.2.2.1 Benefit remained***

The majority of participants talked about how they responded to the NeuroText reminders finishing. Many of them reported that the benefit of the reminders remained even when they had stopped. Spontaneous implementation of other external memory aids helped some participants to maintain the benefits, including using reminder functions on their mobile phones, or using paper-based or electronic calendars.

“Yes, I had to after the messages stopped because I did start forgetting things again... I thought if I wrote things down and stuck them on the fridge because I’m always in and out of the fridge and I would see the messages that I’d written to myself.” (ID 10)

Some participants tried to replicate the NeuroText, by setting up alerts containing the same content at the same time, just using a different platform.

“Well I was going to say since it stopped I left a bit of a gap so I’ve now found I’m recording reminders to myself a lot more than I used to on my mobile phone, so I’m doing similar to what you were doing for me, for myself.” (ID 3)

“I’ve set up reminders, sort of daily tasks that I have to complete... Its been very positive, as I say its just allowed me from those original text message alerts to kind of set up something similar with my work based calendar to kind of send myself text alerts, well not text alerts but email alerts.” (ID 22)

Other participants found that the routine created by receiving NeuroText was maintained even once the reminders were no longer being received. Therefore they were still performing target behaviours at the intended time.

“I enjoyed having them texted, it was a reminder to take me meds at the start of the day. Even when they finished...when they finished I still got into a routine of taking them in the morning. Occasionally I still forget, but normally I remember that because I was taking them religiously at the time when I got the messages, I remembered what it was.” (ID 19)

Interestingly, participants reported that they would notice the time of day, think of the message they would have been receiving, what the content would have been and then act; rather than simply thinking of what they should have been doing at that particular time, and acting on it.

“I found the repetition, sort of ingrains it within my mind, when at certain times of the day I knew that the phone was about to ring, and when it rang, it was going to remind me for my evening Amitriptyline, or my, or my morning tablets and things throughout the day. So, I think that stayed with me and it is still the same now... Yep.” (ID 15)

“Then I got into the habit of taking them as soon as I had the text message and now that I am not getting the text messages, I think ‘Oh this is the time I would get my text message!’ so I take my tablet!... You know, 98% of the time, I do take them when I should. All because of those messages.” (ID 16)

#### **5.2.2.2 Stopped achieving target behaviours**

For some participants, once they stopped receiving reminders, they reverted to baseline and forgot to perform their target behaviours again.

“When would it be, Monday... Putting the bins out on Tuesday, that was really, really good because I’ve started forgetting again already. I don’t know really, that was all that I did, but I did enjoy it and helped with the bins.” (ID 27)

Furthermore, the fact that they had started to forget their intended actions again appeared to dismay participants.

“I miss my Wednesday night one. It’s the thing of... I miss them and I forget things...Yep, exactly how they were before!” (ID 23)

“I mean I found now that I haven’t got them that I’ll sometimes get to like twelve o’clock and I’ll think ‘Blow, I haven’t taken my first one’ and I’m due my second one, so it’s just... it does have an impact on your day.” (ID 29)

#### **5.2.2.3 Concerns**

Since they had started to forget again, numerous participants reported ‘missing’ the messages once they had finished, and that they would have liked them to continue.

“I was expecting them and thought they would be useful to carry on, because they were useful to have... I miss them.” (ID 1)

“Oh that study was marvellous! I didn’t forget nothing, you know when the – ‘cos I was getting the message every day, to check the diary... It was great and I am lost now I haven’t got it... Yes. Big time, I do miss them.” (ID 31)

In fact, some participants appeared to have an emotional response to the cessation of NeuroText.

“It did sort of brighten me up quite a lot really although I was going through quite a bad patch, but I did find it useful. I was quite sorry

when they stopped actually, so you know but as I say that's how life goes on, I was really quite happy to receive them." (ID 7)

Several participants thought NeuroText was so useful that they enquired whether NeuroText would be available outside of the study.

"It was actually really useful and really nice and I think that it would be something that was very useful if you could eventually come up with something I would definitely be interested." (ID 4)

"No, I want them to keep it on. I don't want them to be just a study!" (ID 31)

### **5.2.3 Potential improvements to NeuroText**

#### ***5.2.3.1 Mostly nothing***

The vast majority of participants were happy with NeuroText as it was, thought it was useful, and did not recommend any changes.

"No I think they were the right ones for me and worked well and as I say I am to a large extent am replicating those with my own diarisation in the mobile phone." (ID 3)

"Not particularly no. I thought the reminders were quite useful in the format that they were because I was expecting them and knew what to expect." (ID 15)

"No, I thought they were fantastic as they were. They were direct, straight to the point and they gave me an order and I obeyed." (ID 16)

#### **5.2.3.2 Tailored adjustments**

A couple of participants thought that making the reminders more specific to the individual would make them more useful; this was usually regarding specific appointments.

“I suppose if they could be personalised to me, that would have made them more useful.” (ID 8)

“I suppose it has to be more tailored to the individual and say ‘You’ve got an appointment at 2 o’clock this afternoon’ text at 1’oclock... Maybe, be more specific about the appointment. Instead of just checking your diary, ‘You have a hospital appointment’, or ‘You are going to the theatre’, or to tell you exactly what the appointment is.” (ID 17)

Others suggested that reducing the frequency of reminders, or limiting the days they received specific messages, would have been helpful for them.

“What I was thinking was if instead of having them as regularly as I was getting them they were maybe even spread out and not as frequently as I was getting they would have been helpful.” (ID 4)

“Chores throughout the day, because some days wouldn’t have been the same, say sort of a weekend you know I probably wouldn’t have done the washing and different things, so those ones, not always.” (ID 29)

A few participants thought that reducing the overlap with other reminder services would be an improvement. Again, this was mostly regarding appointments, and the automated reminder services that have been recently introduced.

“They were okay but they are not so important because [the doctors] telephone me with text messages anyway, they send me messages the day before anyway, a text message, so I already get messages from them, so they’re not so important.” (ID 1)

“Having said that, the physio has now started using a text reminder scheme, so I think in my life, my experience, more and more people seem to be using a system similar to what you are talking about.” (ID 33)

It should be noted that most of the participants who suggested the above improvements did acknowledge that they could have altered their NeuroText messages to reflect these recommendations, at any time in the trial.

## **5.3 Control Messages**

### **5.3.1 Potential usefulness of control**

#### ***5.3.1.1 Acting as prompt (control)***

Several participants reported that the control (non-reminder) messages acted as a prompt. Participants recognised that when a control message came through to their phone, it was at the same time as they had previously received a reminder, or had previously performed a target behaviour as a result of a reminder. Therefore, this response of the control acting as a prompt was observed if the participants had already received the NeuroText messages in the previous condition.

“I thought they were round about the time when I was waiting for the calls. I was waiting for the headline, I was waiting for the calls to come and err...the headline came in place of a call about medication.” (ID 15)

“But after a little while I realised that as a reminder, that I would have been checking my medications, so I took me medication. I kind of triggered me memory... I was like ‘Oh, something about the weather, oh, I haven’t taken me meds yet, I’d best go and take them.’” (ID 19)

For some participants, their response to this prompt was to perform the target behaviour, for example, take their medication. However, for other participants, the



priming effect reduced as time went on, and the control messages ceased to act as a prompt.

“Yeah well partly when I was on the placebo one, I would open the message and just see, just look at my phone and it would say BBC whatever, and I would think ‘Oh yeah that’s meant to be for my tablets and then...’ in the beginning, but as time went on, I would just look at it and I wouldn’t think what it’s actually reminding me about. My brain would kind of switch off on it.” (ID 32)

Additionally, some people did not make the connection between the timing of the reminder messages, and the control messages at all.

“I wasn’t at all. I thought they were just random, annoying texts... I hadn’t made that connection.” (ID 33)

#### **5.3.1.2 Gave me a lift**

Another positive response reported by some participants, was that receiving the control messages gave them an on-the-spot mood lift.

“Um they cheered me up! They cheered me up in the morning and I had something to smile about before I had to face the world... it was just something nice before I had to start fighting the world again... I really did like that because they cheered me up even though I didn’t realise I needed cheering up, if you know what I mean... I’ve been through a bit of a rough time the last sort of six, eight months, but yeah, that made it slightly better for me.” (ID 8)

No I was quite happy with them to be honest with you. It was a nice surprise to have them coming through to start off with.” (ID 19)

“Erm, well they really gave me a lift actually, you know, some of them were really good...” (ID 16)

One participant even stated they would enjoy receiving the control messages outside of the trial

“No not really just really, just to say that if you were going to start doing something like this in which you would focus on particular sports, particular teams and stuff like that I would be very interested yeah.” (ID 4)

#### **5.3.1.3 Encouraged engagement**

Several participants reported enjoying receiving the control messages, and finding the content interesting to read.

“I enjoyed having them come through still and then some of the results that came through I was really interested in and I had been following and some of those I wasn’t, so it was nice being able to you know make the choice to what I listened to and what to follow and what not.” (ID 4)

In particular, participants who received current affairs or sport headlines, liked the fact that they were more up-to-date with the news, than if they had not received the messages.

“Err, absolutely brilliant because I might have missed something and then you’ve sent it through, whatever it was, of course that keeps you, you remember it.” (ID 9)

“It’s little pointers in that of oh that’s interesting and that’s interesting and they were really good, I liked those and that because, like now I haven’t put the TV on, you know all morning since I’ve got up and stuff and so by having those little pointers are brilliant, you’re like ‘ahh that’s nice’.” (ID 11)

The control messages encouraged engagement for some participants, who followed the Internet link from the headline, to the full news article.

“If something caught my eye, which it quite often did because the Guardian put some really good stuff out sometimes, I obviously went on to that and really quite enjoyed it... And of course there were certain headlines that were catching my attention.” (ID 7)

One participant reported that they would follow the link to the full article, and then go on to read further articles.

“Yes, definitely so if I got a message of a score or something and then I’d go online and look further at what it was, what the message was, and they were good for that you know... what it does you’d get them through and you’d look, it just makes you look more in depth at whatever it was and you’d find other stuff you know. It’s just like on a search engine, it was good... just encouraged more activity and for you to look at more stuff and things like that.” (ID 11)

Another participant found that the news headlines made him attend more closely to articles in his newspaper, and read them in more depth.

“Well, I received the news headlines and then, it was about the time in the morning when I get my morning paper, so as I went through my morning paper, I’d be looking for headlines that matched something that you had tried to put across to me... I suppose it made me more, look at it in depth for anything coming up. Instead of just accepting the headline, I would read what was behind the headline and why it was presented.” (ID 15)

Additionally, a couple of participants reported feeling that the control messages made them feel a bit more connected to the outside world.

“Well they were just funny, or they made me think about what the messages were, the news ones and I said I thought ‘Oh, I wonder where she’s got that from, I’d like to read that’. You know, but they did give me a bit of a lift and for some strange reason I don’t feel alone! Weird!” (ID 16)

“I think the news and sports information didn’t really, I keep myself quite informed anyway so it, they were nice to receive from a feeling of involved sort of situation but didn’t really do an awful lot in terms of... the main ones were sort of the action to check my to do list, not

to procrastinate and get on and get things done, were much stronger in terms of in pact on me, yeah.” (ID 3)

### **5.3.2 Control not useful**

#### **5.3.2.1 No purpose**

Many participants felt that the control messages were not serving any purpose, and that they did not particularly enjoy receiving them.

“Not particularly useful for anything really. Most of them I thought ‘what?! What is this about?’ Yeah, it weren’t particularly relevant or anything. No.” (ID 17)

“I just lost interest in it you know what I mean, that’s all, I just lost interest. No weren’t too keen on those ones at all.” (ID 21)

Participants reported ignoring the control messages, particularly after they had been receiving them after a while.

“A lot of the time I would just have a look and I wouldn’t, even follow the link through. Maybe because of time, that you know, I’ve got quite a busy household and you know, I wouldn’t have the time to erm, to actually look at them.” (ID 29)

“After a while it came up ‘Oh, ok’ and I didn’t really acknowledge what it was reminding me of. So I just would look at it and then just ignore it.” (ID 32)

The control messages were deemed useless by many participants, and they pointed out that the messages were not effective in reminding them to perform tasks.

“Yes. The one that, I know one of the reminders was on a Monday night to make sure the bins were out and that would come through and when I was on a placebo I didn’t even remember that that was what it was for.” (ID 32)

Some participants stated outright that the NeuroText reminders were more useful than the control messages.

“Didn’t really do an awful lot in terms of... The main ones were sort of the action to check my to do list, not to procrastinate and get on and get things done, were much stronger in terms of in pact on me, yeah... Erm, I think as time went on they became more of a nuisance than a benefit.” (ID 3)

“Well, I’d read them and some of them were a little bit funny so I’d laugh and just put my phone and I’d just carry on and then I’d think ‘Bloody hell, me tablet!’ you know, so although I enjoyed receiving them, they didn’t really get me trained as such, as the more direct ones which worked brilliant.” (ID 16)

#### **5.3.2.2 Confusing**

Initially the control messages confused some participants, as they were unsure of the origin of the messages.

“It was quite funny actually because I kept forgetting that you were sending these messages and I thought ‘what on earth is that’ then I sort of twigged and thought ‘yeah I know what it is’.” (ID 10)

“To be honest with you, the first lot was to do with the news and I kept on thinking ‘what it this weird thing sending me things to do with the news?’ And then after about the fifth one did I think, ‘Oh, I know what it is’.” (ID 14)

One participant pointed out that if they had identified those “random texts” as the trial control messages, they would have found them less annoying.

“Yeah, I think if I’d known why I was getting all these random texts, then I would have found them less annoying because they kept coming through and they didn’t seem to relate to anything I was involved in and I started at one stage to think that my phone had

been hacked, or my emails had been, or that something wrong was going on and I think at one stage I did actually ring you and ask about them, or did you contact me..." (ID 33)

#### **5.3.2.3 Distracting**

The content of the control messages distracted some participants directly away from their target behaviours, for instance, where they found themselves involved in a news story, rather than taking their medication.

"I found me mind wondering once I'd read 'em, wondering where they were from and you know, so, the more direct ones worked far better for me and they were the ones that trained me... I did notice the timing and I knew I'd got to take me tablets, or I'd got to be doing something and they worked to a degree, but not as much as the direct ones. Because as I say, I got that distracted reading them I thought 'Oh, I wonder where she got this from, I love to read that in full' do you know what I mean?" (ID 16)

"My brain would kind of switch off on it. So I would just look at it and think, 'Oh yeah, BBC whatever' and sometimes whatever the current affairs thing was, it might be that that actually interested me, so I would be on my phone looking at it and by the time I came off it, I'd forgotten about [target behaviour] anyway." (ID 32)

#### **5.3.2.4 Irritating**

Many participants reported finding the control messages irritating. Some found that they already knew the content of the news headlines, or that they did not find them relevant.

"Yeah, they were just general information that generally I knew anyway or wasn't particularly exciting for me." (ID3)

“I really don’t know with that one because I read the, I go on the newspaper every day, so I didn’t, if I wasn’t going on the newspaper then maybe, but because I go on the newspaper every day, I wasn’t gaining anything from it. I know that sounds bad, what I am saying, but I am being very honest about.” (ID 14)

“Well I think the new news because I used to look at it anyway.” (ID 20)

Other participants found that the control messages were too repetitive, in terms of content.

“To be honest with you, the news ones, I thought they were repetitive, to say the same story time and time again.” (ID 14)

“No, not really. I think they repeated quite often.” (ID 32)

“So I found the other one, the entertainment news one quite frustrating and annoying, but hey ho... It just seemed to be the same stuff being sent and it was sort of, I felt it became a bit of an inconvenience, but it was all part of the trial, so...” (ID 26)

However, despite the perceived negative elements of the control messages, most participants demonstrated that they understood the purpose of the control messages in the study, and therefore accepted them.

## **5.4 Overall Experience of participating in study**

### **5.4.1 Positive experience of study**

#### ***5.4.1.1 Participation***

Response to participation in the study was overwhelmingly positive, and overall participants were pleased to have been involved in the study.

“They did [help]! They really did. It was a positive experience all ways round.” (ID 16)

“Yeah, I was really pleased with what you did, I tell you. I can’t remember everything now, but I got them on me phone.” (ID 9)

“It would be nice to know that I’ve helped someone achieve something.” (ID 8)

The study provided comfort for participants, and some expressed gratitude for taking part.

“Yeah because [husband’s] memory’s not that great these days and I said mine is better than yours now. So yes, it has helped me an awful lot and I’m grateful that I’ve been on the trial.” (ID 10)

“No, thank you for... thank you for helping me. You have helped me a lot, even though it was only a little thing. It made a great difference to me, so thank you very much Rachel.” (ID 19)

One participant disclosed that they normally dislike engaging with health professionals because it highlights the fact he has MS, which makes him feel disheartened. However, his participation in the study allowed him to acknowledge he had MS, and that he was not alone in the journey.

“I don’t actually like going to see health professionals if I can help it because, it sort of draws attention that there is something wrong with me... so I sometimes can find if I say the doctors been to see me or some other person I sort of feel quite down afterwards but I was finding that actually getting these text messages was actually make me think ‘oh right I’ve got MS I’m not alone in this’ because somebody else is actually contacting me although it being a text message but it, I was actually getting quite a big degree of comfort actually getting these text messages sent so umm but that is definitely an additional point and a very real one to me.” (ID 7)



#### **5.4.1.2 Enjoyed assessment**

An unanticipated response to participation was that several participants reported enjoying the baseline assessments, and finding the tests interesting.

“Was brilliant, really brilliant...Well all the information you taught me about the shapes and everything and what I decide on, you know whether any are right and everything. Then the first stage and all the different images that you gave me, was one the same, or smaller than the other. With squares, circle... yeah.” (ID 9)

“I don’t know what that was, but it was interesting, it was interesting to do. I can’t really remember what the other tests you did, I know the one with the doors because that was really exciting.” (ID 11)

“Ok, initially for the assessment phase of it, I found it really interesting because I do assessments of a similar nature, so it was very good, very useful to see it from the other side of the fence.” (ID 33)

Specifically, one participant likened the tests to “brain training” and enjoyed the fact that the assessment required him to exercise his brain.

“Well it was quite interesting because I was thinking about stuff and using my brain, bits of my brain that I haven’t used for ages. It was quite difficult but I really enjoyed it and you don’t realise, you see I don’t know if it’s because I have MS or not or whether I’m a bit stupid or not but you don’t know how difficult certain things are, but once you get used to it. You know we started doing those looking at doors... I think it was and going over it, the more you go over it, it’s like brain training, the more you do it the better you become at it.” (ID 11)

Furthermore, for some, the assessment provided validation that their memory was not as impaired as they had originally thought.

“Yes! It was completely the opposite to what I would normally say when I was actually doing a practical, completely different. I was ‘Ok,

I'm not that bad actually'. It was good, it was a bit of a confidence boost." (ID 14)

"I actually enjoyed it. I enjoyed knowing I wasn't as bad as I thought." (ID 8)

#### **5.4.2 A few concerns with participation**

Despite the positive reaction to participation in the study, a few concerns were raised. Initially one participant was apprehensive about what level of commitment would be expected.

"And err... And the commitment, what the level of commitment was, but yea it was fine yeah I didn't find it too arduous and my son luckily was happy to take part in it as well." (ID 3)

The same participant was also initially nervous about the prospect of finding out his level of cognitive impairment.

"I think it was sort of what, what might be found out about my good or bad memory traits." (ID 3)

One participant reported that she did not find any benefit of taking part in the study, however she did not mind taking part.

"It was fine, but it made no difference because they were items that I hadn't forgotten. You know you think, if I'd forgotten it would have been a blessing, but because I wasn't forgetting those particular items, it wasn't a big deal to me... I didn't find it beneficial." (ID 14)

## 6 Discussion

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### 6.1 Chapter overview

This chapter will first assess the feasibility of running the study with people with multiple sclerosis. The findings of the randomised control trial and the feedback interviews will then be discussed. Findings will be considered in the greater context of the literature, and the limitations of the present study will be reviewed. The implications for future research and clinical practice will be considered.

### 6.2 Summary of the study

The aims of the study were to evaluate whether receiving NeuroText messages reduced everyday memory problems; increased attainment of target behaviours; and improved mood and quality of life, compared to receiving control messages. A phase II exploratory RCT was successfully employed across multiple sites, to evaluate the effectiveness of the intervention. The feasibility of the study design, intervention, control and outcomes was assessed. The primary outcome measure was the EMQ; quantitative measures of attainment of target behaviours, mood and quality of life were also employed. Feedback interviews were analysed using framework analysis to generate themes.

### 6.3 Discussion of findings

#### 6.3.1 Feasibility

##### *6.3.1.1 Recruitment*

The trial was conducted over 24 months (November 2013 – October 2015), however recruitment took place within 12 months of this period (April 2014 - March 2015). Potential PIs for the original four sites were identified prior to ethical and R&D approval in preparation for recruitment; however the final approval was gained at the end of November, and progress was very slow over the Christmas holidays and in January. Meetings were set up early 2014 to ensure PIs had all the

appropriate documentation and were clear on the referral procedures. The first participant was recruited into the study in April 2014.

Referring clinicians appeared to recognise the potential of the study and seemed keen to refer patients who met the inclusion criteria. Throughout the recruitment period PIs were contacted monthly about referral and recruitment rates, and the researcher attended periodic meetings at PIs' places of work to refresh interest in the study amongst clinical teams. However referral rates remained slow, and it was clear protocol amendments were necessary to boost recruitment, therefore when the trial was halted due to technological problems, amendments were made and gained ethical approval. The protocol changes allowed clinicians to aid the completion of contact details forms and send them to the researcher on behalf of participants, meaning that participants with memory problems didn't have to remember to complete and send them independently. Additionally the screening measure was administered over the phone. These changes reduced the amount of time and effort needed to make a referral by both clinicians and their patients. Furthermore, an additional site was added and recruitment dates were extended. Additional actions boosted recruitment: CRN research nurses referred at two sites; researcher attendance at MS clinics, MS Society research morning and further team meetings. These implemented measures were successful, and therefore the majority of referrals and recruits were made between September 2014 and March 2015. Therefore if a definitive trial was to be performed, the amended protocol should be employed.

One hundred and three people with MS were assessed for eligibility, and of these 50 consented into the study. Of the 53 excluded, the majority 'did not want to take part', most commonly this was because they experienced memory problems, e.g. forgetting names, but not prospective memory problems. It would have been useful if clinicians, prior to referring, had employed a prospective memory screening measure, e.g. the Cambridge Prospective Memory Test (Wilson, Emslie, Foley, et al., 2005). However, this would be an additional task that clinicians would have to perform, which may have slowed recruitment rates further.

The second most frequent reason for not wanting to take part was that they used effective reminders already; others included time-pressures and not wanting to use a mobile phone or pager. Those excluded due to scoring below cut-off on the EMQ, i.e. having few memory problems, probably would not have benefitted from the intervention. As participants were required to give informed consent to participate, there may have been a bias towards people who recognised their difficulties. However, these are likely to reflect the people who would use the service if offered in clinical practice; and those excluded would be unlikely to use the service.

Participants appeared to enjoy the baseline visits, particularly the opportunity to discuss their memory problems with a new, engaged person. For the majority of participants baseline assessment took approximately 3 hours, split over two visits, with the exception of one that took 4 hours over 3 sessions. The majority of participants requested home visits, a few wished to meet at their hospital. The cognitive tests were well received by most, and tolerated by all. Therefore the assessment battery was acceptable and could be used in a definitive trial

All participants appeared to understand the crossover design, and were willing to be randomised. Two participants were considered dropouts after baseline and consent, because the researcher was unable to contact them again using the provided contact details. The retention rate was 98% of those who took part in the trial, and 94% of those who consented into the trial. Therefore the study design was deemed acceptable and feasible for people with MS, and could be used in future trials.

#### ***6.3.1.2 Suitability of intervention***

NeuroText proved feasible to deliver and all participants were able to comply with the intervention. No participants dropped out whilst receiving NeuroText, and informal feedback throughout the trial was overwhelmingly positive. Rotas for the time and frequency of the reminder deliveries were agreed during the baseline

home visits, and most participants did not make adjustments at any point during the trial. The content of the NeuroText messages were in capital letters by default; some participants thought this was useful, some would have preferred the messages to be in lowercase. It is recommended that both options are made available in future trials.

#### ***6.3.1.3 Suitability of control***

Development of the control condition began with researching examples of social text with non-memory content. It was decided that these would include news headlines, depending on interest, e.g. sport, current affairs, quotes. Headlines would be accompanied by URL links to the full corresponding article. Considering the number of control messages that were sent out to each participant during the control condition, it became clear that each individual message could not be manually typed in, unless participants were happy to receive the same content multiple times, as expected in the NeuroText condition. Therefore a range of potential RSS feeds were identified and offered to participants, who chose a maximum of three feeds to receive content from. Consequently this led to the development and introduction of new RSS feed software to the NeuroPage service at the Oliver Zangwill Centre.

Technological problems were experienced with the control at the beginning of the trial because faulty RSS feeds were not consistently or reliably sending content to the NeuroPage system, and so control messages could not be populated and sent at the requested times. Only participants who had requested content from these particular feeds were affected. However, once the problem was identified, the trial was halted, faulty RSS feeds were deleted and replaced with functioning alternatives if possible, and the trial restarted. Only participants starting the trial from this point onwards were included in the outcome analyses. Once restarted there were still some reports that although participants were receiving messages at the correct time and frequency, the content was repetitive. This arose from the RSS feeds not having adequate new material. However due to the fact messages were

still being received as planned, the control was considered received as planned. It is advisable that in future studies only RSS feeds from trusted news websites are employed, e.g. BBC, the Guardian, or ESPN.

Once the trial restarted, the control condition proved feasible to deliver and participants were able to comply with the control. One participant dropped out whilst receiving the control, because they did not find it useful and could not understand why they were receiving the control messages, despite the researcher explaining the trial design to them on many occasions.

Control messages were sent at the same times and frequency as reminder messages, to enable a direct comparison across conditions. A minority of participants requested that the number of control messages was reduced, and therefore they received slightly fewer messages in the control condition, compared to NeuroText condition. Therefore this meant that the frequency, as well as the content, was different between conditions, and could have potentially impacted on the interpretation of findings, e.g. if the control messages were less effective than NeuroText because participants received fewer messages. Some participants also reported that they were initially unsure about the origin of the control messages. This was despite the sender having the same number, and the researcher checking participants had started receiving them. In future trials it is recommended that the researcher telephones participants, rather than text messaging, to check they are receiving the messages and understand their origin. A few participants reported being unable to open the URL links in the control messages, but this was due to limitations of their personal mobile phone. Therefore in future studies mobile phones should be checked for compatibility prior to randomisation.

#### **6.3.1.4 Outcomes**

Following the first condition over 80% of participant outcome questionnaires were returned and rates were comparable in both groups. Return rates of the daily diary and relative questionnaires were slightly lower than the participant outcome

questionnaires, for group 1 (76%; 68%), and considerably lower for group 2 (65%; 52%). The daily diary had to be completed over a week, whereas the outcome questionnaire could be completed in one sitting and returned immediately. Hence the lower rates of daily diary return could be due to the prolonged attention necessary for completion and return. It is recommended that an additional text message be sent to participants on the final day of filling out the daily diary, to remind them to post it. Low-rates of carers/friend questionnaire completion was commonly because participants could not identify someone to complete, and frequently participants reported that their carers underplayed their level of impairment. K. Mackenzie (2014) reported similar findings, where patients with MS reported significantly more problems than carers on the EMQ. This could be due to the disruption in family functioning and friendship, associated with MS (Thomas et al., 2006). Therefore future trials may consider not using the carer/friend outcome questionnaire.

The completion rates for the individual scales, e.g. EMQ, were lower than the rate of outcome return, as participants did not always complete all sections of the questionnaire before returning them to the research team. Participants reported that completing the outcome measures was challenging. Some participants found it hard to describe the frequency of memory problems on the EMQ, or practicing meta-memory; others found that the questionnaire was too long or 'too hard'. Therefore in future trials it may be beneficial to shorten the outcome questionnaire, or employ an independent researcher to aid questionnaire completion. Some participants claimed that the poor response rate was due to low mood or a relapse of physical symptoms, and many lost or forgot to post the questionnaires. A couple of participants returned their daily diaries before the last day of the diary; hence they completed the daily diary in advance. To prevent this from occurring, a text message could be sent each day to remind them to complete only that day.

The majority of participants completed the primary outcome measure, EMQ-frequency, however the EMQ-importance scale and the EQ5d visual analogue scale (VAS) were most commonly incomplete. Therefore for future trials, it is



recommended that the EMQ-importance scale be omitted from the outcome questionnaire, as the frequency scale is sufficient. It is suspected that the reduced completion of the EQ5d VAS was because it was presented at the end of the questionnaire, and in a visually different format to the other items. Therefore in future, placing it earlier in the questionnaire, and perhaps adding a tick-box at the bottom to say they have marked the VAS, would increase completion rates.

Return rates decreased from condition 1 to condition 2 on all measures. Future trials could perhaps run a parallel arm RCT to alleviate this problem. However, this would require a larger sample size. If participants did not return their outcome questionnaire within 2 weeks, they were offered help or administration by phone, to prevent missing data. Five participants requested this help following the first condition, two after the second. The researcher therefore populated the outcome measure; meaning scoring was un-blinded, as the researcher was aware of their group allocation. Therefore future studies need an independent research assistant to check and help participants to complete outcome questionnaires.

### **6.3.2 Effectiveness of intervention**

The two groups were comparable on all baseline measures. The sample had a higher percentage of women than men, which is representative of the MS population (World Health Organisation, 2008). The majority of participants (68%) were unemployed or retired since the onset of the multiple sclerosis, suggesting that the progression of the disease had already affected them cognitively or physically to the degree they could no longer work.

#### **6.3.2.1 Neuropsychology of sample**

Baseline performance on cognitive measures suggested participants had low-average to average memory ability and average executive functioning. Participants overall had low-average attention, with average abilities in selective attention and attention switching. It should however be noted that only 42 of the 50 participants undertook the attention switching subtest, the remaining eight found it too difficult

to proceed after the test examples. Marking these participants with a score of '0' in these subtests was considered, however they did not wish to take part in the subtest, and so their score could not be accurately estimated. Therefore if these participants had been able to complete the subtest, the average performance score of the sample would most likely have been lower.

In summary, the neuropsychological profile of participants overall appears to be slightly below average; and suggests that their everyday memory problems are most likely associated with reduced memory and attention functioning. This supports existing literature that many people with MS have memory problems (Rosti-Otajärvi & Hämäläinen, 2014) , and impairments in complex attention skills (Fischer, 2001; Mohr & Cox, 2001). Executive dysfunction is commonly seen in people with MS (Rosti-Otajärvi & Hämäläinen, 2014), but was not demonstrated in this sample. One explanation could be that the prospective memory problems witnessed in the sample are due to retrospective memory problems, rather than prospective memory, which depend on executive functioning. However the lack of demonstrated executive dysfunction is probably due to the limited range of assessments used.

#### **6.3.2.2 RCT findings**

The most frequently requested reminders in the NeuroText condition were regarding medication, which is what was found in Martin-Saez et al. (2011) study on NeuroPage; and in the control condition were current affairs headlines. Therefore it was anticipated that the NeuroText messages would be more effective in reducing everyday memory problems; as well as increased attainment of target behaviours, which were related to the reminders requested.

No significant difference was found on the EMQ between conditions, suggesting that the content of the messages may not be important in impacting general everyday memory problems. This might indicate that the fact they get a message alert is the most important aspect acting as a reminder, rather than what the

message says. This could be seen to support the Fish et al. (2007) study, where participants were sent content-free messages to act as a prompt to participants to remember their intentions, and hence improve prospective memory functioning.

However, there was a moderate effect size and significant difference between conditions on the daily diary; demonstrating that participants showed improved attainment of target behaviour when receiving NeuroText messages, compared to controls. This discrepancy suggests that the utility of NeuroText lies in its compensation for discrete recall of specific tasks, rather than an ability to compensate for memory dysfunction, as suggested by Lannin et al. (2014), with regard to personal digital assistants. Therefore the findings are probably due to limitations of the EMQ, including the fact it is a general measure of everyday memory, and is unlikely to pick up changes in prospective memory functioning. In future studies it would be useful to use an outcome measure of prospective memory, e.g. the Cambridge Prospective Memory Test (Wilson et al., 2005). These findings are similar to three studies evaluating memory rehabilitation for people with MS, where no significant difference was reported on the EMQ (Carr et al., 2014; das Nair & Lincoln, 2012; Lincoln et al., 2002). However, the EMQ was used because there was no appropriate alternative measure of everyday memory available (Carr et al., 2014). A significant reduction in the frequency of memory problems, following memory rehabilitation, was captured on a daily diary in Lincoln et al. (2003).

A large effect size and significant difference between groups was found on the GHQ, where participants reported fewer symptoms of psychological distress whilst receiving NeuroText, than when receiving control messages. Langdon and Thompson (1996) stated that cognitive impairments negatively interfere with daily functioning. This would suggest that receiving the reminder messages improved their mood, potentially because they were remembering to do the things they needed to do, and so their everyday life was easier. The implication would therefore be that the content of the NeuroText reminder messages were having a greater impact than the control content. Furthermore, these findings were

complemented by a moderate effect size and significant difference on the subscale assessing anxiety and depressive symptoms on the EQ5d. Therefore receiving NeuroText alleviated psychological distress in participants, compared to control, supporting the findings of Carr et al. (2014), who found that group memory rehabilitation significantly improved mood compared to control.

No differences between conditions were found on the mobility, self-care, usual activities and pain subscales of the EQ5d, or on the AMEDO scales measuring adaptation to memory difficulties scales. The AMEDO was developed as a measure of memory rehabilitation outcomes, and so it is surprising that there was no reported impact on this questionnaire. This could perhaps be explained because the items on the questionnaire would be impacted by a comprehensive research programme that aims to educate and provide a toolkit for a variety of memory problems. However NeuroText aimed to tackle specific prospective memory problems, and so participants were unlikely to endorse questions such as, “I understand how memory works” or “I have a range of internal memory aids that I can use for different tasks”.

Carryover and period effects are a common issue associated with crossover designs. A 3-week washout period between conditions was employed in the study design to ensure any benefit from the first condition was not carried-over to the second condition. A carryover effect was detected on four of the EQ5d items, therefore a longer wash-out period is recommended for future studies. Alternatively using a parallel arm RCT would eliminate this risk. A period effect was found on the AMEDO part A, and the daily diary. The period effect associated with the daily diary suggested that groups reported fewer incidents of forgetting over time, regardless of condition. However, on closer inspection, the large reduction of forgetting from the control to NeuroText conditions in Group 2, accounts for the significant period effect. Furthermore, it appears that Group 1’s rate of forgetting did not increase much after moving from the NeuroText to control conditions, which might demonstrate that the benefit of NeuroText was maintained through to their second

condition. This would add to the explanation of why a period effect was detected; but perhaps more importantly suggest there was a carryover effect.

#### **6.3.2.3 Feedback interviews**

Feedback interviews were carried out with 25 participants. Participants were contacted after trial completion and invited to interview. Feedback interviews were performed over the telephone, rather than face-to-face, as there is evidence suggesting that the two modes of interview can yield the same results (Sturges & Hanrahan, 2004). Furthermore, previous home-visits and multiple incidents of communication had allowed for rapport building between the researcher and participants; therefore it was deemed that participants would feel comfortable to share their views over the phone, and that the researcher had sufficient insight to interpret those views. However, because the researcher performed the interview, there is increased risk of social desirability bias.

Seven major themes were identified from the transcripts of the feedback interviews. Regarding NeuroText messages: perceived usefulness, messages ending, potential improvements; Control messages: potential usefulness of control, not useful; and Overall experience of participating in the study: all positive, a few concerns.

The NeuroText-related sub-theme ‘everyday memory related improvements’ included participants’ experiences of achieving target behaviours and improved planning and organisation skills, which largely reflect the daily diary findings, and findings from another qualitative memory rehabilitation study for people with neurological disabilities (das Nair & Lincoln, 2013; das Nair, Martin, et al., 2015). Furthermore the sub-theme ‘improved ability to manage mood’ was identified, which contained concepts of coping better e.g. through being kinder to themselves, and improved control over their life, which could potentially explain the alleviated psychiatric distress portrayed in the GHQ results after NeuroText. Improvements in managing fatigue were also reported, in association with improved ability to plan.

Evidence supporting improvements in mood and fatigue after memory rehabilitation have recently been established in a meta-synthesis of group-based memory rehabilitation (das Nair, Martin, et al., 2015). Additional findings were uncovered from the transcripts, such as reports that the benefits from NeuroText remained for some after the messages finished, either through an established routine, or implementation of replacement aids. This experimentation with other replacement memory aids was not supported by the AMEDO results in the current study, but was also reported in the das Nair and Lincoln (2013) study. These findings suggest that some people might only need to receive NeuroText messages for a short period of time, such as two months, and can then effectively use their own reminders. Furthermore people may only need the initial baseline visit to identify appropriate reminders with a therapist, and then could potentially set their own reminders. Other participants reported missing the messages, and so these are the subgroup that would benefit from longer-term use of NeuroText.

Themes regarding messages acting as prompts appeared with regard to both NeuroText messages and control messages. Therefore the notion that the message content may not be important cannot be ignored. However, it seems that the control messages acted as prompts once participants had already received NeuroText messages, and that the NeuroText messages had themselves acted as prompts first. It was common for participants to report that when a control acted as a prompt, they observed the time, thought about what reminder text they would have received at that time, and what reminder it contained; rather than simply thinking about what task they should be doing at that time. Only one person reported that the control messages acted as prompts, without having received NeuroText first. Therefore it is probable that the content of the message is important initially, and then if a routine is established, the content could be removed. This carryover effect from NeuroText to control condition supports what was hypothesised to have occurred with the maintained target behaviour performance on daily diary scores. However this would not work for everyone, as many participants explicitly said that NeuroText was more effective for them than

the control, and many more did not find that the benefit remained in the control condition.

Interestingly the feedback interviews uncovered unanticipated responses to the control, such as short-term improvements in mood, and encouraging engagement. Sub-themes regarding negative aspects of the control were also found, such as irritating and confusing. Some participants found the control messages distracted them away from their desired target behaviour, which could put them at a disadvantage, compared to NeuroText.

Overall participation was deemed positive, with participants enjoying being involved, and finding the baseline assessments interesting. All participants were interested in receiving a results summary, and many asked to be notified of similar future studies. Feasibility issues were touched on, where most participants suggested nothing needed to be changed to the NeuroText messages, others suggested a few tailored adjustments, e.g. reduce frequency. Therefore it is recommended that the researcher should contact the participants more frequently throughout the trial to ask whether they wish to modify the reminder scheme.

## **6.4 Limitations of the study**

### **6.4.1 Issues with study design**

The RCT methodology was chosen primarily as it is the most robust design for the evaluation of interventions (Higgins & Green, 2013), and to ensure the study could be included in future systematic reviews and meta-analyses. Furthermore, the design allowed the comparison of the intervention to an active control, with randomisation, allocation concealment and blinding, to eliminate bias. A commonly reported issue with RCTs is that the personal story of participants is lost, however the qualitative feedback element of this study recaptured participants' perspectives.

There is some confusion in the literature around the terms 'feasibility' and 'pilot' when describing a study, where some authors use the terms interchangeably (Thabane et al., 2010), whilst others define them as separate (Arain, Campbell, Cooper, & Lancaster, 2010; Lancaster, Dodd, & Williamson, 2004). Whitehead, Sully, and Campbell (2014) performed a literature review aimed at defining the relationship between the two terms. They found that the distinguishing features of a pilot study were that they mimic the design of future larger trials, and therefore have stricter methodology; focus on the trial processes; and are a small version of the main study (Whitehead et al., 2014). The authors also report that pilot studies can also test the feasibility of a larger study, as well as investigating the trial procedures, and therefore it could be said that pilot studies are also feasibility studies (Whitehead et al., 2014). They conclude that a pilot study is a special type of feasibility study, which plans for future trials and mimics the definitive trial; therefore the current study is considered a pilot trial.

The RCT crossover design of this study was deemed feasible. However crossover designs run the risk of carryover effects from the first condition to the second. A washout period of 3 weeks was employed to reduce any carryover, however it appears that this may have not been successful. Therefore a longer washout period between conditions would be recommended, although this could increase the rate of dropout between conditions. Due to the degenerative nature of MS, it is possible that crossover designs are inappropriate, and that only data from the first period should be used (Qizilbash et al., 1998). Although, each participant only took part in the study for six months, and the randomisation should have meant that disease progression was equally likely across groups. Perhaps a better alternative for future trials would be to employ a parallel arm RCT design. However, one benefit of crossover trials is that participants experience both conditions, and can therefore express a preference for or against the treatment. Another benefit is that because each patient receives both conditions, crossover trials usually require half the number of participants to produce the same precision as a parallel group trial (Elbourne et al., 2002).



Despite efforts to boost recruitment, the sample size estimate of 66 was not reached, due to a saturation of eligible referrals at many sites and the timeframe of the study. Therefore more sites, or multiple referring clinicians at each site, are recommended in future. Additionally, recruiting from local charity branches, such as the MS Society, is recommended to boost recruitment. Therefore the study was underpowered to evaluate the effectiveness of the intervention. Recruitment rates in clinical research are unpredictable, and so often are lower than anticipated (Pringle & Churchill, 1995). However, the results will serve as pilot data for a potentially larger multi-centre study.

#### **6.4.2 Issues with intervention**

Due to the nature of the intervention being carried out over two months in participants' personal lives, adherence remains unknown. A literature review on the non-use of assistive technology devices reported high rates of non-adherence (Wessels, Dijcks, Soede, Gelderblom, & De Witte, 2003). Therefore it is probable that some reminder messages went unread, and that mobile phones were switched off or on silent mode. However, due to the study design, these events may also have occurred in the control condition, and were therefore counterbalanced.

#### **6.4.3 Issues with outcomes**

The lack of inclusion of a baseline prospective memory test was a limitation, none were used, as they have lower validity than chosen tests (Roche, Fleming, & Shum, 2002). However, it would be useful to measure prospective memory as part of the baseline assessment, using, e.g. the Cambridge Prospective Memory Test (Wilson et al., 2005) or subtests of the RBMT (Wilson et al., 1985) in future studies.

The outcome measures employed were chosen on the basis of being subjective, self-report tools, which were ecologically valid. However subjective measures rely on participants' ability to report recent or current status, which required intact meta-memory skills, and these are likely to be impaired in the sample population

(Beatty & Monson, 1991). Therefore, participant questionnaires might be inaccurate as a measure of incidence of memory failures. People with worse memories might be worse at recalling instance of memory failure and give themselves low frequency ratings (Sunderland et al., 1983). However, despite this limitation, this form of assessment is the most appropriate for the study.

Another limitation is that the outcome measures were employed because they are well-established measures in memory rehabilitation studies, with good psychometric properties. Therefore findings from this study are more likely to be included in systematic reviews and pooled together in a meta-analysis. However, it appears that the EMQ probably is not sensitive to change in the achievement of target behaviours, and you would not expect to see changes in the majority of items with this intervention, e.g. recognising faces. Changes important to the individual are often lost on global measures, and improvements too small to be statistically significant may still be important to the patient (Hanssen, Šaltytė Benth, Beiske, Landrø, & Hessen, 2015; Khan, Pallant, & Turner-Stokes, 2008; Royle & Lincoln, 2008). However, the EMQ was used because there was no appropriate alternative available with good psychometric properties, (Carr et al., 2014). In future trials it would be useful to include a subjective measure of prospective memory, such as the Comprehensive Assessment of Prospective Memory (Roche et al., 2002), which measures the specific, everyday PM lapses. This recommendation is despite the fact that psychometric properties have not yet been determined.

Some participants did not return the outcome questionnaires, and this must raise doubts over how representative the results were. It is likely that those with the worst memories were under-represented as they often lost or forgot to return the outcome questionnaires. Hence, it is possible that this could have biased the results, however this would be expected in both conditions, and so would be counterbalanced. Some who did not feel able to complete the questionnaires reported that this was due to low mood. Therefore screening for mood problems at baseline could increase outcome return, but could mean that the sample was not representative of the population, where the lifetime prevalence of depression is

50% in people with MS, and is known to interact with cognitive impairment (Feinstein, 2011; Feinstein et al., 1999; Sá, 2008).

#### **6.4.4 Issues with analyses**

The modest sample sizes could have been an issue for the employed statistical tests, and therefore the study was underpowered to detect differences between conditions. However the majority of scales had normal distributions of scores, and so parametric tests were performed. A potential limitation of the analyses was that multiple t-tests were performed, and interpreted without using the Bonferroni correction; hence there is an increased likelihood that any significant differences are due to chance. If the Bonferroni correction had been employed the difference on the GHQ would have remained significant, however the daily diary would not. In future studies with larger samples it is advised that ANOVAs are used, to avoid the issues with multiple testing. Alternatively regression methods could be employed.

Due to the crossover design, tests for carryover and period effects were performed. However the Cochrane Handbook states that the statistical techniques to demonstrate carryover are unsatisfactory and therefore the decision lies on the researcher's judgement (Higgins & Green, 2011). If carryover is detected then the two-stage Grizzle approach, of comparing only condition 1 data is suggested (Grizzle, 1965). However this 'two stage analysis' was not performed as it has been discredited and using the first period removes the main strength of the crossover design, ability to do within-participant comparisons (Freeman, 1989).

Intention-to-treat analysis was used throughout the trial, where all data were categorised as the group in which participants were randomised into. However t-tests only included full data sets. The imputation of missing values, and therefore sensitivity analyses were not performed. However it could be argued that though this would have increased the sample size, it would have probably dampened the detection of any effect. Another common but controversial limitation in health sciences, which is practiced here, is the liberal treatment of ordinal scales as though

they were interval scales. Therefore it would be beneficial to consider using Rasch analysis to convert scales to interval level data in future trials.

The use of null hypothesis significance testing (NHST) has many pitfalls (Field, 2013), as the level of significance does not indicate the importance of an effect. Therefore the effect size, in the form of Cohen's *d*, was also reported, as recommended by the American Psychological Association (Wilkinson, 1999). The effect sizes calculated in this study, complemented the *p* values, in the interpretation of findings.

Qualitative analysis was performed by the researcher for the first time during this study, however supervision from an experienced qualitative researcher ensured quality in the development of the framework matrix and identification of themes.

## **6.5 Implications for practice**

Everyday memory improvements were reported on the daily diary, but not on the EMQ or AMEDO. These results partially support the recommendations of Cicerone et al. (2011) and de Joode et al. (2010), to offer compensatory aids to people with memory problems, and Jamieson's conclusion that there is evidence for prospective memory prompting devices for people with degenerative conditions. Therefore there is some suggestion that people with MS can be supported by electronic memory aids to improve achievement of target behaviours and improve mood.

NeuroText is a service that is currently available, and these findings suggest that the service could be useful for people with progressive neurological conditions, as well as people with ABI. Furthermore this could indicate that rehabilitation approaches commonly used for people with ABI could be translatable to people with neurodegenerative conditions. The study was carried out over five sites, with community-based MS patients, and therefore the findings could be viewed as generalisable.

The aims of the interviews were to elicit and examine feedback from participants who had taken part in the RCT comparing NeuroText with an active control, and to provide suggestions for improvements. Patient partnership, such as this, is a key feature in many NHS services (DoH, 2001). The feedback provided some explanation for the quantitative findings, for example, the maintenance of NeuroText benefit into the control condition for some participants. Therefore indicating that for some people with MS who have memory problems it may be viable to initially have prompts containing reminder content; and then for some the routine will remain, others will independently replace their reminders with an alternative, and some will effectively respond to a simple prompt, such as an alarm.

## **6.6 Implications for research**

The trial is a high quality RCT, that was designed in response to the call for methodologically robust memory rehabilitation research in recent systematic reviews (das Nair et al., 2012; Goodwin, Lincoln, das Nair, & Bateman, 2015; Rosti-Otajärvi & Hämäläinen, 2014). Therefore, the study adds to the evidence-base, and will be eligible for inclusion in future systematic reviews.

The feasibility of the trial design was assessed, and many recommendations for a definitive full-powered RCT have been made. The main recommendations are, that an alternative to the EMQ should be used as the primary outcome measure, and that a prospective memory measure is employed; and that a parallel arm RCT design would be preferable to the current crossover design.

Two sample size estimates were calculated using the GHQ and the daily diary data; the estimates were for 119 and 37 participants, respectively. These estimates indicate that a full powered trial is achievable. The decision to use these measures for the calculations was made in light of the issues found with the EMQ in this study, and the recommendations to use a different measure in future studies. Therefore the calculated sample sizes are indicative for the other measures used in this study. Further research into developing the psychometric properties of memory

rehabilitation outcome measures are strongly recommended, using techniques such as Rasch analysis.

Interviews offer qualitative information that outcome measures used in most trials do not offer (das Nair & Lincoln, 2013). The addition of a qualitative study has been an important addition to better understand the quantitative results, and is the first qualitative evaluation of NeuroPage in the literature. Future trials in the field should include a qualitative element, to allow for the triangulation of evidence, demonstrated in this study (Moffatt, White, Mackintosh, & Howel, 2006).

Previous studies on NeuroPage have compared the intervention to usual-care (Wilson et al., 2001; Wilson, Emslie, Quirk, et al., 2005; Wilson et al., 1997). This study used an active control, containing non-reminder content; which has allowed more exploration of the active ingredient of the intervention, e.g. the content or the prompting alert. If participants had reduced retrospective memory (RM) functioning, as suggested by baseline neuropsychological profile of the sample, then it would be expected that participants would not have remembered the intended action without receiving the reminder content. This was reported in some participants who lost the benefit of NeuroText when the condition finished. However, many participants reported a maintained benefit of NeuroText into the control condition, which is suggestive of intact RM as they could remember the intended action. It is probable this subset of participants therefore had a prospective/executive functioning problem, and so a prompt was sufficient to trigger recollection of the content and perform the target behaviour. A further subset reported that they had developed a routine, following NeuroText, and that they no longer needed the messages, which would suggest that implicit learning had occurred. Hence, it would seem that the most important element of NeuroText, e.g. content or prompt, is dependent on the user's individual impairments. Therefore it is necessary to include an active control in future trials, such as the one used in this study, rather than just comparing to usual-care.

However at this stage, interpretations should be viewed in light of the strengths and weaknesses of the study, such as the study being underpowered to determine effect. MRC Framework for complex interventions (Campbell, Fitzpatrick, Haines, & Kinmonth, 2000) would place this study as a phase II exploratory trial. The study findings justify a full-powered definitive RCT.

## **6.7 Future Directions**

A full powered RCT should be undertaken, using the sample size estimation, and considering the feasibility recommendations documented throughout this chapter. Considering the limitations associated with the crossover design it is suggested that a parallel arm RCT design is employed in this future trial. It is recommended that a third arm containing a content-free prompt is added, in light of the fact that the current control was perceived by some as distracting them away from target behaviours. Additionally this design would allow the observation of how useful the content-free prompts would be without the priming element of NeuroText first seen in Group 1 in this trial.

A further suggestion would be to assess the importance of therapeutic input in the intervention, i.e. the clinician/researcher led identification of target intentions, reminder content and frequency of prompt. Therefore a future study could assess how beneficial this stage alone would be, where participants to implement their own replacement memory aids. Another piece of research could look at the relationship between baseline cognitive data, e.g. memory, attention and executive functioning abilities, and their response to the intervention. For example, “do people with MS and impaired baseline executive functioning, but intact memory, experience benefit from content-free cues?”, in line with the research of Fish et al. (2008).





## 7.0 Conclusions

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Evidence on the effectiveness of external memory aids in MS was gathered by conducting a systematic review on the area. Only one study was identified that specifically evaluated the use of external memory aids with people with MS, despite the inclusion of non-randomised designs. It was concluded that the methodological quality of studies was poor and that high quality trials were necessary in the field.

In an attempt to address the lack of evidence observed in the literature, a single-blind multicentre RCT was conducted to examine the effectiveness of an electronic memory aid, NeuroText. The aim of this study was to evaluate whether people with MS who used NeuroText reminder messages reported reduced subjective reports of memory problems in daily life; increased attainment of target behaviours; and improved mood and quality of life, compared to control messages. A mixed-methods approach, incorporating both quantitative and qualitative information to acquire a fuller understanding of the data was employed. Based on the quantitative data, there was no evidence to suggest that NeuroText improved memory problems in daily life, or quality of life. However there was evidence that NeuroText improved attainment of target behaviours and mood. Interestingly, the qualitative data suggested that participants found NeuroText to be useful across multiple aspects of their everyday life, and some found the benefit remained after the intervention stopped.

Comparing NeuroText with an active control, rather than usual care, allowed the observation of what element of the reminder service might be providing the treatment effect. The content of NeuroText appears important to its effectiveness, but further research is necessary to determine how people with different neuropsychological profiles respond.

Small sample size and lack of appropriate outcome measures may have affected quantitative results. Findings should be interpreted with consideration for the

strengths and weaknesses of the study. The trial was deemed feasible to deliver, and recommendations for future trials were outlined. Therefore we are hopefully one step closer to meeting the unmet needs of people with MS who experience memory problems.

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# Appendices

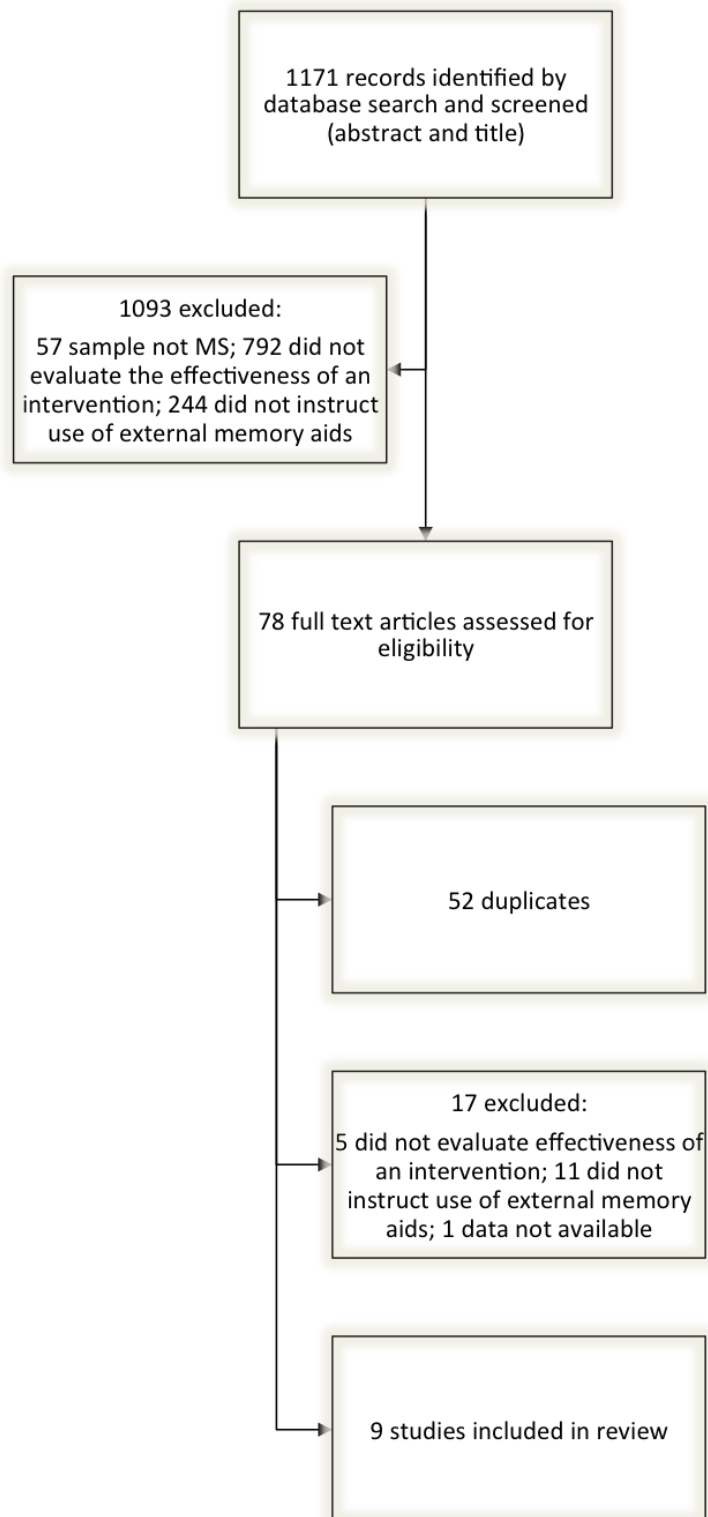
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## Appendix 1: Systematic review search strategy

1. Multiple sclerosis (exp)
2. (Demyelinating and autoimmune and disease) or (demyelination) or (demyelinating and diseases) or (optic and neuritis) or (Myelitis and transverse) or (Neuromyelitis and optica) or (Disseminated and sclerosis) or (Devics and disease)
3. 1 or 2
4. Memory disorder (exp)
5. Memory (exp)
6. Attention or Cognit\* or (Cognit\* and (disorders or impair\*)) or Concentrat\* or Distract\* or Alert\* or Amne?sia or (Planning and problem\*) or Confabulat\* or Recall or (Coniti\* and retention) or Recogni\* or (Prospective and memory) or Forget\* or (Executive and function\*) or (Executive and behavio?r) or dysexecutive or planning
7. 4 or 5 or 6
8. (Assistive and technolog\*) or (Assistive and technolog\* and device) or (Adaptive and technolog\*) or (Assistive and device\*) or pager\* or (paging and system\*) or (Technolog\* and aid\*) or (pocket and (pc or computer)) or (palm and top) or (personal and digital and assistant) or PDA or (self and help and device\*) or (computer\* and handheld)
9. (Memory and aid\*) or (Memory and strateg\*) or Compensat\* or (Electronic and aid\*) or (External and aid\*) or (External and compensat\*) or (memory and device\*) or (remind\* and system) or remind\* or (cogniti\* and prosthetic\*) or substitute\*
10. 8 or 9
-

11.     Rehabilitation (exp)
12.     Neurorehab\* or Therap\* or Treatment or Intervention or Strateg\* or  
Management or (Cogniti\* and rehab\*) or (Therap\* and computer and assist\*)
13.     11 or 12
  
14.     3 and 7 and 10 and 13

## Appendix 2: Systematic review search results flowchart



## **Appendix 3: Letter of ethical approval**

### **NRES Committee East Midlands - Northampton**

The Old Chapel  
Royal Standard Place  
Nottingham  
NG1 6FS

Telephone: 0115 8839440

22 October 2013

Professor Nadina Lincoln  
Professor of Clinical Psychology  
University of Nottingham  
Division of Rehabilitation and Ageing  
Medical School, Queen's Medical Centre  
Nottingham  
NG7 2UH

Dear Professor Lincoln

**Study title:**

**Evaluation of NeuroText as a memory aid for people with Multiple Sclerosis**

**REC reference:**

**13/EM/0324**

**Protocol number:**

**13078**

**IRAS project ID:**

**131028**

Thank you for your letter of 07 October 2013, responding to the Committee's request for further information on the above research and submitting revised documentation.



The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the REC Manager Ms Dawn Denton, [nrescommittee.eastmidlands-northampton@nhs.net](mailto:nrescommittee.eastmidlands-northampton@nhs.net).

### **Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

### **Ethical review of research sites**

#### **NHS sites**

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

#### **Non-NHS sites**

Notification(s) of no objection have been received from local assessors for the non-NHS site(s) listed in the table below, following site-specific assessment (SSA).

I am pleased to confirm that the favourable opinion applies to the following research site(s), subject to site management permission being obtained prior to the start of the study at the site (see under 'Conditions of the favourable opinion below').

#### **Research Site**

Principal Investigator / Local Collaborator

### **Conditions of the favourable opinion**

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

*Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.*

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

*Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.*

*For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.*

*Sponsors are not required to notify the Committee of approvals from host organisations*

### Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett ([catherineblewett@nhs.net](mailto:catherineblewett@nhs.net)), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

**It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

### **Approved documents**

The final list of documents reviewed and approved by the Committee is as follows:

*Document*

*Version*

*Date*

Covering Letter

06 August 2013

Evidence of insurance or indemnity

31 July 2013

GP/Consultant Information Sheets

1.0

30 July 2013

Interview Schedules/Topic Guides

Feedback 1.0

30 July 2013

Interview Schedules/Topic Guides

Interview assessment 1.0

30 July 2013

Investigator CV

17 June 2013

Letter from Sponsor

05 August 2013

Letter of invitation to participant

Invitation to study 1.0

30 July 2013

Letter of invitation to participant

Invitation to feedback interview 1.0

30 July 2013

Letter of invitation to participant

1.0

30 July 2013

Letter of invitation to participant

2.0

07 October 2013

Other: Non NHS SSI

131028/486225/7/603/212521/278328

12 August 2013

Other: CV - Andrew Bateman

17 July 2013

Other: CV - Dr Nair

24 July 2013

Other: CV - Rachel Goodwin

28 May 2013

Other: EMQ - Relative/Friend

1.0

30 July 2013

Other: EMQ - Participant

1.0

30 July 2013

Other: Flowchart of protocol

1.0

30 July 2013

Other: Letter from funder

14 December 2012

Participant Consent Form

1.0

30 July 2013

Participant Consent Form: Relative/Friend

1.0

30 July 2013

Participant Consent Form

2.0

07 October 2013

Participant Consent Form: Relative/Friend

2.0

07 October 2013

Participant Information Sheet

1.0

30 July 2013

Participant Information Sheet

2.0

07 October 2013

Protocol

1.0

30 July 2013

Protocol

2.0

07 October 2013

Questionnaire: Relative/Friends

1.0

30 July 2013

Questionnaire: Participant

1.0

30 July 2013

REC application

131028/486219/1/448

12 August 2013

Response to Request for Further Information

07 October 2013

## **Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

## **After ethical review**

### Reporting requirements

The attached document *“After ethical review – guidance for researchers”* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- ☐ Notifying substantial amendments
- ☐ Adding new sites and investigators
- ☐ Notification of serious breaches of the protocol
- ☐ Progress and safety reports
- ☐ Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

### Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

**13/EM/0324**

**Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at <http://www.hra.nhs.uk/hra-training/>

With the Committee's best wishes for the success of this project.

Yours sincerely

**Mr Ken Willis**  
**Chair**

Email: [nrescommittee.eastmidlands-northampton@nhs.net](mailto:nrescommittee.eastmidlands-northampton@nhs.net)

*Enclosures:* "After ethical review – guidance for  
researchers"

*Copy to:* *Mr Paul Cartledge, Research Innovation Services*  
*Ms Charlotte Davis, Nottingham University Hospitals*

## Appendix 4: Letters of R&D approval

### Cambridgeshire Community Services NHS Trust

09 December 2013

Ms Jenifer Edis  
Rehabilitation Unit  
Hinchingsbrooke Hospital  
Hinchingsbrooke Park  
Huntington  
PE29 6NT

RMG Office  
Lockton House  
Clarendon Road  
Cambridgeshire  
CB2 8FH  
camstrad@cambridgeshire.nhs.uk

Direct dial: 01223 725466

Dear Ms Edis

**Re: L01313 Evaluation of NeuroText for people with Multiple Sclerosis**

**Re: 131028**

**Rec: 13/EM/0324**

Your proposal has been reviewed by the Medical Director of Cambridgeshire Community Services NHS Trust.

I am pleased to inform you that Cambridgeshire Community Services NHS Trust has given permission for the following research to take place.

**This permission is subject to the enclosed standard terms and conditions and conditional upon you notifying the research governance team of any changes to the study-related paperwork.**

Unless we hear from you within a month of this letter, we will assume that you are abiding by these conditions.

The project must follow the agreed protocol and be conducted in accordance with Trust policy and procedures in particular in regard to data protection, health & safety and information governance standards. The research team are required to follow the reasonable instructions of the research site manager and can contact the RMG office for RMG advice or the Trust RMG lead in relation to queries on local policy.

On completion of clinical trials of interventional medicinal products/devices participants need to be aware that local Trust prescribing policy and formulary applies therefore participants cannot expect to continue on the research trial product/device on completion of the trial.

Approval is subject to adherence to the Data Protection Act 1998, NHS Confidentiality Code of Practice, the Human Tissue Act 2004, the NHS Research Governance Framework for Health and Social Care, (2nd edition) April 2005, the Mental Capacity Act and any further legislation released during the time of this study. Approval for Clinical Trials is on the basis that they are conducted in accordance with European Union Directive and the Medicines for Human Use (Clinical Trials) Regulations 2004 principles, guidelines and later revisions, and in accordance ICH Good Clinical Practice.

Members of the research team must where instructed have appropriate substantive or honorary research contracts or letters of access with the Trust prior to commencing work on the study,

Cambridgeshire Community Services NHS Trust: providing services across  
Cambridgeshire, Peterborough, Luton and Suffolk





additional researchers who join the study must also hold a suitable contract or letter of access before they start.

You will be required to complete monitoring information during the course of the research, as requested by the RMG office. Cambridgeshire Community Services NHS Trust reserves the right to withdraw research management approval for a project if researchers fail to respond to audit and monitoring requests.

Should any adverse incidents occur during the research, Cambridgeshire Community Services NHS Trust Incident and Near Miss Reporting Policy should be used, the RMG Office informed and incident procedures adhered to at the research site.

If you make any amendments to your project, please ensure that these are submitted to the research ethics committee and the RMG office and that any changes are not implemented until approval has been received.

We welcome feedback about your experience of this review process to help us improve our systems. May I take this opportunity to wish you well with your research and we look forward to hearing the progress and outcomes for the study.

Please contact the RMG team should you have any queries.

Yours sincerely,



Dr David Vickers  
Medical Director  
Cambridgeshire Community Services NHS Trust

cc: Mr Paul Cartledge

**Research and Development Department**

R&D ref: A092981

29/11/2013

Dr Georgina Browne  
Box 83  
Addenbrookes Hospital

Dear Dr Browne

Box 277  
Addenbrooke's Hospital  
Hills Road  
Cambridge  
CB2 0QQ

Direct Dial: 01223 348492 Ext: 58492

Switchboard: 01223 245151

E-mail: [katrina.gatley@addenbrookes.nhs.uk](mailto:katrina.gatley@addenbrookes.nhs.uk)

[r&denquiries@addenbrookes.nhs.uk](mailto:r&denquiries@addenbrookes.nhs.uk)

[www.addenbrookes.org.uk](http://www.addenbrookes.org.uk)

**Re: 13/EM/0324 Evaluation of NeuroText as a memory aid for people with Multiple Sclerosis**

In accordance with the Department of Health's Research Governance Framework for Health and Social Care, all research projects taking place within the Trust must receive a favourable opinion from an ethics committee and approval from the Department of Research and Development (R&D) prior to commencement.

R&D have reviewed the documentation submitted for this project, and has undertaken a **site specific assessment** based on the information provided in the SSI form, and I am pleased to inform you that we have no objection to the research proceeding within Cambridge University Hospitals NHS Foundation Trust.

Sponsor: University of Nottingham

Funder: MS Society

End date: 29/02/2016

Protocol: final version 1, dated 30/07/2013

**Conditions of Trust Approval:**

- The project must follow the agreed protocol and be conducted in accordance with all Trust Policies and Procedures especially those relating to research and data management. Any mobile devices used must also comply with Trust policies and procedures for encryption to AES 256.
- You and your research team must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice and the Data Protection Act 1998 and are aware of your responsibilities in relation to the Human Tissue Act 2004, Good Clinical Practice, the NHS Research Governance Framework for Health and Social Care, Second Edition April 2005 and any further legislation released during the time of this study.

- Members of the research team must have appropriate substantive or honorary contracts with the Trust prior to the study commencing. Any additional researchers who join the study at a later stage must also hold a suitable contract.
- You and your research team must provide to R&D, as soon as available, the date of first patient first visit.

**If the project is a clinical trial under the European Union Clinical Trials Directive the following must also be complied with:**

- the EU Directive on Clinical Trials (Directive 2001/20/EC) and UK's implementation of the Directive: The Medicines for Human Use (Clinical Trials ) Regulations 2004;
- the EU Directive on Principles and Guidelines for Good Clinical Practice (EU Commission Directive 2005/28/EC); and UK's implementation of the Directive: The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006;

#### **Amendments**

Please ensure that you submit a copy of any amendments made to this study to the R&D Department.

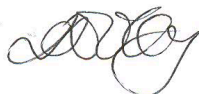
#### **Annual Report**

It is obligatory that an annual report is submitted by the Chief Investigator to the research ethics committee, and we ask that a copy is sent to the R&D Department. The yearly period commences from the date of receiving a favourable opinion from the ethics committee.

Please refer to our website [www.cuh.org.uk/research](http://www.cuh.org.uk/research) for all information relating to R&D including honorary contract forms, policies and procedures and data protection.

Should you require any further information please do not hesitate to contact us.

Yours sincerely



Louise Stockley  
Research Governance Manager

Cc Professor Nadina Lincoln

positive

Nottinghamshire Healthcare   
NHS Trust  
*Positive about integrated healthcare*

Research Support Services  
Institute of Mental Health  
University of Nottingham Innovation Park  
Triumph Road  
Nottingham  
NG7 2TU

E-mail: [Shirley.mitchell@nottshc.nhs.uk](mailto:Shirley.mitchell@nottshc.nhs.uk)  
Direct Line: 0115 748 4321

Date of NHS permission for research: 18<sup>th</sup> December 2013

Dr Lena Palmer  
Clinical Psychologist  
Community Neurology Service  
New Brook House  
385 Alfreton road  
Radford, Nottingham  
NG7 5LR

Dear Dr Palmer

**Study title:** Evaluation of NeuroText for people with Multiple Sclerosis Version 1  
**IRAS/REC ID:** 131028/13/EM/0324  
**Chief Investigator:** Nadina Lincoln  
**Sponsor:** University of Nottingham

Thank you for submitting your project to the Nottinghamshire Healthcare NHS Trust's Research Support Services. The project has now been given NHS permission for research on behalf of:

Sarah Kirkwood, R&D Lead, Nottingham CityCare Partnership

NHS permission for the above research has been granted on the basis described in the application form, protocol and supporting documentation. The documents reviewed were:

| Document                            | Version                  | Date            |
|-------------------------------------|--------------------------|-----------------|
| Protocol                            | 2                        | 07/10/13        |
| Participant Information Sheet       | 2.0                      | 07 October 2013 |
| Letter of invitation to participant | 2.0                      | 07 October 2013 |
| GP/Consultant Information Sheets    | 1.0                      | 30 July 2013    |
| Interview Schedules/Topic Guides    | Feedback 1.0             | 30 July 2013    |
| Interview Schedules/Topic Guides    | Interview assessment 1.0 | 30 July 2013    |
| Letter of invitation to participant | Invitation to feedback   | 30 July 2013    |

The Resource, Duncan Macmillan House, Porchester Road, Nottingham NG3 6AA  
Chair: Dean Fathers, Chief Executive: Professor Mike Cooke CBE



|                                 |               |              |
|---------------------------------|---------------|--------------|
|                                 | interview 1.0 |              |
| EMQ - Relative/Friend           | 1.0           | 30 July 2013 |
| EMQ - Participant               | 1.0           | 30 July 2013 |
| Questionnaire: Relative/Friends | 1.0           | 30 July 2013 |
| Questionnaire: Participant      | 1.0           | 30 July 2013 |

Permission is granted on the understanding that the study is conducted in accordance with the Research Governance Framework, ICH GCP [ONLY if applicable], and NHS Trust policies and procedures available <http://www.nottinghamshirehealthcare.nhs.uk/contact-us/freedom-of-information/policies-and-procedures/>

The research sponsor or the Chief Investigator, or the local Principal Investigator at a research site, may take appropriate urgent safety measures in order to protect research participants against any immediate hazard to their health or safety. The R&D office should be notified that such measures have been taken. The notification should also include the reasons why the measures were taken and the plan for further action. The R&D Office should be notified within the same time frame of notifying the REC and any other regulatory bodies. All amendments (including changes to the local research team) need to be submitted in accordance with guidance in IRAS.

Please note that the NHS organisation is required to monitor research to ensure compliance with the Research Governance Framework and other legal and regulatory requirements. This is achieved by random audit of research.

Yours Sincerely



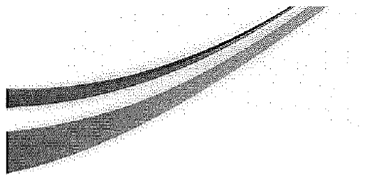
Shirley Mitchell  
Head of Research Management and Governance

CC:

Sponsor

Trent CLRN

NCCP R&D Lead



Nottingham University Hospitals **NHS**  
NHS Trust

Research & Innovation  
Nottingham Integrated Clinical Research  
Centre

18 DEC 2013

C Floor, South Block  
Queen's Medical Centre Campus  
Derby Road, Nottingham NG7 2UH

Tel: 0115 9249924 ext 70659  
[www.nuhrise.org](http://www.nuhrise.org)

Professor Cris S Constantinescu  
Division of Clinical Neurology  
University of Nottingham  
C Floor, South Block  
Queen's Medical Centre  
Nottingham  
NG7 2UH

Dear Professor Constantinescu

Re: 13NS016

CSP 131028

REC 13/EM/0324

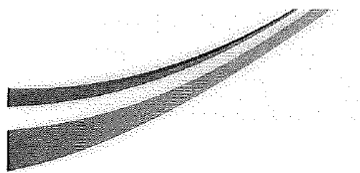
Evaluation of NeuroText as a memory aid for people with multiple sclerosis

The R&I Department have reviewed the following documents and NHS permission for the above research has been granted on the basis described in the application form, protocol, and supporting documentation. The documents reviewed were:

REC Approval letter – dated 30.10.2013  
GP Information Sheet, Version 1.0 dated 30.07.13  
Interview Schedules/Topic Guides., Interview assessment Version 1.0 dated 30.07.13  
Interview Schedules/Topic Guides Feedback, Version 1.0 dated 30.07.13  
Letter of Invitation to participant for feedback interview, Version 1.0 dated 30.07.13  
Letter of Invitation to participant Version 2.0 dated 07.10.13  
EMQ – Relative/Friend Version 1.0 dated 30.07.13  
EMQ – Participant Version 1.0 dated 30.07.13



*We are here for you*



Flowchart of Protocol Version 1.0 dated 30.07.13  
Participant Consent Form Version 2.0 dated 07.10.13  
Participant Consent Form: Relative/Friend, Version 2.0 dated 07.10.13

FIGURE 1

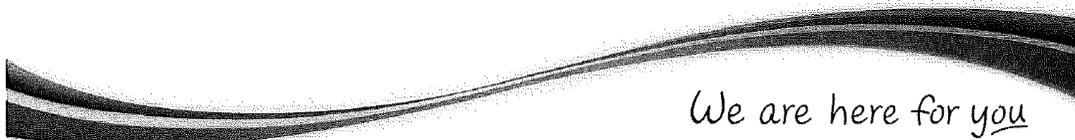
Participants Information Sheet Version 2.0 dated 07.10.13  
Protocol Version 2.0 dated 07.10.13  
Questionnaire: Relative/Friends Version 1.0 dated 30.07.13  
Questionnaire: Participant Version 1.0 Dated 30.07.13

Your study now has NHS permission, on the understanding and provision that you will follow the conditions set out below.

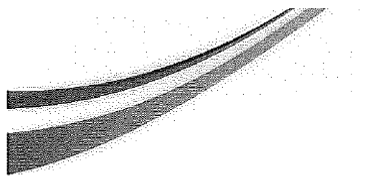
#### Conditions of Approval

The Principal Investigator is responsible for

1. Compliance with all relevant laws, regulations and codes of practice applicable to the trial including but not limited to, the UK Clinical Trials Regulations, Medicines for Human Use (Clinical Trial) Regulations 2004, principles of Good Clinical Practice, the World Medical Association Declaration of Helsinki entitled 'Ethical Principles for Medical Research Involving Human Subjects' (1996 version), the Human Rights Act 1998, the Data Protection Act 1998 the Medicines Act 1968, the NHS Research Governance Framework for Health and Social Care (version 2 April 2005). Should any of these be revised and reissued this will apply. Copies of the up-to-date regulations are available from the R&I Office or via the R&I website <http://nuhrise.org>
2. Submission of study amendments to the Ethics committee and MHRA in accordance with the IRAS guidelines. Amendments and information with regards to changes in study status must be sent to R&I, (this includes changes to the local study team). Within 35 days from the receipt of a valid amendment submission, NUH will inform you if may not locally implement the amendment. If no objections are raised NHS



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permission is valid and the amendment may be implemented.

When submitting documents for studies adopted into the NIHR portfolio please send the information to [NUHNT.TRENTCLR@nhs.net](mailto:NUHNT.TRENTCLR@nhs.net)

When submitting documents for all other studies please use the email address [rdamend@nuh.nhs.uk](mailto:rdamend@nuh.nhs.uk)

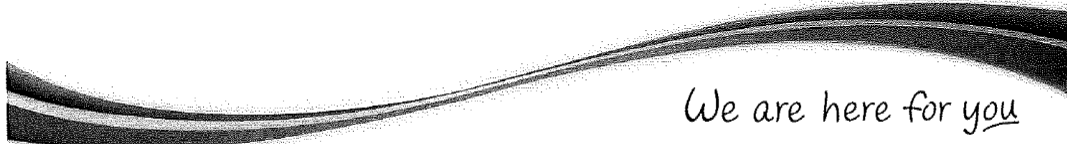
3. Ensuring all study personnel, not employed by the Nottingham University Hospitals NHS Trust hold either honorary contracts/letters of access with this Trust, before they have access to any patients or staff, their data, tissue or organs or any NUH facilities.
4. In accordance with the Department of Health's Plan for Growth, for initialising and delivering research within the NHS the 'first patient, first visit should occur 70 days from receipt of a valid submission in R&I. Therefore for all research where :
  - The sponsor is a commercial partner
  - NUH holds a funding contract with the National Institute for Health Research (NIHR)
  - The research is classed as a "clinical trial" on the IRAS filter page.

The research team is expected to collaborate with the department of R&I in reporting recruitment data to [rdmon@nuh.nhs.uk](mailto:rdmon@nuh.nhs.uk).

1. For GTAC-approved studies, the NHS permission should be forwarded to GTAC via the sponsor. GTAC should then issue a site authorisation letter which must be received by each site prior to recruitment commencing. A copy of this letter must be forwarded to R&I.
2. Comply with requests from NUH R&I to allow monitoring of research to comply with the Research Governance framework.
3. Record all types of adverse events (including Suspected Unexpected Serious Adverse Drug Reaction - SUSARS) in the patient medical records and study documentation and report to the sponsor as required by the protocol. Further guidance can be found in R&I SOP 11 - "Adverse Event Monitoring, Recording and Reporting for investigators".
4. Report any Serious Breach of the UK Clinical Trial regulations in connection with the trial or Serious Breach of the protocol, immediately after becoming aware of the breach to the study sponsor.

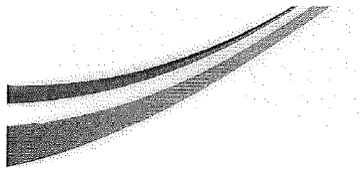
**For NUH sponsored studies only, the Chief Investigator is responsible for:**

- i. All duties as detailed in the "Clinical Trial Delegation of Sponsorship responsibilities to Chief Investigator" agreement.
- ii. Contacting the sponsor for review of all amendment documentation prior to submission to NRES and MHRA. Please note that according to NRES and MHRA regulations, all submissions of amendments need to be signed by the authorised sponsor's representative. All relevant documentation should be emailed



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- to [rdappl@nuh.nhs](mailto:rdappl@nuh.nhs).
- iii. Send copies of the completed Annual Safety, Progress reports and End of Study reports required by the Ethics Committee and the MHRA (if appropriate) to the Quality Assurance manager at NUH R&I.
  - iv. Notify NUH R&I of all SAEs by completing and sending the *"Serious Adverse Event reporting form"* to R&I (only via fax, e-mail or by hand), within 24hrs of becoming aware of the event. If the event is defined as a SUSAR then a follow up report must also be submitted to R&I, via the above channels-no longer than 7 days after the original report was submitted
  - v. Reporting any Serious Breach of the UK Clinical Trial regulations in connection with the trial or Serious Breach of the protocol, immediately after becoming aware of the breach to NUH R&I as sponsor. Further guidance can be found in R&I SOP 12 "Protocol Violation and Serious Breach Reporting"

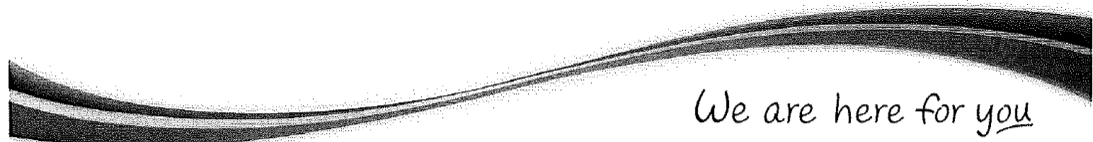
This approval letter constitutes a favourable Site Specific Assessment (SSA) for this site.

Please note that the R&I department maintains a database containing study related information, and personal information about individual investigators e.g. name, address, contact details etc. This information will be managed according to the principles established in the Data Protection Act.

Yours sincerely,

Dr Brian Thomson / Dr Maria Koufali  
Director of Research and Innovation / Deputy Director Research and Innovation

cc Nottingham Research Ethics Committee



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**Direct dial:** 01733 677914/ 7919/ 7912  
**E-mail:** [R&DDepartment@pbb-tr.nhs.uk](mailto:R&DDepartment@pbb-tr.nhs.uk)

**Peterborough City Hospital**  
Edith Cavell Campus  
Bretton Gate  
Peterborough  
PE3 9GZ

Date 17<sup>th</sup> November 2014

Dr Thorpe  
Consultant Neurologist  
PCH

Tel: 01733 678000  
(If DDI prefix extension number with 67)

Dear Dr Thorpe

**Ref:** R&D/2014/41

**Title:** Evaluation of NeuroText as a memory aid for people with multiple sclerosis

**REC Ref:** 13/EM/0324

**Sponsor:** University of Nottingham

With reference to your completed research application, I am pleased to inform you that the **main research proposal** has been approved by the Peterborough and Stamford Hospitals NHS Foundation Trust. It is noted that Peterborough will be identifying and referring patients for this study.

This approval is subject to compliance with the Research Governance Framework and the Peterborough and Stamford Hospitals NHS Foundation Trust Research Governance Policy and Procedures. Copies of both documents can be found on the R&D intranet site.

**The Government wishes to see a dramatic and sustained improvement in the performance of providers of NHS services in initiating and delivering clinical research. The NIHR contract benchmarks, announced in the Government's Plan for Growth, require providers of NHS services to submit performance data on a 70-day benchmark to recruit first patients into clinical trials.**

For the **70-day** benchmark, a *single* measure is taken from the time a provider of NHS services receives a **valid local research application** to the time when that provider recruits the **first patient** for that study. This benchmark measures performance at *an individual site* and we will be required to report on any failures to meet this.

**It is noted that Rachel Goodwin, PhD Student, University of Nottingham will be responsible for the recruitment of participants into this study. Rachel will also be responsible for updating the R&D department of the following milestones:**

- First Participant recruited
- Total number of participants recruited, once the recruitment has closed.

| Milestone                                   | Date       |
|---|------------|
| Initial SSI application received            | 06/10/2014 |
| Valid SSI application received              | 04/11/2014 |
| R&D Committee reviewed                      | 11/11/2014 |
| NHS Permission granted                      | 17/11/2014 |
| 70-day deadline for first patient recruited | 13/01/2015 |

You are reminded that the study must follow the approved protocol. Please note that any protocol amendments or changes to information provided in your original application form must be submitted to the R&D Committee for further review and approval.

You are also reminded that it is your responsibility to comply with the Law and appropriate guidelines relating to the Data Protection Act 1984 and Health and Safety Act 1974.

You are asked to comply, in a timely manner, with project monitoring and auditing requirements of the Trust and to notify the Trust Research & Development Committee of any unexpected serious adverse events/reactions, incidents or near misses involving participants or staff involved in this research project. You are also required to inform the R&D Department when key milestones are reached in the study (Initiation visit performed, closed-in follow-up, closed to follow-up, and close out underway) and any key changes in personnel.

Thank you for your co-operation.

Yours sincerely



Dr M Sivakumaran  
Chairman  
R&D Committee

## Appendix 5: Participant information pack

[TO BE PRINTED ON TRUST HEADED PAPER]



[Potential Participant Address]

### Evaluation of NeuroText as a Memory Aid for People with Multiple Sclerosis

I am sending you information on a study aimed at evaluating whether NeuroText helps reduce memory problems for people with multiple sclerosis.

Many people with MS report having memory problems, which can make their everyday life difficult. Strategies such as memory aids have been found to be useful in people with other neurological conditions. NeuroText is a memory aid device which sends text messages to a mobile or pager at pre-arranged times to remind people to carry out activities or as prompts to check they have done those things they should have done.

Improving memory problems for people with MS is important. The researchers want to compare whether people with MS who receive memory text messages on NeuroText show a reduction in reported memory problems in everyday life, in comparison with those who receive social text messages.

I have enclosed a **Participant Information Sheet** about the study. Please read this before you decide whether you wish to take part in this study.

If you decide to take part, please can you and a relative/friend read and complete the enclosed **Consent Form** each and an **Everyday Memory Questionnaire** each. Could you also fill out the **Contact Slip** detailing the address and phone number we can contact you on.

Could you please send these back to us in the enclosed paid envelope and the team will get in touch to arrange a visit whenever is best for you.

**If you have any questions about the study and want to speak to the research team, you can contact them by:**

- Calling the Research Team Phone on 0758 212 9039, or
- Emailing [lwrag@nottingham.ac.uk](mailto:lwrag@nottingham.ac.uk)

Many thanks.

Yours sincerely,

From clinician

Final Version 1.0 dated 30/07/2013

Page 1 of 2

[TO BE PRINTED ON TRUST HEADED PAPER]



### Participant Contact Details

[Potential Participant Address]

I would like a member of the team to get in touch with me using the details below

1) Name: \_\_\_\_\_

2) Contact number: \_\_\_\_\_

3) Contact Address: \_\_\_\_\_

\_\_\_\_\_

Thank you for your help and time.

[TO BE PRINTED ON TRUST HEADED PAPER]



**PARTICIPANT CONSENT FORM**  
(Final version 1.0: 30.07.2013)

**Title of Study: Evaluation of NeuroText as a Memory Aid for People with Multiple Sclerosis**

**REC ref:** *to be added after approval given*

**Name of Researchers:** Nadina Lincoln, Rachel Goodwin, Shirley Thomas, Andrew Bateman, Roshan das Nair

**Name of Participant:**

**Please initial box**

1. I confirm that I have read and understand the Participant Information Sheet version number 1.0 dated 30.07.2013 for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis. ☐
3. I understand that relevant sections of my medical notes and data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential. ☐
4. I understand that the feedback interview will be audio recorded and that anonymous direct quotes from the interview may be used in the study reports. ☐
5. I give permission for the researchers to contact my GP and inform him/her that I am taking part in this study ☐
6. I understand that should I chose to use a provided pager, I will need to provide addresses of places I will likely be during the trial and a contact number to the NeuroPage service that provides NeuroText. I understand the NeuroPage service will keep my details confidential. ☐
7. I agree to take part in the above study. ☐

\_\_\_\_\_  
Name of Participant                      Date                      Signature

\_\_\_\_\_  
Name of Person taking consent (Researcher)                      Date                      Signature

3 copies: 1 for participant, 1 for the project notes and 1 for the medical notes

Page 1 of 1

[TO BE PRINTED ON TRUST HEADED PAPER]



**RELATIVE/FRIEND CONSENT FORM**  
(Final version 1.0: 30.07.2013)

**Title of Study: Evaluation of NeuroText as a Memory Aid for People with Multiple Sclerosis**

**REC ref:** (to be added after approval given)

**Name of Researchers:** Nadina Lincoln, Rachel Goodwin Shirley Thomas, Andrew Bateman, Roshan das Nair

**Name of Participant:**

**Name of Participant's Relative/Friend:**

**Please initial box**

1. I confirm that I have read and understand the Participant Information Sheet version number 1.0 dated 30.07.2013 for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my legal rights being affected. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis. ☐
3. I understand that relevant sections of my data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential. ☐
4. I agree to take part in the above study. ☐

\_\_\_\_\_  
Name of Participant's Relative/Friend                      Date                      Signature

\_\_\_\_\_  
Name of Person taking consent (Researcher)                      Date                      Signature

3 copies: 1 for participant, 1 for the project notes and 1 for the medical notes



[TO BE PRINTED ON TRUST HEADED PAPER]



**PARTICIPANT INFORMATION SHEET**  
(Final version 1.0: 30.07.2013)

**Title of Study: Evaluation of NeuroText as a Memory Aid for People with Multiple Sclerosis**

**REC ref: (to be added after approval given)**

**Name of Researchers:** Nadina Lincoln, Rachel Goodwin, Shirley Thomas, Andrew Bateman, Roshan das Nair

**You are being invited to take part in a research study.** Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask if there is anything that is not clear, or if you would like more information.

**What is the purpose of the study?**

Many people with MS report having memory problems, which may make their everyday life difficult. Whilst these problems are recognised, they are often not adequately treated. Although some people with MS report memory rehabilitation to be helpful, and experts recommend its use, we are not completely sure how effective this treatment is in reducing memory problems in daily life; and if it is useful, the best way to deliver it. Strategies, such as the use of memory aids have proved to be effective in people with similar conditions, such as stroke and head injuries. Therefore this study will evaluate whether a memory aid, NeuroText, reduces everyday memory problems in people with MS, and improves mood and quality of life.

Page 1 of 7

EVALUATION OF NEUROTTEXT AS A MEMORY AID FOR PEOPLE WITH MULTIPLE SCLEROSIS Participant Information Sheet  
Final Version 1.0 30.07.13



**Why have I been chosen?**

You have been invited to take part because you have multiple sclerosis, and are 18 years or over. We will ask you questions about your memory and on the basis of your answers, we may invite you to continue in the study.

**Do I have to take part?**

You can decide whether or not to take part in the study. If you do decide to take part you will be asked to sign a consent form. You are free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

**What will happen to me if I take part?**

If you agree to take part you will be contacted by a researcher to organise a visit at a place convenient for you, in which the researcher will talk to you about your memory problems. In addition, you will be asked to fill out some questionnaires and do some cognitive assessments. Assistance will be provided if required. The questionnaires will ask about you, the nature of your memory problems and how you are feeling. The assessments will help us get a clearer picture of your memory problems.

A few days after this visit, you will then be randomly assigned to receive NeuroText memory text messages for two months (followed by the social text messages for two months or to receive social text messages for two months followed by NeuroText memory text messages for two months (stage 2). You will be offered the choice of receiving texts to your mobile phone or a provided pager, and a trial message will be sent to ensure you can read the message and respond appropriately. Examples of messages you could receive include 'Remember to phone your brother, it's his birthday today' or 'Do not focus on the things you can't do, focus on what you can do'. You will only receive messages you want and choose to receive, at the times you ask for. You can change these messages at any stage of the study.

If you chose to use a pager (rather than your mobile), we will need to provide details to the Neuropage service which provides NeuroText, about the addresses of places you are likely to be when receiving your messages, e.g. work. This is to make sure there is adequate network coverage for you to receive the messages. We will also need to provide them with a contact number in the case of service issues. The Neuropage service is owned by Cambridgeshire Community Services NHS Trust.

You will be contacted by a researcher after the first or second day after starting to use the message system, to check that everything is going well. Throughout the study you will receive daily messages, in which the content and time of receiving have been agreed during the initial interview.

Any other rehabilitation will continue as usual. Any medication, including MS modifying drugs, will be prescribed as usual.

For the final two weeks of each stage, you will be asked to fill out a daily diary, in which you will record the frequency of memory problems identified in initial interview. At the end of each stage (after 2 months and after 4 months) you will be asked to fill out the questionnaires that were asked at the initial interview, again. You and your relative/carer will also be asked to fill out the Everyday Memory Questionnaire again.

A purposively selected sample of you will be invited to a feedback interview at a place that is convenient for you. This will be audio recorded and will give us more detailed information about your perception of both memory and social text messages.

#### **Expenses and payments**

Participants will not be paid an inconvenience allowance or travel expenses to participate in the study. However all meetings will be held at places that are convenient for you.

**What are the possible disadvantages and risks of taking part?**

There are no risks identified as a result of taking part in this study. Receiving and having to check text messages could be considered a burden. However in the initial interview the content and frequency of received messages is agreed by you.

**What are the possible benefits of taking part?**

We cannot promise the study will help you but the information we get from this study may help alleviate memory problems in your everyday life. As the Neuropage service that provides NeuroText is already available through the Oliver Zangwill Centre, Ely, if you find this study helpful, you could potentially add it to your care plan following completion of the study. Information collated and analysed at the initial assessment and during outcome assessment will be made available to you, which could help to understand your memory problems in more detail.

**What happens when the research study stops?****What if there is a problem?**

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. The researchers contact details are given at the end of this information sheet. If you remain unhappy and wish to complain formally, you can do this by contacting [\[contact details of local PALS\]](#).

**Will my taking part in the study be kept confidential?**

Yes. We will have confidentiality and security agreements in place to ensure your details are dealt with in the strictest confidence.

If you join the study, some parts of your medical records and the data collected for the study will be looked at by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by authorised people to check that

the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

All information which is collected about you during the course of the research will be kept strictly confidential, and any study information about you which leaves an NHS or University of Nottingham site will have your name and address removed so that you cannot be recognised. However, if you do agree to take part, we will let your GP or responsible clinician know that you are a participant in our research project.

Your personal data (address, telephone number) will be kept for 6 to 12 months after the end of the study so that we are able to contact you about the findings of the study (unless you advise us that you do not wish to be contacted). All other data (research data) will be kept securely for 7 years. After this time your data will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team will have access to your personal data.

The only reason that we would discuss the content of the questionnaires with anyone outside of the research team is if we were seriously concerned about your or someone else's safety or well-being. In such a case we would tell you if this was going to happen.

**What will happen if I don't want to carry on with the study?**

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw then the information collected so far cannot be erased and this information may still be used in the project analysis.

**What will happen to the results of the study?**

The study findings will be published in a report, and submitted for peer-review publication in a scientific journal. All information that could be used to identify you will be removed. You

will be asked if you wish to be informed of the results of the study. If you do, we will write to you about these once it is completed and we will destroy your address details once the results have been sent to you. All data will be treated in accordance with the Data Protection Act 1998.

#### **Involvement of the General Practitioner/Family doctor (GP)**

Your GP will be informed that you are taking part in this study. They will be provided with a copy of the Participant Information Sheet and contact details of the research team. They will also be asked to review any relevant prompts, and get in touch with the research team if there are any problems.

#### **Who is organising the study?**

The study is being organised by researchers at The University of Nottingham. The research is funded by the Multiple Sclerosis Society.

#### **Who has reviewed the study?**

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by [to be added when booked] Research Ethics Committee.

#### **Further information and contact details**

Think about whether or not you would like to take part in the study. Once you have decided, please complete the consent forms and Everyday Memory Questionnaire with a relative/friend and send them to us in the enclosed paid addressed envelope. A researcher will contact you and guide you through the next step and the project will begin.

**If you have any questions about this study please contact:**

Rachel Goodwin

Co- Investigator

PhD Student

Division of Rehabilitation and Ageing

Medical School

Queen's Medical Centre

University of Nottingham

Nottingham

NG7 2UH

Research Team Phone : 0758 212 9039

**Chief Investigator :**

Nadina Lincoln

Professor of Clinical Psychology

Division of Rehabilitation and Ageing

Medical School

Queen's Medical Centre

University of Nottingham

Nottingham

NG7 2UH

Tel: 0115 823 0230

**Thank you very much for your time and consideration**



## **Everyday Memory Questionnaire – Participant**

There are two sections to this questionnaire.

### **Section 1**

Below are listed some examples of things that happen to people in everyday life. Some of them may happen frequently and some may happen frequently and some may happen very rarely. We should like to know how often on average you think each one has happened to you over the past month. For each item, tell us if you forgot it:

**Once or less in the last month/ never**

**More than once a month but less than once a week**

**About once a week**

**More than once a week but less than once a day**

**Once or more a day**

Please tick one box for each item.

### **Section 2**

Below is the same list from Section 1 of things that happen to people in everyday life. This time we should like to know how important you think each item is for you. Tell us how important each item is for you by ticking one box for each item:

**Not at all important**

**Unimportant**

**Neither important or unimportant**

**Important**

**Very important**

**Please make sure you complete both sections.**



## Section 1

Tick one box below ☒

**Instructions:** Read each statement below. Tick one box to the right of the statement to indicate how often you experience this problem

|   | Once or less<br>in the last<br>month/<br>never | More than<br>once a<br>month but<br>less than<br>once a week | About once<br>a week | More than<br>once a week<br>but less<br>than once a | Once or<br>more a day |
|---|--|--|----------------------|---|-----------------------|
| X Example item  |  |  |                      | ✓   |                       |
| 1 Forgetting where you have put something. Losing things around the house   |  |  |                      |   |                       |
| 2 Failing to recognise places that you are told you have often been to before   |  |  |                      |   |                       |
| 3 Finding a television story difficult to follow  |  |  |                      |   |                       |
| 4 Not remembering a change in your daily routine, such as a change in the place where something is kept, or a change in the time something happens. Following your old routine by mistake |  |  |                      |   |                       |
| 5 Having to go back and check whether you have done something that you meant to do  |  |  |                      |   |                       |
| 6 Forgetting when it was that something happened; for example, whether it was yesterday or last week  |  |  |                      |   |                       |
| 7 Completely forgetting to take things with you, or leaving things behind and having to go back and fetch them  |  |  |                      |   |                       |
| 8 Forgetting that you were told something yesterday or a few days ago, and maybe having to be reminded about it   |  |  |                      |   |                       |
| 9 Starting to read something (a book or an article in a newspaper, or a magazine) without realising you have already read it before   |  |  |                      |   |                       |
| 10 Letting yourself ramble on to speak about unimportant or irrelevant things   |  |  |                      |   |                       |
| 11 Failing to recognise, by sight, close relatives or friends that you meet frequently  |  |  |                      |   |                       |
| 12 Having difficulty picking up a new skill. For example, finding it hard to learn a new game or to work some new gadget after you have practised once or twice                           |  |  |                      |   |                       |

**Instructions:** Read each statement below. Tick one box to the right of the statement to indicate how often you experience this problem

|    |   | Once or less<br>in the last<br>month/<br>never | More than<br>once a<br>month but<br>less than<br>once a week | About once<br>a week | More than<br>once a week<br>but less<br>than once a | Once or<br>more a day |
|----|---|--|--|----------------------|---|-----------------------|
| 13 | Finding that a word is 'on the tip of your tongue'. You know what it is but you cannot quite find it  |  |  |                      |   |                       |
| 14 | Completely forgetting to do things you said you would do, and things you planned to do  |  |  |                      |   |                       |
| 15 | Forgetting important details of what you did or what happened to you the day before   |  |  |                      |   |                       |
| 16 | When talking to someone, forgetting what you have just said. Maybe saying 'what was I talking about?'   |  |  |                      |   |                       |
| 17 | When reading a newspaper or magazine being unable to follow the thread of a story; losing track of what it is all about                                       |  |  |                      |   |                       |
| 18 | Forgetting to tell somebody something important. Perhaps forgetting to pass on a message or remind someone of something                                       |  |  |                      |   |                       |
| 19 | Forgetting important details about yourself, e.g., your birth date or where you live  |  |  |                      |   |                       |
| 20 | Getting details of what someone has told you mixed up and confused  |  |  |                      |   |                       |
| 21 | Telling someone a story or joke that you have already told them once already  |  |  |                      |   |                       |
| 22 | Forgetting details of things you do regularly, whether at home or at work. For example, forgetting details of what to do, or forgetting at what time to do it |  |  |                      |   |                       |
| 23 | Finding the faces of famous people seen on television or in photographs, look unfamiliar  |  |  |                      |   |                       |
| 24 | Forgetting where things are normally kept or looking for them in the wrong place  |  |  |                      |   |                       |
| 25 | Getting lost or turning in the wrong direction on a journey, on a walk or in a building where you have OFTEN been before                                      |  |  |                      |   |                       |
| 26 | Getting lost or turning in the wrong direction on a journey, on a walk or in a building where you have ONLY BEEN ONCE OR TWICE before                         |  |  |                      |   |                       |
| 27 | Doing some routine thing twice by mistake. For example, putting two lots of tea in the teapot, or going to brush/ comb your hair when you have just done so   |  |  |                      |   |                       |
| 28 | Repeating to someone what you have just told them or asking them the same question twice  |  |  |                      |   |                       |

## Section 2

Tick one box below ☒

**Instructions:** Read each statement below. Tick one box to the right of the statement to indicate how important this problem is to you

|   | Not at all important | Unimportant | Neither important or | Important | Very important |
|---|----------------------|-------------|----------------------|-----------|----------------|
| X Example item  |                      | ✓           |                      |           |                |
| 1 Forgetting where you have put something. Losing things around the house   |                      |             |                      |           |                |
| 2 Failing to recognise places that you are told you have often been to before   |                      |             |                      |           |                |
| 3 Finding a television story difficult to follow  |                      |             |                      |           |                |
| 4 Not remembering a change in your daily routine, such as a change in the place where something is kept, or a change in the time something happens. Following your old routine by mistake |                      |             |                      |           |                |
| 5 Having to go back and check whether you have done something that you meant to do  |                      |             |                      |           |                |
| 6 Forgetting when it was that something happened; for example, whether it was yesterday or last week  |                      |             |                      |           |                |
| 7 Completely forgetting to take things with you, or leaving things behind and having to go back and fetch them  |                      |             |                      |           |                |
| 8 Forgetting that you were told something yesterday or a few days ago, and maybe having to be reminded about it   |                      |             |                      |           |                |
| 9 Starting to read something (a book or an article in a newspaper, or a magazine) without realising you have already read it before   |                      |             |                      |           |                |
| 10 Letting yourself ramble on to speak about unimportant or irrelevant things   |                      |             |                      |           |                |
| 11 Failing to recognise, by sight, close relatives or friends that you meet frequently  |                      |             |                      |           |                |
| 12 Having difficulty picking up a new skill. For example, finding it hard to learn a new game or to work some new gadget after you have practised once or twice                           |                      |             |                      |           |                |

**Instructions:** Read each statement below. Tick one box to the right of the statement to indicate how important this problem is to you

|  | Not at all important | Unimportant | Neither important or | Important | Very important |
|--|----------------------|-------------|----------------------|-----------|----------------|
| 13 Finding that a word is 'on the tip of your tongue'. You know what it is but you cannot quite find it  |                      |             |                      |           |                |
| 14 Completely forgetting to do things you said you would do, and things you planned to do  |                      |             |                      |           |                |
| 15 Forgetting important details of what you did or what happened to you the day before   |                      |             |                      |           |                |
| 16 When talking to someone, forgetting what you have just said. Maybe saying 'what was I talking about?'   |                      |             |                      |           |                |
| 17 When reading a newspaper or magazine being unable to follow the thread of a story; losing track of what it is all about                                       |                      |             |                      |           |                |
| 18 Forgetting to tell somebody something important. Perhaps forgetting to pass on a message or remind someone of something                                       |                      |             |                      |           |                |
| 19 Forgetting important details about yourself, e.g., your birth date or where you live  |                      |             |                      |           |                |
| 20 Getting details of what someone has told you mixed up and confused  |                      |             |                      |           |                |
| 21 Telling someone a story or joke that you have already told them once already  |                      |             |                      |           |                |
| 22 Forgetting details of things you do regularly, whether at home or at work. For example, forgetting details of what to do, or forgetting at what time to do it |                      |             |                      |           |                |
| 23 Finding the faces of famous people seen on television or in photographs, look unfamiliar  |                      |             |                      |           |                |
| 24 Forgetting where things are normally kept or looking for them in the wrong place  |                      |             |                      |           |                |
| 25 Getting lost or turning in the wrong direction on a journey, on a walk or in a building where you have <b>OFTEN</b> been before                               |                      |             |                      |           |                |
| 26 Getting lost or turning in the wrong direction on a journey, on a walk or in a building where you have <b>ONLY BEEN ONCE OR TWICE</b> before                  |                      |             |                      |           |                |
| 27 Doing some routine thing twice by mistake. For example, putting two lots of tea in the teapot, or going to brush/ comb your hair when you have just done so   |                      |             |                      |           |                |
| 28 Repeating to someone what you have just told them or asking them the same question twice  |                      |             |                      |           |                |



## Appendix 6: Invitation to study version 2

[TO BE PRINTED ON TRUST HEADED PAPER]



[Potential Participant Address]

### Evaluation of NeuroText as a Memory Aid for People with Multiple Sclerosis

I am sending you information on a study aimed at evaluating whether NeuroText helps reduce memory problems for people with multiple sclerosis.

Many people with MS report having memory problems, which can make their everyday life difficult. Strategies such as memory aids have been found to be useful in people with other neurological conditions. NeuroText is a memory aid device which sends text messages to a mobile or pager at pre-arranged times to remind people to carry out activities or as prompts to check they have done those things they should have done.

Improving memory problems for people with MS is important. The researchers want to compare whether people with MS who receive memory text messages on NeuroText show a reduction in reported memory problems in everyday life, in comparison with those who receive social text messages.

If you are interested in taking part in this study please could you fill out the **Contact Slip** detailing the address and phone number we can contact you on.

Could you please send this back to us in the enclosed paid envelope and the team will get in touch to arrange a visit whenever is best for you. Your clinician can fill this out and send this to the researcher if you would prefer.

I have enclosed a **Participant Information Sheet** about the study. Please read this before you decide whether you wish to take part in this study. If you decide to take part, please can you and a relative/friend read and complete the enclosed **Consent Form** each, and keep this for when the researcher visits you.

If you have any questions about the study and want to speak to the research team, you can contact the team and ask for Rachel Goodwin by:

- Calling the Research Team Phone on 0758 212 9039, or
- Emailing [lwrag@nottingham.ac.uk](mailto:lwrag@nottingham.ac.uk)

Many thanks.

Yours sincerely,

From clinician

Final Version 2.0 dated 07/10/2013

Page 1 of 2

[TO BE PRINTED ON TRUST HEADED PAPER]



### Participant Contact Details

[Potential Participant Address]

I would like a member of the team to get in touch with me using the details below, and am happy for them to ask me questions about my memory over the phone

1) Name: \_\_\_\_\_

2) Contact number: \_\_\_\_\_

3) Contact Address: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_





## Appendix 7: NeuroText timetable example



Name:

Pager/Mobile No:

### Section 1 REGULAR ONGOING MESSAGES

| Start Date:         | <i>Fill in the time on the days you would like to receive each message.</i> |       |       |       |       |       |       |
|---------------------|---|-------|-------|-------|-------|-------|-------|
| End Date:           |   |       |       |       |       |       |       |
| Message             | Mon   | Tue   | Wed   | Thurs | Fri   | Sat   | Sun   |
| Take your injection |   | 10.30 |       | 10.30 |       |       | 10.30 |
| Take your tablets   | 13.00   | 13.00 | 13.00 | 13.00 | 13.00 | 13.00 | 13.00 |
| Take your tablets   | 21.00   | 21.00 | 21.00 | 21.00 | 21.00 | 21.00 | 21.00 |
| Put the bins out    | 18.00   |       |       |       |       |       |       |
|                     |   |       |       |       |       |       |       |
|                     |   |       |       |       |       |       |       |
|                     |   |       |       |       |       |       |       |
|                     |   |       |       |       |       |       |       |

### Section 2 IRREGULAR OR ONE-OFF MESSAGES

| Message                        | Date | Time  | Frequency e.g. Once / Monthly / yearly |
|--------------------------------|------|-------|--|
| Check your handbag for tablets |      | 18.00 | Every other sunday                     |
|                                |      |       |  |



Cambridgeshire Community Services is responsible for providing a range of NHS and social care services in the Cambridgeshire area, commissioned by and accountable to Cambridgeshire Primary Care Trust

# Appendix 8: Control timetable example



Name: Pager/Mobile No:

RSS Feeds: world headlines

Section 1  
REGULAR ONGOING MESSAGES

| Start Date:<br>End Date: | Fill in the time on the days you would like to receive each message. |       |       |       |       |       |       |
|--------------------------|--|-------|-------|-------|-------|-------|-------|
| Message                  | Mon  | Tue   | Wed   | Thurs | Fri   | Sat   | Sun   |
| RSS Feed                 | 08.20  | 08.20 | 08.20 | 08.20 | 08.20 |       |       |
| RSS Feed                 | 09.00  | 09.00 | 09.00 | 09.00 | 09.00 |       |       |
| RSS Feed                 | 12.00  | 12.00 | 12.00 | 12.00 | 12.00 | 12.00 | 12.00 |
| RSS Feed                 | 15.45  | 15.45 | 15.45 | 15.45 | 15.45 |       |       |
| RSS Feed                 | 22.00  | 22.00 | 22.00 | 22.00 | 22.00 | 22.00 | 22.00 |



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## Appendix 9: Baseline visit topic guide



### Evaluation of NeuroText as a memory aid for people with multiple sclerosis

#### Interview/assessment topic guide and prompts

Final Version 1.0

30.07.2013

*[Note: The following is only a guide of the topics that will be covered during the interview. In line with qualitative research guidelines, the interviews guide is likely to change slightly following each interview, as this is an iterative process.]*

#### For all participants:

- 1) Check they understand what the trial is about
- 2) Introduction to NeuroText and choice of mobile or pager
- 3) Check they can use
- 4) Ask them to describe a typical day, focus on memory problems (daily diary examples)
- 5) What reminders do you think would help? What time of day? Wording?
- 6) Emphasise that they can modify at any time during the trial.
- 7) Chose social text messages from bank of 10 examples
- 8) Want information on memory and MS? Guide to MS Society booklets

#### Possible prompts

- Please could you tell us more about ...?
- Could you give me some examples about ...?

## Appendix 10: Demographic Form

### Demographic Record Form

Today's date:

ID Number:

DOB:

Sex:

Female

Male

Partnership  
status:

Never  
married or  
civil  
partnership

Married or  
civil  
partnership

Separated,  
but still  
legally  
married or  
civil  
partnership

Divorced or  
legally  
dissolved  
civil  
partnership

Widowed or surviving  
partner from civil  
partnership

GP name and  
address:

Ethnicity:  
(see sheet)

Highest  
Educational  
Qualification:  
(see sheet)

Employment  
status :  
(FT/PT)

Occupation:  
(see sheet)

Beliefs:

Type of MS:

Years since  
diagnosis:

Time since  
last relapse:

Using Mobile  
Phone –  
number:

Using Pager:

**If using pager:  
Details of  
address**

**Contact  
number**

**Address of  
anywhere  
likely to  
commonly use  
the service,  
e.g. work**

Appendix 11: Participant outcome questionnaire



NeuroText Study  
Participant Questionnaires

Date form completed:

/

/

D

D

M

M

M

Y

Y

Y

Y

Your study ID:

Thank you in advance for completing this questionnaire. Please check that you answer all questions, and that no pages are missed by accident.

## Instructions

For most of the questions all you need to do is tick a box or circle the answer.

If you need help filling in this questionnaire, please feel free to discuss this with a relative or friend. But please make sure the answers are your own views.

It may take you about 25 minutes to fill in, depending on how much time you wish to spend on it. As you fill it out, don't spend too much time on any one question. There are no right or wrong answers.

Your answers to the questions are extremely valuable for the successful completion of the research. **We also want to remind you that your answers will be kept completely confidential. Therefore, your answers will in no way affect your care.**

Please check that you answer all questions and that no pages are missed by accident.

If you need any information then contact the research team on 0758 212 9039.



## **Everyday Memory Questionnaire – Participant**

## Everyday Memory Questionnaire – Participant

There are two sections to this questionnaire.

### Section 1

Below are listed some examples of things that happen to people in everyday life. Some of them may happen frequently and some may happen frequently and some may happen very rarely. We should like to know how often on average you think each one has happened to you over the past month. For each item, tell us if you forgot it:

**Once or less in the last month/ never**

**More than once a month but less than once a week**

**About once a week**

**More than once a week but less than once a day**

**Once or more a day**

Please tick one box for each item.

### Section 2

Below is the same list from Section 1 of things that happen to people in everyday life. This time we should like to know how important you think each item is for you. Tell us how important each item is for you by ticking one box for each item:

**Not at all important**

**Unimportant**

**Neither important or unimportant**

**Important**

**Very important**

**Please make sure you complete both sections.**

## Everyday Memory Questionnaire – Participant

### Section 1

Tick one box below ☒

**Instructions:** Read each statement below. Tick one box to the right of the statement to indicate how often you experience this

|   | Once or less<br>in the last<br>month/<br>never | More than<br>once a<br>month but<br>less than<br>once a week | About once<br>a week | More than<br>once a week<br>but less | Once or<br>more a day |
|---|--|--|----------------------|--------------------------------------|-----------------------|
| X Example item  |  |  |                      | ✓                                    |                       |
| 1 Forgetting where you have put something. Losing things around the house   |  |  |                      |                                      |                       |
| 2 Failing to recognise places that you are told you have often been to before   |  |  |                      |                                      |                       |
| 3 Finding a television story difficult to follow  |  |  |                      |                                      |                       |
| 4 Not remembering a change in your daily routine, such as a change in the place where something is kept, or a change in the time something happens. Following your old routine by mistake |  |  |                      |                                      |                       |
| 5 Having to go back and check whether you have done something that you meant to do  |  |  |                      |                                      |                       |
| 6 Forgetting when it was that something happened; for example, whether it was yesterday or last week  |  |  |                      |                                      |                       |
| 7 Completely forgetting to take things with you, or leaving things behind and having to go back and fetch them  |  |  |                      |                                      |                       |
| 8 Forgetting that you were told something yesterday or a few days ago, and maybe having to be reminded about it   |  |  |                      |                                      |                       |
| 9 Starting to read something (a book or an article in a newspaper, or a magazine) without realising you have already read it before   |  |  |                      |                                      |                       |
| 10 Letting yourself ramble on to speak about unimportant or irrelevant things   |  |  |                      |                                      |                       |
| 11 Failing to recognise, by sight, close relatives or friends that you meet frequently  |  |  |                      |                                      |                       |
| 12 Having difficulty picking up a new skill. For example, finding it hard to learn a new game or to work some new gadget after you have practised once or twice                           |  |  |                      |                                      |                       |

## Everyday Memory Questionnaire – Participant

**Instructions:** Read each statement below. Tick one box to the right of the statement to indicate how often you experience this

|  | Once or less<br>in the last<br>month/<br>never | More than<br>once a<br>month but<br>less than<br>once a week | About once<br>a week | More than<br>once a week<br>but less | Once or<br>more a day |
|--|--|--|----------------------|--------------------------------------|-----------------------|
| 13 Finding that a word is 'on the tip of your tongue'. You know what it is but you cannot find it  |  |  |                      |                                      |                       |
| 14 Completely forgetting to do things you said you would do, and things you planned to do  |  |  |                      |                                      |                       |
| 15 Forgetting important details of what you did or what happened to you the day before   |  |  |                      |                                      |                       |
| 16 When talking to someone, forgetting what you have just said. Maybe saying 'what was I talking about?'   |  |  |                      |                                      |                       |
| 17 When reading a newspaper or magazine being unable to follow the thread of a story; losing track of what it is all about                                       |  |  |                      |                                      |                       |
| 18 Forgetting to tell somebody something important. Perhaps forgetting to pass on a message or remind someone of something                                       |  |  |                      |                                      |                       |
| 19 Forgetting important details about yourself, e.g., your birth date or where you live  |  |  |                      |                                      |                       |
| 20 Getting details of what someone has told you mixed up and confused  |  |  |                      |                                      |                       |
| 21 Telling someone a story or joke that you have already told them once already  |  |  |                      |                                      |                       |
| 22 Forgetting details of things you do regularly, whether at home or at work. For example, forgetting details of what to do, or forgetting at what time to do it |  |  |                      |                                      |                       |
| 23 Finding the faces of famous people seen on television or in photographs, look unfamiliar  |  |  |                      |                                      |                       |
| 24 Forgetting where things are normally kept or looking for them in the wrong place  |  |  |                      |                                      |                       |
| 25 Getting lost or turning in the wrong direction on a journey, on a walk or in a building where you have <u>OFTEN</u> been before                               |  |  |                      |                                      |                       |
| 26 Getting lost or turning in the wrong direction on a journey, on a walk or in a building where you have <u>ONLY BEEN ONCE OR TWICE</u> before                  |  |  |                      |                                      |                       |
| 27 Doing some routine thing twice by mistake. For example, putting two lots of tea in the teapot, or going to brush/comb your hair when you have just done so    |  |  |                      |                                      |                       |

Everyday Memory Questionnaire – Participant

|    |  |  |  |  |  |  |
|----|--|--|--|--|--|--|
| 28 | Repeating to someone what you have just told them or asking them the same question twice |  |  |  |  |  |
|----|--|--|--|--|--|--|

## Everyday Memory Questionnaire – Participant

### Section 2

Tick one box below ☒

**Instructions:** Read each statement below. Tick one box to the right of the statement to indicate how important this problem is

|   | Not at all important | Unimportant | Neither important | Important | Very important |
|---|----------------------|-------------|-------------------|-----------|----------------|
| X Example item  |                      | ✓           |                   |           |                |
| 1 Forgetting where you have put something. Losing things around the house   |                      |             |                   |           |                |
| 2 Failing to recognise places that you are told you have often been to before   |                      |             |                   |           |                |
| 3 Finding a television story difficult to follow  |                      |             |                   |           |                |
| 4 Not remembering a change in your daily routine, such as a change in the place where something is kept, or a change in the time something happens. Following your old routine by mistake |                      |             |                   |           |                |
| 5 Having to go back and check whether you have done something that you meant to do  |                      |             |                   |           |                |
| 6 Forgetting when it was that something happened; for example, whether it was yesterday or last week  |                      |             |                   |           |                |
| 7 Completely forgetting to take things with you, or leaving things behind and having to go back and fetch them  |                      |             |                   |           |                |
| 8 Forgetting that you were told something yesterday or a few days ago, and maybe having to be reminded about it   |                      |             |                   |           |                |
| 9 Starting to read something (a book or an article in a newspaper, or a magazine) without realising you have already read it before   |                      |             |                   |           |                |
| 10 Letting yourself ramble on to speak about unimportant or irrelevant things   |                      |             |                   |           |                |
| 11 Failing to recognise, by sight, close relatives or friends that you meet frequently  |                      |             |                   |           |                |
| 12 Having difficulty picking up a new skill. For example, finding it hard to learn a new game or to work some new gadget after you have practised once or twice                           |                      |             |                   |           |                |

## Everyday Memory Questionnaire – Participant

**Instructions:** Read each statement below. Tick one box to the right of the statement to indicate how important this problem is

|  | Not at all important | Unimportant | Neither important | Important | Very important |
|--|----------------------|-------------|-------------------|-----------|----------------|
| 13 Finding that a word is 'on the tip of your tongue'. You know what it is but you cannot write it down  |                      |             |                   |           |                |
| 14 Completely forgetting to do things you said you would do, and things you planned to do  |                      |             |                   |           |                |
| 15 Forgetting important details of what you did or what happened to you the day before   |                      |             |                   |           |                |
| 16 When talking to someone, forgetting what you have just said. Maybe saying 'what was I talking about?'   |                      |             |                   |           |                |
| 17 When reading a newspaper or magazine being unable to follow the thread of a story; losing track of what it is all about                                       |                      |             |                   |           |                |
| 18 Forgetting to tell somebody something important. Perhaps forgetting to pass on a message or remind someone of something                                       |                      |             |                   |           |                |
| 19 Forgetting important details about yourself, e.g., your birth date or where you live  |                      |             |                   |           |                |
| 20 Getting details of what someone has told you mixed up and confused  |                      |             |                   |           |                |
| 21 Telling someone a story or joke that you have already told them once already  |                      |             |                   |           |                |
| 22 Forgetting details of things you do regularly, whether at home or at work. For example, forgetting details of what to do, or forgetting at what time to do it |                      |             |                   |           |                |
| 23 Finding the faces of famous people seen on television or in photographs, look unfamiliar  |                      |             |                   |           |                |
| 24 Forgetting where things are normally kept or looking for them in the wrong place  |                      |             |                   |           |                |
| 25 Getting lost or turning in the wrong direction on a journey, on a walk or in a building where you have <b>OFTEN</b> been before                               |                      |             |                   |           |                |
| 26 Getting lost or turning in the wrong direction on a journey, on a walk or in a building where you have <b>ONLY BEEN ONCE OR TWICE</b> before                  |                      |             |                   |           |                |
| 27 Doing some routine thing twice by mistake. For example, putting two lots of tea in the teapot, or going to brush / comb your hair when you have just done so  |                      |             |                   |           |                |

Everyday Memory Questionnaire – Participant

|    |  |  |  |  |  |  |
|----|--|--|--|--|--|--|
| 28 | Repeating to someone what you have just told them or asking them the same question twice |  |  |  |  |  |
|----|--|--|--|--|--|--|



## General Health Questionnaire

# General Health Questionnaire

Please read this carefully:

We should like to know if you have had any medical complaints, and how your health has been in general, *over the past few weeks*. Please answer ALL the questions simply by underlining the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those you had in the past. It is important that you try to answer ALL the questions.

Thank you very much for your co-operation.

---

## HAVE YOU RECENTLY:

- |  |                              |                            |                          |                        |
|--|------------------------------|----------------------------|--------------------------|------------------------|
| 1 — <b>been able to concentrate on</b><br>Much less<br><b>whatever you're doing?</b><br>than usual       | Better than<br><br>usual     | Same as<br><br>usual       | Less<br><br>usual        | than                   |
| 2 — <b>lost much sleep over worry?</b><br>Much more  | Not at all<br><br>than usual | No more<br><br>than usual  | Rather<br><br>than usual | more                   |
| 3 — <b>been having restless, disturbed</b><br>Much more<br><b>nights?</b>                                | Not at all<br><br>than usual | No more<br><br>than usual  | Rather<br><br>than usual | more                   |
| 4 — <b>been managing to keep yourself</b><br>Much less<br><b>busy and occupied?</b><br>than usual        | More so<br><br>than usual    | Same as<br><br>usual       | Rather<br><br>than       | less<br><br>usual      |
| 5 — <b>been getting out of the house as</b><br>Much less<br><b>much as usual?</b><br>than usual          | More so<br><br>than usual    | Same as<br><br>usual       | Less<br><br>usual        | than                   |
| 6 — <b>been managing as well as most</b><br>Much less<br><b>people would in your shoes?</b><br>well      | Better than<br><br>most      | About the<br><br>same      | Rather<br><br>well       | less                   |
| 7 — <b>felt on the whole you were doing</b><br>Much less<br><b>things well?</b><br>well                  | Better than<br><br>usual     | About the<br><br>same      | Less<br><br>than         | well<br><br>usual      |
| 8 — <b>been satisfied with the way you've</b><br>Much less<br><b>carried out your task?</b><br>satisfied | More<br><br>satisfied        | About same<br><br>as usual | Less<br><br>than         | satisfied<br><br>usual |
| 9 — <b>been able to feel warmth and</b><br>Much less<br><b>affection for those near to you?</b><br>well  | Better than<br><br>usual     | About same<br><br>as usual | Less<br><br>than         | well<br><br>usual      |
| 10 — <b>been finding it easy to get on with</b><br>Much less   | Better than                  | About same                 | Less                     | well                   |

## General Health Questionnaire

|             |  |                         |                     |              |                 |
|-------------|--|-------------------------|---------------------|--------------|-----------------|
|             | <b>other people?</b><br>well   | usual                   | as usual            | than         | usual           |
| <b>11 —</b> | <b>spent much time chatting with</b><br>Much less<br><b>people?</b><br>than usual          | More time<br>than usual | More so<br>as usual | Less<br>than | time<br>usual   |
| <b>12 —</b> | <b>felt that you are playing a useful</b><br>Much less<br><b>part in things?</b><br>useful | More so<br>than usual   | Same as<br>usual    | Less<br>than | useful<br>usual |
| <b>13 —</b> | <b>felt capable of making decisions</b><br>Much less<br><b>about things?</b><br>capable    | More so<br>than usual   | Same<br>as usual    | Less<br>than | so<br>usual     |

## General Health Questionnaire

### HAVE YOU RECENTLY:

|  |                       |                       |                |               |
|--|-----------------------|-----------------------|----------------|---------------|
| <b>14 — felt constantly under strain?</b><br>Much more<br>than usual                             | Not at all            | No more<br>than usual | Rather<br>than | more<br>usual |
| <b>15 — felt you couldn't overcome<br/>your difficulties?</b><br>Much more<br>than usual         | Not at all            | No more<br>than usual | Rather<br>than | more<br>usual |
| <b>16 — been finding life a struggle<br/>all the time?</b><br>Much more<br>than usual            | Not at all            | No more<br>than usual | Rather<br>than | more<br>usual |
| <b>17 — been able to enjoy your normal<br/>day-to-day activities?</b><br>Much less<br>than usual | More so<br>than usual | Same as<br>usual      | Less<br>usual  | so<br>than    |
| <b>18 — been taking things hard?</b><br>Much more<br>than usual                                  | Not at all            | No more<br>than usual | Rather<br>than | more<br>usual |
| <b>19 — been getting scared or panicky<br/>for no good reason?</b><br>Much more<br>than usual    | Not at all            | No more<br>than usual | Rather<br>than | more<br>usual |
| <b>20 — been able to face up to your<br/>problems?</b><br>Much less<br>able                      | More so<br>than usual | Same as<br>usual      | Less<br>usual  | able<br>than  |
| <b>21 — found everything getting on top<br/>of you?</b><br>Much more<br>than usual               | Not at all            | No more<br>than usual | Rather<br>than | more<br>usual |
| <b>22 — been feeling unhappy and<br/>depressed?</b><br>Much more<br>than usual                   | Not at all            | No more<br>than usual | Rather<br>than | more<br>usual |
| <b>23 — been losing confidence in<br/>yourself?</b><br>Much more<br>than usual                   | Not at all            | No more<br>than usual | Rather<br>than | more<br>usual |
| <b>24 — been thinking of yourself as<br/>a worthless person?</b><br>Much more<br>than usual      | Not at all            | No more<br>than usual | Rather<br>than | more<br>usual |

## General Health Questionnaire

|  |            |            |        |       |
|--|------------|------------|--------|-------|
| 25 — <b>felt that life is entirely hopeless?</b><br>Much more<br><br>than usual  | Not at all | No more    | Rather | more  |
|  |            | than usual | than   | usual |
|  |            |            |        |       |
| 26 — <b>been feeling hopeful about your<br/>own future?</b><br>Much less<br>hopeful                                      | More so    | About same | Less   | so    |
|  | than usual | as usual   | usual  | than  |
|  |            |            |        |       |
| 27 — <b>been feeling reasonably happy,<br/>all things considered?</b><br>Much less<br>than usual                         | More so    | About same | Less   | so    |
|  | than usual | as usual   | than   | usual |
|  |            |            |        |       |
| 28 — <b>been feeling nervous and<br/>strung-up all the time?</b><br>Much more<br>than usual                              | Not at all | No more    | Rather | more  |
|  |            | than usual | than   | usual |
|  |            |            |        |       |
| 29 — <b>felt that life isn't worth living?</b><br>Much more<br><br>than usual  | Not at all | No more    | Rather | more  |
|  |            | than usual | than   | usual |
|  |            |            |        |       |
| 30 — <b>found at times you couldn't<br/>do anything because your nerves<br/>were too bad?</b><br>Much more<br>than usual | Not at all | No more    | Rather | more  |
|  |            | than usual | than   | usual |
|  |            |            |        |       |

## Adaption to Memory Difficulties Outcome Questionnaire

This is a set of questions about how you think you cope with your memory problems. There are no right or wrong answers. Please take your time and answer all questions. Tick the answer you feel best applies to you:

### Part A

**1. I have had enough information on why I have memory problems.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**2. I understand how memory works.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**3. I find it difficult to come to terms with my memory problems.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**4. I know how to use the strong aspects of my memory to compensate for the weaker aspects.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**5. I understand why I remember some things more easily than others.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**6. I am well organised in how I cope with my memory problems.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**7. I have been doing things that I believe will improve my memory.**

## Adaption to Memory Difficulties Outcome Questionnaire

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

### 8. I have little control over my memory ability.

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

### 9. There are ways to cope with my memory difficulties.

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

### 10. I rely on other people to remind me of what I have to do.

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

### 11. I am confident that I can cope with my memory difficulties.

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

### 12. It upsets me when others notice my memory problems.

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

### 13. I am anxious about my memory problems.

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

### 14. My memory problems make me feel embarrassed.

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

### 15. I panic when I forget something important.

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

## Adaption to Memory Difficulties Outcome Questionnaire

*Agree*

*Disagree*

### Part B. MEMORY AIDS

**Memory aids are strategies we may all use to help us remember things. They can be external or internal:**

**B1. External memory aids:** can be objects or other cues in our surroundings to help us remember things without relying on our memory.

**16. The following is a list of external memory aids. Please indicate which of these you are using. If you are NOT using any external memory aids please go to question 21 on the next page.**

Tick as many as applicable:

- |  |                          |
|--|--------------------------|
| <b>Diary/personal organizer</b>  | <input type="checkbox"/> |
| <b>Alarms/timers</b>   | <input type="checkbox"/> |
| <b>Making notes of anything you need to remember</b>   | <input type="checkbox"/> |
| <b>Calendar/year planner</b>   | <input type="checkbox"/> |
| <b>Dictaphone/ tape recorder</b>   | <input type="checkbox"/> |
| <b>Post it notes</b>   | <input type="checkbox"/> |
| <b>To do lists</b>   | <input type="checkbox"/> |
| <b>Mobile phone</b>  | <input type="checkbox"/> |
| <b>Computer</b>  | <input type="checkbox"/> |
| <b>Object placement</b><br>e.g. putting things in an obvious place where you will notice them.<br>/putting things at the same place all the time | <input type="checkbox"/> |
| <b>Following a routine</b><br>e.g. doing specific things at specific times   | <input type="checkbox"/> |
| <b>Ask someone else to remind you of things to do</b>  | <input type="checkbox"/> |
| <b>Any others:</b>   |                          |



## Adaption to Memory Difficulties Outcome Questionnaire

**Please consider the external memory aids you are using and complete the following questions:**

**17. I believe that I make the most of the external memory aids I am using.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**18. I know which external memory aids work best for me.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**19. The external memory aids I am using are effective.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**20. I have a range of external memory aids that I can use for different tasks.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**21. If you are NOT using any external memory aids please indicate the reasons by ticking one or more of the boxes:**

- I have never tried to use them ☐
- I feel embarrassed to use them ☐
- I have tried but found them too complicated ☐
- I have tried but they don't work for me ☐

Any other reasons:

## Adaption to Memory Difficulties Outcome Questionnaire

**B2. Internal memory aids** are “tricks” to help us remember things when we only have our memory to rely on.

**22. The following is a list of internal memory aids. Please indicate which of these you are using. If you are NOT using any internal memory aids please go to question 27 on the next page.**

Tick as many as applicable:

**Repeating something you want to remember** (silently or out loud) ☐

**Putting similar things into groups** (e.g. things you want to buy into vegetables, clothes, stationary etc.) ☐

**Relating what you want to remember with something you already know** (e.g. a friend's name on the 26<sup>th</sup> December as one day after Christmas) ☐

**Making a picture in your mind of things you want to remember** (e.g. to remember the name Victoria Waters picture Queen Victoria by a waterfall) ☐

**Making up a little story including things you want to remember** ☐

**Paying attention to details** (e.g. when parking the car try to observe the surroundings and watch for a landmark) ☐

**Blocking information into chunks that make sense for you** (e.g. telephone numbers: 9515698 → 95-15-698) ☐

**Acronyms** (e.g. lists of groceries → MEMORY: milk, eggs, matches, olives, rice, yeast) ☐

Any others:

## Adaption to Memory Difficulties Outcome Questionnaire

**Please consider the internal memory aids you are using and complete the following questions:**

**23. I believe that I make the most of the internal memory aids I am using.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**24. I know which internal memory aids work best for me.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**25. The internal memory aids I am using are effective.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**26. I have a range of internal memory aids that I can use for different tasks.**

Agree ☐      Slightly Agree ☐      Slightly Disagree ☐      Disagree ☐

**27. If you are NOT using any internal memory aids please indicate the reasons by ticking one or more of the boxes:**

- I have never tried to use them ☐
- I feel embarrassed to use them ☐
- I have tried but found them too complicated ☐
- I have tried but they don't work for me ☐

Any other reasons:

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

**a) I have no problems in walking about**

☐

b) I have some problems in walking about

☐

c) I am confined to bed

Self-Care

a) I have no problems with self care

☐

b) I have some problems washing or dressing myself

☐

c) I am unable to wash or dress myself

Usual Activities

a) I have no problems with performing my usual activities (e.g. work, study, housework, family or leisure activities)

☐

b) I have some problems with performing my usual activities

☐

c) I am unable to perform my usual activities

☐

Pain/Discomfort

**a) I have no pain or discomfort**

☐

b) I have moderate pain or discomfort

☐

c) I have extreme pain or discomfort

☐

Anxiety/Depression

a) I am not anxious or depressed

☐

b) I am moderately anxious or depressed

☐

c) I am extremely anxious or depressed

☐

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked by 100 and the worst you can imagine is marked by 0.

We would like you to indicate on this scale how good or bad is your own health today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your current health state is.

Best  
imaginable  
health state

100

|                          |
|--------------------------|
| Your own<br>health state |
|--------------------------|

0

Worst imaginable  
health state

Thank you for your help

**Please send the completed Questionnaire to:**

Rachel Goodwin  
NeuroText Study  
University of Nottingham  
Division of Rehabilitation and Ageing  
Medical School  
Queen's Medical Centre  
Nottingham  
NG7 2UH

**If you would like to discuss this questionnaire, or any further information please  
contact the Research Team:**

**Tel: 0758 212 9039      Email: [lwrag@nottingham.ac.uk](mailto:lwrag@nottingham.ac.uk)**



## Appendix 12: Daily diary template

Participant Study Number 1



### **Daily Diary** **Week Commencing:**

At the end of each day, please fill out the **number of times** you have experienced each identified memory problem during your day.

| Memory problem                 | Number of times a day |                       |                         |                        |                      |
|--------------------------------|-----------------------|-----------------------|-------------------------|------------------------|----------------------|
|                                | Monday<br>09/03/2015  | Tuesday<br>10/03/2015 | Wednesday<br>11/03/2015 | Thursday<br>12/03/2015 | Friday<br>13/03/2015 |
| Forgot to take your medication |                       |                       |                         |                        |                      |
|                                |                       |                       |                         |                        |                      |

| Memory problem              | Number of times a day |                       |                         |                        |                      |
|-----------------------------|-----------------------|-----------------------|-------------------------|------------------------|----------------------|
|                             | Monday<br>16/03/2015  | Tuesday<br>17/03/2015 | Wednesday<br>18/03/2015 | Thursday<br>19/03/2015 | Friday<br>20/03/2015 |
| Forgot to go to appointment |                       |                       |                         |                        |                      |
| Forgot to take medication   |                       |                       |                         |                        |                      |





## Appendix 13: Feedback interview topic guide



### Evaluation of NeuroText as a memory aid for people with multiple sclerosis

#### Feedback interviews topic guide and prompts

Final Version 1.0

30.07.2013

*[Note: The following is only a guide of the topics that will be covered during the interview. In line with qualitative research guidelines, the interviews guide is likely to change slightly following each interview, as this is an iterative process.]*

#### For all participants:

1. Please tell us about your experience of being involved in this study.
2. What was it like receiving the memory text messages?
3. What did you find most useful about the memory text messages?
4. What did you find least useful about the memory text messages?
5. What improvements/changes would you like seen made to the memory text messages?
6. What was it like receiving the social text messages?
7. What did you find most useful about the social text messages?
8. What did you find least useful about the social text messages?
9. What improvements/changes would you like seen made to the social text messages?

#### Possible prompts

- Please could you tell us more about ...?
- And how did that make you feel?
- What are your thoughts about ...?
- Could you give me some examples about ...?



## Appendix 14: Example of a framework matrix used in the study

|                    | Overall Experience of Study  | Memory messages   |   |   |   |   | Control messages   |  |                                      |
|--------------------|--|---|---|---|---|---|--|--|--------------------------------------|
|                    | A : Overall experience of study  | B : Experience of memory messages   | C : Most useful about memory messages   | D : Not useful about memory messages  | E : Improvements to memory messages                                 | F : Experience of control messages  | G : Most useful about control messages   | H : Not useful about control messages  | I : Improvements to control messages |
| 1 : Participant 1  | Fine   | Useful<br>Expected to receive them<br>Miss them now they've stopped<br>Since they've stopped, worry I might forget  | Reminded me to do target behaviour<br>That I would otherwise forget to do<br>Made me feel better  | Dr's appointment messages not as important as surgery sends them already  | Nothing   | Not useful  |  |  | Nothing                              |
| 2 : Participant 3  | Disconcerting initially, then fine<br>Interesting<br>Beneficial<br>Worried about finding out level of impairment<br>Worried about commitment<br>Coping better as a result of participation                         | Missed the messages when they stopped<br>Implemented similar memory strategy on phone   | Helped me get more organised and plan more effectively<br>Better problem solving<br>Better at pacing self to avoid fatigue  | Sometimes distracting   | Nothing   |   | Felt involved<br>Prompted to remember something that I'd forgotten               | Less impact than memory messages<br>Enjoyed initially<br>Nuisance as time<br>Not serving a purpose<br>Knew current affairs information already | Choice of different content          |
| 3 : Participant 4  | Didn't think it would have an impact on remembering, but it did  | Very useful<br>Once reminders stopped, couldn't remember again<br>Sometimes didn't read the message, simply the beep acted as a prompt and remembered what it was for<br>Nice not to forget   | Helped achieve target behaviours<br>Pre-empting messages before receiving<br>Jogging memory   | Difficult at the beginning<br>Some of target behaviours required assistance from someone else, and couldn't always have it when received messages | Nothing<br>Reduce frequency, so just an occasional prompt           | Not useful<br>Enjoyed receiving them<br>Nice being given the option to engage with the news   |  | Out of touch with sports news, so hard to follow   | Messages more tailored               |
| 4 : Participant 7  | Useful<br>Receiving the text messages made him feel like he wasn't alone<br>Having someone contacting via the messages provided comfort<br>Improved mood when going through a bad patch<br>Sorry when they stopped |   | Helped achieve target behaviours<br>Acted as a prompt<br>Led to prioritising to do list and planning actions<br>Prevented forgetting<br>Increased concentration focus   | Messages about checking emails didn't have as much impact   | Start them with the same word to prime mindset<br>Make more concise | Interesting<br>Often read full news article in response to receiving the message<br>Enjoyed reading<br>Prompted reading other areas of news   |  |  | Would have liked an uplifting quote  |
| 5 : Participant 8  | Enjoyed knowing impairment wasn't as bad as thought<br>Helped me<br>Nice to know I've helped someone achieve something   |   | Nice being informed of the date<br>Confirmation of the correct day was nice to demonstrate she wasn't always forgetting things<br>Made her feel better able to cope<br>Made her feel oriented to time and date<br>Being presented with correct date made her feel less anxious<br>Made me realise what was going to happen<br>Encouraged her to check the calendar<br>Receiving reminders in the morning enables better management of fatigue | Could have been more specific for appointments  |   | Messages cheered me up/in a better mood<br>They were great<br>Something nice before I had to start fighting the world again<br>Felt more secure in myself<br>Felt more grounded<br>Looked forward to them<br>Upbeat thing | Cheered me up even though I didn't realise I needed cheering up<br>Made me smile | Didn't like biblical quotes  |                                      |
| 6 : Participant 9  | Very good<br>Pleased with participation in study<br>Enjoyed the cognitive assessment<br>Everything was useful  | At first was unusual<br>Then noticed time and anticipated content<br>Basic and to the point   | Reminded me of birthdays I'd forgotten<br>Helped me remember things all the time  | Woke me up a few times  |   | Not bad   | Sends you sports news that you might have missed                                 | Could get the news on the television   |                                      |
| 7 : Participant 10 | Grateful been on trial   | Helped<br>Good thing<br>The messages were the best thing ever<br>After messages stopped started writing things down and putting on fridge<br>Hard after messages stopped, missed them<br>Wrote stuff down to replace messages, but now in routine | Stuck to timings<br>Don't forget target behaviours eg lock doors or eating<br>Remember to do certain things at certain times<br>Don't forget as much as used to<br>In more of a daily routine which didn't have before<br>Due to receiving 'check calendar' reminders, since messages stopped now check calendar automatically every morning to check for appointments<br>Feel a lot happier<br>Husband pleased she remembers to lock doors   | Still forget afternoon meds sometimes   | Nothing   | Read them but wouldn't remember content<br>Confused when started to receive them  | Nothing  |  |                                      |



## Appendix 15: Skew data for baseline measures in full feasibility dataset

| Variable                           | Skewness | Std Error of skewness |
|------------------------------------|----------|-----------------------|
| Age                                | -0.10    | 0.34                  |
| Time since diagnosis               | 0.93     | 0.34                  |
| Time since last relapse            | 1.87     | 0.41                  |
| EMQ Total Score                    | 0.58     | 0.34                  |
| Doors & People Test                |          |                       |
| People                             | 0.14     | 0.34                  |
| Doors                              | -0.01    | 0.34                  |
| Shapes                             | -0.33    | 0.34                  |
| Names                              | -0.57    | 0.34                  |
| Overall Score                      | 2.07     | 0.34                  |
| Combined visual memory             | 0.22     | 0.34                  |
| Combined verbal memory             | -0.12    | 0.34                  |
| Combined recall                    | .043     | 0.34                  |
| Combined recognition               | -0.51    | 0.34                  |
| Verbal forgetting                  | -0.60    | 0.34                  |
| Visual forgetting                  | -1.41    | 0.34                  |
| Hayling & Brixton                  |          |                       |
| Hayling error                      | -1.03    | 0.34                  |
| Hayling overall                    | -1.00    | 0.34                  |
| Brixton                            | -1.33    | 0.34                  |
| Test of Everyday Attention         |          |                       |
| Map search 1                       | -1.43    | 0.35                  |
| Map search 2                       | -2.60    | 0.35                  |
| Elevator counting                  | -1.96    | 0.34                  |
| Elevator counting with distraction | -0.52    | 0.34                  |
| Visual elevator 1                  | -0.11    | 0.35                  |
| Visual elevator 2                  | -0.59    | 0.35                  |
| Elevator counting with reversal    | 0.23     | 0.37                  |
| Telephone search                   | -0.57    | 0.34                  |
| Telephone search while counting    | -0.18    | 0.34                  |
| Lottery                            | -0.29    | 0.34                  |

## Appendix 16: Amendments approval from ethics committee



### Health Research Authority

#### NRES Committee East Midlands - Northampton

Royal Standard Place  
Nottingham  
NG1 6FS

Tel: 0115 8839521

27 October 2014

Mr Paul Cartledge  
Research Innovation Services  
King's Meadow Campus, Lenton Lane  
Nottingham  
NG7 2NR

Dear Mr Cartledge

|                   |  |
|-------------------|--|
| Study title:      | Evaluation of NeuroText as a memory aid for people with Multiple Sclerosis |
| REC reference:    | 13/EM/0324   |
| Protocol number:  | 13078  |
| Amendment number: | Amendment 1  |
| Amendment date:   | 04 September 2014  |
| IRAS project ID:  | 131028   |

The above amendment was reviewed by the Sub-Committee in correspondence.

#### Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

#### Approved documents

The documents reviewed and approved at the meeting were:

| Document  | Version | Date              |
|---|---------|-------------------|
| Covering letter on headed paper                           |         | 23 October 2014   |
| Letters of invitation to participant                      | 2.0     | 07 October 2014   |
| Notice of Substantial Amendment (non-CTIMP) [Amendment 1] |         | 04 September 2014 |
| Research protocol or project proposal                     | 2.0     | 07 October 2014   |

#### Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

## R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

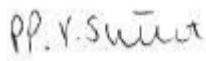
## Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at <http://www.hra.nhs.uk/hra-training/>

|             |  |
|-------------|--|
| 13/EM/0324: | Please quote this number on all correspondence |
|-------------|--|

Yours sincerely



**Mr Ken Willis**  
Chair

E-mail: NRESCCommittee.EastMidlands-Northampton@nhs.net

*Enclosures: List of names and professions of members who took part in the review*

*Copy to: Ms Charlotte Davis, Nottingham University Hospitals  
Professor Nadina Lincoln, University of Nottingham  
Rachel Goodwin*



**NRES Committee East Midlands - Northampton**

**Attendance at Sub-Committee of the REC meeting on 24 October 2014**

**Committee Members:**

| <i>Name</i>           | <i>Profession</i>          | <i>Present</i> | <i>Notes</i> |
|-----------------------|----------------------------|----------------|--------------|
| Mr Ken Willis - Chair | Medical Devices Manager    | Yes            |              |
| Mr John Aldridge      | Senior Lecturer in Nursing | Yes            |              |

**Also in attendance:**

| <i>Name</i>          | <i>Position (or reason for attending)</i> |
|----------------------|---|
| Miss Victoria Strutt | REC Assistant                             |

## Appendix 17: Skew data for baseline measures in RCT dataset

| Variable                           | Skewness | Std Error of skewness |
|------------------------------------|----------|-----------------------|
| Age                                | 0.11     | 0.38                  |
| Time since diagnosis               | 1.26     | 0.38                  |
| Time since last relapse            | 2.01     | 0.44                  |
| EMQ Total Score                    | 0.56     | 0.38                  |
| Doors & People Test                |          |                       |
| People                             | 0.01     | 0.38                  |
| Doors                              | 0.08     | 0.38                  |
| Shapes                             | -0.59    | 0.38                  |
| Names                              | -0.48    | 0.38                  |
| Overall Score                      | 2.12     | 0.38                  |
| Combined visual memory             | 0.10     | 0.38                  |
| Combined verbal memory             | -0.08    | 0.38                  |
| Combined recall                    | -0.14    | 0.38                  |
| Combined recognition               | 0.03     | 0.38                  |
| Verbal forgetting                  | -0.68    | 0.38                  |
| Visual forgetting                  | -1.64    | 0.38                  |
| Hayling & Brixton                  |          |                       |
| Hayling error                      | -1.43    | 0.38                  |
| Hayling overall                    | -1.27    | 0.38                  |
| Brixton                            | -0.41    | 0.38                  |
| Test of Everyday Attention         |          |                       |
| Map search 1                       | -0.23    | 0.39                  |
| Map search 2                       | -0.20    | 0.39                  |
| Elevator counting                  | -1.69    | 0.38                  |
| Elevator counting with distraction | -0.63    | 0.38                  |
| Visual elevator 1                  | -0.10    | 0.39                  |
| Visual elevator 2                  | -0.52    | 0.39                  |
| Elevator counting with reversal    | -0.15    | 0.41                  |
| Telephone search                   | -0.76    | 0.38                  |
| Telephone search while counting    | -0.42    | 0.38                  |
| Lottery                            | -0.43    | 0.38                  |

## Appendix 18: Skew data for outcome measures in RCT dataset

| Variable                                     | Skewness | Std Error of skewness |
|--|----------|-----------------------|
| EMQ Frequency Participant total condition 1  | -0.94    | 0.43                  |
| EMQ Importance Participant total condition 1 | -0.67    | 0.47                  |
| GHQ total condition 1                        | 0.88     | 0.46                  |
| AMEDO Part A total condition 1               | -0.34    | 0.47                  |
| AMEDO Part B1 condition 1                    | -1.95    | 0.46                  |
| AMEDO Part B2 condition 1                    | -0.63    | 0.50                  |
| EQ5d 1 condition 1                           | -0.22    | 0.47                  |
| EQ5d 2 condition 1                           | -0.09    | 0.47                  |
| EQ5d 3 condition 1                           | -0.22    | 0.47                  |
| EQ5d 4 condition 1                           | -0.03    | 0.47                  |
| EQ5d 5 condition 1                           | -0.15    | 0.47                  |
| EQ5d VAS condition 1                         | 0.25     | 0.47                  |
| EMQ Frequency Relative total condition 1     | 0.90     | 0.49                  |
| EMQ Importance Relative total condition 1    | -0.42    | 0.49                  |
| EMQ Frequency Participant total condition 2  | 0.22     | 0.46                  |
| EMQ Importance Participant total condition 2 | -0.01    | 0.47                  |
| GHQ total condition 2                        | 0.78     | 0.47                  |
| AMEDO Part A total condition 2               | -0.08    | 0.47                  |
| AMEDO Part B1 condition 2                    | -0.69    | 0.47                  |
| AMEDO Part B2 condition 2                    | -0.67    | 0.49                  |
| EQ5d 1 condition 2                           | 0.00     | 0.48                  |
| EQ5d 2 condition 2                           | 0.16     | 0.47                  |
| EQ5d 3 condition 2                           | 0.01     | 0.47                  |
| EQ5d 4 condition 2                           | -0.54    | 0.47                  |
| EQ5d 5 condition 2                           | 0.28     | 0.47                  |
| EQ5d VAS condition 2                         | 0.22     | 0.48                  |
| EMQ Frequency Relative total                 | 0.57     | 0.54                  |

|  |       |      |
|--|-------|------|
| condition 2                                  |       |      |
| EMQ Importance Relative total<br>condition 2 | -0.30 | 0.54 |