Using Technology in the Assessment and Rehabilitation of Spatial Neglect

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Abstract

Spatial neglect is characterised by inattention to stimuli in the contralesional side of space. The complexity of the condition (manifesting in personal, near, and far space) make it difficult to assess, with some subtypes not commonly assessed. And, due to the low quality of the current evidence, no single intervention can be formally recommended to effectively rehabilitate neglect. However, technology may offer an opportunity to improve the sensitivity of assessments and facilitate self-administration of rehabilitation at home. In Chapter 1, results from 179 healthy adults (aged 18-94 years-old) revealed that performance on the Computerised Extrapersonal Neglect Test (CENT)'s visuospatial tasks (cancellation, line bisection) were related, sensitive to age-related decline, and sex differences in extrapersonal (far) space. Age-graded normative data was produced to inform the detection of spatial neglect in extrapersonal space in stroke survivors. Chapter 2 found CENT's cancellation test had excellent diagnostic accuracy, sensitivity and validity compared to the widely used, validated paper-and-pencil neglect tests. In a group of 57 stroke survivors, CENT identified 18 cases of extrapersonal neglect which would otherwise go undetected. The results demonstrate the capabilities of a computerised assessment in providing additional attentional measures, as well as the necessity of carrying out a comprehensive assessment of neglect subtypes to inform rehabilitation strategies. Finally, Chapter 3 found that it was feasible for NHS staff to set-up and train 7 participants to self-administer the computerised Spatial Inattention Grasping Home-based Therapy (c-SIGHT) intervention. Though the sample was small and underpowered, there was preliminary evidence of the positive effects of c-SIGHT. This trial demonstrates the value of feasibility studies in providing recommendations to inform future studies. Together these studies offer practical recommendations and novel findings demonstrating the usefulness of technology in detecting spatial neglect and delivering rehabilitation at home to better support and improve people's lives after stroke.

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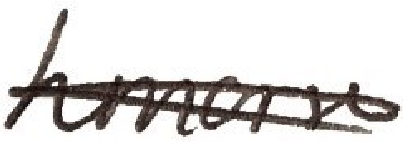
Author's declaration

I declare that the work contained in this thesis has not been submitted for any other award and that it is all my own work. I also confirm that this work fully acknowledges opinions, ideas and contributions from the work of others.

Parts of this work have been presented at conferences and published in an academic journal.

X 

Author's signature

Ethical approval

Ethical approval for part of the work in this thesis had been granted by the School of Psychology Ethics Committee at the University of East Anglia (2018-0026-001469). Health Research Authority approval was also obtained via Cambridge South Research Ethics Committee (IRAS project ID: 275001).

Clinical Trial Registration

Part of the work in this thesis has been registered on the ClinicalTrials.gov registry (identifier: NCT03963661).

Contents

Presentations and publications

Oral Presentations

Morse, H., Pomeroy, V., Clark, A., Bostrom, A., & Rossit, S. (2022). A feasibility randomised controlled trial of a computerised Spatial Inattention Grasping Home-based Therapy (c-SIGHT) for spatial neglect post-stroke: Trial in progress. **Organisation for Psychological Research into Stroke (OPSYRIS; virtual).**

Morse, H., Pomeroy, V., Clark, A., & Rossit, S. (2022). A feasibility randomised controlled trial of a computerised Spatial Inattention Grasping Home-based Therapy (c-SIGHT) for spatial neglect post-stroke: Trial in progress. **School of Psychology Postgraduate Conference Day, University of East Anglia, UK.**

Morse, H., Jolly, A., Pomeroy, V., Biggart, L., & Rossit, S. (2019). Feasibility and potential effects of a portable self-administered computerised therapy for spatial neglect post-stroke (c-SIGHT): preliminary findings of a multiple baseline pilot study. **Organisation for Psychological Research into Stroke (OPSYRIS), Oxford, UK.**

Public Engagement Presentations

Morse, H. (2022). Facebook Live Event: Stroke Researcher. **Stroke Association (virtual).**

Morse, H. (2020). Vision Loss After Stroke. **Stroke Assembly (virtual).**

Poster Presentations

Morse, H., Pomeroy, V., Clark, A., Bostrom, A., & Rossit, S. (2022). A feasibility randomised controlled trial of a computerised Spatial Inattention Grasping Home-based

Therapy (c-SIGHT) for spatial neglect post-stroke: Trial in progress. **UK Stroke Forum, Liverpool, UK.**

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Morse, H., Pomeroy, V., Clark, A., Bostrom, A., & Rossit, S. (2022). A feasibility randomised controlled trial of a computerised Spatial Inattention Grasping Home-based Therapy (c-SIGHT) for spatial neglect post-stroke: Trial in progress. **5th Federation of European Societies of Neuropsychology (FESN) Summer School, Berlin, Germany.**

Morse, H., Pomeroy, V., Clark, A., & Rossit, S. (2021). A feasibility randomised controlled trial of a computerised Spatial Inattention Grasping Home-based Therapy (c-SIGHT) for spatial neglect post-stroke: Trial update. **UK Stroke Forum (virtual).**

Morse, H., Pomeroy, V., Clark, A., & Rossit, S. (2020). Study protocol of a feasibility trial of a computerised Spatial Inattention Grasping Home-based Therapy (c-SIGHT) for spatial neglect post-stroke. **UK Stroke Forum (virtual).**

Morse, H., Pomeroy, V., Clark, A., & Rossit, S. (2020). A feasibility study of a computerised Spatial Inattention Grasping Home-based Therapy for stroke survivors (c-SIGHT). **British Neuropsychological Society (virtual).**

Morse, H., Jolly, A., Pomeroy, V., Biggart, L., & Rossit, S. (2019). Investigating a home-based self-administered computerised therapy and assessment for spatial neglect post-stroke (c-SIGHT): preliminary findings of a usability study. **UK Stroke Forum, Telford, UK.**

Morse, H., Pomeroy, V., Biggart, L., & Rossit, S. (2019). End-user perspectives in developing portable patient-led virtual reality tools for assessment and rehabilitation of spatial neglect post-stroke. **British Neuropsychological Society, London, UK.**

Publications related to this thesis

Morse, H., Jolly, A. A., Browning, H., Clark, A., Pomeroy, V., & Rossit, S. (2023). Aging effects on extrapersonal (far-space) attention: cancellation and line bisection performance from 179 healthy adults. *Aging, Neuropsychology, and Cognition*. DOI: doi.org/10.1080/13825585.2023.2223903

Morse, H., Biggart, L., Pomeroy, V., & Rossit, S. (2020). Exploring perspectives from stroke survivors, carers and clinicians on virtual reality as a precursor to using telerehabilitation for spatial neglect post-stroke. *Neuropsychological Rehabilitation*, 32*(5*), 767-791. DOI: https://doi.org/10.1080/09602011.2020.1819827

Publications unrelated to this thesis

Farmer, H., Hewstone, M., Spiegler, O., **Morse, H.,** Saifullah, A., Pan, X., Fell, B., Charlesford, J., & Terbeck, S. (2020). Positive intergroup contact modulates fusiform gyrus activity to black and white faces. *Scientific Reports, 10* (2700). DOI: https://doi.org/10.1038/s41598-020-59633-9

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Abbreviations

ADHD	Attention-Deficit Hyperactivity Disorder
ADLs	Activities of Daily Living
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
AUC	Area Under the ROC Curve
BIT	Behavioural Inattention Test
CBS	Catherine Bergego Scale
CENT	Computerised Extrapersonal Neglect Test
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	Coronavirus disease
CRN	Clinical Research Network
c-SIGHT	Computerised Spatial Inattention Grasping Home-based Therapy
CT	Computerised Tomography
ESD	Early Supported Discharge
FIM	Functional Independence Measure
HRA	Health Research Authority
IPL	Inferior Parietal Lobule
IQR	Inter Quartile Range
KF-NAP	Kessler Foundation Neglect Assessment
LB	Line Bisection
LHD	Left Hemisphere Damage
M	Mean
MCA	Middle Cerebral Artery
MCSI	Modified Caregiver Strain Index

MDN	Median
MRI	Magnetic Resonance Imaging
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute of Health Research
OCS	Oxford Cognitive Screen
PA	Prism Adaptation
PI	Principal Investigator
PPI	Patient and Public Involvement
RCT	Randomised Controlled Trial
RHD	Right Hemisphere Damage
ROC	Receiver Operating Characteristic
rPPC	Right Posterior Parietal Cortex
rVO	Right Ventral Occipital Cortex
SD	Standard Deviation
SIGHT	Spatial Inattention Grasping Home-based Therapy
SIS	Stroke Impact Scale
SSNAP	Sentinel Stroke National Audit Programme
STG	Superior Temporal Gyrus
SUS	System Usability Scale
TIDier	The Template for Intervention Description and Replication
TMS	Transcranial Magnetic Stimulation
TPJ	Temporoparietal Junction
VAS	Visual Analogue Scale
VFT	Visuomotor Feedback Training

VR	Virtual Reality
WHO-ICF	World Health Organisation International Classification of Functioning, Disability and Health

Impact of COVID-19

This PhD fellowship began in October 2019. Six months later (March 2020) the UK went into the first coronavirus lockdown. By late March the fellow had submitted the Health Research Authority (HRA) ethics application for the project, which involved recruitment of stroke survivors through NHS services.

From March 2020, University restrictions included freezes in department spending (e.g., pausing purchases of equipment in preparation for the trial) and banning of face-to-face research activities. Of more concern to the project was the halting of research within the NHS in March 2020, which delayed starting the project as well as access to Clinical Research Network (CRN) resources necessary for recruitment of stroke survivors.

By June 2020, HRA ethics approval had been obtained however NHS sites listed to be involved in the study did not have capacity to take part. And many research and clinical teams were deployed to other priority roles. As a result, the lead NHS site was unable to begin recruitment until February 2021 (almost 8 months after obtaining HRA approval). The remaining sites did not have capacity to join the study until the summer of 2021, or even February 2022. This, as well as ongoing NHS capacity issues following the COVID-19 pandemic had a negative impact on recruitment for the project. Consequently, the fellow could not conduct face-to-face research until May 2021.

Uncertainty of the feasibility of the project between March 2020 and April 2021 meant that the fellow and supervisory team considered options to redesign the project (e.g., alterative online research studies). However, since the project involved assessing visuospatial attention (i.e., spatial neglect) and investigating a home-based rehabilitation tool (c-SIGHT), it could not be redesigned to carry out study activities virtually without major changes to the original scientific aims submitted to the funder. Additionally, COVID-19 risk assessments meant that face-to-face visits as part of the project were reduced to a maximum of 90 minutes to mitigate the risk of COVID-19 transmission. This was necessary for safeguarding participants, some of whom were considered extremely vulnerable. This meant that a number of exploratory outcome measures included in the original HRA application were removed and key outcome measures were prioritised. Overall, the COVID-19 pandemic negatively affected recruitment meaning the final sample size was significantly smaller than the target sample size in the original funding application and that was registered on ClinicalTrials.gov.

Due to COVID-19 related delays affecting recruitment to the project, a 6-month costed extension was obtained from the funder to extend data collection for the PhD fellow until the end of 2022, and the end of fellowship until March 2023. To date, the primary supervisor/now Chief Investigator continues to recruit for the project. The fellow has since accepted a full-time role as a Clinical Trials Manager. Therefore, the results presented in Chapter 2 and 3 reflect data collected by the fellow up until January 2023 and may not be the final dataset used for publication.

1. General introduction

Stroke is a life-threatening cerebrovascular disease caused by a loss of blood supply to the brain. It's estimated that more than 100,000 people have a stroke annually, meaning there are around 1.3 million stroke survivors living in the United Kingdom (Stroke Association, 2023). A stroke can affect various aspects of an individual's health resulting in psychological, physical, social, and cognitive effects. These effects can range from mild and short-term, to severe and long-lasting. As a result, around 1 million stroke survivors are in need of post-acute care in managing the effects of stroke (Royal College of Physicians Sentinel Stroke National Audit Programme; SSNAP, 2021).

1.1 Post-stroke cognitive consequences

Post-stroke cognitive impairments include problems with memory, thinking, attention, visual perception, and agnosia (recognition and identification problems; Stroke Association, 2019). It is estimated that at least 24% of stroke survivors in the UK experience cognitive impairments (Sun, Tan & Yu, 2014). However, a national survey of just over 11,000 stroke survivors showed that up to 9 out of 10 respondents reported experiencing at least one cognitive problem (Stroke Association, 2019). Some of the highest reported cognitive consequences of stroke were fatigue, memory, difficulty multi-tasking, and concentration (all reported by 80% of respondents; Stroke Association, 2019). Though those most severely affected by significant cognitive and/or visual impairments are likely to be under-represented in the report.

Experiencing just one cognitive or 'hidden' effect of stroke can have a significant impact on stroke survivors' quality of life. For instance, a stroke survivor with memory problems may forget to take their medication or miss medical appointments. While language difficulties (both in production or comprehension), such as Aphasia contribute to social isolation (Northcott & Hilari, 2011). Finally, problems with attention can impair a stroke survivor's sustained attention (concentration), spatial attention (orienting attention to locations in space), divided and selective attention (multitasking, distractibility), and arousal/alertness (causing mental fatigue; Loetscher et al., 2019). They are common problems with at least 80% of 11,000 stroke survivors reporting problems with multi-tasking and concentration (Stroke Association, 2019). Critically, attention plays an important role in other important cognitive processes (e.g., memory, language; Chun & Turk-Browne, 2007; Spaccavento et al., 2017), and deficits in attentional performance have been linked to poorer post-stroke daily functioning (McDowd et al., 2003).

1.2 Spatial neglect

Spatial neglect, or inattention, is a disabling condition following brain injury affecting an individual's attention and spatial awareness (Longley et al., 2022). It can manifest as an inability to respond to sensory stimuli in the side of space opposite to the lesion (contralesional space). The affected side of space is usually the same side in which the stroke survivor may have lost movement (the 'affected' side). It can occur after either left, right or bilateral brain injury, but it is more common (Bowen et al., 1999) and severe after right hemisphere damage (Li & Malhotra, 2015). A stroke survivor exhibiting the classic, or 'core' spatial neglect symptoms may direct their gaze and orient their trunk towards the same side as the lesion (ipsilesional space; Li & Malhotra, 2015). Importantly, for symptoms to be neglect specific, they must not be explained by other sensory impairments (i.e., visual field deficits, hemiparesis; Kerkhoff, 2001).

1.3 Subtypes

As a syndrome, spatial neglect can affect interaction with one side of the world through different sensory modalities, such as auditory, visual (visual neglect), somatosensory, motor, and visual mental imagery (Kerkhoff, 2001). Symptoms can be observed towards the patient's own body (personal space), within arm's reach (peripersonal/near space), and/or beyond arm's reach (extrapersonal/far-space; see **Figure 1.1**) (Berti et al., 2002). Therefore, neglect behavioural symptoms vary depending on which area of space is affected. For example, personal neglect may cause problems grooming or dressing, whereas peripersonal neglect could make reading difficult. Extrapersonal neglect could impact activities involving attention of stimuli in the distance, such as navigation, watching TV or finding people in a crowd.

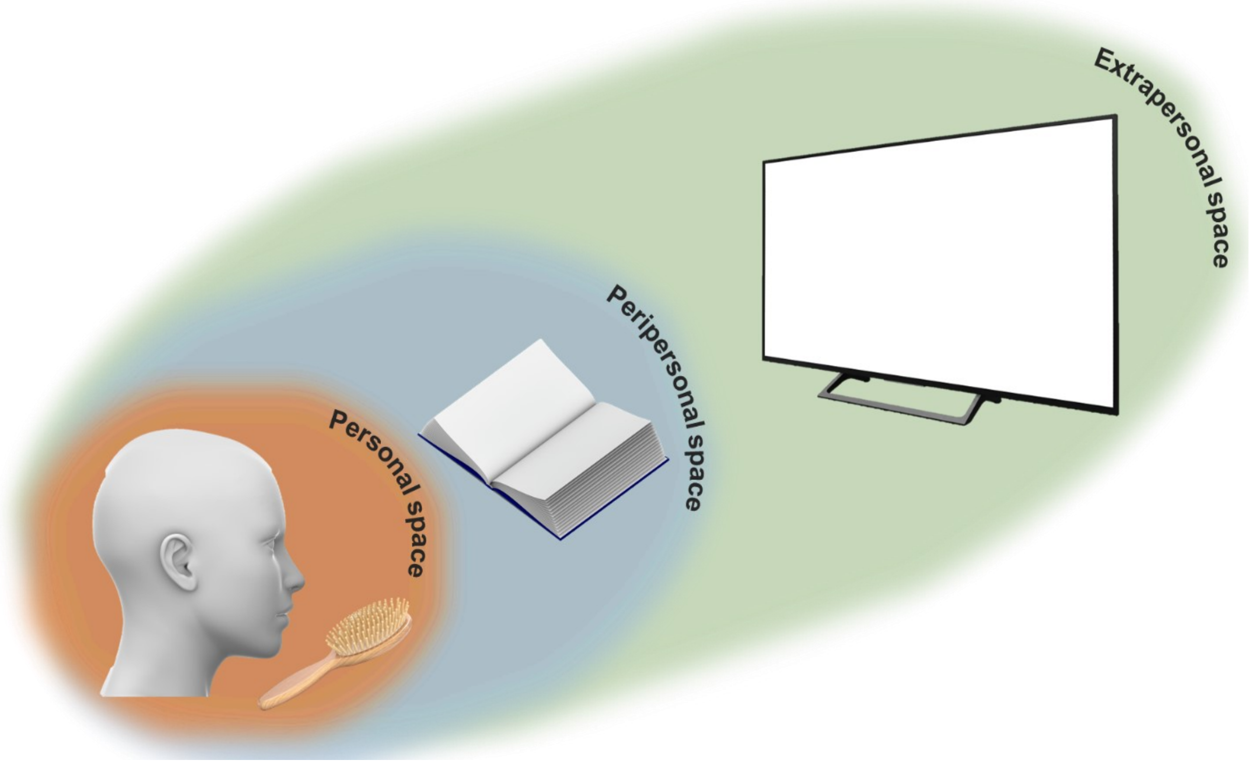

Figure 1.1 Regions of space in which spatial neglect symptoms can occur. Personal space (orange) refers to an individual's own body (e.g., grooming involves interaction with personal space). Peripersonal space (blue) is space within arm's reach (e.g., interacted with while reading) and extrapersonal space (green) is space beyond arm's reach (e.g., interacted with when watching television). Figure created by author using Adobe Stock images.

To add to the complexity, neglect can also impact how we encode information in the space around us (e.g., the locations of objects). To do this, it is hypothesized that we use two reference frames: egocentric and allocentric. Spatial locations encoded using egocentric reference frames are *"represented with respect to the particular perspective of a perceiver, whereas an allocentric reference frame locates points within a framework [...] independent of his or her position"* (Klatzky, 1998, p. 2). In other words, an egocentric reference frame may encode spatial locations relative to one's body (**Figure 1.2a**) and an allocentric reference frame is proposed to encode information based on locations of other objects in space (**Figure 1.2b**). Within the context of spatial neglect, egocentric neglect impairs an individual's awareness to contralesional space relative to their body (**Figure 1.3a**), whereas allocentric neglect impairs an individual's awareness to the contralesional side of an object regardless of where it is in space (**Figure 1.3b;** Demeyere & Gillebert, 2019). Both types of neglect have been reported to occur together and independently of one another in stroke survivors (Demeyere & Gillebert, 2019).

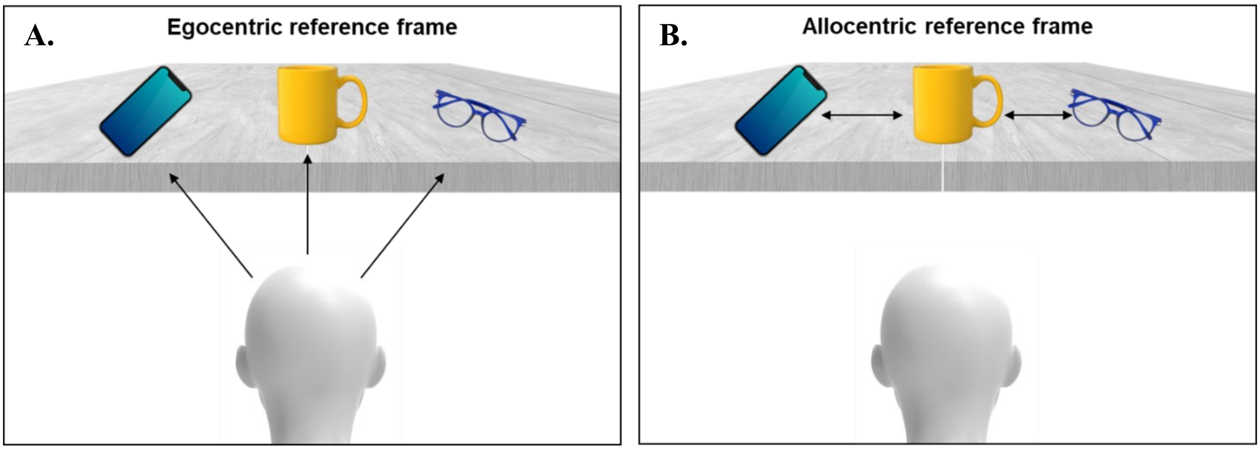

Figure 1.2 Spatial reference frames used to encode information in space. A) Egocentric reference frame (encoding information in space relative to the perceiver's body). B) Allocentric reference frame (encoding information in space relative to other objects). Figure created by author using Adobe Stock images.

Both subsets of neglect can have severe impacts on day-to-day life; egocentric neglect is associated with difficulties finishing meals, finding objects or people around you. Whereas allocentric neglect can impact tasks, such as telling the time and reading (e.g., omitting the left side of words irrespective of their location on the page; Shah, Spaldo, Barrett, & Chen, 2013).

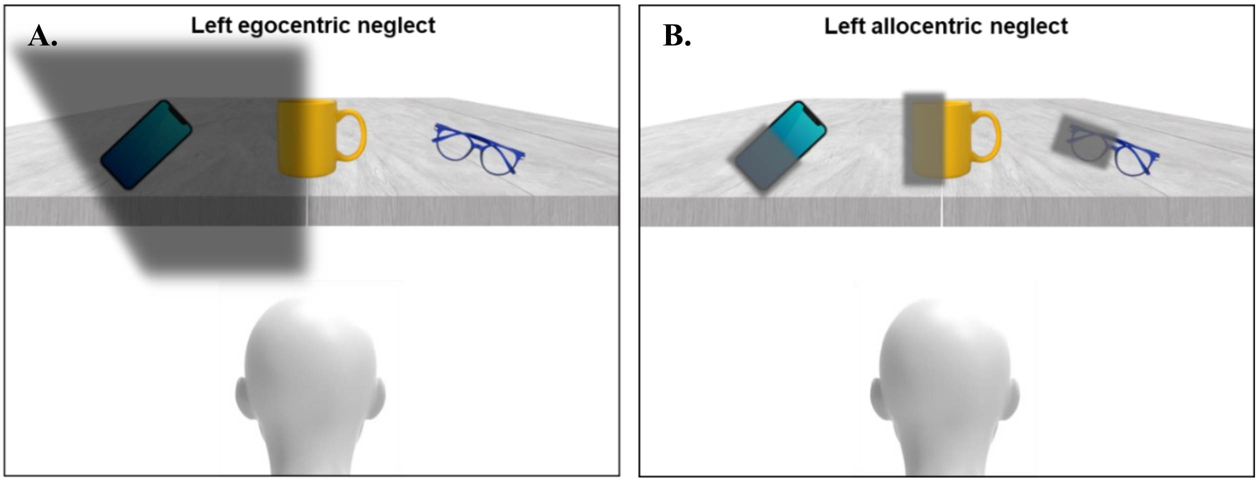

Figure 1.3 Spatial neglect affecting each spatial reference frame. A) Unawareness of contralesional (left) space relative to the patient's body (egocentric neglect). B) Unawareness of the contralesional (left) side of objects, irrespective of the patient's body (allocentric neglect). Figure created by author using Adobe Stock images.

The scope of how neglect symptoms can manifest means daily living activities (e.g., preparing meals, personal care) can become difficult which may lead to higher dependency on others (Hammerbeck et al., 2019). Similarly, spatial neglect has a significant negative impact on patient recovery outcomes (Chen et al., 2015; Jehkonen et al., 2006) and is associated with increased disability (Gillen, Tennen & McKee., 2005). Inpatient hospital stays are twice as long for those with spatial neglect and post-acute care demands are higher (Hammerbeck et al., 2019). We also know that the impact extends to family and friends. For example, informal carers of stroke survivors with spatial neglect have reported higher levels of stress and care (i.e., personal, financial, supervision) compared to carers of stroke survivors without spatial neglect (Chen et al., 2017). However, we must consider that prognosis is likely impacted by increased stroke severity, which is associated with higher rates of spatial neglect (Hammerbeck et al., 2019).

1.4 Rates

Spatial neglect is thought to affect approximately 30% (1 in 3) stroke survivors (Bowen et al., 1999; Ringman et al., 2004; Puig-Pijoan et al., 2018; Rowe et al., 2019; Hammerbeck et al., 2019; Moore et al., 2021; Longley et al., 2022). Rates have been reported as high as 82% of acute strokes (Stone et al., 1993) and 84% of severe stroke cases (Hammerbeck et al., 2019). Variance in reported rates can be influenced by the sample characteristics (i.e., side of hemisphere), 'when' (i.e., stage of stroke) and 'what' assessments are used (Bowen et al., 1999). First, research studies often recruit patients with right hemisphere stroke only (Bowen et al., 1999; Moore et al., 2023). This is likely due to the fact that neglect is more frequent and severe after right hemisphere damage (Li & Malhotra, 2015). As a result there may be an underrepresentation of patients with neglect after left hemisphere damage since there are high rates of exclusion of these samples (Kerkhoff et al., 2013; Luvizutto et al., 2016; Vaes et al., 2018; Volkening et al., 2018). Patients with left hemisphere strokes may also be excluded due to communication difficulties which *could* impair consenting (although we know that using Aphasia friendly materials may help overcome this barrier; Hreha et al., 2017). Next, higher rates of neglect have been reported during acute (within a week of onset) compared to in chronic stages (6-months after onset) of stroke (Bowen et al., 1999; Moore et al., 2021). One recent study using a paper-and-pencil cancellation task reported that 69% of neglect cases had recovered at 6-month follow-up (Moore et al., 2021). Thus, differences in sample recruitment between studies (e.g., acute versus community recruitment) are likely to add to the variation in neglect rates. Finally, the reported frequencies are unlikely to reflect the true number of neglect cases within each subtype (i.e., personal, extrapersonal neglect), since many subtypes are not frequently assessed in research. In fact, most widely used assessments are conducted in peripersonal space only (e.g., paper-and-pencil tests; Checketts et al., 2021).

1.5 Understanding neglect behaviour

It is important to outline the theories explaining spatial neglect behaviour before exploring assessment and rehabilitation methods. Several theories attempt to understand the 'core' neglect behaviour: attentional, motor intentional and representational theories (Heilman, Watson & Valenstein, 2002). Importantly, these theories are not mutually exclusive and individually cannot explain all aspects of neglect as a heterogenous condition (Heilman et al., 2002).

1.5.1 Attentional theories

Attention functions to prioritise and organise the large volume of information we are subject to day-to-day. For example, our attention helps us orient towards stimuli whilst avoiding distraction by other stimuli (e.g., engage in a conversation in a loud room). Attentional theories help explain neglect behaviour since neglect can be associated with lesions other than primary sensory pathways (e.g., primary visual cortex; Heilman et al., 2002). In other words, neglect and sensory deficits, such as visual field deficits can occur independent of one another (Kerkhoff, 2001). Thus, a sensory deficit cannot account for neglect specific impairments. Attentional theories propose that lateralised neglect symptoms are due to attentional deficits, such as a lack of 'conscious' awareness towards contralesional space (inattention hypothesis; Heilman et al., 2002), or an imbalance of attention allocation between hemispheres (hemispheric imbalance hypothesis; Kinsbourne, 1970). In healthy brains, Kinsbourne (1970) stated that there is "*equal and opposing orientational tendencies"*

(p. 143) in attentional allocation between the two hemispheres whereby both hemispheres are competing to attend to stimuli in contralateral space (e.g., right hemisphere attending to stimuli on the left, left hemisphere attending to stimuli on the right). For example, damage to the right hemisphere will mean less competition for the left hemisphere in allocating attention. Thus, this may lead to neglect symptoms where there will be an over attendance to ipsilesional (right) space driven by the 'overactive' intact (left) hemisphere (Kinsbourne, 1970). In practice, a patient with left side neglect may begin their searches in a cancellation test on the right, rather than the left (Heilman et al., 2002). In the case of right side neglect (after left hemisphere injury), Kinsbourne predicts milder forms of neglect since the intact right hemisphere could compensate for the attentional deficits towards the right side (Kinsbourne, 1970; Mesulam, 1981; Corbetta & Shulman, 2011). The imbalance hypothesis, as well as right hemispheric specialisation in attention allocation (Mesulam, 1981) might explain why neglect is more common and severe after right hemisphere injury (Bowen et al., 1999; Li & Malhotra, 2015). Spatial neglect symptoms may also be explained by a patient's inability to shift their attention (or disengage) from one stimulus to another, which is associated with parietal lobe damage (Posner et al., 1984). Together, this makes it more difficult for a patient to inhibit their attention to stimuli on the ipsilateral side and attend to stimuli occurring simultaneously in contralesional space.

Individuals with neglect may have difficulty in sustaining arousal (e.g., alertness; Heilman et al., 2002; Corbetta & Shulman, 2011). In fact, one study observed neglect-like lateralised biases in healthy adults during states of decreased arousal (i.e., drowsiness; Bareham et al., 2014). The study used an auditory spatial discrimination task, whereby 26 healthy volunteers judged if tones were to their left or right during various states of arousal: alert, relaxed wakeful, and drowsy. These states were categorised according to theta waves (neural oscillations appearing during drowsy states) using electroencephalogram (EEG). The researchers found a large effect of drowsiness on judgements; participants were 17 times more likely to report sounds to the right of their body than to the left during states of drowsiness. However, it is worth noting that the authors acknowledge the results could be exclusive to arousal related changes to auditory processes (Bareham et al., 2014). Nonetheless, the results demonstrate the effect arousal can have in biasing our spatial attention which could exacerbate neglect symptoms in patients.

1.5.2 Representational theories

We know spatial neglect is not limited to *visual* neglect, but can be observed in multiple sensory modalities (Kerkhoff, 2001). Thus, it seems logical to consider that some symptoms of neglect may be explained by deficits in our internal representations and memory. A seminal paper by Bisiach and Luzzatti (1978) reported case studies of two stroke survivors who demonstrated inattention towards the left side of their internal representations of space (in their 'mind's eye'). Specifically, one stroke survivor was asked to recall details of a familiar plaza square, the other details of a studio. Upon recall, both omitted descriptions of the left side of the scenes irrespective of their orientation (e.g., facing North or South). This could indeed be an example of representational neglect but also highlights the role of spatial working memory in neglect symptoms. Our spatial working memory functions to retain and update current ('on-line') information about objects in the space around us (Husain & Rorden, 2003). In order to encode this information across both hemifields, one must attend to them. Stroke survivors with neglect, such as those in Bisiach and Luzzatti's study (1978), may omit scene details on the left because their spatial working memory did not encode the left side of the scene due to inattention and low attentional arousal towards the left (Heilman et al., 2002). Spatial working memory deficits may contribute to the severity of neglect (Malhotra et al., 2005) and to understanding of why individuals with neglect often re-visit or re-inspect previously searched areas (perseverate; Husain & Rorden, 2003). Using both a visual search and spatial working memory (Corsi block) task, researchers found that stroke survivors with neglect re-cancelled (perseverated) more previously cancelled targets compared to age-matched controls (Wansard et al., 2014). Moreover, spatial working memory performance and the frequency of re-cancellations were negatively correlated (albeit a small effect; Wansard et al., 2014). The authors explain that individuals may revisit areas due to spatial working memory deficits which impairs their ability to preserve the locations of previously found targets. However, these deficits could not explain re-cancellation behaviour in all 14 participants with neglect. Therefore, it is likely that other cognitive processes (e.g., executive function, spatial attention) are involved in executing efficient visual search and contribute to re-visiting behaviour in neglect (Wansard et al., 2014).

1.5.3 Motor intentional theories

In some cases, failure to interact with contralesional space could be accounted for by motor intentional theories (Heilman et al., 2002). These theories posit that individuals with neglect perceive contralesional stimuli but have deficits in initiating intentional actions. They may fail (akinesia), take longer (hypokinesia) or are unable to sustain (motor impersistence) initiation of movement towards contralesional space (Heilman et al., 2002). Neglect can occur specifically to motor movements on the contralesional side - termed ‘motor neglect’ - where individuals display an underuse of the contralesional limb (Laplane & Degos, 1983). Similarly, motor extinction can occur with neglect, whereby only ipsilesional movements are initiated during bilateral movements (Punt et al., 2013). Interestingly, Punt and colleagues demonstrated that directing gaze towards the contralesional limb somewhat improved motor performance when drawing circles with both hands simultaneously. This leads us to discuss the role of vision and action (e.g., visuomotor control) in spatial neglect which is of particular interest in understanding the mechanisms behind the rehabilitation method used in this thesis.

1.6 Perception and action in neglect

Milner and Goodale's 'two-stream' model of visual perception proposes that the ventral and dorsal visual streams are functionally distinct (Goodale & Milner, 1992; Milner & Goodale, 1995). Specifically, the model states that the ventral stream (primary visual cortex to occipital-temporal cortex) functions to process perceptual information, such as object characteristics (e.g., size) to inform action towards the object. While the dorsal stream (primary visual cortex to occipital-parietal cortex) functions to visually guide actions, such as implementing action towards the object identified by the ventral stream (Milner & Goodale, 2008). Both streams contribute to visually guided actions by providing different information (Milner & Goodale, 2008).

As Goodale and Milner (1992) describe, neuropsychological evidence of this model comes from a dissociation between two disorders: visual agnosia and optic ataxia. Visual agnosia is characterised by problems in recognising objects and is typically associated with damage to ventral areas, such as the occipitotemporal region. Conversely, optic ataxia follows damage to the dorsal system (e.g., posterior parietal region) and results in deficits in visually guided actions, such as reaching and grasping items. A classic case study describes patient DF who had visual agnosia following damage to the ventral stream in the lateral occipital and parasagittal occipitoparietal region (Goodale, Milner, Jakobson & Carey, 1991). DF could not describe object features (e.g., orientation, size) but showed no difficulty reaching and grasping the object (i.e., her estimated grip aperture was accurate; Goodale et al., 1991). This suggests both the ventral and dorsal visual streams could indeed be responsible for two independent processes in our perception and action.

This model has been applied to explaining why some aspects of visuomotor functions (even towards contralesional space) seem to be relatively unimpaired in spatial neglect (e.g., McIntosh et al., 2004; Rossit et al., 2009, 2012; Harvey & Rossit, 2012). In other words, immediate or 'automatic' reaching-to-grasp movements seem to be unaffected in neglect due to spared dorsal areas (Milner & Goodale, 1992). If this is the case, damage to the ventral stream in neglect may primarily affect spatial judgements based on perceptual representations (Edwards & Humphreys, 1999). Early studies have demonstrated similar results in that there was a smaller rightward error (indicating left side neglect) when reaching-to-grasp the middle of rods compared to pointing (Robertson et al., 1995; Edwards & Humphreys, 1999). In accordance with Milner and Goodale's (1992) distinct visual streams hypothesis, it could be that intentional visuomotor actions via the (intact) dorsal stream are less prone to the lateralised biases seen in perceptual judgements (via the affected ventral steam) in neglect (Roberston et al., 1995; McIntosh et al., 2004). One study showed that individuals with left neglect were better able to consider bilateral obstacles when *reaching* through the middle compared to when pointing to the middle (McIntosh et al., 2004). Although McIntosh et al. (2004) acknowledge that visuomotor control may not remain unimpaired in all individuals with neglect.

Subsequent studies have also demonstrated that neglect patients are able to correct their reaching trajectories in response to the target moving, even in contralesional space (Rossit et al., 2009, 2012; Harvey & Rossit, 2012). A study with a group of nine neglect patients following damage to ventral areas (inferior parietal, temporal, occipital) showed impairments in delayed, but not immediate 'automatic' pointing (Rossit et al., 2009). The study included three groups of participants (stroke survivors with neglect, stroke survivors without neglect, healthy participants) who performed immediate ('on-line') or delayed ('off-line') pointing to targets on the left, centre or right of their bodies. Results showed that the neglect group did not have more errors when immediately pointing to targets, even when presented on the left (neglected side) compared to the two control groups. On the other hand, the neglect group showed impairments in accuracy when they had to wait five seconds before pointing to left targets. Specifically, they 'overshot' their pointing or did not point at all (Rossit et al., 2009). The authors found that this deficit was not related to working memory performance and is unlikely due to problems 'holding' the target location in their memory. Rather, deficits in delayed pointing could be due to problems using allocentric reference frames to code the target location to point to later (Rossit et al., 2009; Harvey & Rossit, 2012). This is made more likely by the fact that the sample primarily had damage to ventral areas which Milner and Goodale (1992) suggested code object information using allocentric spatial reference frames. This supports the notion that 'automatic' reaching movements via undamaged dorsal areas are spared compared to perceptual judgements via affected ventral areas (McIntosh et al., 2004; Rossit et al., 2012).

Conversely, Utz et al. (2018) propose that it is unlikely that only the perceptual representations are affected in neglect since they can be beneficial in guiding action (Utz et al., 2018). Utz and colleagues found evidence that withdrawing visual feedback (i.e., viewing the hand during pointing) impaired pointing accuracy in those with neglect more than in those without neglect (Utz et al., 2018). Thus, the authors hypothesized that perceptual tasks also use information used for visuospatial reaching tasks. Perhaps it is more likely that neglect symptoms are not strictly determined by damage to specific areas (e.g., ventral stream; Utz et al., 2018), rather by damage to cortical networks which interferes with communication between the two visual streams (Rossit et al., 2012).

Together, the model and supporting evidence demonstrates that automatic reaching and grasping movements seem mostly intact in neglect. However, this comes with the caveat that this may not be clear cut in each case due to the heterogeneity in lesion locations associated with neglect (discussed below). Nevertheless, researchers have proposed that intact reaching and grasping could be used to rehabilitate neglect symptoms (Robertson et al., 1995; Edwards & Humphreys, 1999; Rossit et al., 2009).

1.7 Anatomy of spatial neglect

A specific lesion site underlying neglect symptoms is still debated, widely researched (Karnath & Rorden, 2012) and complex (Moore, Milosevich, Mattingley, & Demeyere, 2023). Generally, damage to several areas have been associated with neglect, such as the inferior parietal lobule (IPL), superior temporal gyrus (STG; Mort et al., 2003; Rossit et al., 2009; Chechlacz et al., 2010; Karnath & Rorden, 2012), associated white matter (Rossit et al., 2009; Pedrazzini & Ptak, 2020), and temporoparietal junction (TPJ; Pedrazzini & Ptak, 2020).

Lesion-symptom mapping methodology can be used to investigate which brain areas are associated with impairments in behavioural tests. For instance, it will suggest what damaged brain areas are associated with impairments on a cancellation task indicating left-side neglect. Based on this, an assumption is made whether the damaged brain area is involved in being able to successfully complete the task of interest. Very recently, a systematic review of 34 lesion-symptom mapping studies - totalling 2,713 stroke survivors - identified 72 brain areas within the right hemisphere associated with egocentric neglect (Moore et al., 2023). In contrast, five studies found 34 brain areas in the left hemisphere which correlated with egocentric neglect deficits (Moore et al., 2023). For allocentric neglect, only four studies identified 34 regions in the right hemisphere, and only one study found two areas in the left hemisphere. It is worth highlighting that the studies included in the review had samples equal to or more than ten, and used visuospatial neglect tasks only, such as cancellation (97.10%), line bisection (61.80%) and drawing/copying tasks (32.4%). The results of the review revealed five areas in the right hemisphere most frequently associated with egocentric neglect, including subcortical white matter (superior longitudinal fasciculus), parietal (supramarginal gyri, post central gyri, angular gyri) and posterior frontal lobe (precentral gyri). Damage to the angular gyrus (parietal lobe) was also associated with right egocentric neglect in the left hemisphere. Other areas in the left hemisphere associated with right egocentric neglect were distinct from those found in the right hemisphere, such as the temporal (insular cortex) and frontal lobe (Brodmann's area 6, frontal operculum). Within the right hemisphere, allocentric neglect was associated with the posterior temporal lobe (middle temporal gyrus). In contrast, damaged areas within the left hemisphere included subcortical areas (external capsule, anterior limb of internal capsule). To sum, the areas varied for both ego- and allocentric neglect symptoms, suggesting that they can occur independently of one another (Demeyere & Gillebert, 2019; Moore et al., 2023). When they do co-occur, Chechlacz et al. (2010) suggest that this is caused by damage to subcortical white matter which consequently disrupts communication between areas responsible for selecting which spatial reference frame to use. In other words, disconnection between ego- and allocentric reference maps could result in impairments in both subtypes (Chechlacz et al., 2010). Between hemispheres, the review found evidence to suggest that lesions to the left or right hemisphere associated with ego- and allocentric neglect are fairly distinct (i.e., there is minimal overlap; Moore et al., 2023).

The neural underpinnings of neglect occurring in different spatial distances are also debated. Studies have reported that extrapersonal neglect can dissociate with other subtypes (e.g., peripersonal, personal) but also co-occur with peripersonal neglect (Aimola et al., 2012; Nijboer et al., 2014; Ogourtsova et al., 2018). As pointed out in Moore et al's review, two studies ran lesion-symptom mapping of neglect in different spatial regions, but no consensus could be established (Moore et al., 2023). One study found that lesions associated with neglect in extrapersonal (tasks presented 120cm away) and peripersonal (tasks 30cm away) space were not dissociable (Ten Brink et al., 2019). Specifically, there were overlapping lesions in frontal, parietal and temporal areas for neglect in both spatial regions (Ten Brink et al., 2019). Conversely, Committeri and colleagues (2007) have argued that neglect in personal and peripersonal space are independent. From a sample of 160 participants with right hemisphere damage, researchers found that personal neglect was associated with damage to areas involved in proprioceptive and somatosensory processing in the parietal lobe (post central and supramarginal gyrus; Committeri et al., 2007). On the other hand, peripersonal neglect was associated with damage to the frontal lobe (inferior precentral, middle frontal gyrus). Based on these results, the authors propose this as evidence of the role of the ventral areas in orienting and allocating visuospatial attention in extrapersonal space (Committeri et al., 2007). Similar results have been found in a group of 36 young (median age = 26) healthy participants using Transcranial Magnetic Stimulation (TMS) while completing a visual search task on a screen 57cm and 172cm away (Lane et al., 2013). The results implicated the right posterior parietal cortex (rPPC) necessary in visual search in peripersonal space, whereas inhibiting the right ventral occipital cortex (rVO) area impaired visual search in extrapersonal space only. The authors suggest these findings corroborate Milner and Goodale's (1992) two-stream hypothesis, in that they demonstrated that dorsal areas (rPPC) were involved in completing the visual search task in 'actionable' (near) space. Disrupting ventral visual processing areas (rVO) impaired visual search in far space (non-actionable area). Lane et al. (2013) argues that both ventral and dorsal areas are likely involved in processing information in both near and far space. However, according to their results, there may be a preferential bias for the dorsal stream processing visual information in near space since there may be potential to guide action towards objects within reachable space. While ventral processing may be more useful in far-space to identify objects to interact with (Lane et al., 2013).

Going forward, it is clear that neglect is not a unitary condition, but a complex syndrome with multiple subtypes which may not be explained by damage to isolated regions in all cases (Moore et al., 2023). Rather, it could be caused by a disconnection of networks within the brain (Chechlacz et al., 2010; Moore et al., 2023). The studies reviewed here highlight how differences in study methodologies contribute to the variety of brain areas implicated in neglect symptoms (Moore et al., 2023). The large variance in the types of assessments (e.g., space the test is carried out) used between studies (Williams et al., 2021) affects the subtype of neglect detected and introduces a sample bias (Harvey & Rossit, 2012). Selecting participants on strict inclusion and exclusion criteria (e.g., right hemisphere only or specific area) may prevent investigation of other areas outside the area of interest which may contribute to neglect behaviour (Moore et al., 2023). For instance, a study of neglect after right hemisphere using cancellation tests performed in peripersonal space may reveal different lesion sites compared to a study using functional assessments involving all three regions of space. Results from the first example study would be limited in its generalisability in explaining a heterogeneous condition such as neglect (Moore et al., 2023). Therefore, appropriate choice of assessments covering multiple spatial regions (personal, peripersonal, extrapersonal) and frames of reference (ego, allocentric) are necessary in understanding just a few of the dimensions of neglect behaviour.

1.8 Assessing neglect

Spatial neglect is typically assessed using neuropsychological and/or functional tests. Widely used neuropsychological tests are usually paper-and-pencil based tasks and quantify a patient's ability (e.g., using visuospatial attention) to attend to stimuli across both sides of the page. Two examples of commonly used tests are cancellation and line bisection tasks. The former are visual search tasks which require the patient to find and mark ('cancel') target stimuli. An individual with left neglect in peripersonal (near) space would classically demonstrate a lack of awareness towards the left, consequently marking targets only on the right side of the page. Within existing tasks, target stimuli can be stars, lines or letters (Wilson et al., 1987), Bells (Gauthier, Dehaut & Joanette, 1989), hearts (Demeyere et al., 2015), or apples (Bickerton et al., 2011). These tasks (excluding the line cancellation; Wilson et al., 1987) surround target stimuli with distractors to increase attentional demands; making the tasks more sensitive in detecting attentional deficits (Ferber & Karnath, 2001). Using random positioning of stimuli is also thought to better represent our everyday complex visual environments, perhaps making tests more sensitive to detecting mild or moderate neglect (Gauthier, Dehaut & Joanette, 1989). Task demands can also be increased to detect non-lateralised deficits. For example, 'invisible' cancellation conditions - where the mark showing a found target is either not shown or disappears after a few seconds - can be used as a measure of spatial working memory (Benjamins et al., 2019; Dalmaijer et al., 2015, 2018) which has previously been used to explain neglect behaviour (e.g., perseveration; Husain & Rorden, 2003; Wansard et al., 2014). Although cancellation tests are quick to administer and recommended in rapid screening (Moore et al., 2022), they typically only produce one metric of performance (i.e., overall accuracy score).

In contrast, line bisection tasks involve making visuospatial judgements to mark the middle of lines. These are quick to administer and remain one of the most popular cognitive assessments among clinical professionals internationally (Checketts et al., 2021). Horizontal lines are typically presented either centred on the left, middle or right of the page. An underestimation of the left side of the line (left-side neglect) would result in a rightward bisection bias. Multiple lines are used since biases can be inconsistent for each patient

(Ferber & Karnath, 2001; Lezak et al., 2004). Even in healthy individuals, we know that there is a tendency to mark lines more leftward of the true centre (pseudoneglect; Brooks et al., 2016; Learmonth & Papadatou-Pastou, 2022). Importantly, accuracy in the line bisection performance can be influenced by demographic variables (e.g., aging; Morse et al., 2023) and task demands (line length, placement, starting position; see Jewell & McCourt, 2000 for comprehensive review).

More generally, comorbid conditions must be considered when measuring spatial neglect using neuropsychological assessments. Visual field deficits, such as hemianopia (visual field cut) can impact assessment outcome (Kerkhoff et al., 2021) and we know spatial neglect and visual problems co-occur together post-stroke. One UK study found that 97% of stroke survivors with spatial neglect had co-occurring visual impairments (Rowe et al., 2019). The two conditions are distinct; spatial neglect is an attentional disorder whereas visual field deficits are sensory loss to visual field(s) (Halligan, 1999). Yet, one early study noted that individuals with hemianopia can display a deviation towards the affected ('blinded') visual field in line bisection tasks, which may not be indicative of spatial neglect (Ferber & Karnath, 2001; Kerkhoff et al., 2021). Furthermore, individuals with visual field deficits may present with disrupted visual search abilities (e.g., increased response times, unsystematic searches; Kerkhoff et al., 2021) which must be taken into consideration during assessment as to not misattribute these symptoms to spatial neglect. Therefore, it is recommended to conduct visual assessments (e.g., perimetry tests) to inform differential diagnosis (Kerkhoff et al., 2021). On the other hand, spatial neglect can affect screening of other cognitive processes post-stroke (e.g., memory, arithmetic; Lezak, Howieson & Loring, 2004). These may include tests which present stimuli or materials horizontally, such as writing, reading or numerical tasks. This is a potential confound when trying to obtain an accurate cognitive profile since the patient may not have true arithmetic deficits but simply not attend to the necessary stimuli if presented on the neglected side. More recent cognitive batteries, such as the Oxford Cognitive Screen (OCS; Demeyere et al., 2015) have adapted instructions (i.e., realigning materials to the patient's unaffected side) to reduce the impact neglect symptoms may have when assessing other cognitive domains, making it an inclusive post-stroke test battery.

Line bisection, along with reading, drawing tasks (copying or from memory; Wilson et al., 1987), and cancellation tasks remain popular in clinical practice (Checketts et al., 2021) and are recommended as part of the National Institute for Health and Care Excellence stroke care guidelines (NICE, 2013). Yet they do not assess functional behavioural in day-to-day life (Bowen et al., 1999; Chen, Chen, Hreha, Goedert & Barrett, 2015). For example, patients who perform well on paper-and-pencil tests may function poorly in personal care tasks (Bowen et al., 1999). Bowen and colleagues (1999) argue that reliance on paper-and-pencil tests conducted within peripersonal space may "mask" difficulties patients are experiencing in everyday tasks involving multitasking in complex environments. Consequently, paper-and-pencil assessments may lack sensitivity (Azouvi et al., 2002) and potentially misdiagnose milder to moderate cases of neglect (Buxbaum et al., 2004) since the neglect type detected is ultimately determined by the type of assessment used (Grattan & Woodbury, 2017). For instance, most paper-and-pencil assessments (or even tablet-based tasks, e.g., Demeyere et al., 2021) only measure neglect in peripersonal space, thus may not detect deficits in personal or extrapersonal space.

Functional assessments are recommended by the NICE guidelines (NICE, 2013) and are second to neuropsychological assessments in being the most commonly used neglect assessment method (Checketts et al., 2021). The Kessler Foundation Neglect Assessment (KF-NAP; Chen et al., 2015) is a standardised instruction manual for administering the Catherine Bergego Scale (CBS; Azouvi, 1996). Both these assessments require a clinician to observe a patient while carrying out activities of daily living (ADLs). This includes observing: gaze orientation, limb awareness, auditory attention, locating personal belongings, dressing, grooming, navigation, collisions, meals, and cleaning after eating (Azouvi, 1996; Chen et al., 2015). The CBS and KF-NAP both highly correlate with other functional measures (The Barthel Index; Mahoney & Barthel, 1965) and neuropsychological assessments (Azouvi, 1996; Chen et al., 2015). Compared to paper-and-pencil neglect assessments, functional assessments arguably have higher ecological validity (Chen, Chen, et al., 2015; Azouvi, 2017) since they observe neglect behaviour during ADLs. In fact, the CBS detected 50-60% of neglect cases in a sample of 50 right hemisphere stroke survivors versus less than 50% cases detected using reading, cancellation and drawing tasks (Azouvi, 1996).

Unlike paper-and-pencil assessments, functional assessments, such as the CBS and KF-NAP include activities which interact in all three spatial regions: personal (dressing, grooming), peripersonal (meals, locating personal belongings), and extrapersonal space (navigation, auditory attention, gaze orientation; Azouvi, 1996; Chen et al., 2015). Additionally, a self-report version of the CBS provides a measure of anosognosia (lack of insight or denial of condition) which is associated with increased neglect severity (Azouvi et al., 2002; Chen et al., 2012). Some authors argue that these assessments *"capture the heterogeneity of the neglect disorder"* (Chen et al., 2012, p. 424). However, rates of use of standardised and neglect-specific functional assessments, such as the CBS and KF-NAP remain relatively low amongst clinicians internationally (Checketts et al., 2021). An international study by Checketts and colleagues (2021) found that clinical and unstructured observational assessments were the most widely used assessments for neglect, used by 80% of occupational therapists and less than 70% of physiotherapists. Further, 70% of respondents' choice of assessment were informed by professional choice rather than institutional policy. Moreover, of the 454 respondents worldwide, less than 35% of each clinical professional reported using standardised neglect-specific assessments (CBS, KF-

NAP; Checketts et al., 2021). Conversely, usage of standardised generic (non-neglect) measures, such as the Functional Independence Measure (FIM; Keith et al., 1987) was primarily driven by institutional policy. Yet, use of the measures, such as the FIM is not recommended since it does not distinguish spatial neglect impairments from other post-stroke consequences (e.g., hemiparesis; Chen et al., 2012; Checketts et al., 2021).

Finally, functional assessments are necessary to understand the impact of symptoms on ADLs but the large heterogeneity in assessments methods and lack of standardisation can increase the risk of subjective interpretation (Taylor-Rowan, Wilson, Dawson & Quinn, 2018). This is being addressed by some assessments, such as the KF-NAP, which was introduced to increase standardisation of assessment and is feasible to administer amongst clinicians (e.g., occupational therapists; Chen et al., 2015).

Taken together, neuropsychological and functional assessments are widely used to assess spatial neglect in clinical practice (Checketts et al., 2021). Each serve to assess symptoms using different methods and within different subtypes. Neuropsychological assessments are cognitive tasks (e.g., visual search, attentional tasks) which commonly measure neglect in peripersonal space and selected cancellation assessments also measure ego- and allocentric neglect (e.g., The Oxford Cognitive Screen, OCS; Demeyere et al., 2015). Whereas, functional assessments measure symptoms through observations of ADLs and are capable of observing neglect symptoms in all three spatial regions (Chen et al., 2012). Recognising the value in both methods, experts recommend using more than one neuropsychological assessment (e.g., cancellation, line bisection, copying tasks) as well as a functional assessment (e.g., CBS) to obtain a comprehensive understanding of a patient’s neglect symptoms (Lezak et al., 2004; Moore et al., 2022). Both methods fit the World Health Organization’s International Classification of Functioning, Disability and Health (WHO-ICF; World Health Organization, 2002) framework in that neuropsychological assessments identify the *impairment* (i.e., left side personal neglect) and functional assessments identify *limitations* in activities (i.e., personal care) as a consequence (Taylor-Rowan et al., 2018). The application of this model in assessing spatial neglect promotes interdisciplinary working to consider all aspects of an individual's functioning, rather than solely the condition to inform appropriate rehabilitation interventions (World Health Organization, 2002).

1.9 Computerised assessments

Computerised tools have the potential to enhance neglect assessment. For example, computerised assessments can provide performance variables (e.g., reaction times, search paths) not possible to collect using traditional paper-and-pencil tests. Performance variables provided by computerised assessments may be more sensitive in detecting attentional impairments (van Kessel et al., 2013). Moreover, computerised assessments allow for manipulation of stimuli and increased attentional demands (e.g., stimuli number, invisible cancellation conditions) which may decrease the likelihood of patients using compensatory strategies (Giannakou et al., 2022).

As technology becomes more accessible and inexpensive (Threapleton et al., 2016), computerised assessment seem more feasible than ever. A recent review found that computerised neglect tests have been run on several types of apparatus, such as touchscreen monitors, smartphones, tablets, and laptops (Giannakou et al., 2022). Most of which (perhaps with the exception of touchscreen monitors) are widely accessible in homes and workplaces (including health-care environments; Giannakou et al., 2022). For example, one research group has created a neglect test run on a tablet or smartphone which includes a battery of ecological tasks (e.g., laying the table, serving tea, ordering in a café, card distributing; Cipresso et al., 2018). A test of this kind could be helpful in gaining an understanding of neglect behaviour in real-life settings and scenarios when it may not be possible to carry out the tasks physically (e.g., in a hospital setting or due to reduced mobility).

Of the 28 studies identified in a recent review, most (46%) were computer-based versions of conventional tests (i.e., line bisection, cancellation) and 39% were visual search tasks (Giannakou et al., 2022). In practical terms, the tests took between 10-20 minutes at maximum distance of 70cm (peripersonal space). When compared to paper-and-pencil (e.g., line bisection, cancellation) and functional assessments (e.g., CBS), over half (60%) of the computer-based assessments reported equal or increased sensitivity (Giannakou et al., 2022). In other words, some computer-based tasks (particularly those measuring reaction time and visual search tasks) detected cases of neglect which were missed by paper-and-pencil assessments, particularly in mild, chronic and subclinical cases (Giannakou et al., 2022). Based on this review, computer-based assessments have the potential to be more sensitive than paper-and-pencil tests, however the variation in methodologies and assessments used made direct comparisons between studies difficult (Giannakou et al., 2022). These are positive findings, however like paper-and-pencil tests, it seems the current literature continues to focus on computer-based assessments within peripersonal space (Cipresso et al., 2018; Giannakou et al., 2022).

Virtual Reality (VR) based tests can include non-immersive and immersive (via a head mounted display) technology. Immersive VR can be used to manipulate task complexity (Cavedoni et al., 2022) and project stimuli in extrapersonal space (Knobel et al., 2020). Examples of VR-based neglect tasks include navigating along paths (Buxbaum, Dawson & Linsley, 2012), virtual street crossing (Navarro, Llorens, Noe, Ferri, & Alcaniz, 2013), and searching for objects in virtual environments (Kim et al., 2004; Jannink et al., 2009; Cipresso et al., 2014). For example, Ogourtsova et al., (2018) simulated a detection and navigation task including extrapersonal space within an ecologically rich supermarket setting using immersive VR. Importantly, it has been shown that performance on VR assessments significantly correlates with performance with validated, conventional neuropsychological assessments (e.g., star cancellation, line bisection; Fordell et al., 2011; Buxbaum et al., 2012; Navarro et al., 2013) or appeared more sensitive (Peskine et al., 2011). This may be due to increased attentional demands used and/or additional performance metrics, both of which can be sensitive in detecting neglect symptoms (van Kessel et al., 2013; Giannakou et al., 2022) or detection of neglect in subtypes not typically assessed (e.g., neglect in extrapersonal space).

A recent review reported that only four VR assessments were able to measure neglect within extrapersonal space (Cavedoni et al., 2022). Yasuda and colleagues (2020) used a head mounted display to present a target (red sphere) at various distances in virtual space. Using a VR headset enabled the researchers to take precise measurements (in degrees) of one patient's neglected space (Yasuda et al., 2020). Importantly, the study did not report any adverse effects from using a VR headset (such as motion sickness). Unfortunately, the researchers did not report any psychometric superiority or inferiority compared to conventional neuropsychological assessments since it was a proof-of-concept study and only included one participant (Yasuda et al., 2020). Another recent study used immersive VR to stimulate a three-dimensional virtual cancellation task (Knobel et al., 2020). Fifteen right-hemisphere stroke survivors were asked to use a controller to 'touch' targets (spheres) scattered amongst distractors (cubes). Similar to 'real-life' search movements, participants were able to move their head to freely search for targets around the 160-degree horizontal visual angle. After completing the task, participants reported high acceptance and usability of the VR system. Interestingly however, the immersive VR assessment had poorer sensitivity compared to paper-and-pencil tests. The authors argue this may have been due to displaying fewer targets (n= 20) compared to the comparator paper-and-pencil assessment (n= 240;

Knobel et al., 2020). Both studies highlight the capabilities of immersive VR tasks, such as manipulation of virtual environments, stimuli, and precise performance measures. However, Knobel et al.'s (2020) study is a reminder that many properties (e.g., stimuli, number of distractors) of conventional assessments could be embedded into VR or computer-based tests since we know they are capable of detecting neglect symptoms.

Despite their potential and growing use within research, VR-based assessments have practical considerations. For example, immersive VR technology (head mounted displays) are more costly compared to non-immersive computer-based assessments which may run on existing equipment (e.g., tablets, smartphones, laptops; Cavedoni et al., 2022). In terms of convenience in a busy clinical setting, paper-and-pencil assessments may remain superior since they require very basic resources and can take under 5 minutes to administer (Moore et al., 2022). More research is certainly needed to explore the use of computer-based (including VR) assessments since the current evidence is not of high-quality in that it lacks normative data, control groups, and often uses small sample sizes (e.g., n= 1; Cavedoni et al., 2022). The limitations within the literature mean not enough is known about these computerised tools to be used in clinical practice. Going forward, studies should implement increased methodological rigor (larger sample sizes, control groups, normative data), as well as evaluation of usability and patient experience to improve system functionality (Cavedoni et al., 2022).

Overall, some computer-based (including VR) assessments have been reported to be more or as sensitive as paper-and-pencil assessments. Their use could address current gaps in assessment practice, such as providing automatic scoring and additional variables sensitive to attentional deficits (e.g., reaction time; van Kessel et al., 2013). In particular, the technology could be utilised to address the current cap in the underassessment of neglect in extrapersonal space. With both the benefits and limitations of paper-and-pencil and computer-based assessments in mind, perhaps a comprehensive or optimised assessment of neglect behaviour could combine both computer-based and conventional assessments (Giannakou et al., 2022; Cavedoni et al., 2022).

1.10 Rehabilitation

Post-stroke rehabilitation can be challenging due to the complex nature of stroke and its consequences (Clarke & Forster, 2015). For instance, physical and cognitive fatigue is reported to affect up to 86% of stroke survivors in the UK (Stroke Association, 2019). Though one must also consider the impact of post-stroke psychological consequences which affect 1 in 3 stroke survivors (Stroke Association, 2019). These impacts can negatively affect rehabilitation engagement and its effectiveness since mood problems, such as depression (affecting up to 44% of stroke survivors; Stroke Association, 2019) are associated with poorer functional outcome (Pohjasvaara et al., 2001). Therefore, a stroke survivor's rehabilitation plan requires input from multidisciplinary teams across the stroke care pathway (Clarke & Forster, 2015). Yet 44% of stroke community rehabilitation teams do not have access to a clinical psychologist (Royal College of Physicians Sentinel Stroke National Audit Programme; SSNAP, 2021).

Spatial neglect is difficult to rehabilitate due to its complex nature (e.g., symptoms affecting different senses and spatial regions). Therefore, one rehabilitation technique is unlikely to be effective for all stroke survivors (NICE, 2011; Riestra & Barrett, 2013). And cooccurring conditions, such as anosognosia (occurring in ~29-83% of neglect cases; Grattan et al., 2018) can make engagement in rehabilitation interventions challenging (Longley et al., 2022) since patients do not recognise the problems which need addressing (Grattan et al., 2018). Perhaps these factors contribute to poorer recovery outcomes for those with spatial neglect when compared to patients who have equal or comparable stroke severity or physical impairments (Chen et al., 2015).

Rehabilitation interventions aim to help stroke survivors either by restoring or compensating for their loss or impaired function (NICE, 2011). In other words, restorative rehabilitation aims to improve function, whereas compensatory rehabilitation introduces strategies to reduce the effect of the loss of function (Loetscher et al., 2019). A compensatory strategy may be education to increase awareness of neglect symptoms and help the individual voluntarily pay more attention to the neglect side. Alternatively, a restorative approach may increase spatial awareness of the neglected side without needing insight from the patient (Longley et al., 2022), such as after using prism adaptation (PA; prism glasses which shift gaze, discussed below).

Both pharmacological and nonpharmacological (cognitive) techniques have been studied to rehabilitate spatial neglect (Bowen et al., 2013; Riestra & Barrett, 2013; Longley et al., 2022). Although pharmacological interventions are out of scope of this thesis (see Riestra & Barrett, 2013 for a short review), one example is the use of attention-deficit hyperactivity disorder (ADHD) medication (guanfacine) to improve visual search and sustained attention in stroke survivors with spatial neglect (Dalmaijer et al., 2018). In a randomised, double-blinded trial design comparing guanfacine against a placebo, researchers found a moderate improvement in search organisation and sustained attention (i.e., patients found more targets in a cancellation task) after a dose of guanfacine (Dalmaijer et al., 2018). Though there was no improvement in ameliorating the core attentional bias in neglect, the authors propose that using pharmacological and behavioural interventions in conjunction could be more effective than one intervention alone (Dalmaijer et al., 2018).

Broadly, behavioural interventions can be split into two categories: bottom-up and top-down rehabilitation methods (Parton et al., 2004; Bowen, Hazelton, Pollock, & Lincoln, 2013). Top-down methods require the patient to have awareness of their spatial neglect symptoms (Bowen et al., 2013). Some examples include smooth pursuit eye movement training (following stimuli moving towards contralesional space; (Kerkhoff et al., 2013), visual scanning training (encouraging patients to explore stimuli using systematic eye movements) and visual cueing (using bright colours on the neglect side; NICE, 2013; Bowen et al., 2013). Bottom-up approaches (e.g., eye patching) do not require a patient's insight of their symptoms and aim to recalibrate the impaired mechanisms of spatial neglect (e.g., representation of space; Parton, Malhotra & Husain, 2004; Bowen et al., 2013). An example of a widely used bottom-up method is prism adaptation (PA) which involves wearing a pair of goggles with prismatic lenses. These lenses alter, or shift, vision towards the non-neglected side (e.g., right side if left neglect is present). These goggles are worn for a short time (20-30 minutes) while performing visuo-motor tasks (e.g., pointing); these sessions are termed periods of 'prism exposure' (Kerkhoff et al., 2021). Due to the shift in vision towards the ipsilesional side, patients adjust their pointing more towards contralesional side (neglected space) to reach targets. Once the session is over, patients experience 'after-effects' from the shifted vision, whereby their attention is thought to have adapted or reoriented towards the neglected side (Kerkhoff et al., 2021). PA, along with visual scanning training, alerting, and repetitive task techniques are recommended by the stroke rehabilitation NICE guidelines (NICE, 2013). Consequently, PA training has been widely researched to establish it as an effective treatment for spatial neglect (e.g., Rossetti et al., 1998; Gossmann et al., 2013; Ten Brink et al., 2017; Vaes et al., 2018; Longley et al., 2022). Although PA is easy to administer and low-cost, there is no clear consensus that it is effective in reducing spatial neglect, particularly on ADLs (Longley et al., 2021). One study found positive effects in reducing egocentric neglect (e.g., increased targets found on a cancellation task) but not allocentric neglect (e.g., no reduction in cancelling distractors with left-side gaps; Gossmann et al., 2013). Based on this, it seems as though it would be important to understand a patient's full symptomology (i.e., presence of ego- or allocentric neglect) to inform choice of rehabilitation technique.

Visuomotor feedback training (VFT)[1] is a low-cost rehabilitation technique. Unlike PA, Spatial Inattention Grasping Home-based Therapy (SIGHT) can be carried out independently at-home without the need of a therapist (Harvey, Hood, Harvey, & Robertson, 2003; Rossit et al., 2019). As a bottom-up, object centred (allocentric) method, SIGHT does not require insight of symptoms in patients with spatial neglect. SIGHT involves lifting lightweight wooden rods until the patient feels that they are balanced. In the case of left side neglect - since they are not attending to the left side - patients perceive the rod's true middle to be more rightward. Thus, when the patient grasps and lifts the rod, they receive somatosensory (sensory-motor) feedback from the rod tilting and one end hitting the table, indicating that they have not picked it up from the true middle. This feedback enables the patient to readjust their grip and find the true middle through repeating the lifts (Robertson et al., 1997; Harvey et al., 2003). Patients with spatial neglect are able to engage with SIGHT since we know that some individuals with spatial neglect can reach relatively accurately - even towards objects in contralesional space (Rossit et al., 2009, 2012; Harvey & Rossit, 2012).

According to Robertson et al. (1997), SIGHT can help patients attend to the neglect side through motor responses (via dorsal streams). In other words, grasping and lifting the rod provides the patient with more accurate spatial information compared to perceptual feedback (via ventral streams) which is thought to be more vulnerable to the attentional biases observed in neglect (see 'Understanding neglect behaviour' for full discussion). The action responses 'correct' attentional and perceptual mechanisms via "dorsal-to-ventral" visual

[1] For the purpose and clarity of this thesis, VFT will henceforth be referred to as Spatial Inattention Grasping Home-based Therapy (SIGHT).

stream recalibration (Robertson et al., 1995; Harvey et al., 2003; Milner & Goodale, 2006). Harvey and colleagues (2003) investigated this further and demonstrated that using SIGHT for a period of two weeks produced significant improvements in 14 cases of chronic spatial neglect on a real object search task, landmark (judging the shorter ends of lines), and line bisection task (Harvey et al., 2003).

More recently, these effects were replicated in a proof-of-concept, randomised controlled trial where twenty stroke survivors self-administered SIGHT for a 2-week period in their own homes (Rossit et al., 2019). Before carrying out SIGHT independently, participants received two 30-minute experimenter-led sessions over two days. Following this, self-administration was facilitated by paper checklists of which participants had to tick to indicate completion of all 72 trials each day. These self-report checklists were also used to monitor adherence to treatment dosage. Those in the intervention group (n= 10) were required to lift and balance the rods (thus receiving the critical somatosensory feedback) until they felt they had found the true middle/balanced the rod. Those in the control group lifted the rods from one end only. While this group received no somatosensory feedback, these exercises ensured that both groups had similar motor responses (reaching, lifting rods; Harvey et al., 2003). Those in the intervention group showed larger improvements (though the effect sizes were small) compared to the control group on both functional measures (motor hand function, daily activities of living) and paper-and-pencil neglect tests (i.e., the Behavioural Inattention Test including cancellation, line bisection, reading tests; Wilson et al., 1987) up to four-months after the training-phase. Importantly, the equipment used for SIGHT (wooden rods and mat) were simple, inexpensive, and the set-up in stroke survivor's homes enabled patients to carry out therapy without the need of a therapist/researcher to be always present. Based on the evidence so far, the effects of SIGHT suggest that it is a promising rehabilitation method which can be offered to patients to carry out independently at-home at any stage of their stroke recovery. However, further investigations are needed using more rigorous methodologies, such as larger sample sizes and outcome assessor blinding to reduce any possibility of bias (Longley et al., 2021). The authors acknowledge this, as well as using electronic monitoring to measure treatment adherence since the self-report checklists may be unreliable (Rossit et al., 2019).

1.11 Computerised rehabilitation

Technology has the potential to transform monotonous rehabilitation into enjoyable or more engaging activities (e.g., ‘video-game therapy’; Burdea, 2003; Dias et al., 2019). Telerehabilitation uses technology to deliver rehabilitation to patients remotely (Brennan, Mawson & Brownsell, 2009). It can be delivered via telephone, videoconferencing, and wearable devices (e.g., exercise watches; Laver et al., 2020). For example, virtual reality (VR) can facilitate telerehabilitation using exercise games (‘exergames’) in a virtual environment which can provide feedback to the patient (e.g., Morse et al., 2020). Depending on the method, telerehabilitation can be delivered in real time (e.g., via videoconferencing, telephone) or asynchronously (e.g., patient’s performance is remotely shared with a therapist after the session; Brennan et al., 2009). The former is useful for delivering assessments and consultations remotely; particularly during the COVID-19 pandemic when face-to-face appointments were not available or safe (Laver, Walker & Ward, 2022). Asynchronous telerehabilitation can allow patients to carry out rehabilitation autonomously (Morse et al., 2020) in their own time and within a familiar environment (e.g., at-home; Cavedoni et al., 2022).

Telerehabilitation provides some benefits over traditional rehabilitation, such as reaching those in remote areas (Laver et al., 2020) and eliminating travel needs (particularly useful for those with limited mobility; Laver et al., 2020; Cavedoni et al., 2022). These aspects may have economic benefits too, however a recent Cochrane review could not reach a definitive conclusion whether telerehabilitation is cheaper since many studies do not report cost-effectiveness (Laver et al., 2020). Cost aside, telerehabilitation seems feasible to deliver with a clinician present (Svaerke, Niemeijer, Mogensen, & Christensen, 2019) and stroke survivors (Dias et al., 2019) and therapists (Ogourtsova et al., 2017) are generally accepting of the tools (Morse et al., 2020).

We know some of the potential practical benefits, but what do we know about the efficacy of telerehabilitation tools post-stroke? Telerehabilitation delivers rehabilitation in a different format (e.g., remotely, virtually) though the mechanisms are thought to be similar to those of conventional rehabilitation techniques (Laver et al., 2020). A recent Cochrane review evaluated the results of 22 randomised controlled trials (RCT) using various telerehabilitation interventions (Laver et al., 2020); the types of interventions varied but were primarily targeting physical problems (e.g., upper, lower limb, mobility, balance) and aphasia after stroke. The authors could not determine a difference in effectiveness between telerehabilitation and usual care based on assessments of ADLs and quality of life (Laver et al., 2020). In other words, telerehabilitation was neither superior nor inferior to usual care. The authors call for higher quality studies, incorporating reports of patient's acceptability and the feasibility of telerehabilitation methods (Laver et al., 2020). This is particularly important to reduce the chances of user and technical errors when using the technology unsupervised (Threapleton, Drummond & Standen, 2016).

Telerehabilitation for spatial neglect can include both immersive (e.g., VR) and non-immersive (e.g., computer-based) tools. Telerehabilitation using immersive VR may involve creating a rich three-dimensional virtual environment which a patient can interact with using a head mounted display or VR goggles. For example, Yasuda and colleagues (2017) used a head mounted display to immerse ten participants with neglect within a virtual room.

Participants interacted with objects (i.e., touched with their virtual hand) in near-space and carried out a visual search task in far-space. Before and after training, participants also completed conventional neglect tests (cancellation tasks, line bisection) in near (on A4 sheet of paper) and far-space (projected onto a wall, response recorded using a laser pointer). The results showed a significant improvement (more targets found) in far-space cancellation tests after completing the VR tasks (Yasuda et al., 2017). The study provides novel, pilot data on the potential use of immersive VR-based rehabilitation to target neglect in far-space - something not commonly reported in the literature. Though, these results should be interpreted with caution since there was no control group to determine whether the effects were truly due to the VR training. Utilising immersive-VR technology such as this could make it possible to target rehabilitation to neglect in extrapersonal space which can occur independently of peripersonal neglect.

A number of non-immersive applications are freely available for stroke survivors with spatial neglect or visual field loss (British and Irish Orthoptic Society, 2018) which run on laptops and/or tablets. These include both website (e.g., Eye Search which aims to increase visual exploration; Jacquin-Courtois, Bays, Salemme, Leff, & Husain, 2013) and tablet applications (e.g., Durham Reading and Exploration training; DREX; Aimola et al., 2014). Telerehabilitation tools, such as these are designed to facilitate self-administration at home (e.g., providing instructions) and record adherence data automatically (without relying on self-report data).

More recently, one study used augmented reality (overlaying virtual animations onto the real-life environment) to rehabilitate neglect (Stammler et al., 2023). The author's rationale for using augmented reality was to make rehabilitation more engaging and motivate the user by creating a 'game-like' visual exploration exercise. Real-life surroundings were shown on screen using the tablet's camera while a virtual target (an origami bird) was overlayed (augmented) in the environment shown on screen. Ten patients with neglect were asked to either follow the moving bird or find it in a static location. Akin to visual scanning training, these activities encouraged two therapeutic processes: visual exploration of surroundings and rotating the trunk into neglected space (Stammler et al., 2023). Performance feedback (auditory, visual) was given to patients and there was a choice of levels of difficulty. Overall, the application received high ratings on the System Usability Scale and positive ratings of fun, satisfaction and motivation. A clinical trial investigating the efficacy of the application is ongoing but the authors note that augmented reality (or indeed non-immersive VR) could be more cost-effective and accessible compared to VR-based treatments (Stammler et al., 2023). For instance, non-immersive VR applications can utilise technology that may already be in the home or clinic (e.g., smartphone, tablet, PC; Giannakou et al., 2022; Stammler et al., 2023) which bypasses potential side effects from immersive VR, such as cybersickness (brought on by a mismatch between sensory information, e.g., visual, somatosensory; Cavedoni et al., 2022; Stammler et al., 2023).

The current uptake of these tools (particularly those available on application stores) by clinicians and patients outside of research is not known. But we do know that a number of studies have reported positive attitudes towards using non-immersive VR telerehabilitation for spatial neglect (Ogourtsova et al., 2017; Morse et al., 2020). Specifically, stroke survivors, carers and clinicians perceived performance monitoring and virtual feedback (e.g., cheering) as a facilitator of using a VR-based telerehabilitation for spatial neglect. This group of participants also recognised the need for a home-based telerehabilitation tool for spatial neglect, and that it would be accessible (e.g., to those with mobility issues) and convenient (Morse et al., 2020). They also reported that at-home rehabilitation could have psychological benefits, such as increased autonomy, independence, and confidence (Morse et al., 2020). Yet research within this area is still in its infancy; a recent review only identified 13 studies using computerised rehabilitation tools for spatial neglect (Cavedoni et al., 2022). Further research is needed to formally explore the efficacy of computerised tools (Gammeri, Iacono, Ricci, & Salatino, 2020) using controlled, blinded conditions, larger sample sizes, control groups, and usability evaluations (Threapleton et al., 2016; Svaerke, et al., 2019; Cavedoni et al., 2022).

Ultimately, telerehabilitation has the potential to increase enjoyment and motivation of spatial neglect rehabilitation (Morse et al., 2020; Stammler et al., 2023). It can also deliver rehabilitation at home so stroke survivors can receive uninterrupted rehabilitation after discharge. This has potential to help some of the one million stroke survivors needing further care post-discharge (Royal College of Physicians Sentinel Stroke National Audit Programme (SSNAP), 2021) and some of the 41% of stroke survivors who felt they hadn't received the clinical help they needed (McKevitt et al., 2011).

1.12 Conclusions

Spatial neglect is a common consequence following stroke (Hammerbeck et al., 2019). Its symptomology is complex in that it can affect different sensory modalities (e.g., vision, motor), spatial reference frames (ego-, allocentric), as well as spatial regions (personal, peripersonal, extrapersonal space). The evidence suggests that these can occur together or independently of one another and impact different aspects of a stroke survivor's daily living (e.g., Berti et al., 2002; Demeyere & Gillebert, 2019; Kerkhoff, 2001; Moore et al., 2023).

Current paper-and-pencil assessments of neglect have been criticised as they lack ecological validity (Azouvi et al., 2002) and are limited to assessing neglect in peripersonal space. Computerised assessments have capabilities of enhancing neglect assessment, such as facilitating measurement of symptoms in extrapersonal space (e.g., (Yasuda et al., 2020), manipulating attentional demands (van Kessel et al., 2013), and providing additional performance metrics (e.g., reaction time, search paths; Dalmaijer et al., 2015) not provided from paper-and-pencil measures.

Detecting neglect in extrapersonal space is critical in obtaining a comprehensive understanding of an individual's symptomology and inform an appropriate rehabilitation plan. Unfortunately, there is currently insufficient evidence to formally recommend an effective rehabilitation method for spatial neglect (Longley et al., 2021). However, telerehabilitation provides a promising alternative or supplement to rehabilitation methods by facilitating self-administration at home (Cavedoni et al., 2022; Morse et al., 2020; Stammler et al., 2023) and measurement of user adherence (Threapleton et al., 2016). Research in exploring the use of telerehabilitation tools for spatial neglect is still in its infancy and many are still conducted within lab environments (Cavedoni et al., 2022). Going forward, more data is needed to explore the feasibility of using these tools in home environments whilst using more rigorous methodology (Cavedoni et al., 2022; Gammeri et al., 2020; Svaerke et al., 2019). Use of mixed methods is also recommended to better understand the barriers and facilitators of use to inform future development and uptake (Threapleton et al., 2016).

1.13 Thesis rationale

In light of this, the present thesis will investigate the psychometric properties (e.g., diagnostic accuracy) of a new Computerised Extrapersonal Neglect Test (CENT). The test aims to address the current gap in detecting neglect in extrapersonal space since the most widely used assessments (e.g., paper-and-pencil) are only conducted in peripersonal space. The final part of the thesis will investigate the feasibility and usability of using a novel telerehabilitation tool (c-SIGHT) which is based on an existing evidence-based rehabilitation method (SIGHT). The computerised version of SIGHT (c-SIGHT) facilitates self-administration and obtains an objective measure of user adherence at-home. Overall, this thesis will provide novel data on using a computerised assessment to detect neglect in far-space and the feasibility and acceptability of using a self-administered rehabilitation for neglect at home.

1.14 Thesis chapter outlines

Chapter 1 aims to investigate cancellation and line bisection performance in far-space using CENT in a sample of neurologically healthy adults. This includes exploring any effects of demographic variables (i.e., sex, education, handedness) on performance and compiling the tests' first set of age-graded normative data. Establishing normative data is a critical precursor to using CENT with stroke survivors (*Chapter 2 & 3*) to help characterise performance post-stroke and explore which attentional deficits might be neglect-specific. Overall, this chapter will give us a novel insight into visuospatial attention in far-space across age-groups, something which is commonly explored in near-space only.

Chapter 2 aims to investigate attentional impairments (e.g., neglect) in stroke survivors in far-space using CENT when compared to age-matched controls in *Chapter 1*. It will also investigate the diagnostic sensitivity and concurrent validity of CENT compared to paper-and-pencil neglect tests, as well as the relationship between scores on a cognitive screening tool and quality-of-life scores. Results from this chapter will inform us of the frequency of extrapersonal (far-space) neglect in a sample of stroke survivors, as well as establishing whether CENT is a sensitive test in detecting attentional deficits in far-space. It will demonstrate whether computerised assessments could offer more sensitive measures of attentional deficits by using additional metrics not possible to measure using paper-and-pencil tests. If so, the test could help identify cases of extrapersonal neglect which may otherwise go undetected and potentially impact stroke survivor's day-to-day lives (e.g., driving, navigation, watching television).

Chapter 3 will investigate the feasibility of a randomised controlled trial using c-SIGHT, compared to an attentional control version in the homes of stroke survivors with spatial neglect. The trial will estimate key feasibility parameters, such as recruitment, attrition rates, blinding success, follow-up, and adherence rates. Any potential effects of c-SIGHT on outcome assessments (e.g., neglect tests, quality-of-life measures) will be explored between groups. Finally, mixed methods (interviews, questionnaire data) will examine stroke survivor's experience using c-SIGHT at-home to determine its usability and acceptability. The results from this chapter will contribute valued knowledge to trial design of telerehabilitation research in community settings (not limited to neglect). Establishing feasibility will also help support the rationale for further research of telerehabilitation tools (e.g., c-SIGHT) with the potential to provide individuals with neglect rehabilitation at-home. Importantly, usability and acceptability data from c-SIGHT will be useful in future developments of telerehabilitation tools to improve functionality and user-experience.

2. Chapter 1: Aging effects on extrapersonal (far-space) attention: cancellation and line bisection performance from 179 healthy adults

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2.1 Introduction

Visual search is used in everyday life, from searching for people in a crowd to items in a supermarket. Several cognitive processes are thought to be essential to carry out efficient and successful visual search, including orienting attention towards an object or area in space (visuospatial attention), alertness, executive control, and perceptual grouping (Muller-Oehring et al., 2013). These processes are important for conducting organised and efficient (i.e., finding targets successfully in less time) searches in cluttered everyday environments. Organised searches can be measured according to their consistency (maintaining the same search pattern), number of intersections (search path crossing over itself), and distances between targets (finding the next target close to the previous one; Ten Brink et al., 2016). Moreover, our visuospatial attention operates to find stimuli in peripersonal (within reach/near-space) and extrapersonal space (out of reach/far-space), and locate them using egocentric (location of object relative to the body) and allocentric (relative to other objects) reference frames (Lane, Ball & Ellison, 2015). The central role visual search plays in everyday life becomes apparent when observing deficits in visuospatial attention after brain injury or changes with healthy aging.

Cancellation tests (i.e., a visual search task to find targets amongst distractors) are commonly used in clinical and research settings (Checketts et al., 2021; Moore et al., 2022) to detect deficits in visuospatial attention in neurological populations. Currently, they are thought of as the most sensitive measure of spatial inattention (or spatial neglect; Ferber & Karnath, 2001; Moore et al., 2022), a syndrome affecting a person's ability to attend to stimuli on the side of space opposite to the side of the brain lesion. Given that spatial inattention can be observed both in egocentric and allocentric reference frames (Demeyere & Gillebert, 2019), some cancellation tests are able to measure both ego- and allocentric biases (e.g., Ota, Fujii, Suzuki, Fukatsu, & Yamadori, 2001; Bickerton & Samson, 2011; Demeyere et al., 2015). In practice, stroke survivors have been shown to perform less efficient or disorganised searches compared to healthy controls (Ten Brink et al., 2016). Using a computerised cancellation task, Ten Brink and colleagues reported that stroke survivors with spatial inattention after a right hemisphere lesion had increased number of intersections compared to healthy controls, and stroke survivors with spatial inattention after left hemisphere lesions. Deficits in spatial working memory impact the individual's ability to 'update' their internal representation of the scene (i.e., targets already found), meaning they may revisit previously searched areas (perseverate), consequently increasing the number of intersections, resulting in a disorganised search (Ten Brink et al., 2016).

Similarly, performance in aspects of visuospatial attention declines in healthy aging. For example, older people tend to display slower processing speeds (i.e., search duration) in visual search and cancellation tasks compared to younger people (Hommel et al., 2004; Brucki & Nitrini, 2008; Warren, Moore & Vogtle, 2008; Potter et al., 2012; Muller-Oehring et al., 2013; Benjamins et al., 2019; Tamura & Sato, 2020). A large study consisting of 523 healthy participants reported that search duration increased by 59 milliseconds with each year of age (Benjamins et al., 2019). This decline began at around 50-60 years old (Warren et al., 2008; Tamura & Sato, 2020).

In everyday life, most of our visual searches occur in far-space and processing of this space seems different than attentional mechanisms within near-space. In fact, attentional deficits in far-space have been shown to dissociate from deficits in near-space in neurological patients (Halligan & Marshall, 1991; Committeri et al., 2007; Aimola, Schindler, Simone, &

Venneri, 2012). Surprisingly, however, most research on attention has been conducted in near-space (i.e., on a computer screen within reach of the participant), so it remains unknown how different tasks are performed in this section of space and how this is impacted by aging. One study using an everyday-based supermarket task presented in far-space found that search duration was faster for those in their 20s and 30s compared to older adults, particularly those in their 70s and 80s (Potter et al., 2012). This suggests that healthy aging affects visual search duration in far-space.

However, aging effects on visual search seem highly dependent on the task used (Hommel et al., 2004), suggesting that different mechanisms may be involved. For example, older adults take longer than younger participants to complete conjunction than feature searches (Hommel et al., 2004; Potter et al., 2012; Muller-Oehring et al., 2013; Tamura & Sato, 2020). Feature searches utilize a pre-attentive stage (information not yet selectively attended to) of processing to find a target using basic visual features, such as colour and orientation (Treisman 1982; Wolfe, 2021). Targets in feature searches often 'pop-out' from distractors since they are unique in their basic visual features and visually different from distractors (Wolfe, 2021). In contrast, conjunction searches are thought to use both stimulus-driven (bottom-up) and known (top-down) features of a target in the pre-attentive stage to create a priority map that guides where we allocate our attention (Wolfe, 2021). In other words, the priority map acts as an "*attention-directing landscape*", whereby our attention is allocated to 'spikes' until the target is found (Wolfe, 2021 p.6). It has been proposed that older adults are slower at conjunction searches as it relies on later, serial processing stages and requires executive control to shift, inhibit and select attention between targets and distractors (Muller-Oehring et al., 2013; Tamura & Sato, 2020).

Whether aging affects line bisection performance has been more debatable. Like cancellation tasks, line bisection assesses visuospatial attention by measuring the deviation error when individuals mark the centre of lines. To quantify spatial inattention, line bisection tasks are recommended alongside other tests (e.g., cancellation), since biases presented can be affected by motor, visual, and visuomotor impairments (Moore et al., 2022). Generally, healthy individuals bisect lines leftward from the true centre (a phenomenon known as pseudoneglect; Bowers & Heilman, 1980). Right hemisphere dominance in spatial processing is widely used to explain pseudoneglect (i.e., an increased orientation to the left; Brooks, Darling, Malvaso, & Della Sala, 2016). Some studies report rightward biases in participants over 50 years old (Fujii et al., 1995; Jewell & McCourt, 2000; Benwell, Thut, Grant & Harvey, 2014) while others report leftward biases (Varnava & Halligan, 2007). The variance in findings could be due to a high variance between individuals (Manning, Halligan & Marshall, 1990), and task and stimuli used (e.g., line length and placement, hand used, starting position; Brooks et al., 2016; Benwell et al., 2014; for review see Jewell & McCourt, 2000). However, a recent meta-analysis of 63 studies found a leftward bias in studies where all participants were over the age of 50 (Learmonth & Papadatou-Pastou, 2021). The authors propose that preserved right hemisphere dominance could explain why pseudoneglect is observed in older age and that spatial attention may not be as affected by age-related changes compared to other cognitive functions, such as memory (Learmonth & Papadatou-Pastou, 2021; Brooks et al., 2016). Much like visual search research, most studies of line bisection are conducted in near-space, with the exception of one study which found a reduction in pseudoneglect in healthy adults aged between 17 and 41 years old in far versus near-space (Varnava, McCarthy & Beaumont, 2002). To date, it's unclear how (or if) age affects line bisection in far-space and how this relates to visual search performance.

Studying the effects of age on line bisection and visual search is particularly important as these tasks make up a large proportion of neuropsychological assessment of attention impairments (Checketts et al., 2021). For tests where cognitive processes are known to be affected by age (such as visual search duration), age-graded norms can be useful for detecting subtle cognitive changes in older people indicative of early brain disease (Lezak, Howieson, Loring, & Fischer, 2004). However, many paper-and-pencil cancellation tasks used to detect attentional deficits after brain injury do not provide age-specific cut-offs and are limited in the types of performance metrics they can provide (e.g., overall accuracy, spatial bias scores, overall search duration; e.g., Broken Hearts Cancellation test; Demeyere et al., 2015).

Computerised tasks record rich performance metrics, such as search organisation (i.e., search paths, intersections; Dalmaijer et al., 2015), which have been shown to be a sensitive measure of attentional deficits after stroke (Ten Brink et al., 2016). Computerised tests also facilitate the manipulation of attentional demands (thus increasing sensitivity in detecting even mild attentional deficits; Peskine et al., 2011) and the area of space stimuli are presented (e.g., in far-space; Yasuda, Muroi, Ohira & Iwata, 2017; Ogourtsova et al., 2018). Attentional deficits (such as spatial inattention) or age-related declines in search efficiency (success and speed) in far-space could impact the efficiency of activities in daily life (e.g., navigation, finding objects; Potter et al., 2012; Ten Brink et al., 2016). Yet, visuospatial attention tasks (e.g., cancellation, line bisection) are not routinely carried out in far-space in clinical environments.

To address these knowledge gaps, here we investigated cancellation and line bisection performance in far-space across different ages (and other demographic variables, e.g., sex, education, handedness) in a large sample of healthy individuals (Objective 1). This included producing the initial age-graded norms for the tasks for use with clinical populations (Objective 2). To do this, we used our novel Computerised Extrapersonal Neglect Test (CENT) consisting of a cancellation and line bisection task presented in far-space. Based on the literature, we expected to see an increase in processing speed as age increased and evidence of pseudoneglect across the sample. Based on findings from Benjamins and colleagues (2019), we did not expect education or sex to influence performance.

2.2 Methods

2.2.1 Participants

Adult (+18 years of age) members of the public were recruited using convenience sampling in a city centre venue in Norwich, United Kingdom in February 2019. In total, 246 adults took part in the study with 67 participants excluded. Of the 67 excluded, 45 participants (67.16%) did not meet the inclusion criteria: 37.31% had a previous brain injury or disease, 28.36% had uncorrected vision or a visual impairment, and 1.49% had a history of a severe psychiatric condition. Another 15 participants (22.39%) were excluded since they deviated from task instructions (e.g., used both hands, moved closer to the screen during the task). Of these, just under half (n= 7) were over 65 years old. Finally, 7 (10.45%) were excluded due to missing data (e.g., did not finish the study). Thus, the final sample included in the analysis was 179 participants (50% female, 48% male, 2% unspecified). Age ranged between 18 and 94 years (M = 49.29, SD = 18.36). Years of education ranged between 8 and 35 (M = 16.34, SD = 3.84; see **Table 2.1** for full descriptive statistics by age group). Ethical approval was obtained from the Research Ethics Committee at the University of East Anglia (2018-0026-001469). All participants provided informed consent in accordance with the Declaration of Helsinki.

Table 2.1. Descriptive statistics of sample (*n* = 179).

Age group	Mean age (*SD*)	n Female	n Male	n Total	Handedness			Mean years education
					Left	Right	Ambidextrous	
18-29	23.11 (3.21)	20	16	36	3	29	3	16.77 (1.99)
30-39	35.23 (3.11)	11	15	26	5	20	0	17.21 (5.28)
40-49	43.50 (2.93)	13	7	20	2	17	0	17.19 (4.18)
50-59	55.03 (2.68)	19	18	38	2	32	1	16.44 (3.78)
60-69	63.73 (2.99)	13	17	32	4	27	1	15.70 (3.72)
70-79	72.93 (2.32)	8	10	19	3	14	2	14.97 (4.21)
80-89	83.43 (2.67)	4	3	7	2	5	0	15.71 (4.27)
90-99	94 (0)	1	0	1	0	1	0	14 (0)
Overall	49.29 (18.36)	89	86	179	21	145	7	16.34 (3.84)

Note: Years education = from end of UK primary school (11 years old) to end of last education level obtained (e.g., degree or college).

2.2.2 Apparatus and stimuli

Our novel Computerised Extrapersonal Neglect Test (CENT) was projected onto a 60-inch television screen (full HD 1080p/50Hz, pixel size 1920x1080) mounted on a 1.8metre stand. CENT was developed working with end-users and in collaboration with Evolv Rehabilitation Technologies (https://evolvrehab.com/). CENT was programmed on Unity (Unity Technologies) and run on a laptop (OMEN by HP 15-dc0003) connected to the television. Participants used a wireless HTC Vive controller to complete CENT and responses were recorded via an HTC Vive base station placed on a tripod underneath the television and in line with the middle of participants' bodies. Both the HTC Vive base station and controller were connected to the laptop using a Steam wireless dongle.

CENT featured both a cancellation and line bisection task designed to be presented on a large screen (minimum 40 inch). The cancellation task consisted of 50 small (220mm height x 220mm width) and large (280mm height x 280mm width) targets (complete mugs; **Figure 2.1a**) amongst 100 small and large distractors (50 mugs with a left-side gap; 50 with a right-side gap; **Figure 2.1b**) presented across the screen (**Figure 2.1c**). The stimuli were static, positioned within a grid of 10 cells (373.4mm height x 265.6mm width; **Figure 2.1d**) each cell containing 5 targets, 5 left-gap, and 5 right-gap distractors. The line bisection task consisted of 10 short (604mm length x 50mm thickness) black horizontal lines presented one at a time (**Figure 2.2**). Two lines were presented in the middle of the screen (i.e., the midline of the line aligned with the midline of the participant and screen), four on the left and four on the right.

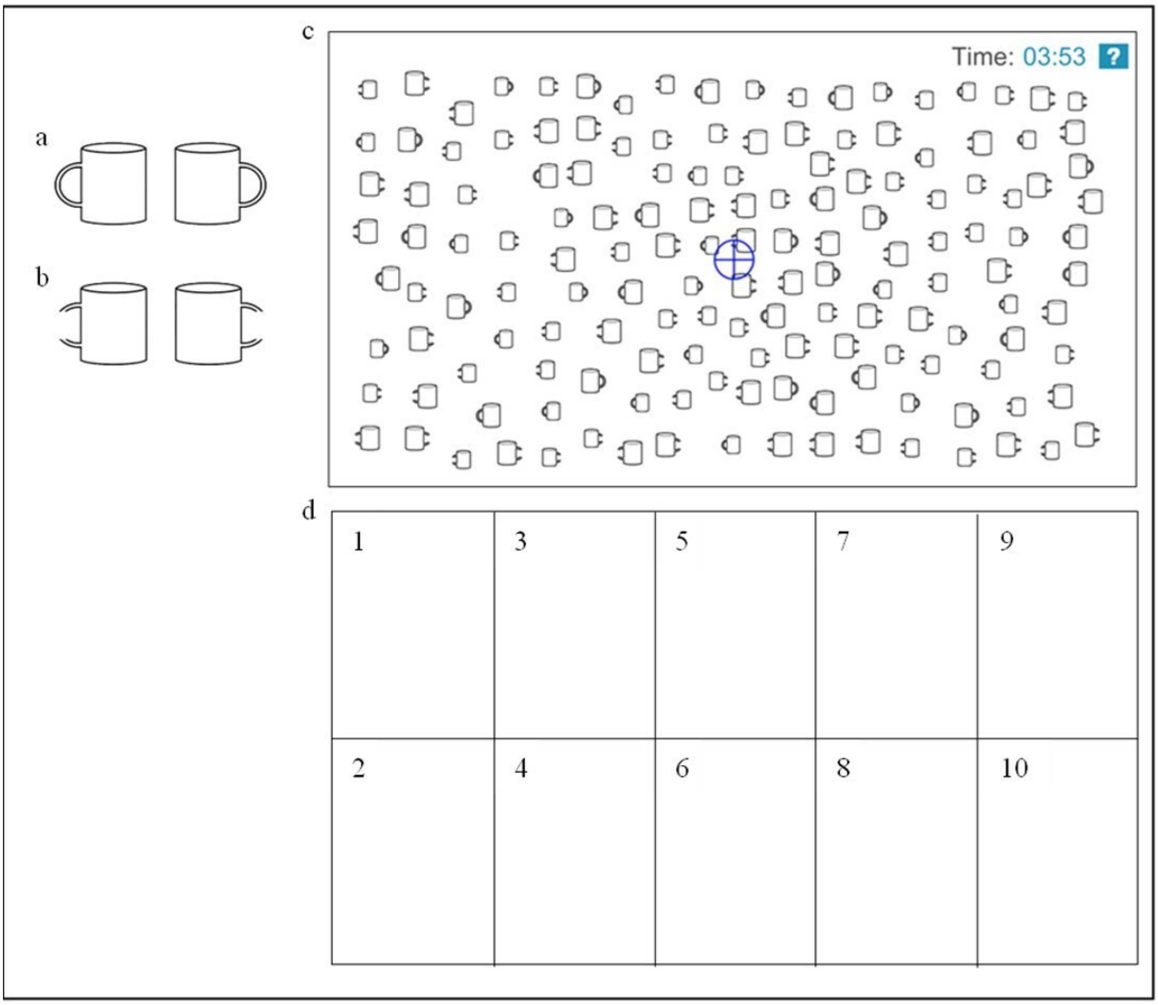

Figure 2.1. a) Cancellation task target stimuli; b) distractor stimuli; c) task display; d) grid used to position stimuli (boxes 1-4 indicate left; 5-6 middle; 7-10 right side of the screen).

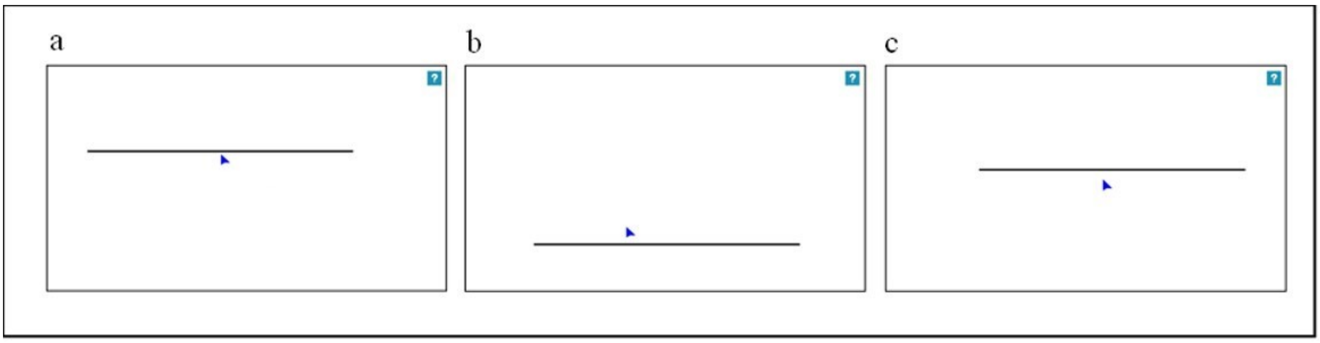

Figure 2.2. Line bisection task. Lines presented on a) left; b) middle; c) right.

2.2.3 Procedure

Participants were seated approximately 170cm away from the television, with their midsagittal plane in line with the centre of the television. Participants were given a wireless HTC Vive controller to click on stimuli (see **Appendix A** for an example set-up). For the cancellation task, participants were instructed to “Please click on all the complete mugs (those with no gaps)” using the Trackpad button. A blue ‘bulls-eye’ symbol was used as a cursor for participants to guide their selection of stimuli on the screen. Upon clicking, a short diagonal line and ‘popping’ noise indicated a registered response.

For the line bisection, a blue arrow was used as a cursor and participants were instructed to “Please click using the controller where you consider the centre of the line to be”. Note that participants were not explicitly encouraged to work quickly since we wanted to collect naturalistic processing speeds across ages.

Participants completed one practice trial with 12 targets and 12 distractors before completing the full cancellation task. Participants received the same instructions for both the practice and the full task. No feedback was given on the cancellation practice trial but was repeated once if participants did not follow the instructions. No practice was completed for the line bisection task since it is not common practice in neuropsychological testing (e.g., Wilson, Cockburn, & Halligan, 1987; Ferber & Karnath, 2001; Lezak et al., 2004). There was no time limit for either task and participants notified the experimenter when they finished the cancellation task. The line bisection task ended automatically after responding to the final line. Task order was counterbalanced across participants.

2.2.4 Outcome variables

Based on CancellationTools (Dalmaijer et al., 2015) and a previous study using computerised visual search (cancellation; Benjamins et al., 2019), we extracted the following variables of visuospatial attentional bias used in standard paper-and-pencil assessments (**Table 2.2**): accuracy (total number of targets cancelled), line bisection error (% left/right deviation from true centre), egocentric score (asymmetry score between the number of targets found on left versus right side of the screen) and allocentric score (asymmetry score between left-gap and right-gap distractors cancelled). To test search organisation (e.g., consistency, intersections, inter-cancellation distance; Ten Brink et al., 2016), we measured search speed (time and distance between consecutive cancellations), quality of search (speed and accuracy of search), and intersections (number of times search path crosses over itself; Dalmaijer et al., 2015). Since previous evidence has shown processing speed declines with age (Hommel et al., 2004; Brucki & Nitrini, 2008; Warren et al., 2008; Potter et al., 2012; Muller-Oehring et al., 2013; Benjamins et al., 2019; Tamura & Sato, 2020), we recorded search duration (total time taken in cancellation task) and total line bisection duration (total response time taken to judge middle of 10 lines). Finally, to measure inhibitory control and short-term memory at different ages we included variables of errors (distractors cancelled) and re-cancellations (cancellation of a target already cancelled, also known as perseverations; Dalmaijer et al., 2015; Benjamins et al., 2019). Further details on each variable of interest and how they were computer are presented in **Table 2.2**.

2.2.5 Statistical analysis

Spearman's rank correlation was first used to test for a relationship between age, education and all cancellation and line bisection variables (Objective 1). Spearman's rank correlation was used since several of the variables were not normally distributed (accuracy, errors, intersections, re-cancellations, ego- and allocentric score). We used Analysis of Variance (ANOVA) to estimate the effect of age group on normally distributed task variables, and Kruskal-Wallis by ranks on all non-normally distributed variables. Distribution of the data was checked graphically using Q-Q and histogram plots, and Levene's test was used to test equality of variances within the age group for normally distributed variables. For these analyses, age was categorised by decade (e.g., 18-29; 30-39; 40-49; 50-59; 60-69; 70-79; 80-94). The oldest age group (80-94) extended to 94 to include our eldest participant rather than having an additional age category with just one participant.

Means, medians (non-normally distributed variables), minimum, and maximum values are reported for each variable. Additionally, 5th and 95th percentiles were calculated to provide cut-off values to determine impairments compared to this sample of neurologically healthy people (Objective 2). Cut-off values were calculated separately for each age group for those variables that were significantly associated with age.

To test our hypothesis predicting a small bias to one side of space (i.e., pseudoneglect), paired t-tests were used to test for the effect of side of space within each task. Additionally, Analysis of Covariance (ANCOVA) and separate rank analysis of covariance (Quade's; Quade, 1967 for non-normally distributed variables) were used to investigate the effect of categorical variables (sex, handedness) on line bisection and cancellation performance whilst controlling for age.

To investigate performance across different ages, K-means clustering analysis was used to explore sub-groups within the sample with shared or similar performance on outcome variables. Variables were transformed into z-scores to standardize variables before running the analysis. Optimal number of clusters was determined using the Elbow method to visually

Table 2.2. Description of each variable from the CENT tasks. Formulas for Quality of Search and Search speed are available in CancellationTools (Dalmaijer et al., 2015).

Variable	Description
Accuracy	Total number of targets cancelled. Max score 50.
Errors	Total number of distractors cancelled. Max score 100.
Intersections	Number of times cancellation path crosses over itself.
Re-cancellations	Cancellation of a target already cancelled (perseverations).
Search duration	Total time (secs) taken in cancellation task.
Quality of search	Shows speed and accuracy of search using a single score (Q score) using number of targets cancelled, total number of targets and total task duration. High score indicated high number of targets detected and high cancellation speed. Formula available in CancellationTools (Dalmaijer et al., 2015).
Search speed	Inter-cancellation (Euclidean) distance in pixels divided by inter-cancellation time (secs). Formula available in CancellationTools (Dalmaijer et al., 2015).
Egocentric score	Measure of bias in finding targets across the screen (space neglect). Calculated by subtracting the number of targets cancelled on left of the screen from number of targets cancelled on right. A positive value represents more targets cancelled on the left side, indicating right egocentric neglect. A negative value represents more targets cancelled on the right side, indicating left egocentric neglect.

Allocentric score	Bias in cancelling distractors with a gap on left or right side (object neglect). Calculated by subtracting the number of left-gap distractors by number of right-gap distractors. A positive value represents more right-gap distractors cancelled, indicating right object centred neglect. A negative value represents more left-gap distractors cancelled, indicating left object centred neglect.
Line bisection error	Deviation (%) from true centre when judging the middle of ten lines on screen.
Total line bisection duration	Total response time (secs) taken in line bisection task (10 lines).

determine when cluster values decline or plateau as the number of clusters increase (Kodinariya & Makwana, 2013).

Chi-squared tests were carried out post-clustering to investigate differences between categorical demographic variables (sex, handedness) and cluster membership. Independent samples t-tests were used post-clustering to test differences in age and education between clusters. ANOVAs were also used to determine which outcome variables had a significant effect on cluster groupings. Accidental re-cancellations (or re-clicks) were defined as clicks performed less than one second apart and removed from the analysis. The alpha level was set at 0.05 for all analyses. Bonferroni correction was used to correct for multiple comparisons (n = 78) and reduce the chance of Type 1 errors, giving an adjusted p-value of p = 0.0006.

2.3 Results

2.3.1 Correlations between age and cancellation and line bisection variables

As can be seen in **Figure 2.3**, search duration, search speed, quality of search and line bisection duration were all significantly correlated with age. More specifically, age was significantly associated with slower timings on the cancellation task: longer search duration [$r_s(179) = 0.38$, $p < 0.001$, 95% C.I. = 0.24, 0.50], slower search speed [$r_s(179) = -0.41$, $p < 0.001$, 95% C.I. = -0.53, -.27], longer line bisection task duration [$r_s(179) = 0.26$, $p < 0.001$, 95% C.I. = 0.12, 0.40], and poorer quality of search [$r_s(179) = -0.40$, $p < 0.001$, 95% C.I. = -0.52, -0.26]. Moreover, some cancellation and line bisection variables were significantly correlated: line bisection duration was positively correlated with search duration [$r_s(179) = 0.43$, $p < 0.001$, 95% C.I. = 0.30, 0.55] but, negatively correlated with search speed [$r_s(179) = -0.33$, $p < 0.001$, 95% C.I. = -0.46, -0.19] and quality of search [$r_s(179) = -0.42$, $p < 0.001$, 95% C.I. = -0.54, -0.29].

In addition, several cancellation variables were significantly correlated with each other: search duration was negatively correlated with search speed [$r_s(179) = -0.76$, $p < 0.001$, 95% C.I. = -0.82, -0.68] and quality of search [$r_s(179) = -0.95$, $p < 0.001$, 95% C.I. = -0.97, -0.93], but positively correlated with number of intersections [$r_s(179) = 0.40$, $p < 0.001$, 95% C.I. = 0.26, 0.52]. Finally, quality of search was significantly correlated with search speed [$r_s(179) = 0.74$, $p < 0.001$, 95% C.I. = 0.65, 0.81] and intersections [$r_s(179) = -0.40$, $p < 0.001$, 95% C.I. = -0.52, -0.26]. There was no significant correlation between any of our variables and years of education ($p > 0.05$).

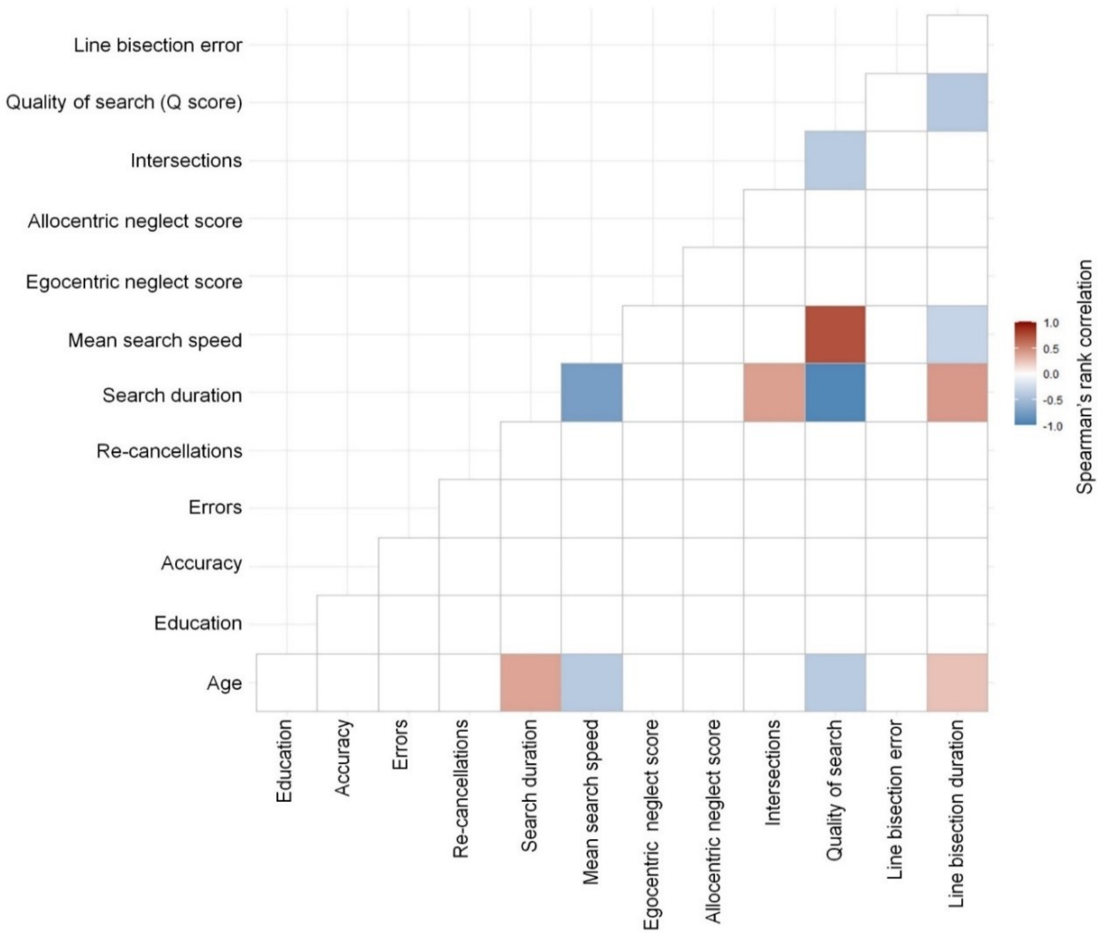

Figure 2.3. Correlation (Spearman's rank) matrix of cancellation and line bisection task variables. Only correlations significant after Bonferroni correction are presented. See **Table 2.2** for variable details.

2.3.2 Age grouping effects on task performance

Search duration

There was a significant effect of age on search duration [F(6, 172) = 5.24, $p < 0.001$, $\eta^2 = 0.16$]. Search duration was significantly slower in age group 80-94 compared to age groups: 18-29 [62.28, $p < 0.001$, 95% C.I. = 20.73, 103.83]; 30-39 [65.10, $p < 0.001$, 95% C.I. = 22.12, 108.07], 40-49 [57.00, $p = 0.002$, 95% C.I. = 12.53, 101.47], and 50-59 [45.70, $p = 0.017$, 95% C.I. = 4.35, 87.05; **Figure 2.4a**). No other significant differences were found.

Quality of Search

A significant interaction was found between age groups and quality of search [F(6, 172) = 6.64, p < 0.001, $\eta^2 = 0.19$]. Quality of search was significantly better in the younger age group, 18-29 compared to older age groups: 60-69 [0.088, $p = 0.019$, 95% C.I. = 0.01, 0.17], 70-79 [0.11, $p = 0.008$, 95% C.I. = 0.02, 0.20] and 80-94 [0.19, $p < 0.001$, 95% C.I. = 0.06, 0.32]. Additionally, quality of search was better in age group 30-39 compared to older age groups: 60-69 [0.10, $p = 0.013$, 95% C.I. = 0.01, 0.19], 70-79 [0.12, $p = 0.006$, 95% C.I. = 0.02, 0.22] and 80-94 [0.20, $p < 0.001$, 95% C.I. = 0.06, 0.33; **Figure 2.4b**]. No other significant differences were found. There were no statistically significant differences between age group 18-29 and age groups 30-59.

Search speed

There was a statistically significant difference in search speed between at least seven age groups [F(6, 172) = 6.573, p < 0.001, $\eta^2 = 0.19$]. Search speed was significantly slower in age group 80-94 compared to younger age groups: 18-29 [-46.40, $p < 0.001$, 95% C.I. = -77.13, -15.67], 30-39 [-45.76, $p < 0.001$, 95% C.I. = -77.54, -13.97], 40-49 [-42.93, $p = 0.002$, 95% C.I. = -75.82, -10.04], and 50-59 [-34.80, $p = 0.012$, 95% C.I. = -65.38, -4.22; **Figure 2.4c**].

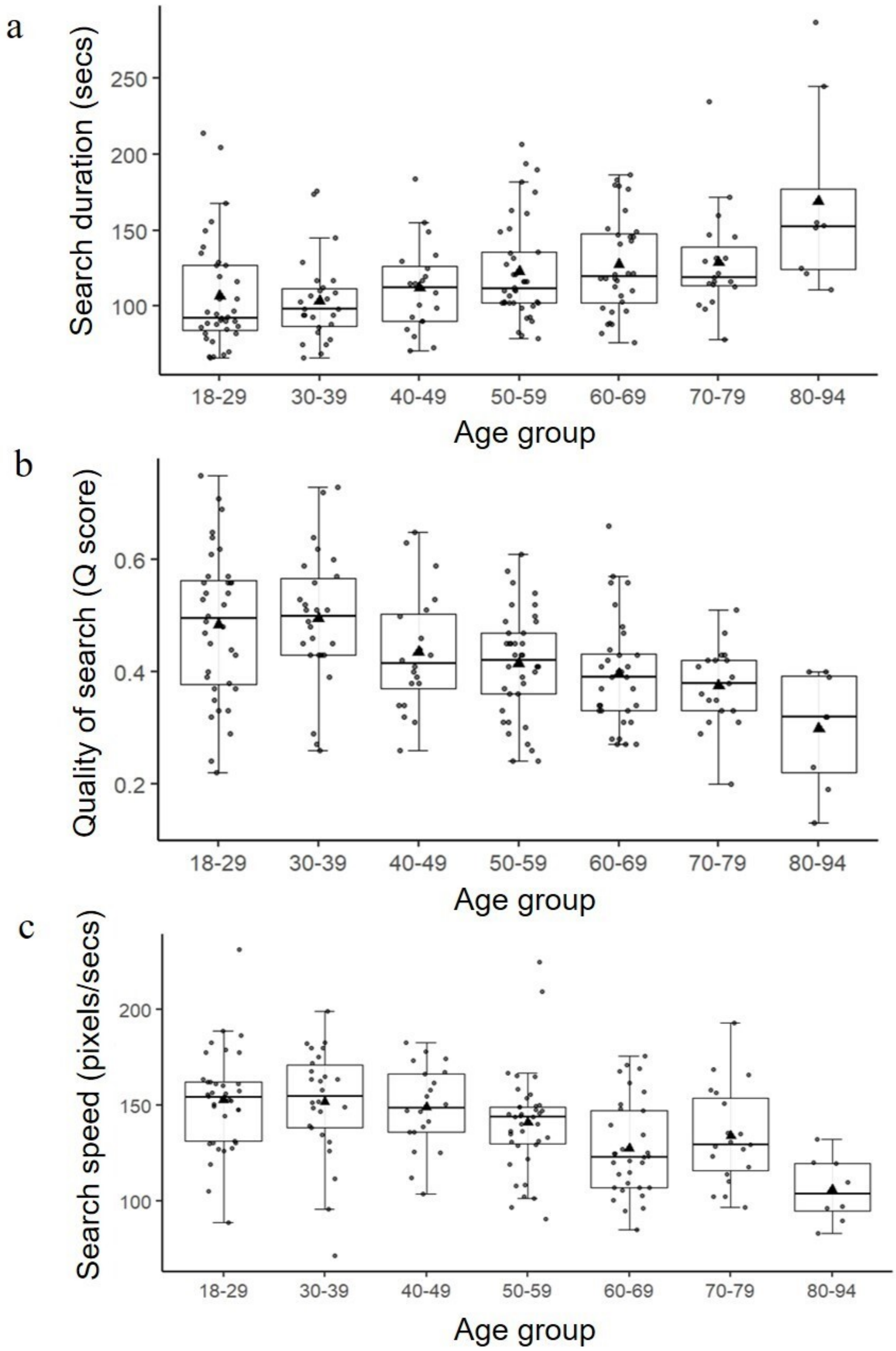

Figure 2.4. Boxplots with error bars showing mean (triangle) and median values of (a) search duration (seconds), (b) quality of search (Q score) and (c) search speed (inter-cancellation (Euclidean) distance in pixels divided by inter-cancellation time (secs) per age group). See **Table 2.2** for variable details.

Search speed was also significantly slower in age group 60-69 compared to: 18-29 [-25.04, p = 0.002, 95% C.I. = -44.14, -5.94) and 30-39 (-24.40, p = 0.008, 95% C.I. = -45.15, -3.64). No other significant differences were found.

Egocentric bias

There was an overall statistically significant interaction between egocentric neglect score and age [H(6) = 13.82, p = 0.032, η_H^2 = 0.05]. However, differences between groups (i.e., increased rightward bias in age group 80-94 compared to all other age groups) were not significant after Bonferroni correction.

Line bisection duration

There was an overall significant effect of age on line bisection duration [F(6, 172) = 2.47, p = 0.026, η^2 = 0.08], however post-hoc tests found no statistically significant difference between the seven age groups.

No effect of age on remaining variables

There was no statistically significant difference in line bisection error, accuracy, errors, intersections, re-cancellations, and allocentric neglect score between the seven age groups.

2.3.3 Normative data for cancellation and line bisection tasks

Data for all variables produced by the cancellation and line bisection tasks are presented in **Tables 2.3a** and **2.3b**. The 5th and 95th percentiles can be used as normal cut-offs for performance. Cut-off scores for each age group by decade (**Table 2.4**) are provided only for variables that significantly correlated with age (see **Figure 2.3**). Note that some variables with higher values indicate worse performance (i.e., search duration, line bisection duration, errors, intersections, re-cancellations), and others with lower values indicate worse performance (i.e., search speed, quality of search). A value close to 0 for line bisection error represents no bias in bisection judgements.

2.3.4 Effect of side on cancellation and line bisection tasks

Overall, participants displayed a small but significant leftward error (*M* = -0.83%, SD = 4.61) in the line bisection task [$t(178) = -2.40$, $p = 0.018$, 95% C.I. = -1.51, -0.15, d = 0.18], replicating previous findings of pseudoneglect in neurologically intact adults (Jewell & McCourt, 2000). This leftward error was not significantly larger when lines were presented on the left side compared to the right side of the screen [$t(179) = -1.63$, $p = 0.106$, 95% C.I. = -6.53, 0.63], nor was there a significant difference in response times for lines presented on the left or right (*M* = 3.48, *SD* = 1.31), [$t(179) = 0.25$, $p = 0.800$, 95% C.I. = -0.53, 0.69].

During the cancellation task, participants spent significantly more time searching on the left side (*M* = 54.12%, *SD* = 6.05) compared to the right of the screen (*M* = 45.88%, *SD* = 6.05), [$t(178) = 9.11$, $p < 0.001$, 95% C.I. = 6.45, 10.03, d = 0.68]. Mean search speed was also faster on the left side (*M* = 135.49, *SD* = 29.33) compared to the right of the screen (*M* = 126.54, *SD* = 27.95), [$t(178) = 6.55$, $p < 0.001$, 95% C.I. = 6.25, 11.64, d = 0.49]. Finally, 89% of the sample started their search on the left side of the screen, compared to 11% who started on the right side. There was no significant difference in finding targets on the left versus right side of the screen (egocentric score), nor was there a bias in selecting distractors with left versus right gaps (allocentric score).

Table 2.3. Tables showing overall normative data for normally distributed (a) and non-normally distributed (b) variables from cancellation and line bisection tasks. 5th and 95th percentiles are shown here to be used as preliminary cut-offs to determine impairment.

A	Variable	Mean score (SD)	Min score	Max score	5th	95th
	Total line bisection duration (secs)	35.47 (13.14)	17	109	21	59
	Search duration (secs)	119.07 (36.85)	66	287	73	187
	Left side (% of search duration)	54.12 (6.05)	35.31	71.28	43.71	63.46
	Right side (% of search duration)	45.88 (6.05)	28.72	64.69	36.54	56.29
	Time asymmetry time score (% time of right – % time on left)	-8.24 (12.11)	-42.57	29.37	-26.92	12.58
	Quality of search	.43 (.12)	.13	.75	.26	.64
	Search speed	140.86 (27.79)	71.19	231.20	96.29	182.68
	Left side	135.49 (29.33)	65.28	209.24	86.12	180.23
	Right side	126.54 (27.95)	64.98	182.69	78.97	171.02
	Line bisection error (%)	-.83 (4.61)	-11.5	29.70	-6.40	5

Note: Time asymmetry time score = negative value shows more time spent searching on the left side of the screen. Quality of search = shows speed and accuracy of search as a single measure. High Q score = high number of targets detected and high cancellation speed. Search speed = pixels per second. Left/right side = side of the screen when completing tasks.

B	Variable	Median score	Min score	Max score	5th	95th
	Accuracy	49	39	50	46	50
	Errors	0	0	4	0	1
	Intersections	3.00	0	43	.00	20.00
	Re-cancellations	0	0	1	0	0
	Egocentric score	0	-3	5	-2	2
	Allocentric score	0	-2	1	0	1

Note: Scores lower than 5th centile and higher than 95th centile indicate an impairment.

Table 2.4. Normative data by age groups (by decade). 5th and 95th percentiles are reported to determine impairment on each variable.

		18-29 (n = 36)	30-39 (n = 26)	40-49 (n = 20)	50-59 (n = 38)	60-69 (n = 32)	70-79 (n = 19)	80-94 (n = 8)
Total line bisection duration (secs)	Mean (SD)	32.67 (13.12)	33.19 (7.83)	30.80 (7.58)	36.82 (17.25)	36.06 (9.77)	40.26 (11.20)	47.00 (22.19)
	Min	17	17	20	22	19	23	29
	Max	72	49	46	109	56	65	96
	5th	18.70	17.35	20.05	22.00	20.30	23.00	29.00
	95th	64.35	47.95	45.95	81.45	56.00	-	-
Search time (secs)	Mean (SD)	106.47 (36.53)	103.65 (27.86)	111.75 (29.08)	123.05 (33.32)	127.38 (32.29)	128.89 (34.05)	168.75 (63.19)
	Min	66	66	71	79	76	78	111
	Max	214	176	184	207	187	235	287
	5th	66.85	67.05	71.10	80.90	79.90	78.00	111.00
	95th	206.35	175.30	182.55	194.65	184.40	-	-
Quality of search	Mean (SD)	.48 (.13)	.50 (.12)	.43 (.11)	.41 (.09)	.40 (.10)	.37 (.07)	.30 (.10)
	Min	.22	.26	.26	.24	.27	.20	.12
	Max	.75	.73	.65	.61	.66	.51	.40
	5th	.24	.26	.26	.24	.27	.20	.13
	95th	.72	.72	.65	.58	.60	-	-
Search speed	Mean (SD)	152.31 (25.93)	151.66 (28.65)	148.84 (21.93)	140.71 (26.39)	127.27 (24.71)	133.90 (25.67)	105.91 (17.05)
	Min	88.82	71.19	103.78	90.47	84.94	96.77	82.93
	Max	231.20	198.97	182.68	224.58	175.57	192.72	132.13
	5th	102.75	79.69	104.19	96.49	91.29	96.77	82.93
	95th	194.93	193.20	182.45	209.77	172.52	-	-

2.3.5 Sex effects on cancellation and line bisection variables

There was a significant effect of sex on search speed [$F(1, 172) = 4.15$, $p = 0.043$, $\eta^2 = 0.24$], whereby males had a faster search speed (*m* = 144.15) compared to females (*m* = 137.71). We also found a statistically significant difference in allocentric neglect score (non-normally distributed variable; [$F(1, 173)= 6.01$, $p = 0.015$, $\eta^2 = 0.03$] between males (unstandardised residuals; *m* = 5.09) and females (*m* = -4.89), when controlling for age. No other significant effects of sex were found on remaining variables.

2.3.6 Handedness effects on cancellation and line bisection variables

There were no effects of handedness on cancellation and line bisection variables.

2.3.7 K-Means clustering analysis

A k-means cluster analysis revealed two clusters (**Figure 2.5a**) of participants based on cancellation and line bisection variables. Cluster 1 (*n* = 103; mean age = 43.87) is characterised by participants with shorter search and line bisection durations, faster search speed, fewer intersections in search path, higher quality of search score (indicating a more efficient search) and increased rightward error in line bisection task. In contrast, Cluster 2 (*n* = 76; mean age = 56.53) included participants with longer search and line bisection durations, slower search speed, more intersections, lower quality of search, and more leftward error in line bisection judgements. Moreover, participants in Cluster 1 were significantly younger (*m* = 43.87, *SD* = 16.86) than those in Cluster 2 (*m* = 56.63, *SD* = 17.85), [$t(177)= -4.88$, $p < 0.001$, d = .74]. These variables all had a significant impact on cluster groups: search speed [$F(1, 177) = 163.76$, $p < 0.001$, η^2 = 0.48]; search duration [$F(1, 177) = 219.65$, $p < 0.001$, $\eta^2 = 0.55$]; intersections [$F(1, 177) = 24.69$, $p < 0.001$, $\eta^2 = 0.12$]; quality of search [$F(1, 177) = 222.68$, $p < 0.001$, $\eta^2 = 0.58$]; line bisection error [F(1, 177) = 4.49, $p = 0.035$, $\eta^2 = 0.03$]; line bisection duration [F(1, 177) = 51.95, $p < 0.001$, $\eta^2 = 0.23$]. Remaining performance variables (accuracy, errors, re-cancellations), education, sex, and handedness did not have a significant impact on cluster groupings.

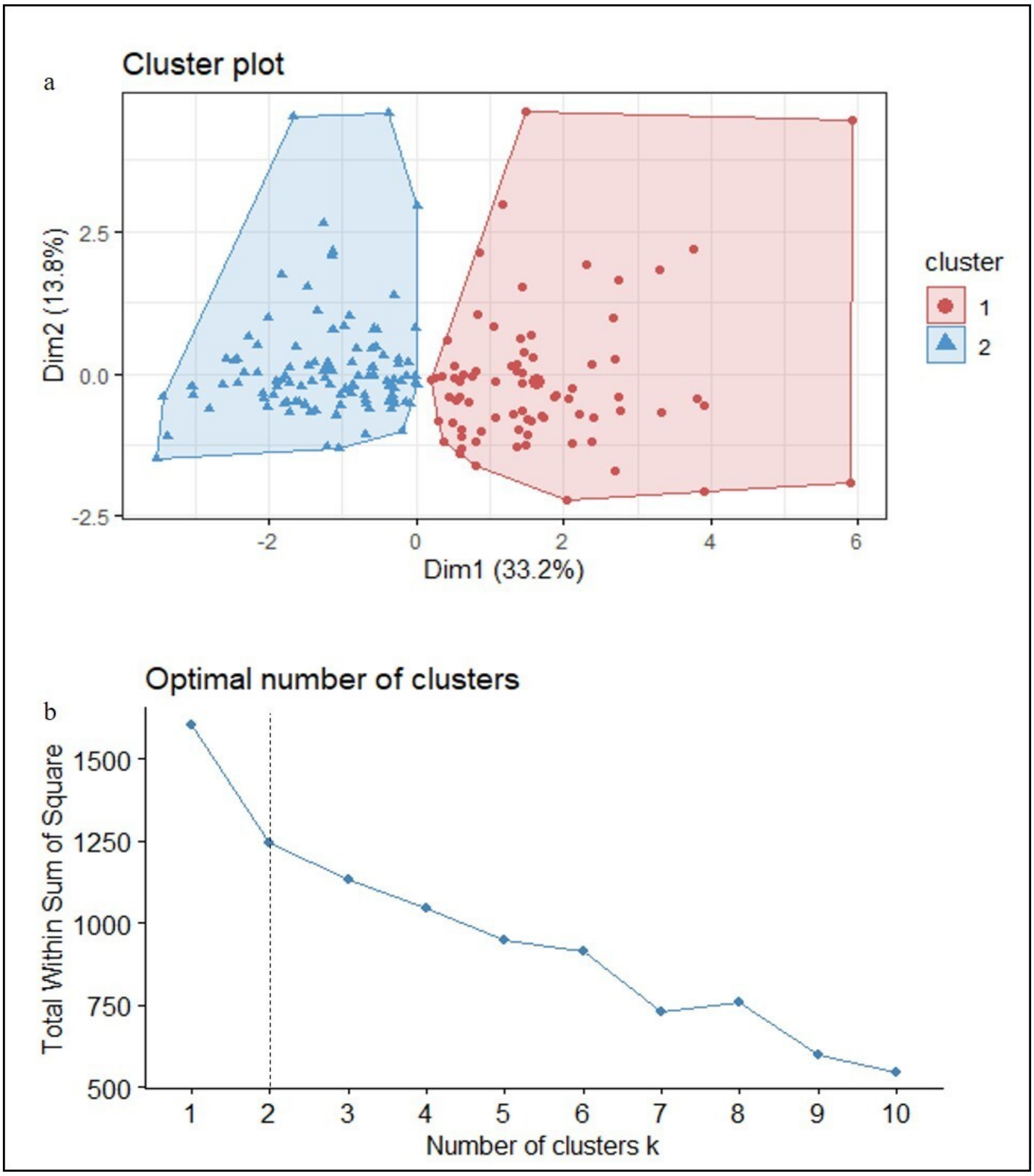

Figure 2.5. (a) Cluster plot representing Cluster 1 (*n* = 103) and Cluster 2 (*n* = 76) in cancellation and line bisection task performance. Dim = Dimensions. (b) Elbow method for determining the optimal number of clusters.

2.4 Discussion

We aimed to investigate the effect of aging on performance on computerised cancellation and line bisection tasks in far-space. We found older age was associated with slower task processing speed, slower search speed, and poorer quality of search. Males were faster on the cancellation task compared to females. In addition, we found a leftward bias on the line bisection task akin of pseudoneglect, and increased search duration and speeds on the left side of space in the cancellation task. Finally, our cluster analysis found two age-related groups: the younger cluster had more efficient (faster, organised) searches compared to the older cluster.

Age was the primary demographic factor affecting performance on our cancellation task. This pattern of results is consistent with previous literature showing that processing speed in visual search and cancellation declines with aging (Hommel et al., 2004; Warren et al., 2008; Potter et al., 2012; Muller-Oehring et al., 2013; Benjamins et al., 2019; Tamura & Sato, 2020). Exhaustive search behaviour (e.g., increased caution) could contribute to this increased processing speed in older adults (Hommel et al., 2004; Potter et al., 2012).

Older age was also associated with longer processing times in the line bisection task. There was good convergent validity between tasks: line bisection duration was positively correlated with cancellation duration, and negatively correlated with search speed and quality of search. This suggests that the time taken to complete line bisection is a predictor of performance in cancellation. This is surprising given the controversy around whether the two tasks do (Keller et al., 2005; Ferber & Karnath, 2001), or do not (Molenberghs & Sale, 2011) measure different aspects of attention. In future studies, it would be interesting to compare performance on CENT in near versus far-space to see if our findings replicate in near-space.

We observed a decrease in search organisation, or efficiency (i.e., slower search speed, poorer quality of search) in older adults. More specifically, quality of search began to decline significantly in those older than 60 years old. These changes could reflect a decline in processing speed, difficulties with inhibitory control when navigating around distractors to find targets (Potter et al., 2012; Muller-Oehring et al., 2013; Tamura & Sato, 2020), or fine motor skills (e.g., movement time, speed variability; Rossit & Harvey, 2008; Hoogendam et al., 2014).

More generally, omissions and re-cancellations were rare, and accuracy was high among the sample (e.g., Uttl & Pilkentot-Taylor, 2001; Benjamins et al., 2019). The sample also displayed a methodical and efficient search pattern (i.e., few intersections, quality of search score as high as 0.75), such as searching for the next nearest target following a vertical (i.e., top to bottom, moving rightward) or horizontal (i.e., left to right, moving downward) 'snake pattern' search path (Ten Brink et al., 2016). Like Benjamins and colleagues (2019), some participants showed a relatively inefficient search (i.e., many intersections), with a mean quality of search score just 0.43. On this basis, poor search organisation alone may not be sensitive to attentional changes (Benjamins et al., 2019).

Pseudoneglect was evident across the sample, irrespective of age, replicating previous studies in near (e.g., Learmonth & Papadatou-Pastou, 2021) and far-space (Stancey & Turner, 2010). However, contrary to previous studies (Fujii et al., 1995; Jewell & McCourt, 2000), we did not find an effect of age on line bisection error. It seems the role of age and pseudoneglect is still unclear and highly dependent on task factors (e.g., hand use, starting position, line placement; Brooks et al., 2016; for review see Jewell & McCourt, 2000), none of which were manipulated here.

In a similar vein, we found novel findings of an 'over-attendance' (English et al., 2021), or pseudoneglect in both line bisection and cancellation in far-space. More specifically, participants showed a leftward bias when bisecting lines and were faster finding targets on the left side of space (like English et al., 2021). One interpretation of this may be due to dominance of the right hemisphere in visuospatial attention (e.g., inferior parietal lobe; Cicek, Deouell & Knight, 2009; Cona & Scarpazza, 2019). Alternatively, this leftward bias could reflect learned processes, such as Western reading systems (i.e., reading from left to right) which may impact our search organisation (e.g., 'reading-experience' hypothesis; Ransley et al., 2018; Brucki & Nitrini, 2008; English et al., 2021). For example, participants in a rural, illiterate Amazonian community exhibited random search patterns compared to those who had been exposed to reading and writing (Brucki & Nitrini, 2008). On the other hand, Arabic speakers show faster reaction times detecting Arabic letters presented on the right side, compared to on the left and when using English letters (Ransley et al., 2018). We found no relationship between education level and task performance. Based on this finding, our novel CENT test has potential for use across individuals with varying levels of formal education and cultures.

Contrary to previous evidence (Saykin et al., 1995; Brucki & Nutrini, 2008; Uttl & Pilkenton-Taylor, 2001; Benjamins et al., 2019), we found that males had a significantly (albeit small effect size) faster search speed compared to females (irrespective of age). Two previous studies have found similar sex differences in younger samples, whereby males were faster than females in near-space conjunctive visual search paradigms (Stoet, 2011; English et al., 2021). The authors propose this as evidence for increased hemispheric asymmetry in males (English, 2021), or the evolutionary hunter-gatherer theory (i.e., men's 'innate' hunting behaviours predict them to be better at visual search; Eals & Silverman, 1994; Stoet, 2011; Stancey & Turner, 2010). Alternatively, a large (n= 21,781) study using a sustained attention task found faster reaction times and more commission errors (erroneous response in quick succession) in males, compared to females (Riley et al., 2016). The authors suggest that increased speed and commission errors could reflect increased impulsivity in males (though these sex effects varied between cultures). Although we did not include commission errors within our analysis and no measure of impulsivity (or indeed any personality traits), these previous findings may be helpful in explaining our sex effects in our visuospatial attention task. Nevertheless, previous studies were conducted in near-space, and so our findings could provide evidence of sex differences in search speed in far-space.

2.4.1 Limitations

We did not take a measure of experience with technology; however, we do not believe this contributed to the age-related decline in CENT performance. Age-related decline in processing speed in visual search tasks are well documented (see Introduction). We also argue that the technology used in the study (the controller) was not overly complex in that it was very similar to a television remote. Importantly, there is no evidence to suggest that poorer performance on tasks in those older than 65 years old is due to use of novel technologies (e.g., augmented reality; Peleg-Adler, Lanir & Korman, 2018). The assumption that less experience with technology would exclusively affect older people contributes to ageist beliefs surrounding technology use in older people and widens the digital health divide (Mace, Mattos, & Vranceanu, 2022). Moreover, we provide the first set of age-graded normative data for our new task, though some age-groups are small (e.g., n= 8) and underpowered, the sample sizes are not unlike other studies (Webb et al., 2020). Finally, our study was carried out in a public setting with an unselected sample, but the average years of education was still 16 years, and all participants were English speakers. Future studies could explore CENT performance across different education levels and cultures

Despite these limitations, we believe that the preliminary cut-offs provided here could be useful in evaluating attentional deficits (e.g., ADHD), motor or impulse control impairments (particularly re-cancellations; Benjamins et al., 2019), or potentially early onset of cognitive impairment and brain disease. Going forward, normative data for age-groups could continue to grow since CENT is open access and free to use to researchers and clinicians.

2.4.2 Conclusion

To the best of our knowledge, we offer novel findings that computerised visuospatial attention tasks in far-space are sensitive to aging with changes in performance beginning at 60 years of age. Our testing methods of a far-space measure of visuospatial attention could be considered to have more ecological validity compared to the ones previously tested (conducted in a laboratory environment; e.g., Uttl & Pilkenton-Taylor, 2001; Hommel et al., 2004; Brucki & Nutrini, 2008; Warren et al., 2008; Muller-Oehring et al., 2013; Tamura & Sato, 2020), since most everyday visuospatial attention tasks are indeed performed in our busy and noisy day-to-day lives just like in the current experiment. We are currently investigating if these tasks have potential to be used with clinical populations (i.e., stroke survivors). If so, they could be useful in detecting subtle cognitive changes in older people, which could be indicative of early brain disease.

2.4.3 Data availability. The data and analyses scripts conducted in R (version 2022.07.0 Build 548; R Core Team, 2018) are available at https://osf.io/uzdwk/. The CENT task is available at https://github.com/UEANeuroLab.

2.4.4 CRediT author statement. Helen Morse: Conceptualization, Software, Analysis, Resources, Data curation, Writing – Original Draft, Writing – Review & Editing, Visualization; Amy A. Jolly: Investigation, Resources; Hannah Browning: Data curation; Allan Clark: Software, Analysis, Writing – Review & Editing, Visualization; Valerie Pomeroy: Writing – Review & Editing; Stéphanie Rossit: Conceptualization, Methodology, Software, Analysis, Resources, Writing – Review & Editing, Supervision, Project administration, Funding acquisition.

3. Chapter 2: Assessing spatial neglect in extrapersonal space after stroke: diagnostic accuracy of a Computerised Extrapersonal Neglect Test (CENT)

3.1 Introduction

Spatial neglect is a heterogeneous condition (Loetscher et al., 2012). Symptoms can be multidimensional (Williams et al., 2021), presenting themselves in different sensory modalities (auditory, visual, somatosensory; Kerkhoff, 2001), areas of space (personal/body, peripersonal/near-space, extrapersonal/far-space) and/or reference frames (egocentric/space, allocentric/object). The complexity of the condition makes it difficult to measure (Williams et al., 2021), particularly since widely used assessments (e.g., line bisection, cancellation tests) commonly measure one subtype (e.g., in peripersonal space; Loetscher et al., 2012). Some of these paper-and-pencil tests also lack normative data (Azouvi, 1996; Azouvi et al. 2002) and sensitivity, in that they misdiagnose milder to moderate cases (Buxbaum et al., 2004). Consequently, underdiagnosis of subtypes could negatively impact patients' recovery outcomes and safety (i.e., since they are unaware of deficit; Williams et al., 2021).

There is currently no 'gold standard' assessment for spatial neglect (Bowen et al., 1999). In fact, there are approximately 292 assessment tools for spatial neglect, yet 65% do not specify which subtype is targeted (Williams et al., 2021). The volume of assessments and inconsistency of terminologies used around the condition (e.g., subtypes) makes it increasingly difficult for clinicians to choose an assessment (Williams et al., 2021). As a result, there has been little consensus or standardisation in clinical practice about which assessments should be used. An international study reported that the most widely used cognitive assessments are carried out using paper-and-pencil within peripersonal space (Checketts et al., 2021). These include line bisection, clock drawing, star, and letter cancellation tests. There is a similar trend within research studies, where 97.6% of studies use cancellation tasks (Moore et al., 2022).

A recent study, involving experts, recommended using a cancellation test when only one test can be used (e.g., due to time pressures; Moore et al., 2022). Cancellation tasks (a type of visual search task) are considered to be the most sensitive paper-and-pencil neglect assessment (Ferber & Karnath, 2001; Azouvi et al., 2002; Moore et al., 2022). In fact, accuracy on cancellation tasks is a predictor of recovery 6-months post-stroke (Demeyere & Gillebert, 2017). Typically, cancellation tasks involve searching and 'cancelling' (i.e., crossing out) targets among distractors across a display (usually an A4 sheet of paper). These tasks are quick (e.g., less than 5 minutes; Demeyere et al., 2015) and easy to administer at bedside. Examples of widely used cancellation tasks include The Star Cancellation (Wilson et al., 1987), Line Cancellation (Wilson et al., 1987), Ota Test (Ota et al., 2001), Broken Hearts Test (Oxford Cognitive Screen; Demeyere et al., 2015), and Apple Cancellation Test (Bickerton et al., 2011). Outcome variables and attentional demands in these tasks can be sensitive measures of neglect behaviour, such as the starting point on the page (Azouvi et al., 2002) and numbers of distractors (Ferber & Karnath, 2001; Guest et al., 2002), respectively. More specifically, cancellation tasks with visually matched, or similar targets and distractors (e.g., Broken Hearts, Ota Test, Apple Cancellation) are thought to be more attentionally demanding due to the lack of 'pop-out' effects (Ferber & Karnath, 2001). Some cancellation tasks are able to measure additional subtypes of neglect, such as ego- and allocentric neglect behaviours by manipulating stimuli type (e.g., Broken Hearts Test; Demeyere et al., 2015). It is thought that cancellation tasks measure deficits in visuospatial attention (since they are in essence visual search tasks), which relate to lack of exploration in daily life (lack of attendance to one side; Ferber & Karnath, 2001).

After cancellation tests, line bisection tests are popular in assessing spatial neglect in clinical practice (Checketts et al., 2021). These tests require participants to mark the middle of horizontal lines and provides the assessor with a directional error, or deviation from the true middle (McIntosh et al., 2017). Originally devised as a measure of hemianopia by physician Axenfeld in

1984 (translated in Kerkhoff & Bucher, 2008), line bisection is quick and simple to administer. Historically, individuals with homonymous hemianopia (visual field cut in left or right side of both eyes) have been reported to show an opposite error to those with neglect, in that they bisect a line towards their blind field (Kerkhoff & Bucher, 2008). In other words, an individual with left visual field cuts in both eyes may bisect a line more leftward due to a compensatory process to pay more attention to the blind field (something which individuals with neglect do not exhibit; Kerkhoff & Bucher, 2008; Lanyon & Barton, 2013). More recently however, researchers did not observe this 'hemianopic line bisection error', but instead found that the classic neglect rightward bisection error was more pronounced in acute stroke survivors with visual field and neglect co-occurring together (Sperber & Karnath, 2016). The authors propose that the 'hemianopic line bisection error' may be more likely to occur in chronic cases as a compensatory strategy (Sperber & Karnath, 2016; Lanyon & Barton, 2013). Therefore, the line bisection test may lack the specificity in differentiating between visual field deficits and other post-stroke impairments, such as neglect since a line bisection error may not be neglect-specific (Ferber & Karnath, 2001; Sperber & Karnath, 2016).

There is also evidence that line bisection performance can dissociate with cancellation performance (Ferber & Karnath, 2001; Azouvi et al., 2002; Keller et al., 2005; Sperber & Karnath, 2016). For example, Ferber and Karnath (2001) reported a dissociation between performance in line bisection and cancellation tasks, as well as no significant line bisection error in 14 of 35 (40%) individuals classified with 'severe neglect'. To add to this, factor analyses in two separate studies found cancellation and line bisection performance loaded onto two independent factors and did not correlate with one another (Azouvi et al., 2002; Sperber & Karnath, 2016). More specifically, Azouvi et al. (2002) found that line bisection performance loaded onto a factor along with clock drawing and reading, whereas cancellation, figure copying, and writing test performance loaded onto the same factor. However, this isn't to say that the line bisection task isn't an informative and useful test since a significant error (i.e., above cut-off) is still indicative of a spatial deficit (Rorden, Berger & Karnath, 2006).

Taken together, the evidence suggests that line bisection and cancellation tasks may measure different behaviours, such as allocentric/object-based (line bisection) versus egocentric/space-based (cancellation) representations of space (Ferber & Karnath, 2001; Sperber & Karnath, 2016). Nonetheless, both serve as quick and convenient assessments of neglect (Ferber & Karnath, 2001), and each have a role in assessing specific subtypes of neglect behaviour (e.g., allocentric, egocentric neglect) which could help identify more appropriate treatments for individuals (Checketts et al., 2021). However, these tests are still limited to assessing neglect behaviours in a small area of space (sheet of paper) close to the patient. Additional assessment methods should be incorporated to assess other subtypes to give a comprehensive examination of neglect symptoms (Williams et al., 2021).

Studies have reported that extrapersonal neglect can dissociate and co-occur with other subtypes (peripersonal, personal neglect; Aimola et al., 2012; Nijboer et al., 2014; Spaccavento et al., 2017; Ogourtsova et al., 2018). However, these relationships are often complex. For example, one participant has been reported to display paradoxical neglect behaviour on matched cancellation tasks between spatial areas, whereby they had left-side neglect in peripersonal space, but right-side neglect in extrapersonal space (Van der Stoep et al., 2013). Moreover, increased severity of neglect symptoms on conventional neglect assessments (e.g., cancellation, line bisection) is associated with neglect in both peripersonal and extrapersonal space (Van der Stoep et al., 2013).

We know that neglect in extrapersonal space is associated with poorer cognitive (e.g., memory, problem solving, social interactions) and motor (e.g., locomotion, eating) outcomes (Spaccavento et al., 2017). Yet, there is no specific test for neglect in extrapersonal space routinely used in clinical practice (e.g., Checketts et al., 2021). Studies report rates of extrapersonal neglect between 3-72% (Aimola et al., 2012; Nijboer et al., 2014; Spaccavento et al., 2017; Van der Stoep et al., 2013). The large variance in the incidence of extrapersonal neglect is likely due to the different methods of assessment in each study; many used classic tests (e.g., line bisection, cancellation; Aimola et al., 2012; Van der Stoep et al., 2013; Nijboer et al., 2014) while some used more functional assessments (e.g., tea serving, card dealing, room description tasks; Spaccavento et al., 2017). Critically, nearly all these studies presented the tests at different distances away from the participant, such as 320cm (Aimola et al., 2012), 120cm (Nijboer et al., 2014; Van der Stoep et al., 2013) or no distance specified (Spaccavento et al., 2017). These are just a few examples, however the variance in assessment methods highlights that there seems to be little consensus within studies on what space is included in extrapersonal space (Williams et al., 2021). For example, of 45 studies reporting extrapersonal neglect (also referred to by 12 other terms), less than half (42%) defined extrapersonal neglect as affecting "beyond reaching distance" (Williams et al., 2021). Another example is that one study claimed to assess extrapersonal space, yet the neuropsychological assessments used in the study were presented in peripersonal space (i.e., within reaching distance; Committeri et al., 2007). The lack of standardisation of the definition of extrapersonal space and the space it covers is likely to impact the incidence rates reported (Williams et al., 2021).

The reported incidence rates of extrapersonal neglect within the general stroke and brain injury population are unknown since the samples used to base these incidence rates can be unrepresentative (i.e., often excluding those with left hemisphere strokes, haemorrhages, aphasia, multiple strokes, cognitive and/or visual impairments; e.g., Aimola et al., 2012; Spaccavento et al., 2017). In some cases, extrapersonal neglect may be detected using functional observations or assessments, but only a few are neglect specific (e.g., Kessler Foundation Neglect Assessment Process; Chen & Hreha, 2015) and are not as widely adopted clinically compared to non-neglect specific functional assessments (Checketts et al., 2021). Assessments, such as The Catherine Bergego Scale (CBS; Azouvi, 1996) involve activities of daily living which rely on interaction in extrapersonal space, such as navigation (e.g., travelling from place to place), gaze direction and collision avoidance (Cunningham et al., 2017). However, it is difficult to isolate the assessment of extrapersonal neglect using these methods since the activities involve both personal and peripersonal space processing (Williams et al., 2021). For this reason more 'fine-grained' assessments are needed (Nijboer et al., 2014; Whitehouse et al., 2019).

Of 292 assessment tools, Williams and colleagues (2021) identified 21 'standardised' tests which explicitly measured extrapersonal neglect, compared to 216 used for measuring neglect behaviour in peripersonal space. Within the research literature, some studies have administered line bisection and cancellation tasks at various distances (120cm-320cm away) and used laser pointers (Berti et al., 2002; Aimola et al., 2012; Buxbaum et al., 2012; Ogourtsova et al., 2018) or a computer mouse to respond (Van der Stoep et al., 2013). Other assessments involved visual search tasks (i.e., searching for a target among distractors), such as finding objects around a room or corridor (Stone et al., 1991; Dublin Extrapersonal Neglect Assessment; Cunningham et al., 2017), within a picture presented 250cm away (Lindell et al., 2007), or locating words on a large board (Halifax Visual Scanning Test; Whitehouse et al., 2019). Although some of these tests were digitalised (e.g., the task was shown on a computer monitor; Van der Stoep et al., 2013), many relied upon manual scoring which was limited to basic performance metrics, such as overall score (e.g., Berti et al., 2002; Buxbaum et al., 2012; Van der Stoep et al., 2013).

Although it may be possible to measure additional performance metrics for paper-and-pencil tests (e.g., starting position, search path) the process would be far more labour-intensive for the tester compared to using automatic scoring provided by computerised tools (Dalmaijer et al., 2015). Introducing additional measures other than overall accuracy or number of omissions in cancellation tasks may tell us more about an individual's symptomology since neglect can include non-lateralised attentional deficits, such as working memory, selective and sustained attention (Husain & Rorden, 2003; Huygelier et al., 2020).

Ten Brink and colleagues (2020) used a computerised visual search task with a group of 129 stroke survivors with either left or right hemisphere damage, with or without spatial neglect. Their task presented participants with coloured circles and were instructed to tap on circles which matched the cued colour (target), while surrounded by distractors (other circles) in peripersonal space. In contrast to the digitised assessments above, the computerised visual search task produced performance metrics, such as search time, search consistency (e.g., search organisation), and revisits (delayed, immediate returns to already cancelled targets; Ten Brink et al., 2020). Right hemisphere damaged (RHD) stroke survivors with neglect missed more targets on both sides of the screen (ipsilesional, contralesional space), and had a larger asymmetry score (i.e., missed more targets on contralesional versus ipsilesional space) compared to left hemisphere damaged (LHD) and RHD stroke survivors without neglect. RHD participants with neglect were also more likely to begin their search in ipsilesional (right) side of space, whereas RHD and LHD without neglect begun on the left (more like healthy controls; Morse al., 2023) (Ten Brink et al., 2020). Moreover, RHD with neglect showed more delayed revisits (perseverations) compared to LHD and RHD with no neglect, indicating that these individuals may have had non-lateralised attentional deficits in spatial working memory which can occur with neglect (Husain & Rorden, 2003; Ten Brink et al., 2020). Interestingly, there was no difference in task duration nor search consistency between RHD and LHD with or without neglect. This contradicts previous work by the same group in which RHD stroke survivors (particularly those with neglect) demonstrated poorer searches (less efficient, disorganised) compared to healthy controls (Ten Brink et al., 2016). Based on this, it's not clear whether deficits in search duration and search consistency are neglect-specific deficits. Not only did this study provide additional "*attention-related parameters*" which seem to be distinctive to those with neglect (i.e., revisits, asymmetry in detection rates), but its performance showed agreement with conventional assessments, such as cancellation, line bisection, a neglect-specific functional assessment (CBS; Ten Brink et al., 2020). This study demonstrates the capabilities of computerised assessments for spatial neglect, particularly that they can detect non-lateralised attentional (e.g., spatial working memory) deficits which might otherwise go undetected using conventional assessments. It would be interesting to know whether similar visuospatial attention deficits would be observed in stroke survivors with and without neglect in far-space since these deficits can exist independently from near-space (e.g., Aimola et al., 2012; Nijboer et al., 2014; Spaccavento et al., 2017; Ogourtsova et al., 2018).

Similar (open source) computerised visual search tasks exist which provide additional attentional parameters, such as search efficiency (e.g., quality of search) and organisation (e.g., intersection rates, search speed; CancellationTools by Dalmaijer et al., 2015). However, these tools still only inform us about visuospatial attention (e.g., visual search) in peripersonal space and some lack normative data (Ten Brink et al., 2020). Comparing performance to normative data can help characterise impairments in clinical populations while taking the effect of demographic variables into account, such as age (Lezak et al., 2004). This is particularly important to consider in visuospatial attention tasks since as we know that healthy aging affects processing speeds (Benjamins et al., 2019; Morse et al., 2023), and healthy populations tend to exhibit an over-attendance to the left-side of space in both line bisection and visual search (Morse et al., 2023).

To sum, spatial neglect in extrapersonal space often co-occurs with peripersonal neglect, but rates vary, and it is not routinely assessed despite the impact on functional outcomes. Computerised tests can facilitate the assessment of spatial neglect in far-space and provide additional measures of attentional performance not possible with paper-and-pencil tests. Ultimately, assessing multiple subtypes of spatial neglect, such as ego- and allocentric neglect in extrapersonal space could inform rehabilitation strategies (Dalmaijer et al., 2015; Demeyere & Gillebert, 2019).

Age-graded normative data from 179 healthy adults is available for the Computerised Extrapersonal Neglect Test (Morse et al., 2023). CENT consists of a cancellation and line bisection task, capable of measuring ego- and allocentric neglect (similar to Demeyere et al., 2015), and provides several measures of attention (e.g., reaction times, asymmetry scores, search speed, quality of search, search path, intersections, accuracy, re-cancellations). The test has been shown to be sensitive to age-related changes in visuospatial processing, such as reaction time, search speed and quality of search (Morse et al., 2023). Thus, the next step is to investigate its use with clinical populations in detecting attentional impairments (i.e., spatial neglect) in extrapersonal space. Therefore, the present study first aims to report the rates of extrapersonal neglect based on CENT performance compared to normative data (Morse et al., 2023). Unlike many computerised assessments of neglect, CENT will be administered within the community in stroke survivor's homes. Secondly, it will investigate the psychometric properties (i.e., diagnostic sensitivity, concurrent, convergent, divergent validity, internal consistency) of CENT compared to conventional neuropsychological paper-and-pencil measures. Third, CENT performance will be compared between healthy controls and stroke survivors (with and without neglect) to investigate neglect-specific attentional deficits in extrapersonal space. Finally, the study will explore any relationships between performance on CENT, cognitive domains (measured using a cognitive screening battery), and post-stroke quality-of-life scores.

3.2 Methods

3.2.1 Participants

In total, 74 stroke survivors took part in the study in their own homes. Of those, 57 completed CENT and 17 did not complete the task due to: insufficient space to set-up task (n = 11);

difficulty following instructions (n = 2); technical issues (n = 2); unable to use controller (n = 1); or withdrew from study (n = 1). Normative data for the CENT task was previously collected from a cohort of 179 healthy adults (age ranged from 18-94 years; Morse et al., 2023).

Stroke survivors were recruited between May 2021 and December 2022 via a parent study: c-SIGHT feasibility trial (ClinicalTrials.gov identifier: NCT04752982). Ethics for the trial was approved by South Cambridge Ethics Committee (20/EE/0107). There were four recruiting sites (acute and community NHS stroke services) across the East of England. Potential participants were screened for eligibility upon admission and consented by NHS and Clinical Research Network (CRN) staff.

Stroke survivors were invited to the study if they met the following inclusion criteria: over 18 years old, mental capacity to give informed consent, medically stable (both confirmed by site Principal Investigator or usual care team), able to follow and execute a two-step command, confirmed diagnosis of stroke using clinical CT and/or MRI, and lived within 70 miles of the University of East Anglia. Stroke survivor participants were excluded from the study if they had a history of other neurological conditions (e.g., dementia, brain tumour, Parkinson's disease), bilateral upper limb impairments or were taking part in a stroke rehabilitation trial. Information sheets and consent forms were provided in Aphasia friendly format (i.e., simplified text, picture aids) to reduce exclusion of those with speech and language difficulties.

3.2.2 Measures

Computerised Extrapersonal Neglect Test (CENT)

CENT (run on Unity; Unity Technologies) included both a cancellation and line bisection task completed in extrapersonal space (at least 170cm away from participant). Full technical details of the task can be found in the 'Apparatus and stimuli' section in Morse et al. (2023) and the previous chapter. CENT was presented on stroke survivors' television screen (≧40 inch) using a

HDMI cable connected to the laptop (OMEN by HP 15-dc0003) running the task. If no television was suitable (i.e., <40 inch, no HDMI input), the task was projected onto a portable screen (image size ≧40 inch) using a portable projector (Metroplan Budget Tripod Project screen ET1000, image size 125cm width x 125cm). Identical to Morse et al. (2023), stroke survivors used a wireless HTC Vive controller to complete CENT. Responses were recorded via an HTC Vive base station placed on a tripod or flat surface in-line with the middle of participants' body. The HTC Vive base station and controller were paired to the laptop using a Steam wireless dongle. Participants had a maximum of four minutes to complete the cancellation task. This is based on time taken to complete the task by healthy adults (Morse et al., 2023) and time limits used for paper-and-pencil cancellation measures (e.g., between 3-5 minutes; Demeyere et al., 2015; Moore et al., 2022). In line with other standardised line bisection tests used in clinical practice, there was no time limit for the line bisection task.

As per Morse et al. (2023), the same variables used to create normative data were extracted for stroke survivors. These included lateralised variables to represent visuospatial attentional bias, such as: line bisection error (% left/right deviation from true centre), egocentric score (difference between the number of targets found on left versus right of the screen), allocentric score (difference between left-gap and right-gap distractors cancelled), and asymmetry time score (difference in search time in left versus right side of the screen). Other variables included measures of search efficiency and organisation: search speed (time/seconds and distance/pixels between consecutive cancellations), quality of search (speed and accuracy of search), and number of intersections (number of occurrences the search path crosses over itself). The number of errors (distractors cancelled) and re-cancellations (cancellation or revisit of a target previously cancelled) were recorded as measures of inhibitory control and spatial working memory, respectively. Finally, overall accuracy (total number of targets cancelled), search duration (total time to complete cancellation task) and total line bisection task duration (total time taken to judge middle of 10 lines) were recorded. Definitions of these variables are identical to those stated in Morse et al. (2023).

3.2.3 Paper-and-pencil spatial neglect assessments

Participants completed the Star Cancellation Test (Wilson et al., 1987) which presents 54 small stars amongst distractors (52 large stars, 13 letters, 10 short words) on a landscape A4 sheet of paper. Performance is measured by totalling the number of targets cancelled. The line bisection task (e.g., Rossit et al., 2012; Rossit et al., 2019) presented ten horizontal 200mm long black lines on a landscape A4 sheet of paper and participants were required to mark the middle of each line. One line was presented at a time while other lines were occluded using two sheets of paper during bisection. Error from the true middle was measured in millimetres to determine an attentional bias. As per author instructions, there was no time limit for these tasks (Wilson et al., 1987; Rossit et al., 2012; Rossit et al., 2019). These tasks were chosen since they are both widely used in clinical practice (Checketts et al., 2021) and thus act as comparators against CENT in peripersonal space.

The Oxford Cognitive Screen (OCS; Demeyere et al., 2015) measured various cognitive domains: language, memory, vision, number, praxis, executive, and attention. As a comparator test to CENT, the OCS Cancellation test presented 50 complete hearts (without gaps) amongst distractors (hearts with right- or left-gaps) on a landscape A4 sheet of paper. Participants had 3 minutes to complete the task and provided the following variables: overall accuracy (max 50), egocentric and allocentric score (Demeyere et al., 2015). The OCS was chosen since it is an inclusive post-stroke battery (i.e., Aphasia friendly) and the cancellation test is a direct comparator to CENT cancellation task, in that it has the same number of targets and measures both ego- and allocentric neglect (Demeyere et al., 2015). Matching the number of targets between CENT and comparator tasks is important to match attentional demands, since performance in stroke survivors (especially those with neglect) decreases as target numbers increase (Ten Brink et al., 2020).

A short Visual Analogue Scale (VAS; based on Ronchi et al., 2020) was used as a self-report measure of neglect severity and anosognosia (i.e., awareness of symptoms). Participants were required to mark their perceived spatial neglect symptoms on a scale of 0 (green, no symptoms) to 10 (red, severe). This measure was included since neglect severity has been associated with co-occurrence of both peripersonal and extrapersonal neglect (Van der Stoep et al., 2013). Finally, the One-item extended task (Fortis et al., 2010) was used as a quick and COVID-19 safe (i.e., no contact) measure of personal neglect to explore rates alongside neglect in extrapersonal space. For this task, participants were asked to point to their body parts on the contralesional side.

3.2.4 Quality-of-life after stroke questionnaire

The Stroke Impact Scale (SIS; Duncan et al., 2003) collected participants' subjective ratings of the impact of their stroke on their: physical abilities, emotions, memory, thinking, communication, daily living activities (ADLs), social interaction, and overall recovery score. Responses were on a five-point Likert scale and were normalised (i.e., transformed into percentages up to 100%) for each domain (Duncan et al., 1999). A higher domain score indicated higher quality of life after stroke. This measure was selected since it captures aspects of a stroke survivor's life other than just physical functioning (Duncan et al., 2003)

3.2.5 Procedure

Measures were administered over a 90-minute testing session (or over two shorter visits if preferred) at stroke survivors' homes. Demographic information (handedness, years of education) was collected by the researcher during the testing session. Measures were completed in order of priority to answer the research questions (i.e., paper-and-pencil neglect tasks, OCS, CENT, SIS). All paper-and-pencil neglect tests were positioned in-line with the participant's midline and administered following the standardised instructions provided by the authors. The researcher aimed to position stroke survivors 170cm from the screen when presenting CENT. Distance varied depending on space and participant mobility, thus the true distance ranged from 103cm to 369cm (*m* = 217.62cm, *SD* = 55.20). Distance from the screen did not correlate with a change in accuracy or processing speed ($p > 0.05$). Due to the sensitive nature of some questions, the SIS was posted ahead of the visit for participants to complete independently. If incomplete at the visit, the researcher and stroke survivor completed the SIS together.

3.2.6 Neglect group classifications

Stroke survivors were assigned to the no neglect or neglect group if they scored below cut-offs in contralesional space on any validated neglect assessment in peripersonal space. Neglect in peripersonal space was determined using the following cut-offs: ≤ 51 in the Star Cancellation Test (Wilson et al., 1987); line bisection error < -6mm or > 6mm (Rossit et al., 2012, 2019); < 42 overall accuracy in OCS Cancellation test; < -2 or > 3 egocentric (space) asymmetry score, and < -1 or > 1 allocentric (object) asymmetry score in OCS Cancellation test (Demeyere et al., 2015).

Rates of extrapersonal neglect was determined based on performance outside of cut-offs on CENT variables similar to those used to classify neglect on validated neglect assessments (i.e., Star Cancellation Test, OCS Cancellation test, line bisection; Wilson et al., 1987; Demeyere et al., 2015; Rossit et al., 2019) and shown to be neglect-specific in previous research (e.g., asymmetry scores; Ten Brink et al., 2020). For the CENT cancellation task, the following cut-offs were used to categorise stroke survivors with extrapersonal neglect: < 46 overall accuracy; < -2 or > 2 egocentric score; < 0 or > 1 allocentric score; < -26.92% or > 12.58% asymmetry time score. Neglect on the CENT line bisection was determined if the bisection error was < -6.40% or > 5%. For lateralised variables, the impairment must have been in contralesional space. Impairments on remaining non-lateralised CENT variables (errors, intersections, search speed, quality of search, search duration, line bisection duration) were not used to determine extrapersonal neglect since these measures are not commonly used to diagnose neglect in isolation. Additionally, poorer search organisation (e.g., intersections) has been associated with neglect and without neglect after right hemisphere damage (Ten Brink et al., 2016, 2020). Thus, performance on these remaining variables may be indicative of other cognitive problems (e.g., inhibitory control; Benjamins et al., 2019; Ten Brink et al., 2020) rather than neglect-specific impairments per se.

3.2.7 Statistical analyses

One-way Analysis of Variance (ANOVA), Mann-Whitney U, independent samples t-tests, or Chi-Squared tests were used to compare demographic data between groups. CENT's Cancellation task sensitivity and specificity was determined using the Receiver Operating Characteristic (ROC) curve analysis. Here, sensitivity refers to CENT's ability to correctly classify true attentional deficit (e.g., neglect) cases, and specificity the ability to correctly classify no deficits. ROC analysis was run separately against two validated paper-and-pencil cancellation tests (BIT Star Cancellation, OCS Cancellation test). The Area Under the ROC Curve (AUC) value was used as a measure of diagnostic accuracy (i.e., test discriminatory power; Grech, Stuart, Williams, Chen & Loetscher, 2017). An AUC value of 1.0 represents 'perfect accuracy' (Zou, O'Malley & Mauri, 2007) in correctly classifying an individual with or without attentional deficits. A statistically significant AUC value provides evidence of diagnostic accuracy. Thus, AUC values have the following discriminatory power ranges: 0.90-0.99 (outstanding), 0.80-0.89 (excellent), 0.70-0.80 (acceptable), 0.51-0.69 (poor), or < 0.50

(performs worse than chance; Zou et al., 2007; Hosmer, Lemeshow & Sturdivant, 2013; Grech et al., 2017).

Spearman's rank correlation was used to establish the concurrent, convergent, divergent validity and internal consistency of CENT compared to validated paper-and-pencil neglect assessments. The correlation analysis also included all cognitive domains from the OCS, Visual Analogue Scale scores, and SIS domain scores. Next, Analysis of Variance (ANOVA) and Kruskal-Wallis tests were used to test the effect of group (healthy controls, no neglect, neglect) on CENT performance. Groups were not split into left or right hemisphere damage due to uneven or small sample sizes within some groups (e.g., left hemisphere stroke). Distribution of the data was checked graphically using Q-Q and histogram plots, and Levene's test was used to test the equality of variances within the group. Finally, independent samples t-tests were used to test the difference in SIS scores between neglect and no neglect groups. CENT variables were processed as per Morse et al. (2023). Within the CENT cancellation task, accidental re-cancellations (or re-clicks) performed less than one second apart caused by hardware issues with the controller were removed from the analysis. Bonferroni corrected alpha levels were used for all multiple comparisons within each statistical test.

3.3 Results

3.3.1 Demographic and clinical characteristics

An age-matched sample of 57 neurologically healthy controls were randomly selected from the normative dataset to include in the analysis to compare CENT performance. See **Table 3.1** for demographic data for all participants. There was no significant difference in age [$F(2, 113) = 0.10$, $p = 0.905$] and years education [$F(2, 113) = 1.14$, $p = 0.325$] between healthy controls (n= 57), stroke survivors with (n= 20) and without neglect (n= 37). Nor was there a significant difference in sex [$\chi(4) = 3.79$, $p = 0.435$] or handedness [$\chi(4) = 3.63$, $p = 0.459$] between groups.

Table 3.1. Demographic and clinical data for stroke survivors (neglect, no neglect groups) and healthy controls.

	Neglect (n = 20)	No neglect (n = 37)	Healthy controls (n = 57)	Group differences
Age; mean (*SD,* min, max)	69.70 (*8.95*, 48-88)	68.49 (*13.20*, 32-90)	69.00 (*7.26*, 60-88)	F(2, 113) = 0.10, p = 0.905
Sex; N (%)				χ(4) = 3.79, *p* = 0.435
Female	7 (35%)	17 (45.90%)	24 (42.10%)	
Male	13 (65%	20 (54.10%)	30 (52.60%)	
Missing			3 (5.30%)	
Years education; mean (*SD,* min, max)	7.08 (*3.67, 4*-16)	7.08 (*3.53,* 2-16)	11.47 (*21.59*, 8.50-26)	F(2, 113) = 1.14, p = 0.325
Handedness; N (%)				χ(4) = 3.63, *p* = 0.459
Right	18 (90%)	31 (83.80%)	45 (78.90%)	
Left	2 (10%)	6 (16.20%)	9 (15.8%)	
Ambidextrous	0 (0%)	0 (0%)	3 (5.30%)	
Side of stroke; N (%)				χ(2) = 1.07, *p* = 0.587
Left	5 (25%)	14 (37.80%)		
Right	14 (70%)	22 (59.50%)		
Bilateral	1 (5%)	1 (2.70%)		
Type of stroke; N (%)				χ(1) = 0.09, *p* = 0.764
Ischaemic	17 (85%)	34 (91.90%)		
Haemorrhagic	2 (10%)	3 (8.10%)		
Missing	1 (5%)	0 (0%)		
Side of weakness; N (%)				χ(2) = 0.78, *p* = 0.676
Left	11 (55%)	16 (43.20%)		
Right	3 (15%)	6 (16.20%)		
None	6 (30%)	15 (40.50%)		
Days post-stroke; mean (*SD*, min, max)	103.25 (*59.24*, 32-252)	105.76 (*124.26,* 19-783)		t(55) = -0.09, p = 0.933
Length of stay; mean days (*SD*, min, max)	21.82 (*25.20*, 1-98)	13.46 (*20.38,* 1-91)		t(50) = 1.29, p = 0.205

Notes: Group differences reported using one-way ANOVA (normally distributed variables), Chi-square (categorical variables), or independent samples t-test (normally distributed variables). Standard deviation (*SD*); maximum value (min); maximum value (max); Male (M); Female (F); Handedness refers to hand used post-stroke.

3.3.2 Clinical characteristics

A summary of demographic and clinical characteristics for stroke survivors are presented in **Table 3.1**. The neglect group had a longer length of stay (m = 21.82) compared to the no neglect group (m = 13.46), however, this difference was not significant [t(50) = 1.29, p = 0.205]. There was no significant difference in days post-stroke to date of testing between both groups, meaning both groups were tested at similar times following stroke; [t(55) = -0.09, p = 0.933]. There was also no significant difference between neglect and non-neglect groups in: side of lesion [$\chi(2)$ = 1.07*, p* = 0.587], side of weakness [$\chi(2)$ = 0.78, *p* = 0.676], type of stroke [$\chi(1)$ = 0.09, *p* = 0.764].

3.3.3 Rates of neglect

In total, 57 stroke survivors were included in analyses. Of these 20 (35.09%) were categorised to the neglect group and 37 (64.91%) no neglect group based on performance below cut-offs on validated neglect assessments (in peripersonal space). **Table 3.2** presents behavioural assessment for neglect and no neglect groups. CENT detected 18 cases of extrapersonal neglect (31.58% of the sample). **Table 3.3** summarises the rates of neglect within peripersonal and extrapersonal space. Within peripersonal space, 10.53% (n= 6) had egocentric neglect, 14.04% (n= 8) had allocentric neglect, and 5.26% (n= 3) had both types. In extrapersonal space, 7.02% (n= 4) had egocentric and 7.02% (n= 4) had allocentric neglect. No stroke survivors had ego- and allocentric neglect occurring together in extrapersonal space. No stroke survivors had personal neglect on the one-item extended test (Mdn score = 18.00, min = 16, max = 18).

Table 3.2. Behavioural assessment and questionnaire scores for neglect and no neglect groups.

	Neglect (n= 20)	No neglect (n= 37)	Group differences
BIT Star Cancellation (mdn, min, max)	51.50 (13-54)	54 (52-54)	**U = 596.50, p < 0.001, r = 0.55**
Line bisection* (mm, mdn, min, max)	5.33 (-10.00-28.25)	-1.15 (-13.90-5.10)	**U = 204.50, p < 0.05, r = 0.37**
OCS Cancellation test (mdn, min, max)			
Overall accuracy	42 (19-50)	49 (45-50)	**U = 663.50, p < 0.001, r = 0.66**
*Egocentric score**	0 (-7-19)	0 (-2-3)	U = 325.00, p = 0.437
*Allocentric score**	1 (0-24)	0 (-1-1)	**U = 150.00, p < 0.001, r = 0.60**
OCS profile overview; N (% impaired)			
Memory	4 (20%)	3 (8.10%)	$\chi(1) = 1.70$, $p = 0.192$
Number	4 (20%)	3 (8.10%)	$\chi(1) = 1.70$, $p = 0.192$
Language	5 (25%)	3 (8.10%)	$\chi(1) = 3.07$, $p = 0.080$
Praxis	7 (35%)	5 (13.50%)	$\chi(1) = 3.61$, $p = 0.058$
Vision	6 (30%)	0 (0%)	**$\chi(1) = 12.41$, $p < 0.001$, $\varphi = 0.47$**
Attention	15 (75%)	4 (10.80%)	**$\chi(1) = 24.07$, $p < 0.001$, $\varphi = 0.65$**
Stroke Impact Scale (*m, SD, min, max)*			
Physical	57.89 (*28.48*, 6.25-100)	74.16 (*26.65*, 0-100)	**$t(54) = -2.33$, p < 0.05, d = 0.59**
Cognition	75 (*26.43*, 0-100)	83.98 (*15.87,* 28.57-100)	$t(54) = -1.59$, p = 0.118
Mood	67.69 (*17.03*, 27.78-88.89)	74.77 (*16.52,* 41.67-100)	$t(54) = -1.50$, p = 0.138
Communication	86.09 (*16.01*, 39.29-100)	90.15 (*13.38*, 35.71-100)	$t(54) = -1.01$, p = 0.319
ADL	69.87 (*28.99*, 17.50-100)	80.54 (21.04, 30-100)	$t(54) = -1.58$, p = 0.121
Mobile	62.13 (*31.61*, 5.56-100)	76.73 (*23.99*, 25-100)	$t(54) = -1.93$, p = 0.059
Hand	50 (*38.48*, 0-100)	71.62 (*34.52*, 0-100)	**$t(54) = -2.14$, p < 0.05, d = 0.59**
Social	48.36 (*28.09*, 0-100)	67.31 (*23.62*, 3.13-100)	**$t(54) = -2.67$, p < 0.05, d = 0.73**
Recovery scale	55.53 (*26.45*, 10-85)	70.41 (*20.53*, 20-100)	**$t(54) = -2.33$, p < 0.05, d = 0.63**
Visual Analogue Scale (mdn, min, max)	2.00 (0-9)	0.00 (0-7)	**U = 211.50, p < 0.05, r = 0.34**
Personal neglect test (mdn, min, max)	18 (16-18)	18 (18-18)	U = 370.00, p = 0.163

Notes: Group differences reported using Mann-Whitney U (non-normally distributed variables), Chi-square (categorical variables) or independent samples t-test (normally distributed variables). Significant differences are highlighted in **bold**. Median (mdn); Minimum (min); Maximum (max); Millimetre (mm); Mean (m); Standard deviation (SD); A lower score on the Stroke Impact Scale domains indicates more impairment/lower quality-of-life.

Table 3.3. Summary of neglect rates within each subtype.

Subtype	% stroke survivors (n= 57)
Peripersonal (total)	35.09% (20)
Extrapersonal (total)	31.58% (18)
Both	21.05% (12)
Peripersonal only	14.04% (8)
Extrapersonal only	8.77% (5)

Notes: Rates (%; N) of neglect based on performance below cut-offs on validate paper-and-pencil tests (cancellation, line bisection); Rates in extrapersonal neglect calculated based on performance below cut-offs on CENT (cancellation, line bisection; See 'Neglect group classifications' for full detail on variables used.

3.3.4 Diagnostic accuracy

The CENT cancellation test accuracy had 'excellent' diagnostic accuracy (Hosmer, Lemeshow & Sturdivant, 2013) against the BIT Star Cancellation (AUC = 0.92, p < 0.001, 95% C.I. 0.83, 1.00) and OCS Cancellation test (AUC = 0.95, p < 0.001, 95% C.I. 0.88, 1.00; **Figure 3.1**). The CENT cancellation test had high percentage (80-87.50%) of true positives (sensitivity) and low percentage (10.60-12.20%) of false negatives (specificity) compared to the validated paper-and-pencil neglect tests; the BIT Star Cancellation classified 10 (17.54%) and the OCS Cancellation test classified 8 (14.04%), whereas the CENT Cancellation accuracy score classified 13 (22.81%) as having neglect. In other words, the CENT test accuracy score was accurate in classifying stroke survivors with neglect (sensitivity), while also not classifying those without spatial neglect as having the condition (specificity). **Table 3.4** presents sensitivity and specificity rates against each validation test.

In comparison, the CENT cancellation test egocentric and allocentric scores performed worse than chance [AUC = 0.41, p = 0.459, 95% C.I. 0.07, 0.74] and [AUC = 0.43, p = 0.550, 95% C.I.

0.18, 0.69], respectively (Hosmer, Lemeshow & Sturdivant, 2013). The OCS Cancellation test classified 6 (10.53%) stroke survivors with egocentric neglect, while CENT classified 4 (7.02%) with egocentric neglect in far-space. In other words, the CENT egocentric neglect score had a high rate of false positives (low specificity) and would only correctly detect right side neglect (sensitivity) in half of the sample (low sensitivity). Conversely, when detecting left neglect, the CENT egocentric score had high specificity (detecting few false positives), but a high rate of false negatives (e.g., may miss cases; low sensitivity). For allocentric neglect, the OCS cancellation task detected 8 (14.04%) stroke survivors with allocentric neglect and CENT detected just 4 (7.02%) with allocentric neglect in far-space. The CENT cancellation test had poor sensitivity in detecting both right and left allocentric neglect, but high specificity in that it did not have a high rate of false positives.

Finally, the CENT line bisection test had poor diagnostic accuracy compared to the paper-and-pencil line bisection task (AUC = 0.62, $p = 0.199$, 95% C.I. 0.40, 0.86). The paper-and-pencil line bisection task classified 13 (22.81%) as having neglect, compared to the CENT cancellation test which classified 5 (8.77%). Therefore, CENT line bisection test had a high rate of false positives in classifying stroke survivors with right neglect (low specificity) and detected few true cases (low sensitivity) of left neglect in far-space. These results are likely influenced by the spread of data, whereby many stroke survivors in the sample scored 0 (indicating no ego-, allocentric, and line bisection bias). It is also important to note that the difference in the number of cases detected between the tasks may reflect that both peripersonal and extrapersonal neglect can occur independently of one another.

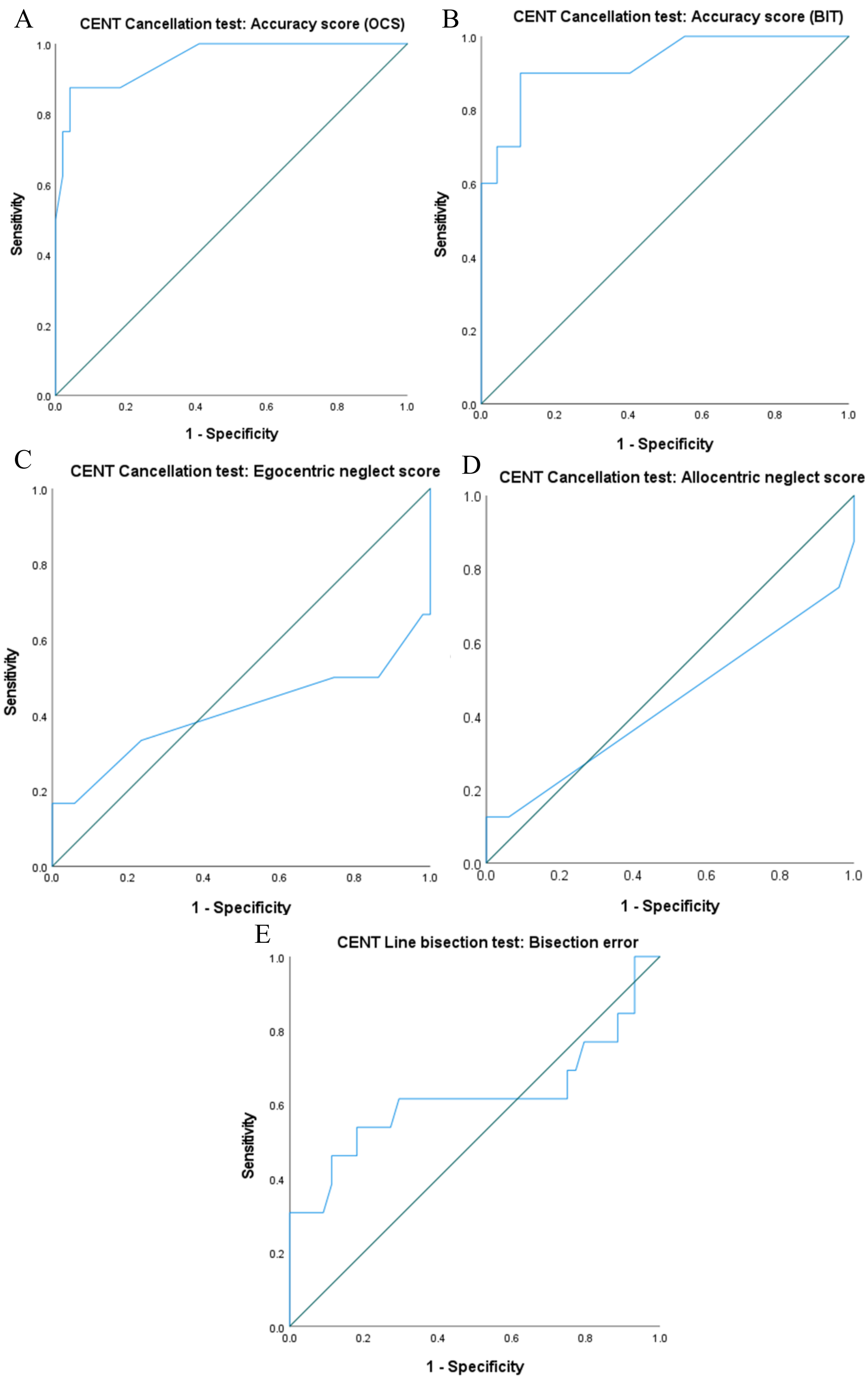

Figure 3.1. ROC curves showing CENT Cancellation test accuracy against: A) OCS Cancellation test overall accuracy score; B) BIT star cancellation test accuracy; C) OCS Cancellation test egocentric score; D) OCS Cancellation test allocentric neglect score; and E) Paper-and-pencil line bisection error. The green line represents no test diagnostic accuracy (performing at chance level). The blue line represents ROC curve. High diagnostic accuracy would be as close to top right corner (Zou, O'Malley & Mauri, 2007). Note that graphs C-E contain positive and negative value scores.

Table 3.4. Sensitivity and specificity values for CENT Cancellation and line bisection test compared to validated paper-and-pencil comparator tests.

		Validation test	*N*	Score direction	Sensitivity rate (true positives)	False positives	Specificity rate (true negatives)	False negatives
CENT Cancellation test	Overall accuracy score	BIT Star Cancellation	57		80% ↑	10.60%	89.40% ↑	20%
		OCS Cancellation	57		87.50% ↑	12.20%	87.80% ↑	12.50%
	Egocentric score	OCS Egocentric score	57	Right neglect	50% ↓	86.30%	13.70% ↓	50%
				Left neglect	16.70% ↓	5.90%	94.10% ↑	83.30%
	Allocentric score	OCS Allocentric score	57	Right neglect	12.50% ↓	6.10%	93.90% ↑	87.50%
				Left neglect	12.50% ↓	2%	98% ↑	87.50%
CENT Line bisection test	Line bisection error	Paper-and-pencil line bisection	57	Right neglect	84.60% ↑	93.20%	6.80% ↓	15.40%
				Left neglect	23.10% ↓	0%	100% ↑	76.90%

Note: Arrows indicate high (↑) or low (↓) values. For example, 80% sensitivity rate would indicate that extrapersonal neglect was correctly detected in 80% of the sample. Whereas, 80% specificity means CENT correctly classified 80% of the sample without the condition.

3.3.5 Concurrent, convergent and divergent validity

A strong positive correlation was found between CENT cancellation test accuracy and the Star Cancellation test score (Wilson et al., 1987), [$r_s(57) = 0.70$, $p < 0.001$]. Overall accuracy on the CENT cancellation test also correlated moderately with the OCS Cancellation test accuracy [$r_s(57) = 0.61$, $p < 0.001$]. In other words, CENT cancellation test accuracy scores increased as accuracy scores did on both validated cancellation tests in peripersonal space. Stroke survivors' quality of search was positively correlated with the OCS Cancellation test accuracy [$r_s(57) = 0.57$, $p < 0.001$] and star cancellation test score. [$r_s(57) = 0.58$, $p < 0.001$]. This indicates that increased search efficiency (i.e., quality of search) was associated with finding more targets on both validated cancellation tests in peripersonal space. Finally, there was a negative relationship between OCS visual field test score and re-cancellations in the CENT cancellation test [$r_s(57) = -0.69$, $p < 0.001$]. This suggests that stroke survivors with visual field deficits measured using the OCS battery had an increased number of re-cancellations in CENT.

A number of the existing neglect assessments were highly correlated with each other, such as the star cancellation and OCS Cancellation test [$r_s(57) = 0.70$, $p < 0.001$]. All significant correlations are presented in **Figure 3.2**.

3.3.6 Internal consistency

Accuracy on the CENT cancellation task was positively correlated with both search speed [$r_s(57) = 0.57$, $p < 0.001$] and quality of search [$r_s(57) = 0.73$, $p < 0.001$]. Remaining correlations presented in **Figure 3.2** replicate previous work (Morse et al., 2023).

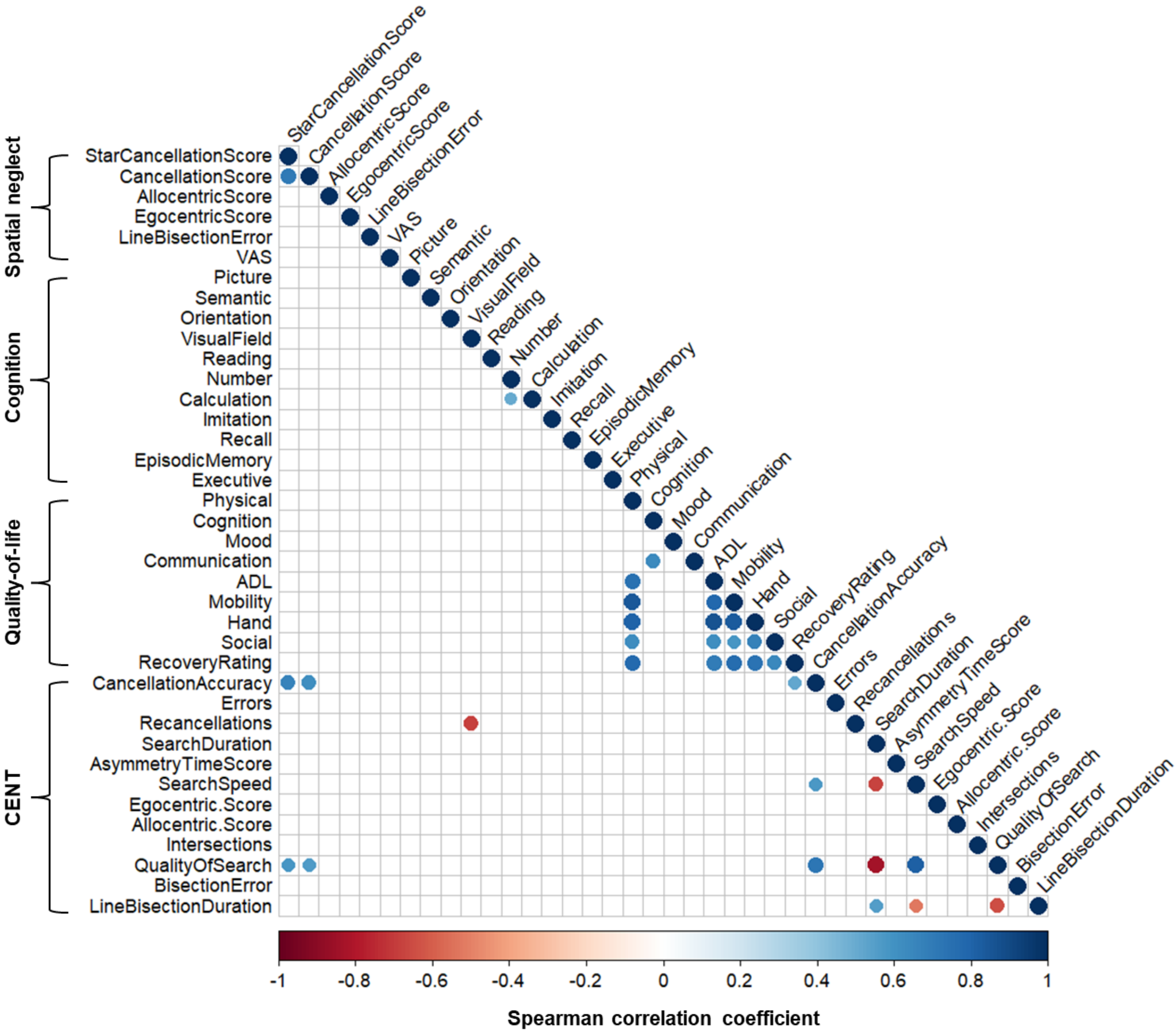

Figure 3.2. Spearman's rank correlation matrix of scores from validated spatial neglect (paper-and-pencil) assessments, cognitive, quality-of-life measures, and CENT variables. Only Bonferroni corrected correlations ($p < 0.00007$) are presented. Created in R Studio.

3.3.7 Group comparisons

CENT cancellation task

There was a main effect of group on CENT cancellation accuracy score [$\chi^2(2) = 18.56$, $p < 0.001$, $\eta^2_H = 0.13$; **Table 3.5**]. The difference was specific to the neglect group, who had lower accuracy (mdn = 47) compared to the no neglect (mdn = 50, p = 0.001) and healthy controls group (mdn = 49, $p < 0.001$; **Figure 3.3A**). This neglect-specific effect on accuracy remained significant after controlling for side of lesion [$F(1, 55) = 19.22$, $p < 0.001$]. Accuracy was not significantly different between healthy controls and no neglect group (p = 1.00). A main effect of group on re-cancellations was found [$\chi^2(2) = 8.17$, $p < 0.05$, $\eta^2_H = 0.04$]. Specifically, the neglect group had significantly more re-cancellations (mdn = 0, max = 4) compared to the no neglect (mdn = 0, max = 2, $p < 0.05$) and healthy control group (mdn = 0, max = 1, $p < 0.05$; **Figure 3.3B**). This effect remained after controlling for side of lesion [$F(1, 55) = 4.06$, $p < 0.05$]. There was no difference in re-cancellations between the no neglect and healthy controls (p = 1.00). **Table 3.5** presents CENT performance for each group.

Additionally, there was a significant effect of group on search duration [$\chi^2(2) = 42.63$, $p < 0.001$, $\eta^2_H = 0.35$]. More specifically, stroke survivors with (mdn = 240.50) and without neglect (mdn = 179) spent longer searching during the cancellation task compared to healthy controls who were significantly faster (mdn = 122, $p < 0.001$; **Figure 3.3C**). There was no significant difference in search duration between the no neglect and neglect group (p = 0.681). There was a main effect of group on search speed [$F(2, 113) = 47.93$, $p < 0.001$, $\eta^2 = 0.46$]. Post-hoc comparisons revealed that healthy controls were significantly faster (m = 126.39, SD = 24.59) compared to stroke survivors with (m = 66.47, SD =29.74, md = 60.12, $p < 0.001$, 95% C.I. 42.93, 77.32) and without neglect (m = 84.52, SD = 29.60, md = 42.06, $p < 0.001$, 95% C.I. 28.09, 56.03; **Figure 3.4A**). There was no significant difference between stroke survivors with and without neglect (md = -18.06, p = 0.055, 95% C.I. -36.42, 0.30).

Table 3.5. CENT performance across groups.

	Neglect (n = 20)	No neglect (n = 37)	Healthy controls (n = 57)	Group differences
CENT Cancellation test	Score	Score	Score	
Overall accuracy (mdn, min, max)	47 (6 - 50)	50 (39 - 50)	49 (41 - 50)	**$\chi^2(2) = 18.56$, $p < 0.001$, $\eta_H^2 = 0.13$**
Egocentric score	0 (-19 - 5)	0 (-5 - 2)	0 (-2 - 3)	$\chi^2(2) = 0.24$, $p = 0.889$
Allocentric score	0 (-3 - 3)	0 (-1 - 2)	0 (-2 - 1)	$\chi^2(2) = 0.001$, $p = 1.00$
Errors	0 (0 - 13)	0 (0 - 2)	0 (0 - 4)	$\chi^2(2) = 2.89$, $p = 0.236$
Re-cancellations	0 (0 - 4)	0 (0 - 2)	0 (0 - 1)	**$\chi^2(2) = 8.17$, $p < 0.05$, $\eta_H^2 = 0.04$**
Search Duration (secs)	240.50 (116 - 246)	179 (117 - 330)	122.00 (76 - 287)	**$\chi^2(2) = 42.63$, $p < 0.001$, $\eta_H^2 = 0.35$**
Asymmetry time score (%)	-9.80 (-29.80 - 129.80)	-13.18 (-40.61 - 10.47)	-7.28 (-42.56 - 18.08)	$\chi^2(2) = 3.35$, $p = 0.188$
Intersections	4.50 (0 - 20)	5 (0 - 41)	3.00 (0 - 23)	$\chi^2(2) = 4.56$, $p = 0.102$
Mean search speed (*m*, *SD*, min, max)	66.47 (*29.74*, 17.20 - 131.82)	84.53 (*29.60*, 39.20 - 161.94)	126.59 (*24.59*, 84.94 - 192.72)	**$F(2, 113) = 47.93$, $p < 0.001$, $\eta^2 = 0.46$**
Quality of Search	0.18 (*0.09,* 0.01 - 0.33)	0.27 (*0.08*, 0.11 - 0.43)	0.38 (*0.10*, 0.13 - 0.66)	**$F(2, 113) = 47.93$, $p < 0.001$, $\eta^2 = 0.46$**
CENT Line bisection test				
Error (%, mdn, min, max)	0.85 (-6.80 - 28.80)	-0.20 (-11.60 - 3.70)	-1.80 (-11.30 - 5.00)	**$\chi^2(2) = 7.51$, $p < 0.05$, $\eta_H^2 = 0.03$**
Task duration (secs, mdn, min, max)	71.50 (38 - 155)	50 (33 - 207)	39.00 (19 - 96)	**$\chi^2(2) = 39.22$, $p < 0.001$, $\eta_H^2 = 0.32$**

Notes: The neglect group includes those impaired in at least one neglect test in peripersonal space. Group differences are reported using Kruskal-Wallis (non-normally distributed variables) or one-way ANOVA (normally distributed variables). Significant differences are highlighted in **bold**. Median (mdn); Minimum (min); Maximum (max); Millimetre (mm); Mean (m); Standard deviation (SD).

Quality of search was significantly different between all groups [$F(2, 113) = 47.93$, $p < 0.001$, $\eta^2 = 0.46$]. Specifically, stroke survivors with neglect had the poorest search organisation (m = 0.18, SD = 0.10) compared to stroke survivors without neglect (m = 0.27, SD = 0.08, md = 0.09, p = 0.001, 95% C.I. 0.03, 0.15) and healthy controls (m = 0.38, SD = 0.10, md = 0.20, p < 0.001, 95% C.I. 0.15, 0.26; **Figure 3.4B**). Stroke survivors without neglect also had poorer search efficiency (quality of search) compared to healthy controls (md = -0.11, p < 0.001, 95% C.I. -0.16, -0.63). The significant difference between stroke survivors with and without neglect survived after controlling for side of lesion [$F(1, 54) = 13.69$, $p < 0.001$, $\eta^2 = 0.20$]. Although the side of lesion did have a significant effect (albeit small effect size) on quality of search performance [$F(1, 54) = 11.44$, $p = 0.001$, $\eta^2 = 0.18$].

No significant differences were found between groups in: the number of distractors cancelled (errors) [$\chi^2(2) = 2.89$, p = 0.236], intersections [$\chi^2(2) = 4.56$, p = 0.102], asymmetry time score [$\chi^2(2) = 3.35$, p = 0.188], allocentric neglect score [$\chi^2(2) = 0.001$, p = 1.00], or egocentric neglect score [$\chi^2(2) = 0.24$, p = 0.889].

CENT Line bisection task

There was a main effect of group on average line bisection error [$\chi^2(2) = 7.51$, p < 0.05, $\eta^2_H = 0.03$]. However, post-hoc comparisons were not significant (p > 0.05). There was a significant effect of group on line bisection task duration [$\chi^2(2) = 39.22$, p < 0.001, $\eta^2_H = 0.32$] (**Figure 3.3D**). Similar to search duration where there was no neglect-specific effect (p = 0.323), line bisection task time was longer for both stroke survivors with (mdn = 71.50) and without neglect (mdn = 50) compared to age-matched healthy controls, who were faster at judging the centre of lines (mdn = 39, p < 0.001).

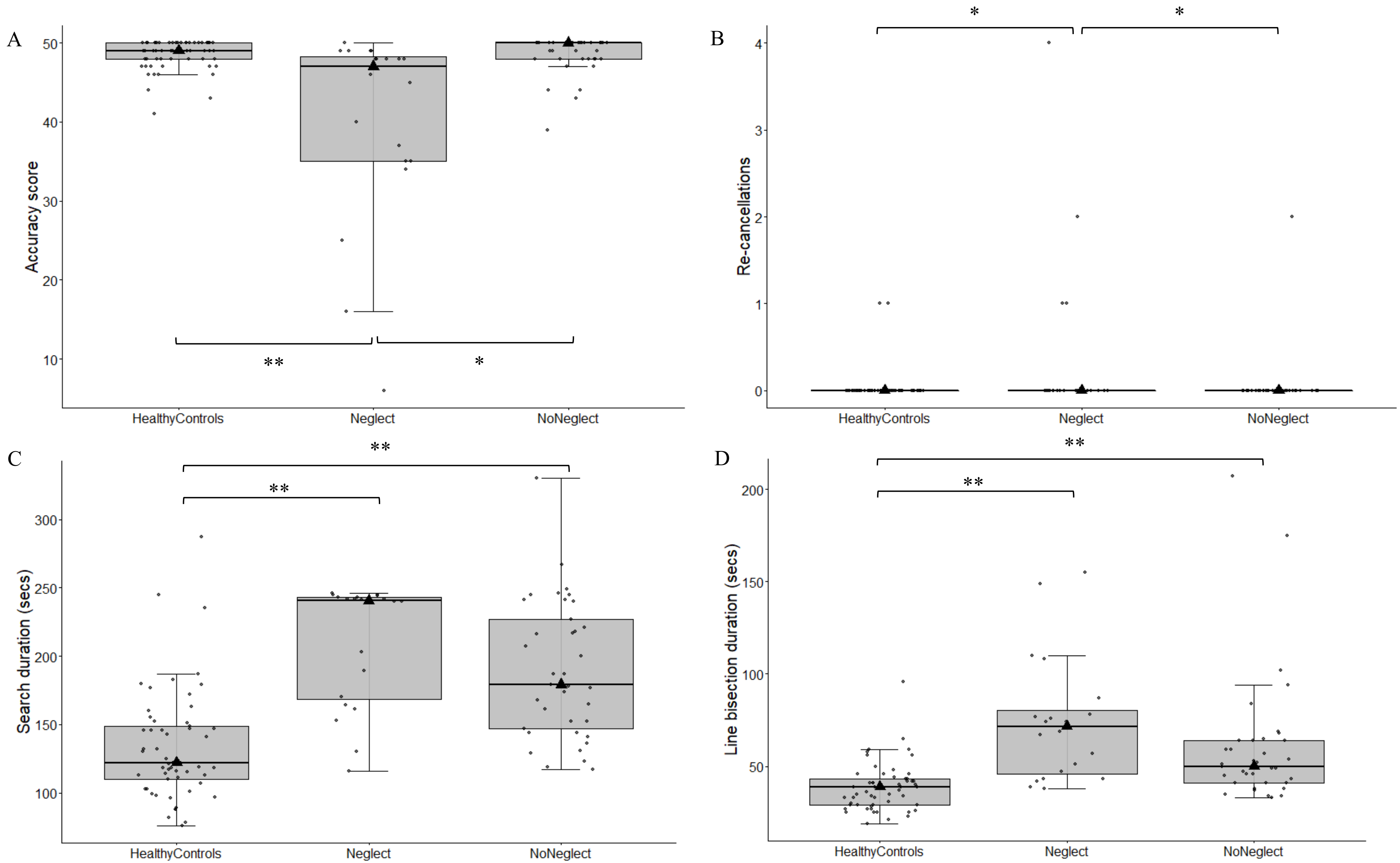

Figure 3.3. Boxplots with error bars showing median values (triangle, line) of CENT cancellation task performance: (A) Accuracy score; (B) Re-cancellations; (C) search duration (seconds); (D) line bisection duration (secs) per group. Significant differences shown above using * ($p<0.05$) and ** ($p<0.001$). Created in R Studio.

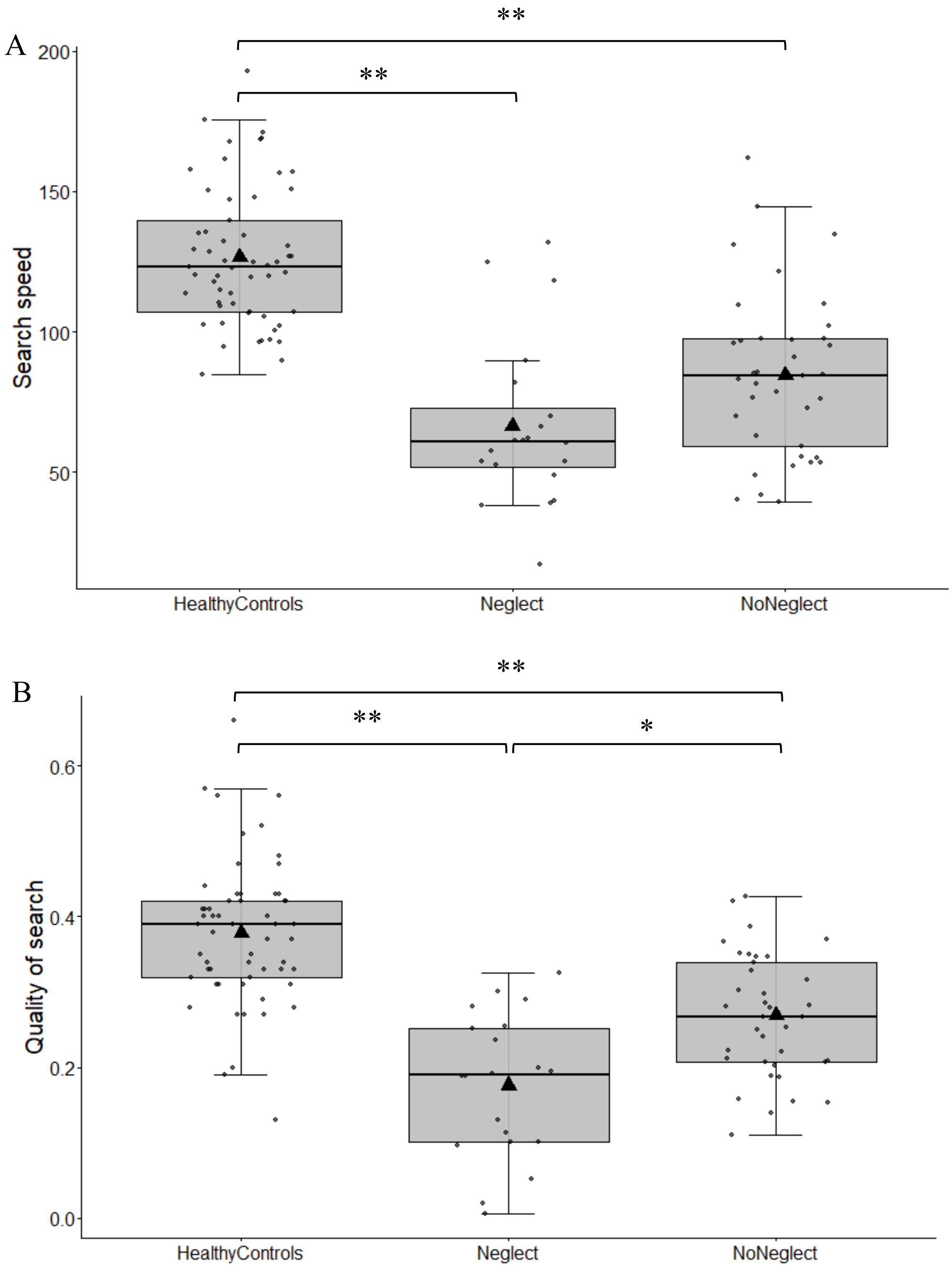

Figure 3.4. Boxplots with error bars showing mean (triangle) and median (horizontal line) of CENT cancellation task performance: (A) Search speed and (B) Quality of search per group. Significant differences shown above using * (p<0.05) and ** (p<0.001). Created in R Studio.

Quality-of-life scores

There was a moderate significant correlation between SIS recovery rating and CENT cancellation test accuracy [$r_s(56) = 0.52$, $p < 0.001$]. SIS domains were intercorrelated (**Figure 3.2**). No other spatial neglect test correlated with domains in the SIS ($p > 0.00007$).

The neglect group self-reported significantly poorer physical movement abilities [$t(54) = -2.33$, $p < 0.05$, $d = 0.59$, 95% C.I. -27.71, -2.05], hand functionality [$t(54) = -2.14$, $p < 0.05$, $d = 0.59$, 95% C.I. -41.93, -1.31], social activities [$t(54) = -2.67$, $p < 0.05$, $d = 0.73$, 95% C.I. -33.22, -4.70], and recovery score $t(54) = -2.33$, $p < 0.05$, $d = 0.63$, 95% C.I. -27.71, -2.05] compared to the no neglect group. Full means and standard deviations are displayed in **Table 3.2.** There were no significant differences between groups for remaining SIS domains.

3.4 Discussion

This study aimed to report the rates of extrapersonal neglect in a group of stroke survivors using a novel computerised test (CENT). We also aimed to investigate the psychometric properties of CENT compared to conventional neuropsychological paper-and-pencil neglect assessments. And compare CENT performance between healthy controls, stroke survivors with and without neglect to investigate any neglect-specific deficits in visuospatial tasks (i.e., cancellation, line bisection) in extrapersonal space. Finally, we set-out to explore whether performance on CENT was associated with scores on cognitive domains and quality-of-life measures.

Crucially, CENT identified 18 cases of neglect in extrapersonal space which would otherwise go undetected using just peripersonal neglect assessments. In agreement with previous evidence (Aimola et al., 2012; Van der Stoep et al., 2013), the results here demonstrate that peripersonal and extrapersonal neglect co-occurring together was more common than neglect deficits isolated to one spatial region. While peripersonal tests detected

10 cases of neglect, it is not possible to say if one test was more sensitive than another (i.e., CENT), since the tests were measuring neglect in different spatial regions. As we can see here (though less common) neglect symptoms can occur independently of one another in peripersonal and extrapersonal space. For instance, more cases of neglect were detected in the line bisection task in peripersonal space (n= 13), compared to CENT's line bisection task in extrapersonal space (n= 5). Perhaps this replicates Aimola and colleagues (2012), who found that neglect patients' line bisection performance was poorer (i.e., larger error) in peripersonal versus extrapersonal space. This contradicts previous studies (Keller et al., 2005) who found that line bisection performance was poorer in extrapersonal space. Authors have speculated that lesions affecting ventral and/or dorsal streams may influence whether a stroke survivor has neglect in extrapersonal and/or peripersonal space, respectively (Aimola et al., 2012; Van der Stoep et al., 2013).

In line with previous evidence (Aimola et al., 2012; Ferber & Karnath, 2001; Sperber & Karnath, 2016), the CENT Cancellation task detected more cases of neglect compared to the line bisection task in extrapersonal case. CENT Cancellation task accuracy score also had excellent diagnostic accuracy compared to validated paper-and-pencil cancellation tasks. That is, it was able to accurately detect neglect (high sensitivity), but also correctly identify those who do not have neglect (specificity, i.e., low false positive rate). Not only this, but CENT positively correlated with two widely used validated paper-and-pencil cancellation tasks (Checketts et al., 2021), demonstrating high concurrent validity. Interestingly, search efficiency (quality of search) on the CENT Cancellation task correlated with overall accuracy on both validated paper-and-pencil neglect assessments. Although this isn't unexpected since accuracy correlated between these tasks, which is a variable used in calculating quality of search. Nonetheless, it demonstrates that CENT Cancellation accuracy score has both concurrent and convergent validity when compared with validated neglect tasks in peripersonal space.

We found evidence of good internal consistency within CENT variables; cancellation test accuracy positively correlated with both search speed and quality of search. These correlations were not present in a previous study of CENT in a healthy sample (Morse et al., 2023), and demonstrate that all three variables are measuring a similar construct (search efficiency) in this sample of stroke survivors. Processing times in the line bisection and cancellation task were positively correlated with each other. This is a replication of previous findings within a healthy sample (Morse et al., 2023). At first this may suggest that performance in the two tasks could be related (something which has been controversial within the literature; Ferber & Karnath, 2001; Keller et al., 2005; Molenberghs & Sale, 2011). However, we must also consider the fact that many more stroke survivors were impaired on the cancellation task (n= 13) than the line bisection (n= 2) within extrapersonal space. This may add to the evidence that cancellation tasks are one of the most sensitive neglect assessments (Azouvi et al. 2002; Ferber & Karnath, 2001; Moore et al., 2022). It may also lend support to the dissociation between the two tasks (Azouvi et al. 2002; Ferber & Karnath, 2001; Keller et al., 2005; Sperber & Karnath, 2016) since many stroke survivors who were impaired on the cancellation task were not impaired on the line bisection task (in both peripersonal and extrapersonal space; e.g., Aimola et al., 2012, see **Appendix B** for rates of neglect in each region of space). This warrants more investigation since it was not the objective of this study. CENT would need to be completed in both peripersonal and extrapersonal space to make direct comparisons as to whether line bisection and cancellation tasks within CENT are or are not related.

More generally, and consistent with previous literature, we found that 35% of the sample of stroke survivors had peripersonal neglect (Bowen et al., 1999; Hammerbeck et al., 2019;

Longley et al., 2022; Moore et al., 2021; Puig-Pijoan et al., 2018; Ringman et al., 2004; Rowe et al., 2019). The neglect group also had a higher proportion of impairment on visual field and attention (including executive attention) cognitive domains compared to the no neglect group (similar to Demeyere & Gillebert, 2019). Similarly, we found a dissociation between ego- and allocentric neglect in peripersonal space, which has previously been replicated also using the OCS Cancellation task (Demeyere & Gillebert, 2019). Interestingly, this dissociation was also present in extrapersonal space, but unlike peripersonal space, no stroke survivors had both ego- and allocentric neglect in extrapersonal space. To the best of our knowledge, this study (albeit small sample) could be the first to explicitly report rates of allocentric neglect in extrapersonal space since many extrapersonal neglect assessments do not measure allocentric neglect. Here, rates of both ego- (10%) and allocentric neglect (14% of sample) in peripersonal space were lower than previously reported (Demeyere & Gillebert, 2019). This could be due to the difference in stroke survivor samples; Demeyere and Gillebert (2019) tested stroke survivors within 3 weeks of stroke, whereas our sample consisted of a heterogenous group of community-dwelling stroke survivors (e.g., ranging from early subacute to chronic stages of stroke). It is possible that cases of ego- and allocentric neglect in our sample had recovered since recovery rates have been reported as high are 81% and 74% for egocentric and allocentric neglect, respectively (Demeyere & Gillebert, 2019).

Group comparisons of CENT performance revealed that accuracy, re-cancellations and quality of search all had neglect-specific deficits. In other words, stroke survivors with neglect found fewer targets (poorer accuracy) and performed more revisits (re-cancellations). Poorer accuracy could reflect both lateralised and non-lateralised visuospatial deficits in the neglect group. For example, some stroke survivors may have shown an impaired ability to find targets across the whole screen (non-lateralised) or within contralesional space (lateralised; Ten Brink et al., 2020). Increased re-cancellations within the neglect group replicates previous work (e.g., Ten Brink et al., 2020; Wansard et al., 2014) and supports the notion that those with neglect have increased non-lateralised attentional deficits in spatial working memory compared to stroke survivors without neglect (Husain & Rorden, 2003). Though our effect here was small and could be influenced by outliers (i.e., more severe neglect cases) and/or visual deficits (e.g., hemianopia) since a poorer score on the OCS visual field test was associated with more re-cancellations in CENT.

The neglect group also demonstrated less efficient searching (quality of search); they found fewer targets in a longer amount of time. Similarly, Ten Brink et al., (2016) found that the consistency of search direction (a measure of search organisation) was more impaired in participants with neglect following a right hemisphere stroke. It is likely that search efficiency is more impaired in neglect due a lower accuracy caused by inattention to targets in contralesional space and a bias towards finding targets in ipsilesional space (Corbetta & Shulman, 2011). It is also possible that longer processing speeds (i.e., search duration) influenced search efficiency via lower arousal levels in those with neglect (Corbetta & Shulman, 2011). However, we did not find a neglect-specific effect of search speed and processing time (in either task), and more recent evidence replicated these findings in a visual search task (Ten Brink et al., 2020). Instead, longer search duration, search speed, and line bisection task duration in CENT in stroke survivors is likely to reflect slowed processing speed which is prevalent in up to 50% of individuals 4-years following their stroke (Mahon et al., 2020).

Similarly, search organisation variables (such as the number of intersections) did not differ between healthy controls and stroke survivors with and without neglect. Initially this is surprising since previous research deemed the number of intersections as "*the most sensitive measure"* of search organisation post-stroke (Ten Brink et al., 2016). Specifically, they found that right hemisphere stroke participants with neglect had the highest number of intersections, compared to left hemisphere and healthy controls. On the other hand, our results may not be unexpected since a previous study found that poor search organisation (e.g., inefficient search) was fairly common in healthy samples (Benjamins et al., 2019; Morse et al., 2023). Specifically, 24% of a large (n = 523) sample of healthy individuals had a poor search organisation (Benjamins et al., 2019). For this reason, the authors recommend against using search organisation alone in determining attentional problems post-stroke since they may not be stroke-specific, rather reflect the variance in search organisation in the general population (Benjamins et al., 2019).

Neither stroke survivors with or without neglect made more errors (i.e., incorrectly cancelled distractors) compared to healthy controls. Instead, all three groups made a similar number of errors, except for an outlier in the neglect group. It seems that this group of stroke survivors did not have poorer inhibitory control (as measured by number of errors made) compared to age-matched healthy controls. This highlights the advantage of using age-graded normative data since we know that a change in inhibitory control in visual search (such as ignoring distractors) is known to decline with healthy aging (Morse et al., 2023; Müller-Oehring et al., 2013; Potter et al., 2012; Tamura & Sato, 2020).

The heterogeneity of the stroke survivors within the sample may have contributed to this since there were a higher frequency of milder, than severe cases of neglect. For example, the neglect group had a relatively high median accuracy score on validated neglect measures (e.g., borderline to cut-off score) and there was a large range of scores. Having said that, the neglect group had significantly lower scores (indicating poorer function) in physical movement abilities, hand functionality, social activities, and recovery rating score (indicating more severe post-stroke effects). Yet, they did not have a significantly longer hospital stay compared to the no neglect group which is common finding (Hammerbeck et al., 2019). To sum, this suggests that the heterogeneity within the sample may contribute to the lack of differences in errors between groups.

Similarly, heterogeneity within the sample may have also contributed to the lack of differences between groups in lateralised variables, that is asymmetry time score, allocentric, egocentric neglect, and line bisection error. This was surprising since these variables (except allocentric neglect score) measure 'core' spatial neglect deficits (a bias towards ipsilesional side of space; Li & Malhotra, 2015). It is probable that grouping left- and right-side neglect (i.e., left, right hemisphere stroke survivors) together reduced the biases by averaging them closer to 0 (no bias). For example, there was no significant difference in peripersonal egocentric score between the neglect and no neglect group despite the large range in scores. A more speculative explanation could be that visuospatial deficits (i.e., neglect) were less severe in extrapersonal space. This may also account for the lack of spread in data necessary to determine the diagnostic accuracy of CENT's lateralised variables (i.e., line bisection bias ego-, allocentric neglect scores). Two previous studies found a similar effect, where line bisection error was larger (Aimola et al., 2012) and more stroke survivors were impaired on a letter cancellation task in peripersonal versus extrapersonal space (Van der Stoep et al., 2013). In future investigations of CENT, larger groups should be recruited in order to perform comparisons between left- and right-side neglect in extrapersonal space.

CENT Cancellation task accuracy score was the only neglect test to correlate with self-reported recovery rating in the Stroke Impact Scale. Based on this, it is possible that cancellation test performance in extrapersonal may better reflect quality-of-life post-stroke compared to cancellation tests in peripersonal space. This is a promising finding since many paper-and-pencil tests do not reflect quality-of-life (e.g., day-to-day functioning) after stroke (Azouvi, 2017). Since the recovery rating was self-reported, therefore prone to bias and anosognosia, it would be important to investigate this further by comparing CENT performance and scores on observational functional assessments (e.g., The Catherine Bergego Scale; Azouvi, 1996).

Interestingly, we observed some paradoxical neglect behaviour between different tasks (similar to Van der Stoep et al., 2013). For example, four stroke survivors exhibited a contralesional bias (i.e., bisection error towards the neglected side) in line bisection tasks in peripersonal or extrapersonal space. In extrapersonal space, seven stroke survivors with right-hemisphere stroke showed an increased search time on the left (‘neglected’/contralesional) side of the screen. These cases of contralesional biases could be cases of ipsilesional neglect (e.g., recorded in line bisection; Williamson et al., 2018) and/or reflect compensatory strategies in chronic stroke (e.g., neglect patients made aware of bias and trained to scan on neglected side; similar cases in Van der Stoep et al., 2013). The latter is possible given that our sample includes stroke survivors from subacute to chronic stages of stroke. Finally, given we know that hemianopia can influence how stroke survivors bisect lines (Ferber & Karnath, 2001; Sperber & Karnath, 2016) and that 30% of the neglect group were impaired on the vision domain of the OCS, it is also likely that co-occurring visual problems (i.e., visual field cuts) could contribute to the contralesional bisection error.

3.4.1 Limitations

Several limitations of this study should be considered alongside the current findings. First, the overall sample size (n= 57) and subsequent group sizes (e.g., n= 5 left hemisphere with neglect) is a limitation since it was not possible to run sub-group analyses by side of lesion. Previous studies using analyses by side of lesion had overall sample sizes between 107 and 280 (Ten Brink et al., 2016; Van der Stoep et al., 2013), and between 18 and 115 per group (e.g., right hemisphere with neglect; Ten Brink et al., 2016, 2020). The benefits of running analyses per side of lesion is that it would help isolate neglect-specific deficits from those that may arise due to lesion of a particular hemisphere. For example, Ten Brink et al., (2016) found that poorer search organisation was exclusive to neglect following right versus left hemisphere. We attempted to control for this during analysis as a covariate, however splitting the sample into sub-groups would be advantageous in understanding whether the side of lesion has a mediating effect on any of the attention-related parameters (e.g., search organisation) produced by CENT in extrapersonal space.

Second, although all efforts were made to control the set-up of the CENT task, the distance from the screen varied between stroke survivors mainly due to differences in space in each home. This highlights the additional considerations (and potential barriers) of using computerised tasks (especially those testing in extrapersonal space) within 'realistic' (i.e., home, care home) settings. It is possible that the increased distance from the screen could have influenced performance on CENT tasks. For example, there is evidence to suggest that line bisection error (i.e., magnitude, direction) may be mediated by the length of the line (see Jewell & McCourt, 2000 for review). Specifically, early evidence showed that a small sample (n= 8) of stroke survivors with neglect made paradoxical, leftward errors on shorter lines, compared to larger rightward errors on longer lines (e.g., Harvey, Milner, & Roberts, 1995). The implications of this in the current study are that lines appeared shorter within the retinal image the farther the participants were sat from the prescribed distance (170cm). This may have contributed to why fewer stroke survivors were impaired on the line bisection task in extrapersonal space (i.e., the error was reduced). However, the effect of line length on magnitude of error is not definitive and a recent meta-analysis of line bisection error in healthy populations found no evidence of a moderating effect of line length (Learmonth & Papadatou-Pastou, 2022). CENT is portable meaning its use can extend to within the community, but perhaps future use of CENT could be conducted in a controlled environment (e.g., clinic room) to maintain a more consistent task set-up which is challenging in a community setting.

Third, although confrontation tests were carried out as part of cognitive screening (i.e., OCS; Demeyere et al., 2015), formal assessments and diagnoses of visual field defects were not known within this sample. Knowledge of which participants had visual defects could have helped explain paradoxical bisection errors (i.e., bias towards neglected space).

Fourth, lesion-symptom analysis (e.g., lesion-symptom mapping) was not utilised in this study due to time constraints. Integrating this methodology with the current data could add to the scarce literature (n= 2 studies; Committeri et al., 2007; Ten Brink et al., 2019) on understanding the neural underpinnings of spatial neglect in different spatial regions. It would be particularly interesting to investigate whether stroke survivors in the sample had lesions affecting the ventral and/or dorsal visual processing streams and whether this corresponds to neglect deficits in peripersonal and/or extrapersonal space, respectively (Aimola et al., 2012; Van der Stoep et al., 2013).

Finally, the personal neglect measure (One-item extended task; Fortis et al., 2010) appeared to lack sensitivity as almost all of the sample scored at ceiling. It is unlikely that no stroke survivor had personal neglect since it is reported to co-occur with extrapersonal neglect in up to 85% (63 of 74) of stroke survivors (Caggiano & Jehkonen, 2018). In retrospect, a neglect-specific functional assessment (e.g., CBS; Azouvi, 1996) would have been superior as it would offer a measure of ADLs in personal, peripersonal, and extrapersonal neglect to compare to CENT performance rather than relying on self-report quality-of-life questionnaires. However, this was not possible due to time constraints and social distancing measures during testing visits throughout the COVID-19 pandemic.

3.4.2 Conclusion

This study has demonstrated test accuracy, sensitivity and validity of CENT. First and foremost, CENT's cancellation task found that approximately 32% (n = 18) of our sample had extrapersonal neglect, which would otherwise go undetected following current neglect assessment practices primarily consisting of paper-and-pencil assessments in peripersonal space. CENT's cancellation task showed agreement with validated neglect assessments, and therefore, could be used alongside, such assessments within a clinical setting to optimise detection of spatial neglect in multiple regions of space. Moreover, CENT demonstrated how attentional parameters, such as quality of search produced by computerised assessments provides an insight into neglect-specific deficits in search organisation. Like ego- and allocentric neglect (Demeyere & Gillebert, 2019), detecting deficits in search organisation in extrapersonal space may be helpful in focusing rehabilitation strategies (e.g., training search organisation; Ten Brink et al., 2016). In turn, this targeted rehabilitation may improve functional outcomes known to be affected by extrapersonal neglect, such as navigation (Spaccavento et al., 2017). Future research should aim to use CENT in a larger sample of stroke survivors in a clinical setting to investigate attentional deficits in extrapersonal space in a variety of stroke cohorts.

4. Chapter 3: A feasibility randomised controlled trial of a computerised Spatial Inattention Grasping Home-based Therapy (c-SIGHT) post-stroke

4.1 Introduction

Reducing the long-term effects of a stroke benefits the individual, their family, but also society. From a societal perspective, the average cost of a stroke stands at more than £45,000 per person over 5 years (Stroke Association, 2018), with this increasing for those needing longer hospital stays and additional inpatient rehabilitation. Post-discharge, Early Supported Discharge (ESD) in the UK lasts between 2 to 6 weeks and is typically available for 5 or less days a week rather than the recommended 7 days (25% meet this recommendation; Royal College of Physicians Sentinel Stroke National Audit Programme; SSNAP, 2021). Following ESD care, up to 40% of community rehabilitation teams have a limited duration (e.g., months) to their service (SSNAP, 2021). This may contribute to why as many as 38% (1 in 3) of 1,546 stroke survivors surveyed felt they had not had enough support after leaving hospital (Stroke Association, 2020).

Home-based rehabilitation could be applied to help (particularly chronic) problems after-stroke. This may include cognitive problems, such as spatial neglect which affects around 30% of stroke survivors (Bowen et al., 1999; Chen et al., 2015; Hammerbeck et al., 2019; Moore et al., 2021; Puig-Pijoan et al., 2018; Ringman et al., 2004), and is typically defined as an unawareness to contralesional space. It is linked to poorer recovery outcomes (Chen et al., 2015) and is a major predictor of post-stroke disability (Gillen et al., 2005). Those with neglect experience increased difficulty participating in rehabilitation (e.g., physical therapy) due to a lack of awareness to one side of the body (Barrett & Muzaffar, 2014). This, and increased stroke severity, may partially account for longer hospital stays and higher dependency on others following discharge (Hammerbeck et al., 2019). For example, carers of stroke survivors with spatial neglect report greater stress levels and carer burden (Chen et al., 2017). It is estimated that up to a third of spatial neglect cases persist into the chronic stages of stroke (e.g., over a year; Umeonwuka et al., 2022). Thus, many individuals are living with the negative long-term effects of the syndrome within the community long after rehabilitation services have ended.

More than thirty different rehabilitation techniques exist for spatial neglect, including prism adaptation (PA; widely researched), visual scanning, mental imagery, mirror neuron therapy, limb activation, Transcranial Magnetic Stimulation (TMS), Somatosensory stimulation, Optokinetic stimulation, neck vibration, pharmaceutical treatments, robot and computer-based therapies (Umeonwuka et al., 2022). However, most techniques are carried out with a therapist (or researcher) present in a clinical (e.g., in-patient) setting. Although, the evidence of the efficacy of PA is inconsistent and inconclusive (Bowen et al., 1999; Longley et al., 2021), PA is still widely researched (perhaps since it is non-invasive and low-cost; Fortis et al., 2020). Like many interventions, PA has historically been carried out with the assistance of a trained personnel (e.g., therapist) in a rehabilitation facility (Longley et al., 2022; Ten Brink et al., 2017) which incurs extra costs (Fortis et al., 2020). Despite the potential benefits of providing rehabilitation to more stroke survivors in the community for a longer period of time (Fortis et al., 2020), reports of home-based rehabilitation interventions for spatial neglect are scarce. In fact, Umeonwuka and colleagues (2022) only reported two studies which investigated a treatment for spatial neglect in a home setting (i.e., Fortis et al., 2020; Rossit et al., 2019).

Recognising the need for stroke survivors with spatial neglect to access rehabilitation in the chronic stages of stroke, Fortis and colleagues (2020) explored using PA delivered by informal carers in stroke survivors' homes. Nine participants with spatial neglect after a right hemisphere stroke used PA at home, delivered with the help of family and/or caregivers (Fortis et al., 2020). Time post-stroke varied between 4 to 60 months, thus seven were classified as having chronic spatial neglect. The authors deviated slightly from the conventional PA procedure, which usually involves pointing to targets whilst wearing prismatic goggles which shift the visual field rightward. Instead, participants were required to wear prism goggles whilst carrying out 'ecological' tasks (e.g., serving tea, playing cards) and hobbies involving visuo-motor actions. Both of which better reflected activities of daily living and were reported to be more enjoyable (Fortis et al., 2010) than simple pointing. Neuropsychological assessments (e.g., spatial neglect tests) were carried out before the control and active intervention phase, then followed-up 1, 3 and 6-months post-intervention. Though the sample was small (and underpowered), there was an improvement lasting up to 6 months in cancellation and functional tasks (e.g., CBS) following ecological PA for two sessions per day (totalling 30 minutes) for two weeks (Fortis et al., 2020). Importantly, delivering ecological PA with the help of carers was feasibility and acceptable; adherence (self-reported by carers) was high with most participants averaging 10 sessions per week (though ranging as low as 3) and carers rated the exercises as 'pleasant'. The study demonstrated that a home-based rehabilitation intervention was feasible to deliver without the presence of a therapist (Fortis et al., 2020).

Spatial Inattention Grasping Home-based Therapy (SIGHT) is a patient-led and home-based intervention for spatial neglect. As described in the general introduction, SIGHT is a bottom-up intervention (e.g., requiring no insight/awareness of symptoms) which requires patients to lift and balance light-weight wooden rods. In practice, an individual with spatial neglect towards the left side of space will initially lift the rod more rightward of the true centre. Repeated lifts and tilting of the rods prompt the patient to gradually re-adjust their grip towards the neglected (left) side until the rod is successfully balanced (Harvey et al., 2003; Robertson et al., 1997). The mechanistic hypothesis surrounding how SIGHT ameliorates neglect is discussed fully within the general introduction, however in sum, it is thought that the sensorimotor and proprioceptive feedback (e.g., tipping) from lifting the rods prompts patients to readjust their grip away from ipsilesional space and towards the middle (Harvey et al., 2003; Robertson et al., 1997). Thus, helping patients become aware of the previously neglected side of space.

To date, improvements on neglect tests have been reported after 20 minutes (Robertson et al., 1997), two-days, one-month (Harvey et al., 2003) and 4-months after using SIGHT (Rossit et al., 2019). Rossit and colleagues (2019) compared the SIGHT intervention (grasp-to-lift and balance rods) versus a control group (lift from one end, receiving no feedback; Harvey et al., 2003) in a group of 20 stroke survivors. Though the sample size was small, there were some promising (albeit small) effects, such as improvements in paper-and-pencil neglect tests (e.g., cancellation, line bisection tasks) lasting up to 4-months after self-administering SIGHT for 2-weeks at-home (Rossit et al., 2019). SIGHT used inexpensive and simple equipment in participants' homes, and did not require the presence of a therapist/instructor at all times (Rossit et al., 2019). Although this study provides proof-of-concept for SIGHT and its potential beneficial effects, like Fortis et al., (2020), the study lacked methodological rigour (Longley et al., 2021). Specifically, the method of randomisation meant there was an increased chance of selection bias, and single (participant) blinding meant the outcome assessor was unblinded to group allocation (Longley et al., 2021). Finally, participant fidelity (e.g., adherence) to the intervention dosage was recorded using self-report checklists which could be subject to bias (Rossit et al., 2019).

Rossit et al. (2019) and Fortis et al. (2020) are among the first to demonstrate the feasibility of delivering a home-based rehabilitation intervention for spatial neglect. However, future studies could implement more robust methodologies (e.g., blinded randomised controlled trial design) and technology (e.g., motion sensors; Rossit et al., 2019) to reduce potential biases and improve measurement of participant adherence, respectively. Applying technology to SIGHT could be useful, not just in reliably (and objectively) measuring adherence remotely, but also in enhancing the delivery of rehabilitation at home in general (Threapleton et al., 2016).

Carrying out rehabilitation remotely at home using technology (telerehabilitation) has the potential to support post-acute rehabilitation alongside and/or beyond NHS stroke service provisions (Laver et al., 2020). Stroke survivors and therapists have recognised this potential; in a recent focus group, 15 participants from these groups felt that technology could empower stroke survivors to engage with rehabilitation when they no longer had access to rehabilitation via stroke services (Faux-Nightingale et al., 2022). The role of technology is recognised within the NICE guidelines (written almost a decade ago), which recommend the use of computer or smartphone-based therapies for stroke survivors with communication difficulties (National Institute for Health and Care Excellence, 2013). To date, the COVID-19 pandemic accelerated the use of technology to deliver health-care remotely (tele-health; Doraiswamy et al., 2020), including telerehabilitation for stroke (Laver et al., 2022). In a recent survey, almost a third of stroke survivor respondents received therapy (e.g., occupational therapy, physiotherapy) via tele-health methods (on the phone or online; Stroke Association, 2020). It is promising that over 60% of these stroke survivors were satisfied with their experience (Stroke Association, 2020).

Within the emerging literature, computerised therapies for spatial neglect seem feasible to deliver with a clinician present (Svaerke et al., 2019). However, many of these innovative interventions (e.g., using virtual reality) have not been explored in a home setting. Computer-based or virtual reality can enable stroke survivors with spatial neglect to carry out rehabilitation whilst being monitored remotely over time, as well as potentially increasing enjoyment, engagement and autonomy (Cavedoni et al., 2022). For instance, exergames have been developed in an effort to make rehabilitation exercises more enjoyable (Tobler-Ammann et al., 2017). Though it seems user input is required during development since some stroke survivors reported that the exergames were too easy/simple or childish (Tobler-

Ammann et al., 2017). A recent review of virtual reality interventions found 14 studies, including the use of non-immersive (e.g., computer monitors, joysticks, keyboards) and immersive (e.g., head mounted displays) technologies (Cavedoni et al., 2022). For example, one pilot study immersed stroke survivors (n = 7) within a virtual outdoor world (e.g., forest) using a virtual reality headset while they completed an attention cueing task (Huygelier et al., 2022). While no evaluations of efficacy were performed, usability was positive (e.g., low rates of cybersickness) which were facilitated by involvement of stroke survivors in the early phases of design (Huygelier et al., 2022). Another study found positive improvements in visuospatial and attentional performance after completing ADL tasks (e.g., purchasing items in a shop) within a non-immersive virtual reality stimulated city ('Reh@City') compared to 'traditional' cognitive rehabilitation (e.g., puzzles, shape sorting; Faria et al., 2016).

Critically, stroke survivors (Dias et al., 2019) and therapists (Ogourtsova et al., 2017) are generally accepting of computerised tools. Stroke survivors and therapists have shared that feedback provided by technology (e.g., clapping, scores) increased their engagement and enjoyment of using non-immersive virtual reality, and would be a facilitator to using a home-based computerised therapy (Morse et al., 2020). For these reasons, computerised therapies could be a promising method for rehabilitation of spatial neglect (see Gammeri et al., 2020; Pedroli et al., 2015 for a review). However, the overall quality of the studies exploring the efficacy of computerised therapies (e.g., for upper limb rehabilitation) remains low, with many studies using small sample sizes and are at a high risks of bias (Laver et al., 2017). Much like most of the 'traditional' treatments for spatial neglect, many of the existing tools still require the presence of a clinician and are administered in hospitals or rehabilitation centres (Svaerke et al., 2019). Further research is required to formally explore the efficacy of computerised tools (Gammeri et al., 2020) using blinded conditions, larger sample sizes, control groups (Svaerke et al., 2019), and in different settings (i.e., at home). Specifically, research is needed to explore the feasibility of using computerised rehabilitation at-home, particularly for groups who may have increased difficulty accessing this support (e.g., communication difficulties, cognitive deficits, less digitally literate; Stroke Association, 2020). For this reason, collaboration with users (e.g., stroke survivors, carers, therapists) is necessary to improve the usability and acceptability of computerised rehabilitation tools (e.g., Huygelier et al., 2022). This would reduce the barriers associated with using technology and improve uptake (Threapleton et al., 2016).

Based on the proof-of-concept study demonstrating the potential positive effects of SIGHT self-administered at home (Rossit et al., 2019), we have developed a computer enhanced version of SIGHT (c-SIGHT). C-SIGHT was developed in collaboration with stroke survivors, clinicians, and carers (Morse et al., 2020) and facilitates self-administration at home. Specifically, visual and auditory instructions are delivered using a computer program and adherence data (e.g., repetitions, sessions) is collected using a small low-cost motion tracking sensor. The addition of the motion tracking sensor addresses challenges of recording adherence using self-report checklists used in the preceding study (Rossit et al., 2019). We collected end-user feedback in the early stages of development of c-SIGHT with the hopes of reducing barriers of use and improving adherence at-home (Morse et al., 2020). The next step following this co-development work was to design a feasibility study incorporating recent recommendations set out by Longley et al. (2021). These recommendations aim to improve the quality of studies going forward, including the use of randomisation, participant and assessor blinding, larger sample sizes, control group, and transparent reporting (Longley et al., 2021). Feasibility studies are an important precursor to a full randomised control trial to inform which aspects of the trial design are successful (e.g., recruitment). This can save future funding of trials which may not be success (Morgan et al., 2018). Feasibility studies do add significant time (around 3 years) to reaching final results of the efficacy of an intervention (Morgan et al., 2018). But it is estimated that 20 feasibility studies deemed unfeasible have saved the British government's major funder of health research (National Institute of Health and Care Research; NIHR) at least £20 million (Morgan et al., 2018).

Thus, the present study aimed to determine the feasibility of a randomised controlled trial using c-SIGHT intervention (c-SIGHT 1) compared to an attentional control (c-SIGHT 2) in the homes of stroke survivors with spatial neglect. Various aspects of feasibility will be investigated: recruitment and success of allocation to groups (objective 1a); intervention fidelity and adherence rates (objective 1b); data completeness, follow-up and drop-out rates (objective 1c). Investigating these aspects of feasibility will determine whether a trial of this kind can be run and inform future trial design. Next, the study will explore any potential effects between groups (Objective 2). In other words, whether c-SIGHT 1 (active intervention) reduces spatial neglect symptoms. Finally, the study aims to explore stroke survivors' (and carers') experiences using c-SIGHT independently at home (Objective 3). This will inform us whether the technology used to deliver c-SIGHT is usable and accepted by stroke survivors. Ultimately, a feasibility study is a necessary precursor to a future trial to formally assess c-SIGHT's efficacy in rehabilitating spatial neglect.

4.2. Methods

4.2.1 Study design

This was a mixed-methods, quadruple-blinded (participants, usual care team, outcome assessors, investigators) two-arm feasibility randomised controlled trial. Participants were allocated using minimisation to one of two-arms: c-SIGHT active intervention (c-SIGHT 1) or an attentional control version (c-SIGHT 2). Assessments were administered at baseline (T0), post-training phase (T1), and one-month (T2) after using c-SIGHT 1 or 2. **Figure 4.1** displays a flowchart of trial procedure. This trial was registered on ClinicalTrials.gov (NCT04752982) prior to the first participant randomisation. This research project was funded by the Stroke Association Postgraduate Fellowship (PGF 19/100016). Ethics approval was granted by the Health Research Authority (HRA) East of England Cambridge South Research Ethics Committee (reference 20/EE/0107) on 5th June 2020. Full pre-registered protocol is available here: https://osf.io/x2jg9/.

4.2.2 Setting

Recruitment was conducted in acute and community stroke settings across the East of England. In total, five NHS sites (Norfolk Community Health and Care NHS Trust, Cambridge University Hospitals, East Coast Community Healthcare, Norfolk and Norwich University Hospital, Cambridgeshire and Peterbough NHS Foundation Trust) were involved in study activities, such as recruitment (n= 4) and intervention delivery (n= 3). Note that three sites carried out both activities, and two recruitment only. Study activities (i.e., baseline, follow-up visits) were carried out by the (blinded) research fellow within the community in stroke survivors' homes (or temporary placements, such as a care homes or an inpatient rehabilitation unit).

4.2.3 Participants and recruitment

Recruitment for this study occurred between February 2021 and January 2023. One NHS site delivered the intervention but did not have capacity to recruit participants. Carers of stroke survivors were invited to act as a study partner. Carers were defined as an unpaid friend or family member who provided help to the stroke survivor. Inclusion and exclusion criteria for stroke survivors and carers are shown in **Table 4.1**. Demographic and clinical data was extracted by clinical teams following enrolment onto the trial. This included length of stay, stroke information and clinical brain scan(s).

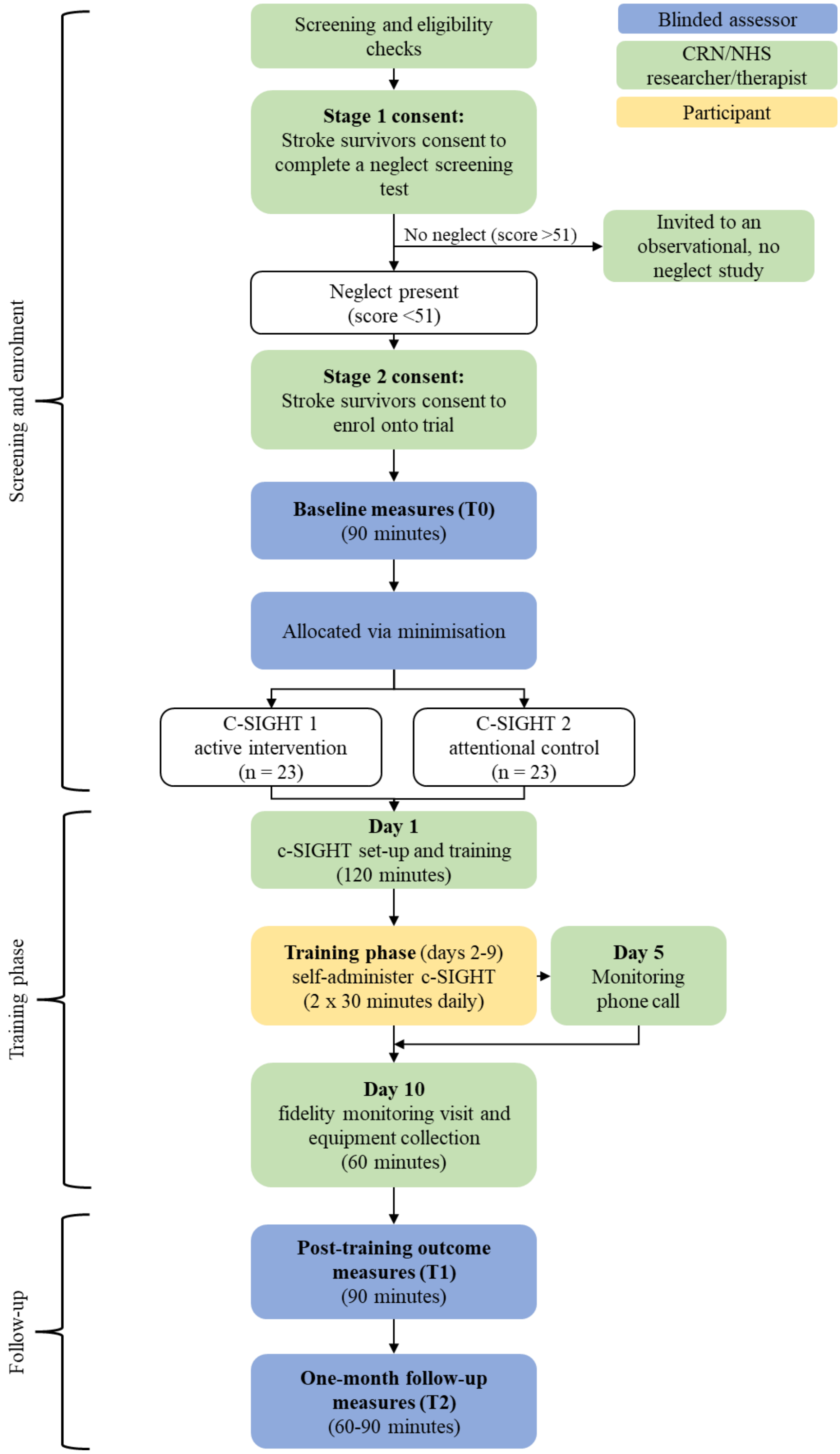

Figure 4.1. Flowchart of trial procedure.

Table 4.1. Participant inclusion and exclusion criteria.

Inclusion criteria	Exclusion
Stroke survivor participants	
≥ 18 years of age	History of other neurological conditions (dementia, brain tumour, Parkinson's disease, previous strokes)
At least one-week post-stroke	Bilateral impairment in arms (unable to move both arms)
Stroke confirmed using clinical neuroimaging (head CT or MRI)	Taking part in a stroke rehabilitation trial (which includes an intervention)
Medically stable (confirmed by the stroke service medical team)	
Capacity to give informed consent (confirmed by stroke service medical team or site Principal Investigator; PI)	
Able to follow and execute a two-step command (e.g., "lift and balance this pen/pencil")	
Signs of spatial neglect either via clinical assessment (e.g., score < 51 on BIT Star Cancellation test; Wilson et al., 1987; line bisection error < -6mm or > 6mm; Rossit et al., 2012, 2019; < 42 overall accuracy in OCS Cancellation test; < -2 or > 3 egocentric (space) asymmetry score, and < -1 or > 1 allocentric (object) asymmetry score in OCS Cancellation test; Demeyere et al., 2015) or in observational tests used in clinical practice	
Live within 70 miles of the University of East Anglia (UEA)	
Carer participants	
≥ 18 years of age	
Capacity to give informed consent	
Carer of a stroke survivor in trial	
Live within 70 miles of the University of East Anglia (UEA)	

Stroke survivors were screened for eligibility and consented by the central research team, local research staff (e.g., physiotherapists, occupational therapists) or Clinical Research Network (CRN) researchers. Stroke survivors first consented to complete a short spatial neglect screening test (Stage 1; BIT Star Cancellation Test; Wilson, Cockburn & Halligan, 1987). If neglect was present (score < 51; Wilson et al., 1987) participants were invited to consent to join the trial (Stage 2). Carers were nominated by stroke survivors and provided written informed consent. Participants who exhibited neglect on additional validated tests (e.g., line bisection, Oxford Cognitive Screen; Demeyere et al., 2015) were invited to take part in the study. These assessments were chosen since they are widely used in clinical practice (Checketts et al., 2021) and cancellation tasks are recommended by experts as a sensitive tool for rapid screening of neglect (Moore et al., 2022)

4.2.4 Sample size

A formal sample size calculation is not recommended for a feasibility study (Lancaster et al., 2004). Using the latest recommendations (Bell et al., 2018), and based on previous results (Rossit et al., 2019) which suggests a moderate to small effect size, a sample size of 46 stroke survivors (n = 23 per group) was appropriate for this feasibility study and to estimate parameters required for the sample size calculation of a future efficacy study.

4.2.5 Baseline measures

An investigator from the central research team (H.M) carried out baseline visits at stroke survivors' homes. Visits lasted approximately 90 minutes but could be split into two separate visits to better suit stroke survivors (e.g., for those with fatigue). Measures administered at baseline are presented in **Table 4.2**. These are listed in the order completed and prioritised based on the study objectives. Peripersonal paper-and-pencil neglect assessments, such as the Star Cancellation Test (Wilson et al., 1987) and line bisection test (Rossit et al., 2019) were administered as a baseline measure of the participants' neglect behaviour. These were selected as measures to assess any changes in neglect behaviour since they are widely used in clinical practice (Checketts et al., 2021) and experts recommend use of cancellation tasks in assessing spatial neglect (Moore et al., 2022). Next, CENT was used as a measure of neglect in extrapersonal (far-space) since this is not commonly assessed in clinical practice (Williams et al., 2021). CENT provides attention performance metrics not produced using paper-and-pencil tests (e.g., search organisation, efficiency) and has high diagnostic accuracy compared to paper-and-pencil comparators (see previous chapter). Details of the administration of CENT is described fully in Chapter 2. The OCS (Demeyere et al., 2015) was administered (including the OCS Cancellation test) to obtain an overall cognitive profile for each stroke survivor at baseline only. This battery is quick to administer (15-20 minutes) and inclusive for stroke survivors (e.g., with language or visual deficits; Demeyere et al., 2015). The Stroke Impact Scale (Duncan et al., 1999) was used as a self-report measure of disability and quality-of-life. This questionnaire was chosen since it included many aspects of daily living activities (ADLs): physical abilities, emotions, memory, thinking, communication, social interaction, and overall recovery score. Due to the sensitive nature of some questions, this questionnaire was posted ahead of time for participants to complete privately. A spatial neglect visual analogue scale (VAS; Ronchi et al., 2020) was used as a brief self-report measure of neglect symptoms and anosognosia.

Finally, a measure of personal neglect (one-item extended; Fortis et al., 2010) was included. This test was chosen for its brevity and was 'COVID' safe (i.e., involved no physical contact with others or objects). These measures served to investigate any subsequent potential effects (i.e., changes in scores) and effect sizes between groups following use of c-SIGHT 1 or 2. Carer outcome assessments are shown in **Table 4.3**.

Table 4.2. Stroke survivor measure description, extracted variable and point of collection.

Measure	Description	Dependent variable extracted	T0	T1	T2
Star Cancellation test (BIT) (Wilson et al., 1987)	Paper-and-pencil cancellation task	Total accuracy score (stars cancelled; max 54). A score < 51 indicates impairment.	X	X	X
Line bisection (Rossit et al., 2019)	Paper-and-pencil 10-line bisection task	Bisection error (deviation from true center; mm).	X	X	X
CENT (Computerised Extrapersonal Neglect Test)	Computerised spatial neglect test, including a cancellation and line bisection test. Stimuli is presented out of reach (extrapersonal space; >170cm away from participants) on a TV or using a projector (full details in previous chapter).	Cancellation: Overall accuracy (max 50, <46 indicates impairment); errors; re-cancellations; time asymmetry score; quality of search; intersections; ego- and allocentric neglect score. Line bisection: bisection error (%)	X	X	X
Oxford Cognitive Screen (OCS) (Demeyere et al., 2015)	Short cognitive battery assessing major cognitive domains: memory, language, number, praxis, executive functions, attention after stroke.	Scores on domains (following cut-offs).	X		
OCS Cancellation test (Demeyere et al., 2015)	Sub-task within OCS. Paper-and-pencil cancellation task	Total accuracy score; ego- and allocentric asymmetry scores	X	X	X
Stroke Impact Scale (SIS) (Duncan et al., 1999)	Self-report questionnaire evaluating disability and quality of life after stroke.	Scores on each domain transformed from five-point Likert scale to percentages. A higher percentage score indicates less impairment.	X	X	X
Spatial neglect visual analogue scale (VAS; e.g., Ronchi et al., 2020)	Self-rated visual scale measuring perceived spatial neglect severity.	Self-rated score (0-10; higher score indicates more severe neglect)	X	X	X
One-item extended test (Fortis et al., 2010)	Short personal neglect test requiring participants to point to parts of their body on the contralesional side.	Score (0-18; 18 indicates no impairment)	X	X	X
1:1 interview (see **Table 4.4** for interview schedule)	Short (~15 minutes) semi-structured interview.	Qualitative themes and feedback		X	
System Usability Scale (Brooke, 1996)	Self-report questionnaire measuring the usability of c-SIGHT.	Curved grading scale score (0-100; 100 = high usability or A+; Sauro & Lewis, 2016)		X	

Notes: T0 = baseline; T1 = post-training; T2 = one-month follow-up visit; BIT = Behavioural Inattention Test (Wilson et al., 1987)

Table 4.3. Carer measure description, extracted variable and point of collection.

Measure	Description	Dependent variable extracted	T0	T1	T2
Modified Caregiver Strain Index (Robinson, 1983; Thornton & Travis, 2003)	Self-rated questionnaire measuring caregiver strain.	Total score (0-26; higher score indicated higher level of caregiver strain)	X	X	X
Informant spatial neglect VAS (e.g., Ronchi et al., 2020)	Self-rated visual scale measuring perceived spatial neglect severity.	Self-rated score (0-10; higher score indicates more severe neglect)	X	X	X
Catherine Bergego Scale (CBS; Azouvi, 1996)	Checklist/scale completed by the carer used to detect presence of spatial neglect in everyday activities	Total score (0-30; higher score indicates more severe neglect)	X	X	X
1:1 interview (see **Table 4.4** for interview schedule)	Short (~15 minutes) semi-structured interview.	Qualitative themes and feedback		X	
System Usability Scale (Brooke, 1996)	Self-report system (e.g., c-SIGHT) usability questionnaire.	Curved grading scale score (0-100; 100 = high usability or A+; Sauro & Lewis, 2016)		X	

Notes: T0 = baseline; T1 = post-training; T2 = one-month follow-up visit.

Carer measures served to provide an additional perspective on spatial neglect severity and impact on ADL's using an Informant version of the VAS scale and Catherine Bergego Scale (Azouvi, 1996), respectively. The Modified Caregiver Strain Index (Robinson, 1983; Thornton & Travis, 2003) provided a measure of the impact of spatial neglect on carers.

4.2.6 Allocation and blinding

Following completion of the baseline measures, participants were allocated using an allocation system built by Norwich Clinical Trials Unit. The lead researcher/outcome assessor (H.M) used the system to blindly allocate participants to the c-SIGHT active intervention (c-SIGHT 1) or c-SIGHT attentional control version (c-SIGHT 2) via minimisation. Allocation emails were sent directly to intervention delivery staff at the relevant site. The following parameters were used for allocation: age (<65 or ≥65 years old), days since stroke (<90 or ≥90 days), side of hemisphere lesion (left, right, bilateral), and neglect severity (0-25 very severe or 26-51 less severe on Star Cancellation Test score; Wilson et al., 1987; Strata based on Volkening, Kerkhoff & Keller, 2018). Minimisation was chosen over unrestricted randomization to reduce heterogeneity between groups (Scott et al., 2002). Participants, carers, outcome assessor, and usual care teams (e.g., General Practitioner) were blinded to group allocation. Participants were told not to describe the exercises they had been performing to the investigator during follow-up assessment visits.

4.2.7 Intervention

Two versions of c-SIGHT (c-SIGHT 1/intervention & c-SIGHT 2/attentional control) were compared. C-SIGHT was based on the non-computerised version of SIGHT used in Rossit et al., (2019). Both c-SIGHT groups used the same equipment and set-up in stroke survivors' home and participants were asked to self-administer (following training) c-SIGHT for 30-minutes (36 trials), twice a day (e.g., morning, afternoon) for ten consecutive days. C-SIGHT 1 involved grasping, lifting and balancing rods using the less impaired upper limb and a pincer grip (e.g., forefinger and the thumb; **Figure 4.2A**). Participants were instructed to lift until they felt the rod was balanced, with no limit on repetitions. Lifting the rods provided visual, motor, somatosensory and proprioceptive feedback (i.e., tilting of rods; Rossit et al., 2019). No other feedback (e.g., verbal) was given to the participant as to whether the rod was correctly balanced. Participants in c-SIGHT 2 group were required to lift the rods from one end only (**Figure 4.2B**). This group acted as an attentional control comparator to the active intervention since participants do not balance the rod. Thus, they receive no visual, motor, somatosensory and proprioceptive feedback of the tilting rods. However, grasping-to-lift from one end ensured the group were carrying out similar motor responses (Harvey et al., 2003).

Participants used three wooden rods of different lengths (red = 100cm, blue = 75cm, green = 50cm) to perform the exercises (**Figure 4.3**). Each colour matched specific lifting positions on the laminated mat (sized 160cm width x 30cm height). The nine rod lifting positions (small squares paired with a letter; A – I) corresponded to where each rod should be placed on a given trial (Rossit et al., 2019). For example, the red rod may have been placed on letter C. To reduce the use of an external reference point to lift and balance the rods more accurately, each lifting position meant the rods would either be placed in the centre (in-line with participant's midsagittal plan) or 10cm to the left or right (Rossit et al., 2019).

C-SIGHT was built on Unity (Unity Technologies) in collaboration with Evolv Rehabilitation Technologies (https://evolvrehab.com/) and a computer scientist at the University of East Anglia (A.B). C-SIGHT was run on an OMEN by HP 15-dc0003na gaming laptop. The laptop was connected to the participants' television to deliver intervention instructions (visually and auditorily).

A **c-SIGHT 1 (active intervention)**

Grasping-to-lift and balance rods.

B **c-SIGHT 2 (attentional control)**

Grasping rods from one end only.

Figure 4.2. Active intervention (A) and attentional control (B) instructions. Note that participants in the control group always grasped the rod in the non-neglected field. Images from Rossit et al., (2019).

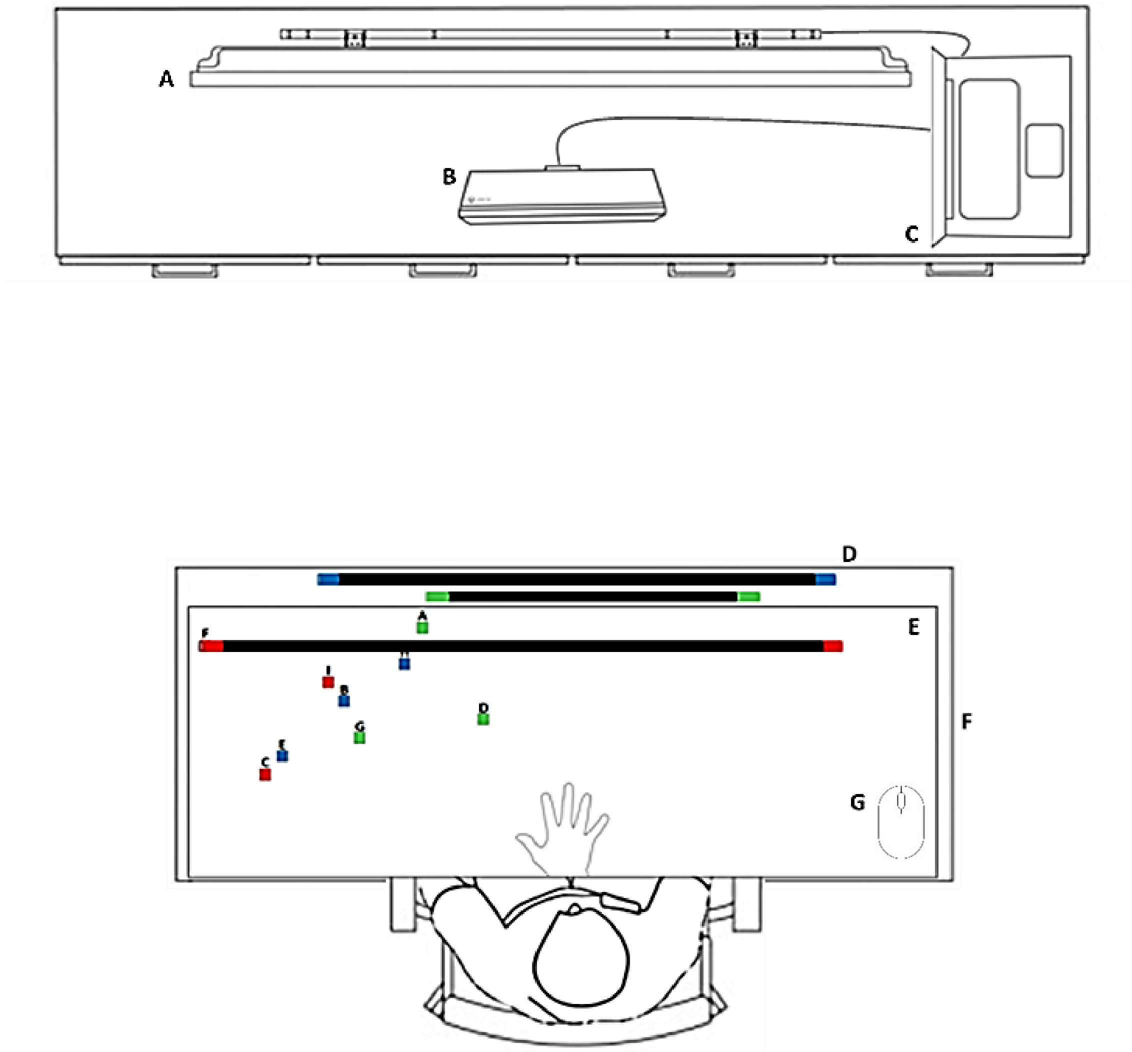

Figure 4.3. Schematic illustration of c-SIGHT set-up including all equipment: A) participant's television (if available/compatible); B) Microsoft Kinect Sensor; C) gaming laptop used to run c-SIGHT; D) c-SIGHT wooden rods (red = 100cm, blue = 75cm, green = 50cm); E) training mat; F) foldable picnic table (if required); G) wireless mouse. This example is a set-up used with a stroke survivor with left-side neglect using their unimpaired (right) hand (note the hand drawing on the mat matches hand used). The reverse set-up (i.e., left hand, lifting positions on right-side) is used for individuals with right-side neglect. Figure made by author.

If no TV was available, the laptop was used independently with the screen facing participants. An Xbox One Microsoft Kinect® sensor was used to record adherence (e.g., session length) and rod lift repetitions (e.g., each time a rod was lifted to shoulder height). Participants were positioned approximately 120cm from the sensor and positioned with their midsagittal plane in-line with both the sensor and mat (indicated using the hand outline on the mat). A wireless mouse was positioned on the mat to navigate through the training sessions (i.e., move onto the next trial). A portable picnic table (120cm L x 60cm W x 55-70cm H) was provided to attach the mat to if no table was available at participants' houses. Participants begun each session by selecting the session (e.g., Day 1 Block A) from the menu shown on the c-SIGHT application. A print-out of short step-by-step instructions were given to participants to remind them how to open the c-SIGHT application (**Appendix C**). During the exercises, instructions were given visually on screen and read-out auditorily by the programme for each trial. The session ended once all 36 trials had been completed. Participants could exit the session early by pressing 'Esc'. Full instructions for each group are shown in **Figure 4.4**. The Template for Intervention Description and Replication (TIDier) checklist (Hoffmann et al., 2014) for this trial is shown in **Appendix D**.

4.2.8 Intervention delivery staff and training

Thirteen staff members from three community NHS sites were trained in delivering c-SIGHT, including participant training, set-up, and final equipment collection sessions with participants (**Figure 4.1**). Local Principal Investigators at each of the three NHS community sites (e.g., stroke care or dedicated research teams) selected staff within their team to act as intervention delivery persons.

There were no formal criteria set by the research team for selecting delivery staff. Professional backgrounds of the 13 trained included occupational therapists (n = 5), clinical research nurses (n = 4), physiotherapists (n = 2), a trainee clinical psychologist (n = 1), and a research practitioner (n = 1).

All staff received identical half-a-day, in-person training on equipment set-up and training participants how to use c-SIGHT, delivered by the study Chief Investigators (H.M and S.R). The training included sharing 'how-to' videos and guides (i.e., step-by-step written, pictorial instructions) which could be used subsequently, independently as memory aids.

4.2.9 Intervention delivery

Intervention delivery staff contacted participants following completion of the baseline assessment visit carried out by the blinded investigator (H.M; **Figure 4.1**). The initial set-up visits required staff (unblinded to group allocation) to set-up the c-SIGHT equipment and show participants how to use the equipment and system (i.e., turn on laptop and start a session). Staff were instructed to be present during the first c-SIGHT session to ensure participants were following instructions in accordance with their group allocation. Following this visit, participants were instructed to self-administer c-SIGHT independently, each day, until Day 10. Staff carried out a 'Check-in' phone call on Day 5 to monitor any issues. On the final day of the training phase (Day 10), staff re-visited participants to observe the final session and remove the equipment from participant's home.

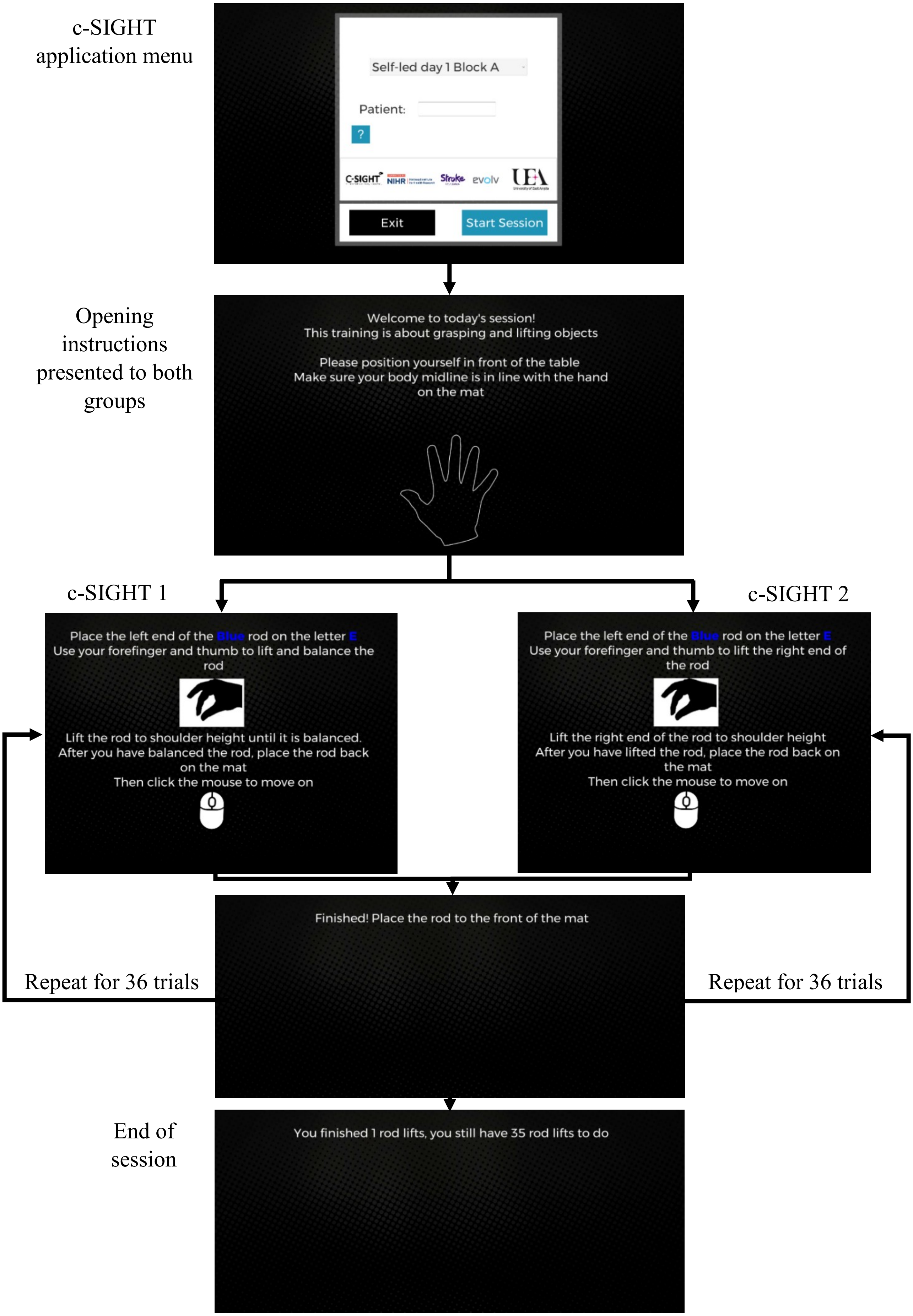

Figure 4.4 c-SIGHT 1 and 2 instructions delivered via the c-SIGHT application on a laptop. Instructions were presented visually and read using an automated voice. A counter was presented in the corner showing the number of repetitions (lifts) participants has completed per trial. This example shows instructions for a right-handed stroke survivor with left-side neglect. Images and instructions are modified for left-handed stroke survivors with right-side neglect.

4.2.10 Study measures

Feasibility of recruitment was recorded using eligibility, exclusion rates, and the proportion of those consented onto the study. Moreover, allocation rates to each group and frequency of unblinding were recorded to assess allocation success (Objective 1a). The feasibility of the delivery of the trial intervention and control (c-SIGHT 1 & 2) was assessed using intervention fidelity and adherence rates (defined below; Objective 1b). Data completeness, follow-up rates, and drop-out rates were recorded as a measure of the final aspect of feasibility in the trial (Objective 1c).

4.2.11 Staff intervention fidelity

Fidelity is defined as the "*degree to which an intervention is implemented as intended*" (Pérez et al., 2015). As stated in the 'Intervention delivery' section, all three delivery sites received the same training and materials. This was implemented to optimise fidelity by standardising staff intervention delivery instructions (Carroll et al., 2007). To monitor fidelity to intervention set-up and participant training (i.e., delivering the correct instructions; Objective 1b), intervention delivery staff took photographs (with participant's consent) of c-SIGHT set-up on Days 1 and 10. These photographs were used to assess whether staff had correctly set-up c-SIGHT and whether there were any modifications to the set-up during the 10-day training phase. Staff were also instructed to record short videos of participants (occluding faces) using c-SIGHT 1 or 2 on Days 1 and 10. This data was used to monitor whether staff were delivering, and participants were following, the correct instructions according to group allocation. To avoid unblinding, these photographs were not viewed by the investigator (H.M) until analysis and write-up.

4.2.12 Participant intervention fidelity (adherence)

Adherence is one of five dimensions of fidelity (Carroll et al., 2007) and refers to whether participants followed the prescribed intervention usage. This includes frequency, duration and dose (Carroll et al., 2007; Pérez et al., 2015). Participant's adherence to c-SIGHT (Objective 1b) was monitored using electronic data extracted from c-SIGHT (i.e., session length, frequency, repetitions).

4.2.13 Outcome measures

The blinded outcome assessor (H.M) returned to see participants for follow-up visits; T1 was carried out as soon after Day 10 equipment collection as possible and T2 was conducted one-month after Day 10. Measures administered during both these visits (**Table 4.2**) involved repeating all measures at baseline (expect the full OCS battery; Demeyere et al., 2015). Any change in performance on these measures from T0 were used to investigate any potential effects (i.e., changes in scores) of c-SIGHT between groups (Objective 2). This also applied to carer measures. Semi-structured interviews and a self-report usability questionnaire administered at T1 (details below) were used to explore participants' (and carers') experiences using c-SIGHT (both intervention and control) at home (Objective 3).

4.2.14 Participant interviews and usability measure

One-to-one semi-structured interviews were conducted with stroke survivors during the T1 visit (i.e., as close to using c-SIGHT as possible). Carers were interviewed separately during the same visit. All interviews were audio recorded with participants' consent. The interview schedule is presented in **Table 4.4**. Supported conversations techniques (e.g., use of short sentences, repetition, paraphrasing, use of high frequency words) were used for those with language deficits. Usability was formally measured using a quick and simple questionnaire (System Usability Scale; Brooke, 1996). The usability measure scores were used as a quantitative measure of perceived usability (Objective 3). Interviews were chosen to inform and supplement quantitative data to gain a richer understanding of participant experience, obtain feedback and recommended improvements to future trial planning and c-SIGHT (Objective 3).

Table 4.4. Interview schedule to guide one-to-one semi-structure interviews.

Topic:	**Example questions:**
1. User experience	"How did you feel during/after using c-SIGHT?"
2. Usage	"How did you feel about the frequency you were using c-SIGHT?"
3. Equipment	"What did you think about the equipment you used for c-SIGHT?"
4. Sounds, displays, text, and instructions	"What did you think about what you saw on screen or the noises you heard while using c-SIGHT?", "What did you think about the instructions?"
5. Perceived benefits and/or limitations	"What do you feel are the benefits or limitations of using c-SIGHT?"
6. Possible changes in spatial neglect	"Have you felt or noticed any changes in yourself after using c-SIGHT?"
7. Estimated (financial) cost	"How much do you think c-SIGHT would cost?"

4.2.15 Patient and Public Involvement

Participant facing documents were reviewed by a stroke survivor independent from the research team. Aphasia 'friendly' participant information sheets and consent forms (created following Accessible Information Guidelines; Stroke Association, 2012) were used to facilitate recruitment of stroke survivors who may have mild language impairments. These materials were also reviewed by an experienced stroke speech and language therapist (S.N). Two stroke survivors, a carer and clinicians working on the study attended an annual meeting to share and discuss trial progress. Monthly meetings with recruiting sites informed necessary ethics amendments to improve recruitment and simplify study processes for clinicians working on the study.

4.2.16 Data analyses

Feasibility of recruitment (Objective 1a) is reported using descriptive statistics (e.g., frequencies, percentages) and presented following the CONSORT 2010 guidelines (Schulz, Altman, Moher & the CONSORT Group, 2010) (see both CONSORT and TIDIeR checklist in **Appendix D**). Allocation success (homogeneity of groups) is reported using demographic data for each group (Objective 1a). The feasibility of the delivery of the trial intervention and attentional control (Objective 1b) is reported as percentages, generated using a fidelity checklist (**Appendix E)** adapted from Powers et al. (2022). The checklist considers sources of evidence (Case Report Forms, photographs, videos, correspondence) in assessing staff fidelity to delivering the intervention as set out in the study protocol. Participant adherence rates (i.e., frequency of use, session length, repetitions) are reported using descriptive statistics for each c-SIGHT group (Objective 1b). Significant outliers were removed for this analysis (e.g., sessions that ran for over an hour and had no repetitions as participants left the system running). Data from participants who withdrew part-way through the training phase was excluded from adherence rate reports and estimates of effects due to missing data. Completion rates of measures, follow-up rates, and drop-outs are reported using descriptive statistics and percentages (Objective 1c). The CONSORT 2010 statement (Schulz et al, 2010) flowchart also presents this data visually as participant flowed through the trial. Missing data was coded for analysis. Serious Adverse Events (SAE's) and Serious Events (SE's) are reported as part of trial safety.

Descriptive statistics were calculated for each participant at each time point (T0, T1, T2) to investigate any potential effects (i.e., changes in scores) of c-SIGHT between groups (Objective 2). Interviews were transcribed verbatim by the lead investigator (H.M) and student research assistant (H.C). Similar to Morse et al., (2020), transcriptions were then coded by the lead investigator (H.M) and entered into a coding grid in Microsoft Excel (Microsoft Corporation, 2018). Themes and codes were reviewed by a second-rater (S.R) to ensure agreement in grouping of codes. Any disagreements were discussed between the research team until an agreement was reached. The data was analysed using deductive thematic analysis (Braun et al., 2014) to group and extract common themes within the coding grid (Objective 3).

4.3 Results

4.3.1 Feasibility outcomes

Recruitment

The trial did not achieve its original target of 46 stroke survivors (n = 23 per group) with spatial neglect. In total, 704 stroke survivors were screened for eligibility (**Figure 4.5**). Of the 668 excluded, 23 were eligible but were not consented to the study due to: no staff capacity to recruit (n = 10) or declined to participate (n = 13). Therefore, 36 (5.11%) were consented to the trial.

CONSORT
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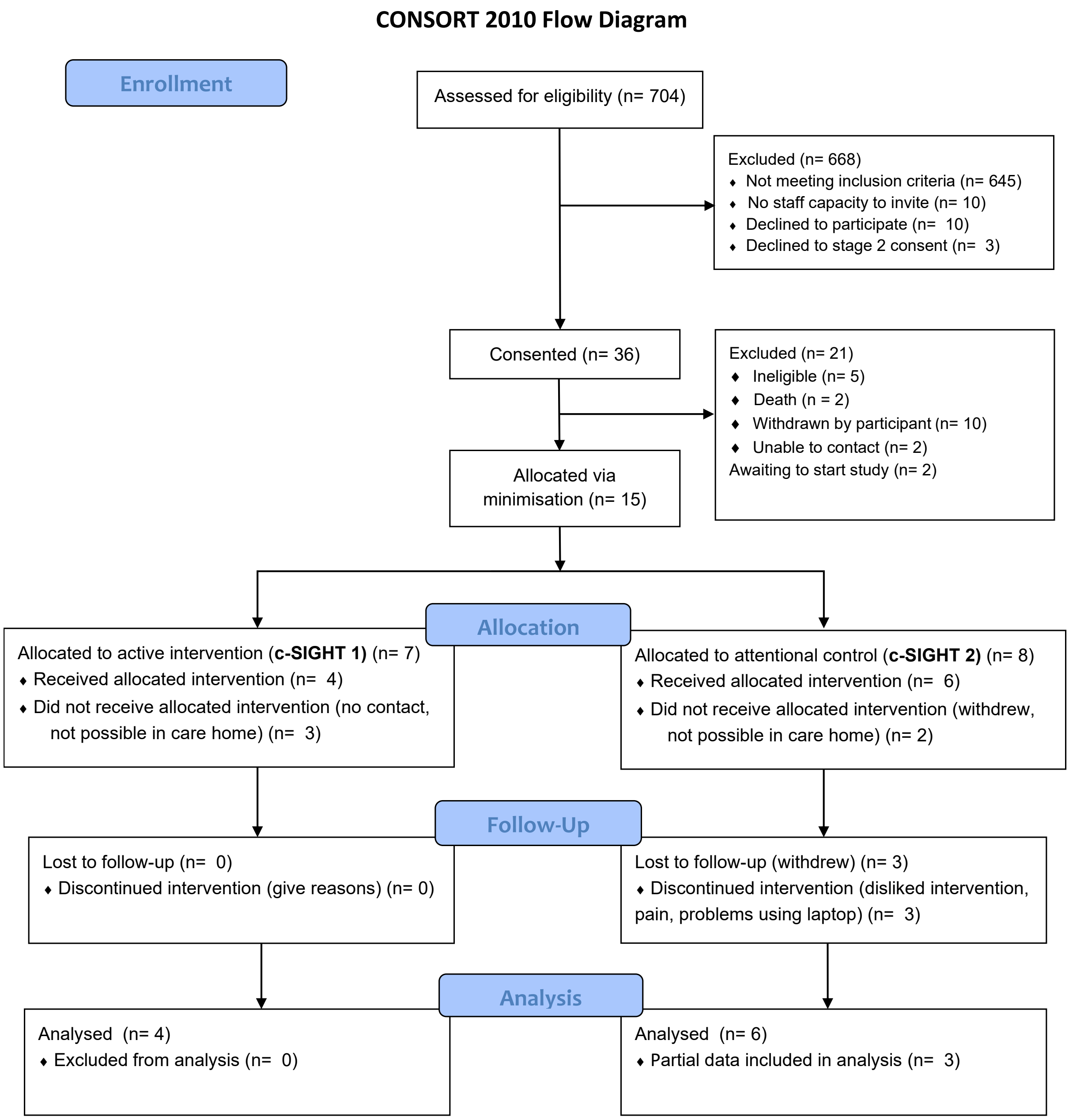

Figure 4.5. CONSORT (Schulz et al., 2010) diagram of participant flow. Note: the screening and recruitment procedure included recruitment of some stroke survivors with no spatial neglect, who were invited to an observational sub-study within the trial (n = 71; Chapter 2 of this thesis).

Note that 71 stroke survivors met all eligibility criteria, except symptoms of neglect thus were consented to a parallel study (see previous chapter). One carer was recruited as part of the trial. Reasons for stroke survivor ineligibility were as follows: no capacity to consent (23.29%), history of neurological condition (20.47%), unable to follow two-step command (16.47%), not medically stable (14.35%), lived out of recruitment area (14.12%), speech impairment (10.59%), stroke not confirmed with neuroimaging (8.00%), enrolment in another rehabilitation trial (2.12%), and bilateral impairments in arms (0.47%). Note some stroke survivors met multiple exclusion criteria.

Figure 4.6 shows screening figures for all four recruiting sites. The effects of the COVID-19 pandemic on NHS site capacity (i.e., staffing levels, redeployment) meant some sites opened later than others. Two sites approached during study set-up had no capacity to recruit for the study. Staff capacity fluctuated across the 22-month period which impacted site capacity to screen all stroke admissions (**Figure 4.6**). This was particularly true in July 2021 and 2022 due to staff leave. Community 1, Community 2, and Acute 2 had dedicated research staff and time, whereas Acute 2 primarily used clinical staff with no protected research time. Community 1 and 2 were the only two sites who had capacity to continue screening all stroke admissions throughout their participation. Acute 1 and 2 were unable to continue screening all admissions due to limited capacity (e.g., time, staffing).

Recruitment figures across all sites are presented in **Figure 4.7**. Overall recruitment per month (median = 1) was lower than expected over 22-months. The first half of the recruitment period (Feb – Dec 2021) saw a total of 11 recruits. In October 2021, the target sample size was revised to aim for a minimum of 16 (n = 7 per group) over 11 months until September 2022 (the planned end-date at the time). This revised sample was conservative (e.g., accounting for potential drop-outs), and based on the recruitment rates between February 2021 and October 2021 (n = 1 per month).

Recruitment was monitored through inspection of screening logs to identify any high rates of exclusion. This informed amendments to eligibility criteria, such as removal of '*must be one-week post-stroke*' and '*no previous strokes*' in October 2021 and March 2022, respectively. Following this change, recruitment figures doubled to 25 recruits in the second half of the recruitment period (Jan – Nov 2022). Exclusion criteria '*must have capacity to consent*' was removed and consent via consultee was introduced in November 2022. The impact of this amendment was not yet known at the time of write-up. To reduce workload at NHS sites and simplify recruitment, an amendment was submitted in August 2022 to change the two-step consent process to a single step (i.e., combined consent for screening and enrol onto study). Both amendments were informed by a trial progress meetings including site clinicians working on the trial and Patient and Public Involvement (PPI) representatives. Recruitment is ongoing.

Baseline measures completeness and drop-outs

Of the 36 participants consented to the trial, 16 (44.44%) begun the baseline assessment visit (T0). Of these, 15 (93.75%) completed T0. One participant partially completed T0 but withdrew part-way since they felt overwhelmed with taking part in a trial and adjusting to post-stroke consequences. One carer (67 years old female) was recruited as study partner for SS02. Demographic and clinical data for all 15 who completed T0 are presented in **Table 4.5**, baseline assessment scores in **Table 4.6**, and CENT performance in **Table 4.7**. Participants who completed the baseline visit were able to complete all assessments, apart from 3 (20%) participants who could not complete CENT due to insufficient space to set-up the task.

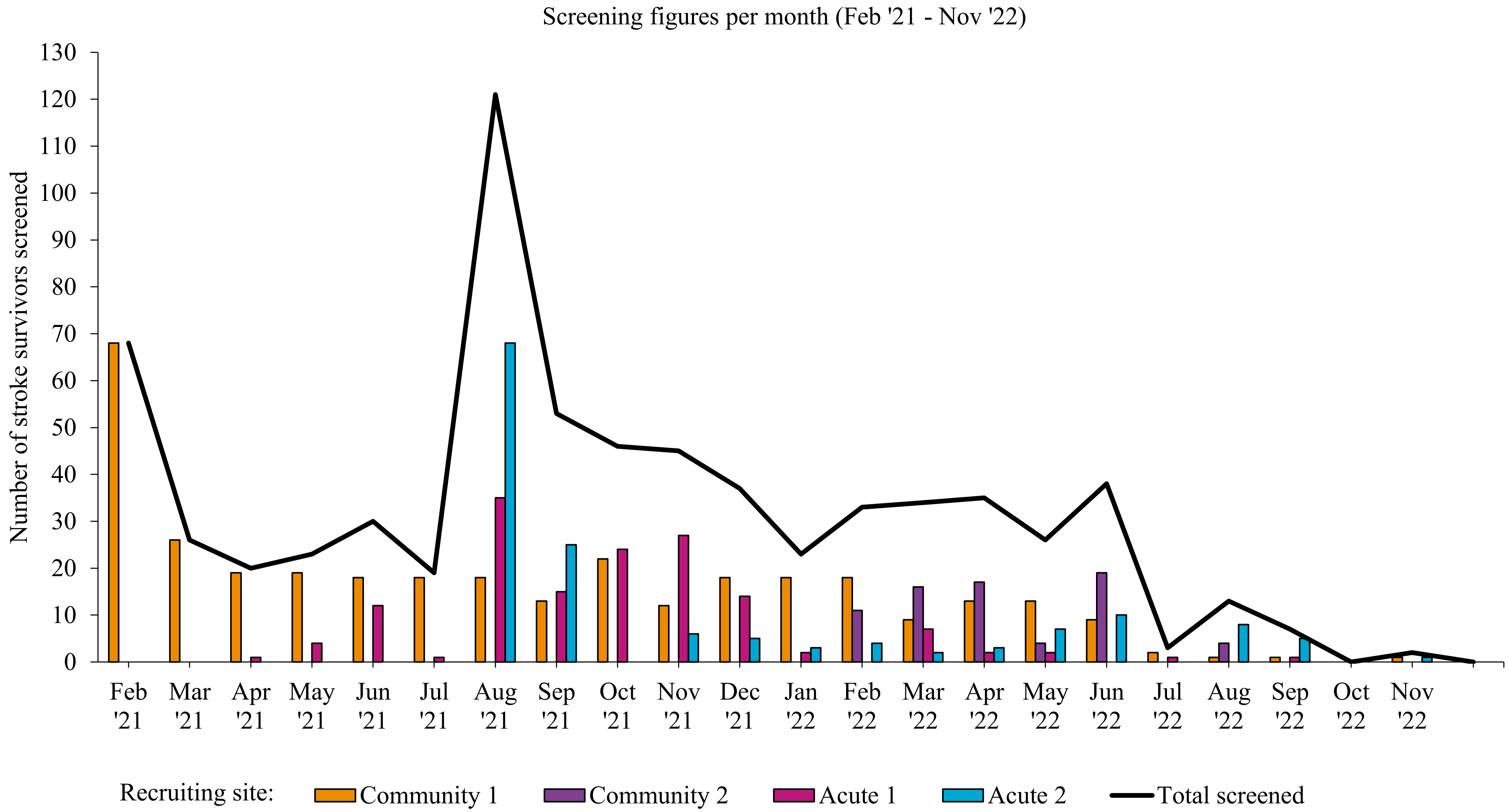

Figure 4.6. Screening figures across four recruiting sites (n= 2 community; n= 2 acute) over a 22-month period. The black line represents total recruitment trend. Opening dates for each site were as follows: Community 1 (February 2021); Acute 1 (April 2021); Acute 2 (June 2021); Community 2 (February 2022).

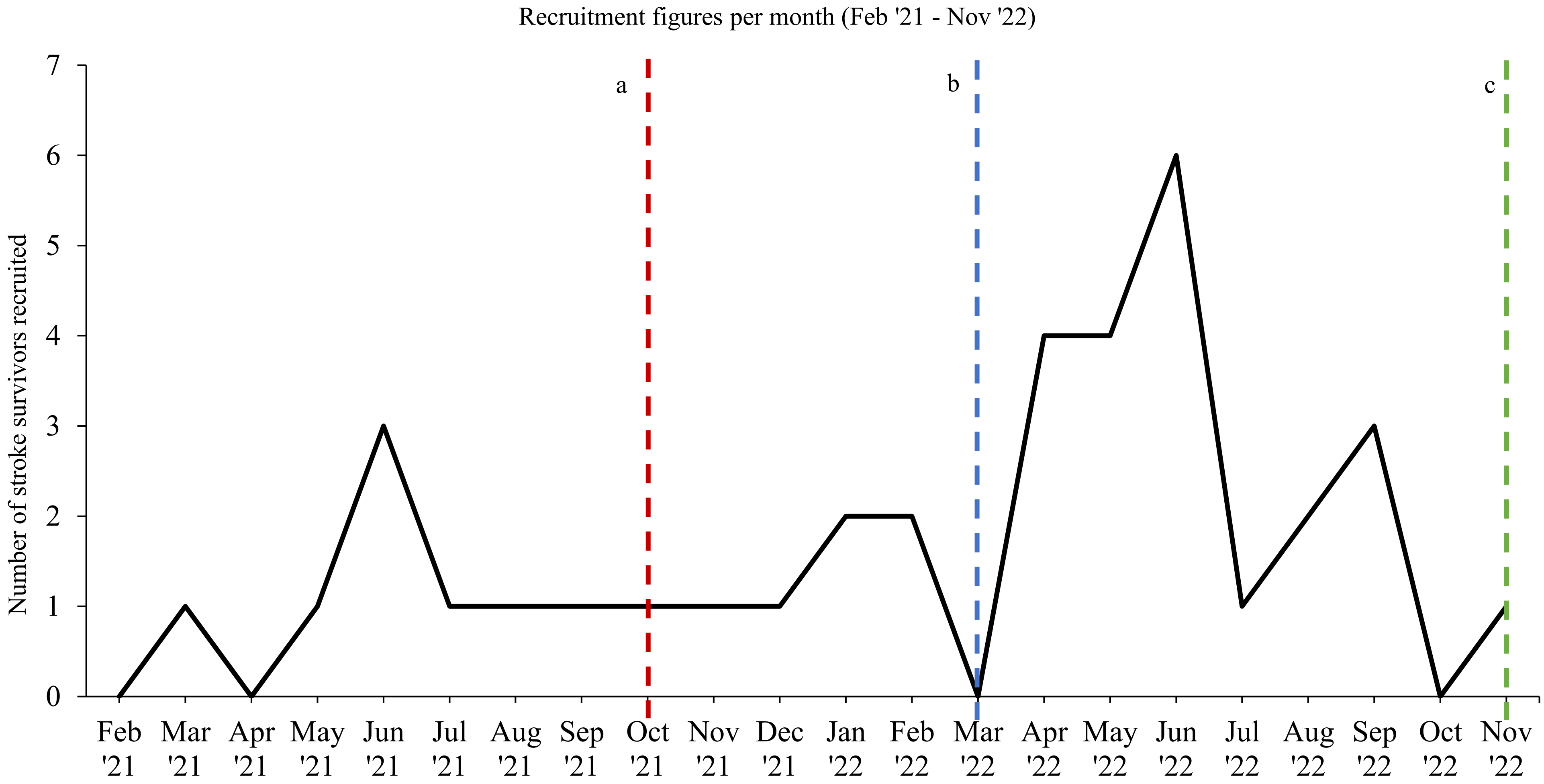

Figure 4.7. Recruitment figures over all recruiting sites over a 22-month period. Dotted lines show amendments to eligibility criteria to increase recruitment. Red line A shows removal of inclusion criteria '*one-week post-stroke*'; Blue line B shows removal of exclusion criteria '*no previous strokes*'; Green line C shows removal of inclusion criteria must '*have capacity to consent*'.

On average, participants completed T0 106.07 days (SD = 55.19) post-stroke and 52.88 days (SD = 33.97, 19-138) after recruitment. The large number of days between recruitment and T0 was often due to delayed discharge from inpatient care (i.e., hospital, rehabilitation units) or ill health. The time needed from stroke onset to baseline visit reflects the time taken for screening for eligibility, recruitment, and notification of new recruit to the research team and collection of paperwork.

Two stroke survivors showed no signs of spatial neglect at T0 and were moved to the no neglect study (previous chapter). The remaining 17 (47.22%) of stroke survivors recruited did not complete T0. Of these, 8 (22.22%) participants withdrew due to: anticipation using computer-based intervention (n= 2), poor health (n= 1), plans to move abroad (n= 1), refused home visit (n= 1), and no reason given (n= 3). Three (8.33%) were excluded due to disease progression (i.e., end-of-life care; n= 2) and second stroke (prior to exclusion criteria change; n= 1). Two (5.56%) did not respond to contact attempts and two (5.56%) passed away. Finally, two were awaiting to completed T0 visit at the time of write-up.

Allocation and blinding

The 15 participants who completed baseline assessments were allocated using minimisation. Blinding was successful; there were no reports of unblinding of participants, carers or outcome investigator. Group sizes are presented in **Figure 4.5** and **Table 4.5** and **4.6**, and were balanced in size; active intervention (n = 7) and control (n = 8). Mean age for both the active intervention (m = 70.43) and control group (m = 71.38) were similar. As seen in **Table 4.5**, the control group had slightly more stroke survivors with right hemisphere lesions (n = 6 of 8; 75%) compared to the active intervention group (n = 4 of 7; 57%).

Table 4.5. Demographic and clinical data for intervention and attentional control group.

	ID	Age	Sex	Side of stroke	Type of stroke	Location	Length of stay	Days post-stroke
Intervention (n= 7)	**SS01**	72	M	R	Isch	Frontal, lateral parieto-occipital, cortical border	13	139
	SS06	88	F	B	Isch	L. midbrain, pons, occipital pole, R. cerebellar	57	113
	SS09	54	M	L	Isch	Occipital region, putamen	1	62
	SS14	74	F	R	Isch	MCA, occipital lobe	-	252
	SS03	72	F	R	Isch	Posterior MCA	21	70
	SS10	66	M	L	Isch	MCA	-	118
	SS08	67	M	R	Haem	MCA	136	167
	M (*SD*)	**70.43 (*10.23*)**					**45.60 (*54.68*)**	**131.57 (*64.52*)**
Control (n= 8)	**SS02**	74	M	R	Isch	MCA	43	57
	SS07	77	M	R	Isch	MCA, superior temporal gyrus, Wernicke's area	7	32
	SS11	78	M	R	Isch	MCA	4	50
	SS04	71	M	R	Isch	Thalamus, temporal	7	77
	SS12	71	M	L	Isch	MCA	103	136
	SS05	67	M	R	Isch	Occipital, temporal, basal ganglia	-	100
	SS13	64	F	R	Haem	Posterior internal capsule	98	121
	SS15	69	M	L	Isch	-	14	97
	M (*SD*)	**71.38 (*4.81*)**					**39.43 (*43.76*)**	**83.75 (*36.13*)**

Note: Participants in bold completed the trial; M = mean; SD = standard deviation; M = male; F = female; R = right hemisphere; L = left hemisphere; Isch = Ischaemic; Haem = Haemorrhage; MCA = middle cerebral artery; Length of stay (days); Days post-stroke refers to time from stroke onset to baseline visit.

Table 4.6. Baseline assessment and quality-of-life scores for intervention and attentional control group.

Group	ID	OCS Impairment		BIT Star	OCS Cancellation: Acc	OCS Cancellation: Egocentric	OCS Cancellation: Allocentric	VAS	Personal neglect		Line bisection error	Stroke Impact Scale (%): Phys	Cog	Mood	Comm	ADLs	Mob	Hand	Social	Recov
Intervention (n= 7)	**SS01**	P, A		48 *	42	0	24 *	8.5	18		7.55 *	100	100	86.11	100	97.50	100	100	62.50	80
	SS06	P, V, A		48 *	35 *	-1	0	1.5	16		1.05	37.50	100	27.78	85.71	37.50	16.67	20	9.38	50
	SS09	A		51 *	46	-1	0	4.5	18		3.15	87.50	85.71	77.78	78.57	100	77.78	85	59.38	85
	SS14	M, N, V, A		24 *	24 *	19 *	3 *	3	18		28.25 *	37.50	35.71	58.33	71.43	22.50	16.67	0	0	10
	SS03	A		52	44	0	4 *	0	18		2.2	81.25	89.29	75	100	77.50	58.33	55.00	40.63	45
	SS10	L, M, A		48 *	42	1	2 *	3	18		-12.35 *	62.50	75	72.22	64.29	55	69.44	0	46.88	30
	SS08	M, V, A		16 *	10 *	10 *	5 *	5	18		66.35 *	6.25	96.43	25	96.43	65	16.67	25	28.13	90
			Mdn (*IQR*)	**48 (*27*)**	**42 (*20*)**	**0 (*11*)**	**3 (*5*)**	**3 (*3.50*)**	**18 (*0*)**	**M (*SD*)**	**13.74 (*26.15*)**	**58.93 (*26.04*)**	**83.16 (*34.45*)**	**60.32 (*21.97*)**	**85.20 (*27.16*)**	**65.00 (*29.30*)**	**50.79 (*37.19*)**	**40.71 (*35.80*)**	**35.27 (*22.77*)**	**55.71 (*19.63*)**
Control (n= 8)	**SS02**	N, P, V, A		13 *	44	-1	8 *	0.5	18		6.65 *	68.75	82.14	58.33	89.29	67.50	77.78	0	53.13	65
	SS07	A		54	43	0	0	3	18		7.8 *	37.50	85.71	66.67	96.43	97.50	61.11	70	18.75	60
	SS11	M, P, A		52	42	-5 *	0	2	18		8.7 *	68.75	35.71	88.89	71.43	82.50	88.89	75	75	60
	SS04	L, V, A		54	37 *	8 *	1	8	18		-6.1 *	81.25	85.71	86.11	92.86	97.50	94.44	75	59.38	70
	SS12	L, M, N, A		44 *	14 *	-6 *	2 *	4	15		-7.1 *	18.75	25	22.22	28.57	30	5.56	15	28.13	45
	SS05	V, A		32 *	19 *	11 *	2 *	8	18		21.9 *	37.50	89.29	52.78	100	32.50	19.44	0	50	20
	SS13	N, A		52	36 *	4 *	5 *	1	18		9.05 *	6.25	75	83.33	85.71	32.50	5.56	0	9.38	25
	SS15	L, M, V, A		51	39 *	-6 *	0	9	18		0.7	43.75	0	66.67	39.29	45	72.22	10	25	30
			Mdn (*IQR*)	**51.50 (*15*)**	**38 (*15*)**	**-0.5 (*11.50*)**	**1.50 (*3.50*)**	**3.5 (*6.5*)**	**18 (*0*)**	**M (*SD*)**	**5.20 (*9.37*)**	**45.31 (*26.04*)**	**59.82 (*34.45*)**	**65.63 (*21.97*)**	**75.45 (*27.16*)**	**60.63 (*29.30*)**	**53.13 (*37.19*)**	**30.63 (*35.80*)**	**39.84 (*22.77*)**	**46.88 (*19.63*)**

Note: Participants in bold completed the trial; Mdn = median; IQR = inter quartile range; Oxford Cognitive Screen (OCS) Impairment summarises which domain participant has a deficit; P = praxis; A = attention; V = vision; M = memory; N = Number, L = language; * denotes impairment; M = mean; SD = standard deviation; Behavioural Inattention Test (BIT) Star Cancellation Test (cut off ≤51; Wilson et al., 1987); Acc = overall accuracy (cut-off <42); Egocentric neglect score (cut-off <-2, >3); Allocentric neglect score (cut-off <-1, >1; Demeyere et al., 2015); VAS = Visual Analogue Scale (Ronchi et al., 2020); Personal neglect measured using One-item Test (Fortis et al., 2010); Line bisection error in millimetres (mm); The Stroke Impact Scale (Duncan et al., 1999) scores out of 100%, higher score indicates higher functioning; Phys = Physical domain; Cog = Cognition; ADLs = Activities of Daily Living; Hand = hand functionality; Recov = Recovery rating score 0-100 (0= no recovery; 100 = complete recovery).

Table 4.7. CENT performance for intervention and attentional control group.

Group	ID	**CENT Line Bisection test** Error	**CENT Cancellation Test** Accuracy	Egocentric score	Allocentric score	Errors	Re-cancellations	Asymmetry time score	Intersections		Search speed	Quality of Search
Intervention (n= 7)	**SS01**	25.60% *	35 *	0	0	0	0	-27.25% *	10		53.98 *	0.10 *
	SS06	-1.70%	34 *	-2	1	1	1 *	17.11% *	19		52.50 *	0.10 *
	SS09	-1.70%	49	1	0	0	0	-15.91%	4		66.40 *	0.24
	SS14	2.90%	25 *	-19 *	0	0	2 *	82.05% *	20		38.18 *	0.05 *
	SS03	-0.30%	48	1	-1 *	1	0	0.17%	0		49.07 *	0.19 *
	SS10	-	-	-	-	-	-	-	-		-	-
	SS08	-	-	-	-	-	-	-	-		-	-
	Mdn (*IQR*)	**-0.30% (*15.95*)**	**35 (*19*)**	**0 (*11.5*)**	**0 (*1*)**	**0 (*1*)**	**0 (*1.50*)**	**0.17% (*71.16*)**	**10 (*17.50*)**	**M (*SD*)**	**52.03 (*10.14*)**	**0.14 (*0.08*)**
Control (n= 8)	**SS02**	6.70% *	45 *	3 *	0	0	4 *	-17.16%	12		89.80 *	0.25
	SS07	5.10% *	48	1	0	0	0	-19.67%	13		118.29	0.28
	SS11	1.00%	49	-1	0	0	0	-2.91%	9		54.02 *	0.20
	SS04	-6.80% *	48	-2	0	0	1 *	-23.19%	1		69.82 *	0.19 *
	SS12	-	-	-	-	-	-	-	-		-	-
	SS05	28.80% *	6 *	-6 *	0	0	0	100.00% *	0		17.20 *	0.01 *
	SS13	-5.20%	37 *	5 *	3 *	5 *	0	-29.80% *	13		61.41 *	0.11 *
	SS15	2.10%	40 *	4 *	0	0	0	-5.17%	15		60.47 *	0.13 *
	Mdn (*IQR*)	**2.10 (*11.90*)**	**45 (*11*)**	**1 (*6*)**	**0 (*0*)**	**0 (*0*)**	**0 (*1*)**	**-17.16 (*20.28*)**	**12 (*12*)**	**M (*SD*)**	**67.29 (*31.31*)**	**0.17 (*0.09*)**

Note: Participants in bold completed the trial; Mdn = median; IQR = inter quartile range; * denotes impairment; Error in % from true centre of line (cut-off <-6.40, >5); Accuracy (cut-off <46); Egocentric score (cut off <-2, >2). Positive score = right egocentric neglect. Negative score = left egocentric neglect; Allocentric score (cut-off <0, >1). Positive score = right allocentric neglect. Negative score = left allocentric neglect; Errors (distractors cancelled; cut-off >1); Re-cancellations (cut-off >0); Asymmetry time score in % (cut-off <-26.92, >12.58). Positive score = more time on right. Negative score = more time on left; Intersections (frequency search path crosses over itself; cut-off >20.00); M = mean; SD = standard deviation; Search speed (age related cut-offs; 50-59 <96.49, 60-69 <91.29, 70-79 <96.77, 80-94 <82.93); Quality of Search (age related cut-offs; 50-59 <0.24, 60-69 <0.27, 70-79 <0.20, 80-94 <0.13); SS10, SS08, SS12 unable to complete CENT due to insufficient space for equipment set-up.

The active intervention group was tested slightly later post-stroke (m = 131.57 days) and had a longer average hospital stay (m = 45.60 days), compared to the control group (m = 83.75 days post-stroke; m = 39.43 length of stay). This may be related to the fact that the active intervention group had more severe neglect according to their group average paper-and-pencil and CENT scores. Full demographic and clinical characteristics for each group are reported in **Table 4.5.**

Staff intervention fidelity

There was a mean fidelity rate of 78.72% across the sample who received the allocated intervention (n= 10). **Figure 4.8** shows the mean fidelity rates at each intervention delivery stage. Fidelity was highest during c-SIGHT set-up, training and telephone check-in call (>85%). Within these sections, fidelity was lacking due to lack of evidence of correct set-up or instruction delivery, either through lack of photographs, videos, or Case Report Forms. However, fidelity was relatively high for both groups in terms of set-up and training of the intervention.

The lowest fidelity was on the final training days (m = 34.56%) since all seven participants who completed the 10-day intervention phase did not complete the final session with the delivery staff present. Three participants did not complete the final session with the staff member since the Day 10 visit was completed later than true Day 10, as it fell on a weekend (n = 2) or the participant missed the appointment (n = 1). Other reasons included: participant had packed equipment away prior to staff arrival (n = 2); participant had very low engagement (i.e., hadn't been using c-SIGHT regularly; n = 1); no reason recorded (n = 1).

It is worth noting that SS08 with severe neglect did not receive the allocated intervention due to a lack of space for equipment set-up in the participant's care home room. Another (SS12) did not receive c-SIGHT 2 due to *"specialist seating [meant the] motion sensor*

[Kinect sensor was] unable to pick up patient's movements". Unfortunately, no other details were provided, nor was there a suitable alternative seating based on the participant's mobility needs.

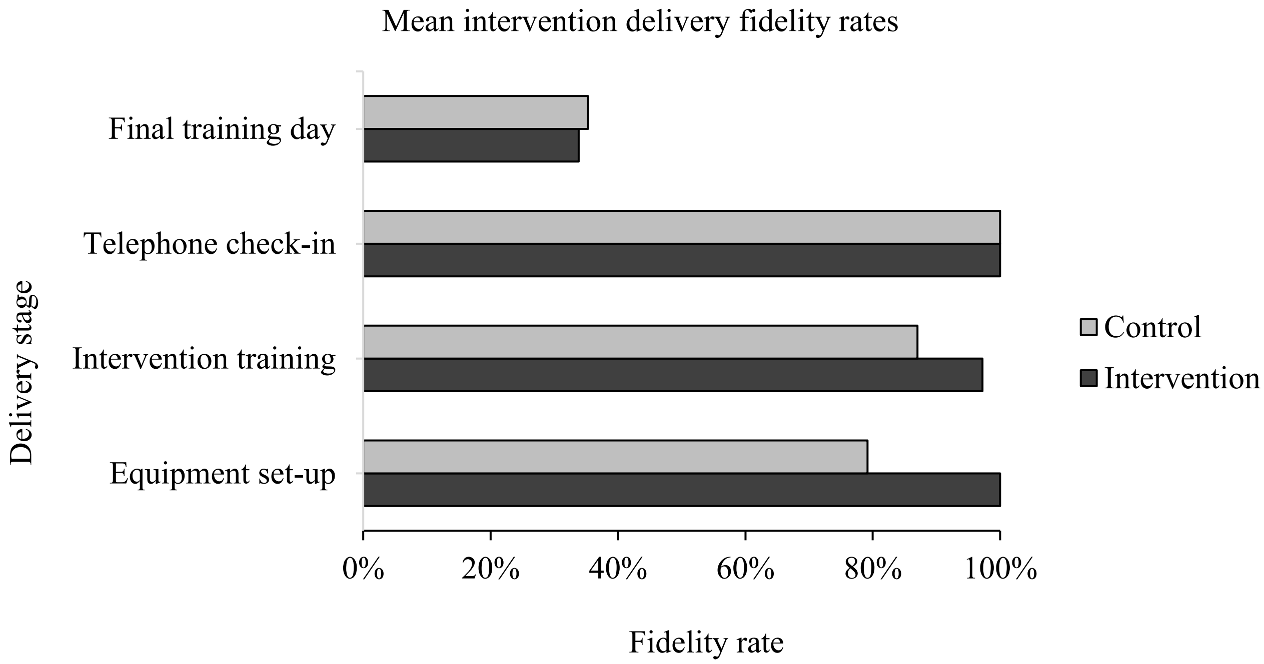

Figure 4.8. Bar graph showing mean fidelity rates (%) at each intervention delivery stage for each group.

Participant intervention fidelity (adherence)

Of 15 participants randomised, 10 had c-SIGHT successfully set-up in their homes. Of these, seven (70%) completed the training phase. Adherence data for all participants by group is shown in **Table 4.8**. Of the six who received the control version of c-SIGHT, three (50%) withdrew part-way through. One participant (SS05) disliked the exercises (i.e., lifting the rods from one end), while another (SS13) experienced pain in their (less impaired) upper limb from lifting the rods. The final participant (SS15) withdrew part-way through since they found using the equipment (i.e., laptop) "*too confusing*" due to problems retaining new information (e.g., using the laptop to start up the c-SIGHT application).

Overall, fidelity to dosage was moderate. Participants completed 70.42% of the 20 prescribed sessions and there were a high number of repetitions (m= 802.29, SD= 786.81) across groups. Though the intervention group completed more sessions (m= 16.5) compared to the control group (m= 11.67). This is likely due to drop-outs and the nature of the exercises (e.g., though the number of sessions were the same in each group, those in the intervention group generally performed more repetitions in order to balance the rods).

Only one participant had a 100% fidelity score as they completed the correct number of sessions, twice a day for 10 days. Remaining participants did not have 100% fidelity due to: completing more than the set sessions (20%), repeating sessions (80%), or not completing 20 sessions (70%). Participant SS06 unknowingly experienced technical difficulties whereby the sensor did not detect lifts in 22 of 23 sessions.

Outcome measure completeness and drop-outs

Of the 15 allocated participants, six (40%) completed the post-training assessment visit (T1). All six participants completed the outcome assessments, aside from one participant who did not complete CENT due to problems seeing the stimuli on the television. The remaining nine (60%) participants did not complete the T1 visit since they did not receive the allocated intervention (n = 5; **Figure 4.5**) or withdrew part-way through receiving the allocated intervention (n = 3). One participant missed the T1 visit due to a holiday abroad but completed the one-month follow-up (T2).

In total, seven (100%) of the participants who received their allocated intervention completed T2 and all accompanying outcome assessments (**Table 4.2**). At group level, all participants who received the active intervention (c-SIGHT 1) completed all follow-up visits

(T1, T2). Whereas 50% (n = 3) of participants in the control group (c-SIGHT 2) completed the T1 and T2 visits since there was a higher number of drop-outs (n = 3) in the control group. Half of the participants at T1 and T2 completed the Stroke Impact Scale questionnaire (Duncan et al., 1999) posted to them ahead of the visit.

Table 4.8. Adherence data for participants by group.

Group	ID	Mean session length	Total time	Sessions started	Sessions finished	Total repetitions	Sessions complete
Intervention (n= 4)	SS01	17m 23s	07hr 14m 25s	26	25	1539	125%
	SS06	13m 44s	05hr 02m 00s	23	21	39	105%
	SS09	17m 10s	05hr 43m 11s	20	20	1639	100%
	SS14	05m 30s	00hr 16m 31s	3	0	127	0%
	M	**13m 27s**	**04hr 34m 02s**	**18**	**16.5**	**836**	**82.50%**
	(*SD*)	**(*05m 33s*)**	**(*03hr 00m 22s*)**	**(*10.30*)**	**(*11.21*)**	**(*871.19*)**	**(*56.05*)**
Control (n= 6)	SS02	17m 19s	03hr 45m 06s	14	13	320	65%
	SS05	12m 33s	01hr 15m 21s	6	3	221	15%
	SS07	16m 22s	05hr 11m 05s	19	19	1731	95%
	SS11*	12m 52s	01hr 55m 44s	9	7	224	35%
	SS13*	16m 50s	01hr 07m 22s	4	3	325	15%
	SS15*	16m 16s	00hr 48m 49s	3	2	182	10%
	M	**15m 25s**	**3hr 23m 48s**	**13**	**11.67**	**757.33**	**58.33%**
	(*SD*)	**(*02m 31s*)**	**(*1hr 59m 23s*)**	**(*6.56*)**	**(*8.08*)**	**(*844.67*)**	**(*40.41*)**

Note: M = mean; SD = standard deviation; Participants with * shows they withdrew part-way through training phase and were not included in calculation of means; m = minutes; s = seconds; hr = hours; repetitions refer to number of rod lifts; sessions complete shows % of the 20 sessions completed.

4.3.2 Safety

There were no SAE's related to c-SIGHT 1 or 2. Although one participant withdrew due to pain in their shoulder from lifting the rods in the control group. There were nine Serious Events (SE's) not related to c-SIGHT 1 or 2 including: three deaths; five hospital admissions (due to new stroke event, infection, fall, progressive disease); one participant was referred to end of life care. Three of these events involved participants who had begun study activities (i.e., at least baseline assessment visit). Of these, one participant reported (SS02) a chest infection during the intervention training phase which limited their ability to continue with intervention temporarily (3 days).

4.3.3 Potential effects of c-SIGHT

i. Neglect measures

Overall cancellation test accuracy scores improved following the training phase in the intervention group. More specifically, these participants found more targets in cancellation tasks both in peripersonal (i.e., paper-and-pencil tests; **Table 4.9**) and extrapersonal (CENT; **Table 4.10**) space. The improvements were largest immediately following the training phase in the BIT Star and CENT cancellation task. In the control group, there was a temporary improvement in OCS cancellation task immediately after the training phase, however there was no improvement in the BIT Star cancellation task nor the CENT cancellation task over time.

The control group showed a reduction in rightward bias over time in both the paper-and-pencil and the CENT line bisection task. Similarly, this group spent more time searching on the left side of the screen in extrapersonal space (see asymmetry time score; **Table 4.10**) immediately after the training phase, which then reduced one-month later. The intervention group spent more time searching on the left side of the screen at one-month follow-up. Paradoxically, the intervention group displayed a larger rightward bias over time in both the paper-and-pencil and CENT line bisection tasks. Similarly, the intervention group had a larger rightward bias (egocentric score; i.e., found more targets on the right versus left) in the OCS cancellation task immediately after the training phase. The control group showed an opposite effect; they found more targets on the left side immediately after the training phase.

There were minimal changes in allocentric scores in peripersonal neglect assessments and the CENT task in either group over time. According to the median VAS scores, the intervention group self-reported lower neglect severity following the training phase. In contrast, the control group had a slight increase in self-reported neglect severity. There was no change in personal neglect scores in either group, since both groups performed at ceiling at each time-point.

Outcome measures for the carer of SS02 (in the control group) are presented in **Figure 4.9**. Caregiver strain and carer (n= 1) rated neglect severity was highest at T0 (except VAS which was marginally higher at T2), lowest at T1 and increased slightly at T2 (**Figure 4.9**). In other words, this carer perceived improvements in their partner's neglect severity immediately after the training phase.

ii. Search organisation and efficiency

The intervention group showed an improvement in search organisation (fewer intersections) and efficiency (quality of search) immediately following and one month after the training phase. The improvement in quality of search was larger immediately after the training phase. Search speed showed no change immediately following the training phase but became faster (more efficient) at one-month follow-up. In contrast, the control group had a faster mean search speed immediately after the training phase, but minimal change at one-month follow-up. The control group also showed a decline in both search organisation and efficiency immediately after the training phase, but a small improvement at one-month follow-up.

Table 4.9. Scores on neglect assessments at each time point per group: active intervention (n = 4) and attentional control (n = 3).

Measure	Group	T0	T1	T2
LB error (mean, *SD*)	Intervention	10.00 (*12.46*)	13.93 (*8.98*) ▼	10.80 (*7.88*) ▼
	Control	7.72 (*1.03*)	5.98 (*0.25*) ▲	3.18 (5.28) ▲
BIT Star (mdn, *IQR*)	Intervention	48 (*20*)	53 (*25*) ▲	50.50 (*36*) ▲
	Control	52 (-)	40.50 (-) ▼	51 (-) ▼
OCS cancellation				
Accuracy	Intervention	38.50 (*18*)	39.50 (*26*) ▲	42 (*23*) ▲
	Control	43 (-)	46 (-) ▲	42 (-) ▼
Egocentric	Intervention	-0.50 (*15*)	4.72 (*9*) ▼	1 (*15*)
	Control	-1 (-)	-2.50 (-) ▼	0 (-) ▲
Allocentric	Intervention	1.50 (*19*)	0 (*18*) ▲	1 (*17*) ▲
	Control	0 (-)	3 (-) ▼	1 (-) ▼
VAS	Intervention	3.75 (*5.60*)	1.75 (*5.30*) ▲	1 (*3.13*) ▲
	Control	2 (-)	5.50 (-) ▼	4.50 (-) ▼
Personal neglect	Intervention	18 (*2*)	18 (*0*)	17.50 (*1*) ▼
	Control	18 (*0*)	18 (*0*)	18 (-)

Note: T0 = baseline; T1 = post-training; T2 = one-month follow-up visit; M = mean; SD = standard deviation; Line bisection error in millimetres (mm); ▲ indicates an improvement in group mean/median score (e.g., a reduction in spatial neglect bias score) compared to baseline and ▼ indicates a decline (e.g., increase in spatial neglect bias score), no arrow indicates no change; Behavioural Inattention Test (BIT; Wilson et al., 1987); VAS = Visual Analogue Scale (Ronchi et al., 2020); Personal neglect measured using One-item Test (Fortis et al., 2010). Missing n = 1 from control group for measures collected at T1.

Table 4.10. CENT scores at each time point per group: active intervention (n= 4) and attentional control (n= 3).

Measure	Group	T0	T1	T2
Line bisection error (mdn, *IQR*)	Intervention	0.60% (*21.63*)	3% (*18.68*) ▼	7.20% (*21.38*) ▼
	Control	5.10% (-)	4.60% (-) ▲	5.10% (-)
Cancellation task				
Accuracy	Intervention	34.50 (*18*)	43 (-) ▲	32.50 (*22*) ▼
	Control	48 (-)	47 (-) ▼	48 (-)
Egocentric	Intervention	-1 (*16*)	-1 (-)	0.50 (*18*) ▲
	Control	1 (-)	1.50 (-) ▼	-1 (-) ▼
Allocentric	Intervention	0 (*1*)	0 (-)	-1 (*6*) ▼
	Control	0 (*0*)	0 (*0*)	0 (*0*)
Errors	Intervention	0 (*1*)	0 (-)	1 (*16*) ▼
	Control	0 (*0*)	0 (*0*)	0 (*0*)
Re-cancellations	Intervention	0.50 (*2*)	0 (*0*) ▲	0.50 (*2*)
	Control	0 (-)	0 (*0*)	0 (*0*)
Asymmetry time score	Intervention	0.60% (*90.23*)	0.31% (-) ▲	-8.11% (*81.81*) ▲
	Control	-17.16% (-)	-24.13% (-) ▼	-9.95% (-) ▲
Intersections	Intervention	14.50 (*14*)	8 (-) ▲	7 (*20*) ▲
	Control	12 (-)	19.50 (-) ▼	11 (-) ▲
Search speed (mean, *SD*)	Intervention	52.76 (*11.55*)	52.05 (*18.09*) ▼	63.42 (*7.98*) ▲
	Control	87.37 (*32.20*)	98.76 (*16.12*) ▲	88.91 (*17.57*) ▲
Quality of search	Intervention	0.12 (*0.08*)	0.16 (*0.13*) ▲	0.13 (*0.12*) ▲
	Control	0.24 (*0.04*)	0.23 (*0.04*) ▼	0.27 (*0.61*) ▲

Note: T0 = baseline; T1 = post-training; T2 = one-month follow-up visit; Mdn = median; IQR = inter quartile range; Error in % from true centre of line; ▲ indicates an improvement in group mean/median score (e.g., a reduction in spatial neglect bias score) compared to baseline and ▼ indicates a decline (e.g., increase in spatial neglect bias score), no arrow indicates no change; Egocentric score = positive score = right egocentric neglect, negative score = left egocentric neglect; Allocentric score = positive score = right allocentric neglect, Negative score = left allocentric neglect; Asymmetry time score in % = positive score = more time on right, negative score = more time on left; M = mean; SD = standard deviation. Missing n = 1 from control group for measures collected at T1. Missing n = 1 from intervention group at T1.

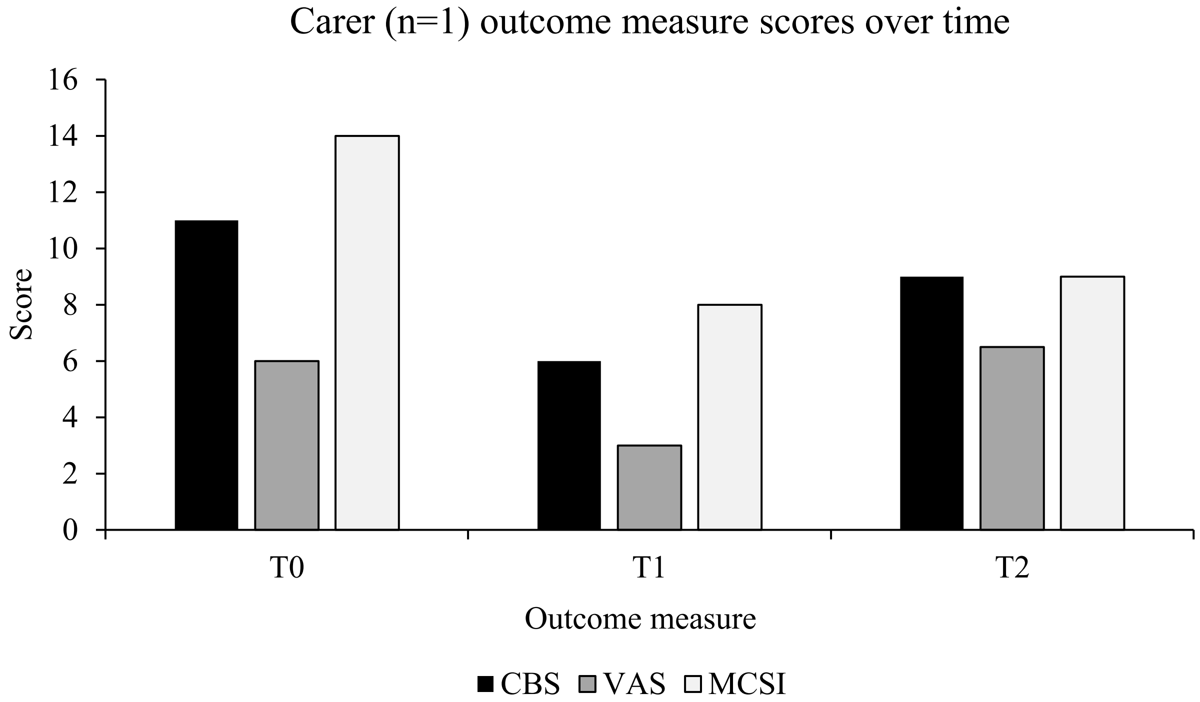

Figure 4.9. Bar graph showing outcome measure scores for carer of participant SS02. Carer outcome measures shown include, the Catherine Bergego Scale (CBS), Visual Analogue Scale for neglect (VAS), and Modified Caregiver Strain Index (MCSI). Higher scores indicate higher neglect severity and caregiver strain.

iii. Quality-of-life

The Stroke Impact Scale (Duncan et al., 1999) domain scores over time for each group are presented in **Figure 4.10**. Overall, participants in the control group self-reported more improvements in all domains (except mood) following the training phase. In contrast, the intervention group had minimal or no improvements over time across all domains. The only exception was within the social domain where there was a large increase in the mean score immediately after the training phase, which declined at one-month follow-up. There was a large spread of scores in both groups, perhaps representing the heterogeneity of post-stroke consequences within each group.

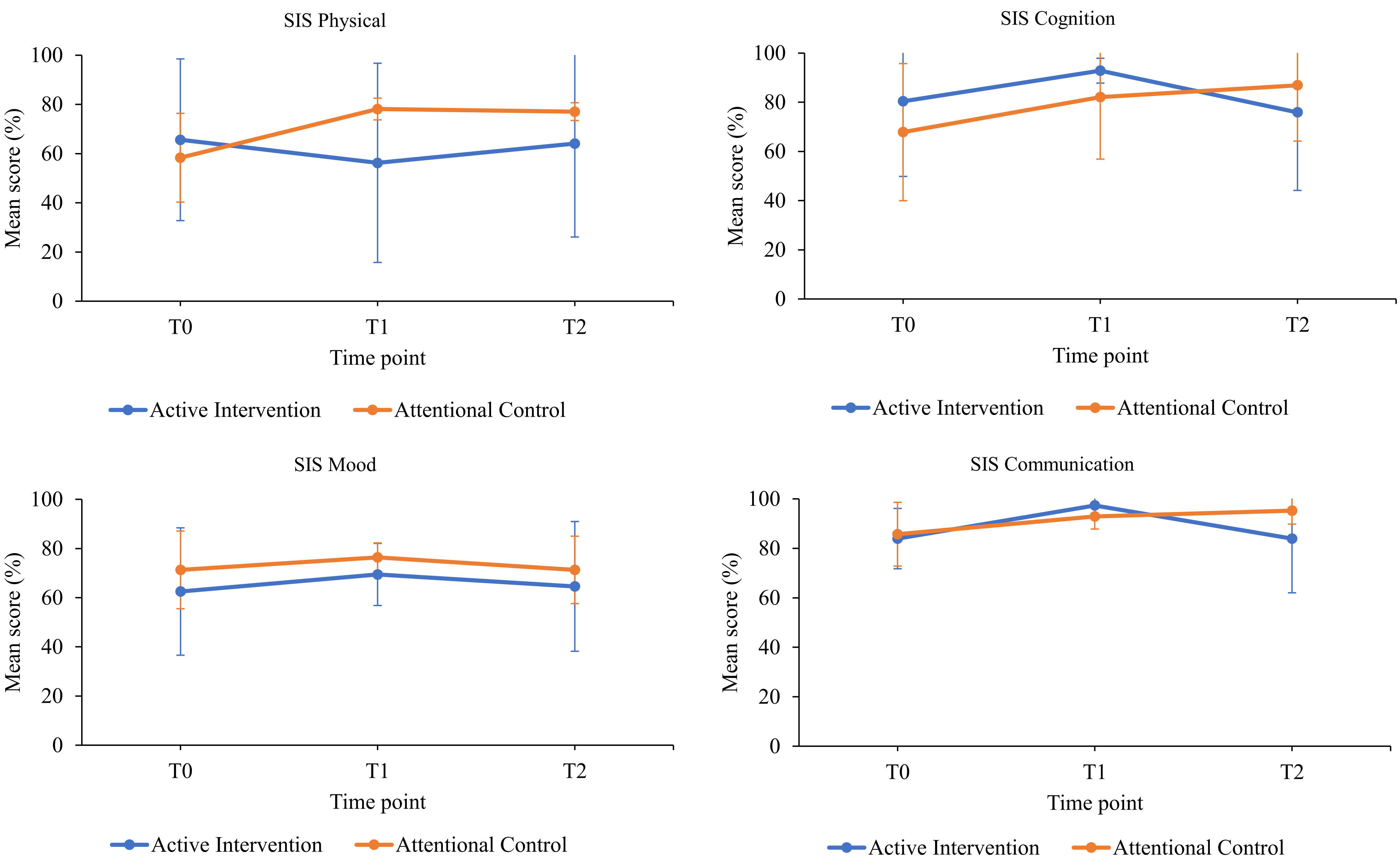

Figure 4.10. Graphs showing Stroke Impact Scale (Duncan et al., 1999) domain scores at each timepoint (baseline; T0, post-training; T1, one-month follow-up; T2) per group: active intervention (n= 4) and attentional control (n= 3). Error bars show standard deviation. Higher score indicates higher functioning. Recovery rating score 0-100 (0= no recovery; 100 = complete recovery).

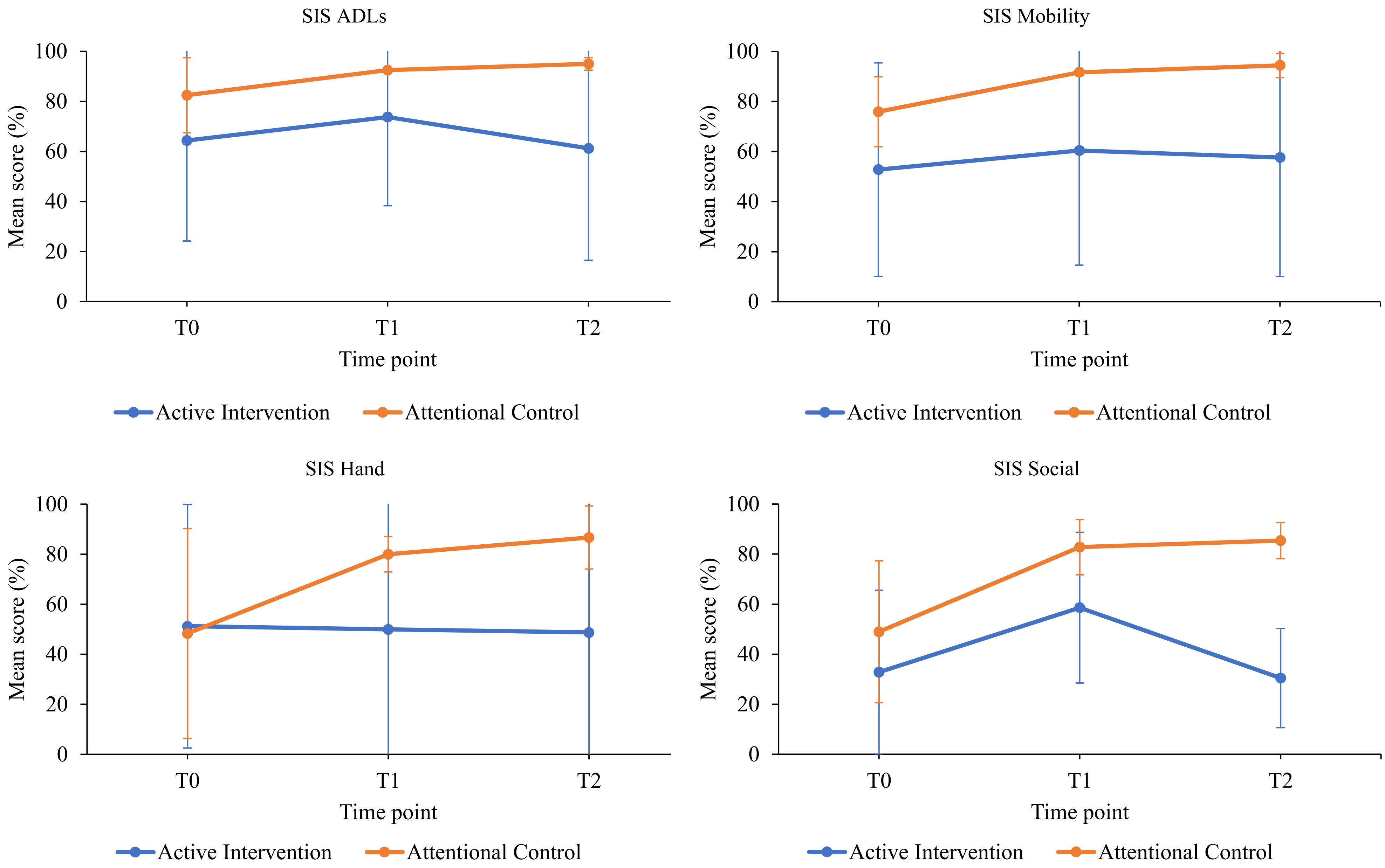

Figure 4.10. Graphs showing Stroke Impact Scale (Duncan et al., 1999) domain scores at each timepoint (baseline; T0, post-training; T1, one-month follow-up; T2) per group: active intervention (n= 4) and attentional control (n= 3). Error bars show standard deviation. Higher score indicates higher functioning. Recovery rating score 0-100 (0= no recovery; 100 = complete recovery).

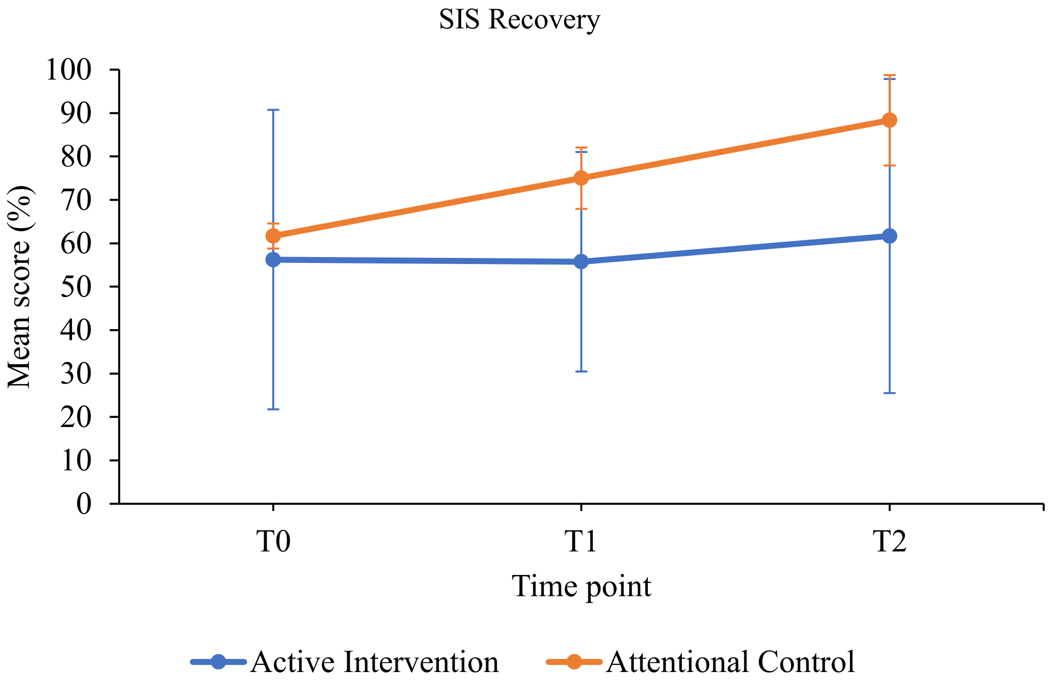

Figure 4.10. Graphs showing Stroke Impact Scale (Duncan et al., 1999) domain scores at each timepoint (baseline; T0, post-training; T1, one-month follow-up; T2) per group: active intervention (n= 4) and attentional control (n= 3). Error bars show standard deviation. Higher score indicates higher functioning. Recovery rating score 0-100 (0= no recovery; 100 = complete recovery).

4.3.4 Participant experience and feedback

Exploring participants' experience using c-SIGHT revealed three major themes: considerations in a home environment, engagement factors, and future suggestions. **Table 4.11** presents a summary of codes used to create major themes, along with corresponding quotes.

i. Considerations in a home environment

Participants highlighted that c-SIGHT required sufficient space and noted the volume of equipment left in the home.

"It's a lot of equipment lying around" – SS14

"finding somewhere to put it … it was tight" – SS09

Although participants didn't report any issues with having the equipment in their homes, SS14 was worried about equipment getting damaged.

"Technology is probably quite expensive … I didn't want anything to get damaged" – SS14

SS01 and SS11 liked the convenience of having the equipment at home.

"Come down in the morning, and I'd sit here and set this up" – SS01

However, older age and the lack of familiarity with technology made it difficult for SS11 to switch the system on. Consequently, they requested an additional home visit to provide assistance and additional training.

"I've just got too old to be flexible enough to remember how to do things I was use to do" – SS11

Carer (C01) of SS02 noted relief that the system was simpler than they expected to use. Likewise, carer and family involvement were noted by SS14 and SS11 as a consideration in use at home, since their partners either weren't interested or not confident using technology.

"I thought it was very straightforward to understand, which was a great relief … 'cause we're not a computer generation" – C01

Finally, SS07 noted that they were uncertain about what to do when their c-SIGHT sessions were interrupted at home (e.g., by telephone, doorbell), since there was no pause functionality.

"Interruptions, so I didn't know whether and if...didn't know what I was meant to do" – SS07

ii. Engagement factors

Three stroke survivors (one in the intervention arm) and the carer did not understand the purpose of the exercises, nor how they could be beneficial. This was more frequent in the control group.

"I personally didn't see any benefits, and I didn't understand how" – SS07

"Mystified really about what that was trying to do" – SS14

All but SS07 reported good tolerance to the exercises. SS11 thought of the exercises as a game, which he found enjoyable and engaging. In contrast, SS01 and SS06 expressed relief when they had finished their daily sessions. SS07 found them over simplistic, repetitive and wanted something more challenging.

"They're the sort of things I enjoy … playing games" – SS11

"I don't want to do it because it's boring" – SS07

Conversely, C01 and SS11 were positive that the exercises were simple to follow. This enabled SS11 and SS02 to carry out the control group exercises independently. Within the intervention arm, SS09 found the exercises difficult at first, but soon became familiar and no longer needed the instructions.

"Once he'd got into what he was supposed to be doing, I didn't need to help him or anything" – C01

"Once you know what to do, you don't, well I didn't need the instructions" – SS09

Motivators in engagement varied between participants. SS09 and SS06 were motivated by being instructed to complete the exercises. Whereas, SS01 viewed the exercises as a challenge. SS06 and SS14 were motivated to complete the exercises to help others.

"I did it… Because I was told to … I hope it benefits somebody one day" – SS06

"I felt some good could come out of it and could help someone" – SS14

Participants either thought the dosage was too much (n= 3; control) or manageable (n= 3; intervention group). These participants also noted that their adherence to dosage deviated to what was recommended. For example, two participants reported lower engagement and completed less than recommended. C01 shared that SS02 completed both sessions back-to-back to avoid setting-up the equipment multiple times a day. Similarly, three stroke survivors (n= 2 intervention group) experienced achiness in their (unimpaired) arm from the repetitive exercises.

"I broke it up … ten days was manageable" – SS09

"He just did one, had a little break, and then did the other one … it was more convenient to do two together" – C01

"Eventually your arm does get a little bit tired" – SS01

Finally, participants did not report any perceived benefit in their neglect symptoms from using c-SIGHT 1 or 2. If they did experience a change in post-stroke symptoms, it was attributed to improving over time. However, SS02 reported physical improvements in their left hand from the repetitive exercises.

"This movement has improved the situation of the left hand" – SS02

iii. Future suggestions

Participants provided a number of suggested changes to improve the usability of c-SIGHT. The first suggestion was to reduce the repetitiveness of instructions. SS07 thought the length of the instructions made the sessions too long, and SS09 did not need the instructions after the first few sessions. Although most (n= 4) participants thought the instructions were clear, SS02, SS07 and SS11 felt they misinterpreted the instructions in where to place the rod. Specifically, they believed the instructions could be clearer in their sequencing and where to place the rod on the mat. SS09 proposed this could be made clearer by colouring the whole rod, rather than just the ends.

"I made errors in lifting the rod a bit too early" – SS02

Participants reported some technical barriers, such as: the sound of the robotic voice delivering instructions, sensor sensitivity (i.e., either overly sensitive or not detecting lifts), and no record of session completion (e.g., completed sessions not indicated on the drop-down list). C01 and SS01 shared that they experienced difficulty remembering what session had been completed, resulting in repeating sessions. C01 suggested adding a function to display a 'tick' next completed sessions, and SS09 requested 'humanising' the computerised voice.

"I put up with it, but it was a bit of a drone" – SS09

"If it could just have like a tick to say you've definitely done that one" – C01

Additionally, SS01 suggested adding a function to go back to the menu mid-session to enter their name if forgotten. These suggestions could be considered going forward to reduce any risks to engagement.

4.3.5 c-SIGHT usability

Across stroke survivors (n= 7) and a carer, the system was graded C (m= 65.94, *SD*= 20.18), or ‘OK’ usability. Within groups, participants in the control group had a higher average rating (grade C, m= 70, *SD*= 12.08) than the intervention group (grade D, ‘Poor’, m= 61.88, *SD*= 27.57). System Usability ratings are presented in **Figure 4.11**.

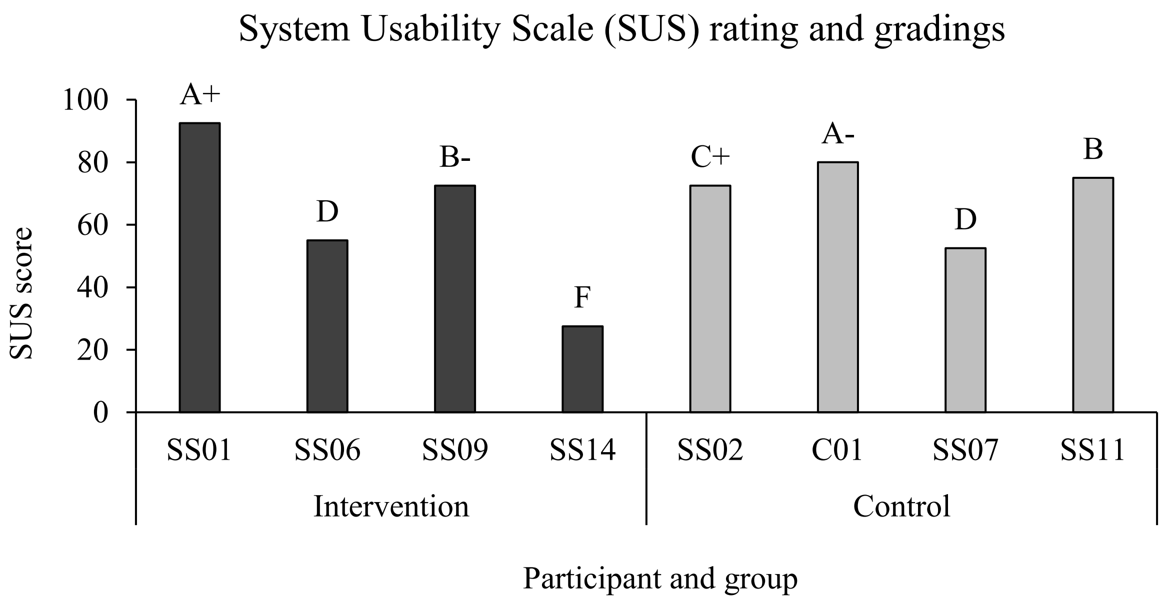

Figure 4.11. Bar graph showing SUS ratings and gradings for c-SIGHT Intervention and Attentional control groups. C01 denotes data for carer of SS02.

Table 4.11. Table displaying three major themes, corresponding codes and example quotes from one-to-one semi structured interviews with stroke survivors (n = 7) and one carer.

Theme	Code	Example
Considerations in a home environment	Cost/value	"Technology is probably quite expensive … I didn't want anything to get damaged" – SS14
	Space	"finding somewhere to put it … it was tight" – SS09
	Age and technology	"I've just got too old to be flexible enough to remember how to do things I was use to do" – SS11
	Carer involvement	"I thought it was very straightforward to understand, which was a great relief … 'cause we're not a computer generation" – C01
	Equipment	"It's a lot of equipment lying around" – SS14
	Convenience	"Come down in the morning, and I'd sit here and set this up" – SS01
	Interruptions	"Interruptions, so I didn't know whether and if...didn't know what I was meant to do" – SS07
	Considering others	"might be one or two people, perhaps who might find that a bit difficult" – SS01
	Help	"I had to invite, ask them to come out again to explain how to switch the screen on" – SS11
	User	"mistake by the user" – SS01
Engagement factors	Purpose of exercises	"Mystified really about what that was trying to do" – SS14
	Perceived benefits	"This movement has improved the situation of the left hand" – SS02
	Dosage	"He just did one, had a little break, and then did the other one … it was more convenient to do two together" – C01
	Motivators	"I felt some good could come out of it and could help someone" – SS14
	Enjoyment (or lack of)	"I don't want to do it because it's boring" – SS07
	Experience with technology	"I worked with computers when I was working … so that wasn't something that bothered me" – SS14
	Fatigue	"Eventually your arm does get a little bit tired" – SS01
	Simple exercises	"Once you know what to do, you don't, well I didn't need the instructions" – SS09
	Tolerance	"I think feeling while using it was fine" – SS01
	Symptom awareness	"I wasn't aware before that I was not seeing things" – SS01
	Games	"They're the sort of things I enjoy … playing games" – SS11
	Levels of difficulty	"It wasn't challenging enough" – SS07
	Familiarisation	"It was a bit slower because he was working it out" – C01
	Independence	"Once he'd got into what he was supposed to be doing, I didn't need to help him or anything" – C01
	Repetitiveness	"It was so repetitive" – SS07
	Focus	"I was watching what I was doing" – SS07
Future suggestions	Instructions (e.g., clarity, repetitiveness)	"I made errors in lifting the rod a bit too early" – SS02
	Technical barriers	"When I raised my hand, it wouldn't see me" – SS14
	Session list	"If it could just have like a tick to say you've definitely done that one" – C01
	Voice/instructions	"I put up with it, but it was a bit of a drone" – SS09

4.4 Discussion

The primary aim of this study was to determine whether a trial of this kind - using a home-based computerised rehabilitation intervention post-stroke - could be run (feasibility). The results would inform if a larger, subsequent trial should follow. Here, though the effect of COVID-19 was significant, the results demonstrate that further review of aspects of the trial, such as recruitment, eligibility criteria, attentional control intervention, participant adherence, and c-SIGHT usability are required before moving forward to a larger trial. Other aspects of the trial (allocation, blinding, staff delivery fidelity) were successful and some preliminary potential effects from the active intervention are promising. To the best of our knowledge, this trial shows for the first time, that it is feasible for NHS staff (e.g., research and non-research clinicians) to set-up and train participants to use a home-based computerised intervention for spatial neglect post-stroke.

The largest risk to the success and validity of the trial was recruitment, which was significantly lower than expected; averaging one participant per month across five recruiting sites. In total, approximately 5% of stroke survivors screened were enrolled onto the trial, and the final sample size was dramatically less than originally planned (n= 7 instead of n= 46 stroke survivors with spatial neglect). This is substantially lower than similar feasibility studies with the same clinical population, which enrolled 22% of screened participants (Longley et al., 2022). However, one must consider that the previous trial was carried out in an inpatient rehabilitation unit prior to the COVID-19 pandemic, and screened stroke survivors with spatial neglect only over 10 recruitment sites. In contrast, the present trial screened all stroke admissions which included recruitment to a no spatial neglect sub-study (which successfully recruited n = 71 stroke survivors). Although, our average monthly recruitment rate was similar to the previous study which averaged around two participants per month (Longley et al., 2022).

Recruitment for the current trial was challenging due to the effects of the COVID-19 pandemic. The COVID-19 lockdowns and measures between March 2020 and December 2021 (Institute for Government, 2022) had both a direct (i.e., suspension of non-COVID-19 trials; Thornton, 2020) and indirect (i.e., 14% of NHS redeployed; YouGov, 2021) impact on recruitment rates. The direct effects to this trial were twofold. First, the study was due to begin in April 2020, but much like 80% of non-COVID-19 trials (van Dorn, 2020), key trial activities (i.e., data collection visits) were paused until May 2021. Second, two sites who expressed interest in participating no longer had capacity to take part and another recruiting site did not open until February 2022 (12 months after the first site opened). Indirect effects were to staff capacity at sites. For instance, 10 eligible potential participants were not invited since sites did not have staff to consent these stroke survivors prior to discharge. Staff capacity was also variable between sites and impacted study activities other than recruitment. For example, sites with dedicated research teams or protected research time screened and recruited significantly more participants compared to those without (e.g., at the acute hospital). Those with limited capacity were also unable to report data on usual care (e.g., rehabilitation) set-out in the protocol or screen all stroke admissions.

Overall, the effect of the COVID-19 pandemic on recruitment nationally was substantial. In April 2022 almost 46% of trials adopted onto the National Institute of Health Research (NIHR) study portfolio were "*recruiting at a significantly lower rate than expected*" (Department of Health & Social Care, 2023). For this reason, planning future research studies using the recruitment rates from this trial must be done with caution since it may be overly conservative. Recruitment rates may have been slightly higher (e.g., similar to Longley et al., 2022) if recruitment was carried out pre- or post-COVID-19 pandemic, particularly since up to 52.10% of NIHR studies are now meeting or exceeding recruitment targets (Department of Health & Social Care, 2023).

The effect of COVID-19 on recruitment aside, there was a high exclusion rate at screening. This was a direct effect of the inclusion/exclusion criteria implemented at the beginning of the trial but may also reflect the fact that all stroke admissions were screened (i.e., those with spatial neglect were not screened in isolation thus many who did not have neglect were excluded). With a future RCT in mind, this is a lesson learnt to broaden inclusion/exclusion criteria as much as possible to better reflect the stroke population. However, this decision would be highly dependent on the aim of the trial. An explanatory trial, that is, a trial evaluating the efficacy of an intervention "*under ideal conditions*" (p. 285, Roland & Torgerson, 1998) may have stricter exclusion criteria. Arguably, this trial took an explanatory approach since the original eligibility criteria aimed to recruit a homogenous stroke population (e.g., first stroke only, no other neurological conditions, capacity to consent). Explanatory trials are useful in answering specific scientific questions (Roland & Torgerson, 1998), such as investigating which stroke survivors may respond better to the intervention based on their lesion location. However, when the eligibility criteria begun to negatively impact recruitment and was subsequently changed, the trial took a more pragmatic approach. Pragmatic trials are designed to better reflect the heterogeneity of patients in usual care settings, and in other words "*represent the patients to whom the treatment will be applied*" (p. 285, Roland & Torgerson, 1998). This approach to intervention trials is superior if the ultimate aim of the feasibility study is to investigate whether the intervention would be beneficial to patients within routine clinical practice (Roland & Torgerson, 1998). Future research following this trial should consider which approach is more appropriate for answering the aims of the study, taking the ultimate goal of the research into consideration; whether it is to investigate the *effectiveness* in clinical practice (pragmatic), or the *efficacy* of an intervention in ideal conditions (explanatory; Roland & Torgerson, 1998). This decision would affect other aspects of the design (e.g., delivery setting, standardised versus flexible delivery). Of course, the choice between the two approaches is not mutually exclusive. Instead a trial could sit within a continuum between the two (e.g., by using The Pragmatic-Explanatory Continuum Indicator Summary 2 Wheel in **Appendix F**; Loudon et al., 2015).

Another risk to the trial was the high drop-outs compared to similar trials (Aimola et al., 2014; Longley et al., 2022). Drop-outs were highest between enrolment to receiving the allocated intervention. Almost half of drop-outs between enrolment and allocation were due to participant withdrawal. A potential contributing factor to this may have been that often consent was taken while participants were in hospital/inpatient rehabilitation units and upon returning home were too overwhelmed or unwell to take part in a clinical trial. This links to the report that up to 45% of stroke survivors report feelings of abandonment post-discharge (Stroke Association, 2018), and that being discharged from hospital to the community often feels like "*falling off a cliff*" (Stroke Association, 2015 p. 6). With this in mind, future recruitment methods could instead identify participants within stroke care settings but obtain consent once participants have returned home to reduce withdrawal. Involving community rather than acute (e.g., inpatient hospitals) NHS stroke services to act as recruitment sites may be more a more pragmatic approach to target stroke survivors within the community, especially since c-SIGHT is a home-based intervention. The recruitment and drop-out rates in this trial tell us that a trade-off may be required between obtaining higher recruitment rates (e.g., including acute hospitals who were high recruiters), or higher participant retention by recruiting participants post-discharge (e.g., recruiting from community NHS stroke services only).

Importantly, blinding of participants and outcome assessors was successful. This is an improvement on the proof-of-concept study (Rossit et al., 2019) and reduces the risk of bias in collecting outcome measures. Therefore, the use of a blinded outcome assessors and computer-generated method of allocation (including automated email notifications) should be considered for future trials given the high risk of bias in the current evidence exploring the efficacy of computerised therapies (Laver et al., 2017). Despite the use of minimisation, there was more heterogeneity (i.e., side of stroke, neglect severity) in the intervention versus control group in the final analyses. The control group had right hemisphere strokes only, whereas the intervention group had a mix of left, right, or bilateral strokes. Although these groups were smaller than originally planned and unbalanced in sample size, minimisation parameters could be reviewed to include more than two strata to better reflect the range of neglect severities (e.g., very, severe or mild/suspected; Volkening et al., 2018).

We found that NHS staff were able to deliver the novel computerised therapy (c-SIGHT) as intended. However, set-up of c-SIGHT was not feasible in a care home setting due to inadequate space for set-up (i.e., space for motion sensor) and lack of staff capacity to help the participant use the equipment. Unless changes are made to the system (e.g., replacing the sensor to reduce the space needed), then future trials may consider excluding residents in care homes. Within participants' homes, fidelity was highest during set-up/training participants and all participants were correctly trained to the allocated intervention. Unfortunately, fidelity was lowest towards the end of the training-phase as most participants did not complete the final session with NHS staff present. This was an issue in monitoring whether participants were following the same instructions and/or whether the equipment had moved. Going forward, increasing clarity of trial instructions may be required to ensure participants understand not to move the equipment until the NHS staff return on the final day.

Importantly, stroke survivors were able to self-administer c-SIGHT at home without the need of a therapist. Participants liked the convenience of a home-based intervention, and the technology was not a barrier to use. Some participants were positive about the use of technology, referring to it as a game and that it was simpler to use than expected. Although there were considerations in using the system at home. Most pointed out that the system needed substantial space within their (or other's) homes and that home-life (e.g., doorbell, phone ringing) interrupted some sessions. Other participants noted concern that the system may be difficult for those living alone, without the support of a carer or family member to help them use the system. However, some of the participants within this sample were able to use the system without the assistance of a partner/family member. The suggestions provided by participants are helpful to consider in further iterations and development of c-SIGHT, such as addressing technical barriers to use, including using a less robotic voice to deliver instructions, reducing the repetitiveness of instructions (in turn reducing length of sessions), and providing an indicator of which sessions are already completed. As technology advances, alternative equipment could be used to replace the Microsoft Kinect Sensor. The sensor requires space to use (over a metre) and some participants reported frustration with its sensitivity. Further refinement of the system is required based on participant feedback, with hopes to improve the current usability rating ('OK'), and ultimately participant adherence.

Fidelity to the dosage was low; only one participant successfully followed the prescribed dosage. Interviews with stroke survivors suggest that low adherence could have been due: to a lack of understanding of the purpose of the exercises, levels of difficulty (i.e., some found the control group exercises too easy), and fatigue. Fatigue (e.g., achy arm) was reported by participants in both groups, however more participants in the attentional control group did not understand the purpose of the exercises. Another participant (with mild neglect) found the control group exercises unchallenging and 'too simplistic'. These factors may contribute to the higher drop-out rate in the control group (n= 3) and low adherence. This finding was unexpected since previous studies using the same attentional control group exercises (i.e., lifting the rod from one end) reported no drop-outs during training phases (Harvey et al., 2003; Rossit et al., 2019).

Attentional control groups are used to improve the internal validity of a trial (Aycock et al., 2018). In other words, they are implemented to help us determine whether any therapeutic effects are related to the active intervention rather than other factors (e.g., trial participation, time; Spieth et al., 2016). Aycok et al. (2018) set-out nine considerations when designing an attentional control group, one being to ensure that exercises remain "*interesting and acceptable*", otherwise there is a risk of attrition (Aycock et al., 2018). The final sample from the attentional control group (n = 3) is too small to make any definitive conclusions as to whether the current attentional control was 'unacceptable', but the attrition rates suggest that the active intervention was more acceptable. This is unfortunate since the current attentional control exercises are well 'equalised' to the active intervention (Aycock et al., 2018), in that it uses the same equipment, set-up, training, therapist contact, and dosage, while removing the key therapeutic element of the intervention exercises (e.g., tilting of the rods; Harvey et al., 2003). Future studies could consider using a waitlist design which can overcome ethical issues of allocating participants to a control group (Aycock et al., 2018). Though the design is financially and time intensive, it enables all participants to use the active intervention (e.g., control group accesses the active intervention after the study ends) and may reduce feelings of unfairness in the control group (Aycock et al., 2018). Alternatively, future trials could also consider using an 'intention-to-treat' approach which retains all randomised participants until the end of the trial (e.g., follow-ups) irrespective of their noncompliance to the intervention (Gupta, 2011). This approach reduces risks of missing data and smaller samples sizes, thus improving statistical power (Wertz, 1995). It also takes a pragmatic approach since it better reflects clinical practice (Gupta, 2011). In this trial, an intention to treat approach would have meant more data at follow-up, including qualitative data collected from participants with very low adherence rates which could provide key information on improving c-SIGHT.

Potential effects of c-SIGHT will be discussed, but with the caveat that the sample size was unbalanced between groups and under-powered as a whole. The generalisability of the results is limited, particularly given the heterogeneity within the sample (e.g., side of hemisphere, neglect severity, time since stroke). Inspection of outcome measures revealed that there were some potential effects in the intervention group. Specifically, the intervention group was able to find more targets in both peripersonal and extrapersonal space at follow-up compared to the control group. Rossit et al. (2019) also reported improvements in (peripersonal) visual cancellation tasks after using SIGHT. Although our effects occurred more frequently immediately after training, while Rossit et al. (2019) found improvements in these tasks up to four-months after using SIGHT. Here, not only did the intervention group show an improvement in the accuracy in visual cancellation tasks, but they also demonstrated improved search organisation and efficiency in extrapersonal space. The intervention group also begun to spend more time searching on the left-side in extrapersonal space after using c-SIGHT. These are promising preliminary findings since it shows, for the first time, that c-SIGHT exercises carried out in peripersonal space could also improve visual search in extrapersonal space.

We did not see an improvement in the line bisection task in either peripersonal or extrapersonal space in the intervention group. In fact, the control group showed a reduction in line bisection error in both peripersonal and extrapersonal space. This was unexpected given that previous studies have found a reduction in line bisection bias following c-SIGHT (Rossit et al., 2019). Equally, previous research found no improvement (Harvey et al., 2003). This is interesting from a theoretical perspective since the line bisection task and c-SIGHT active intervention both involve bisecting (e.g., finding the middle) of horizontal lines and rods, respectively. In other words, both tasks are object-focused (or allocentric-based; (Demeyere & Gillebert, 2019; Ferber & Karnath, 2001; Sperber & Karnath, 2016). Here, it seems that an object-based intervention (c-SIGHT) produced improvements in egocentric tasks (e.g., visual search tasks) rather than object-based tasks (e.g., line bisection).

Finally, there were no substantial or long-lasting improvements in self-rated quality-of-life scores in the intervention group. In fact, the control group reported more improvements in various aspects of their quality-of-life post-stroke (e.g., physical, cognition, ADLs, mobility, hand function, social, recovery domains). The control group reported worsening neglect severity over time compared to the intervention group. Moreover, the carer of a participant in the control group reported improvements immediately following the training-phase. Perhaps this reflects recovery over time upon returning home and/or receiving usual care rehabilitation. Nonetheless, it is positive that the intervention group perceived an improvement in their neglect severity after using c-SIGHT. With this in mind, future studies could consider including an observational neglect assessment (e.g., KF-NAP; Chen et al., 2015) to reduce the potential biases in self-reporting, including anosognosia.

4.4.1 Limitations

Like previous studies investigating computerised therapies post-stroke (Gammeri et al., 2020; Laver et al., 2017) and rehabilitation for spatial neglect (Bowen et al., 2013; Longley et al., 2022), the major limitation of the current study is the small sample size. Consequently, the study results lack generalisability and power to make estimates in the potential effects of c-SIGHT. Similarly, the present study had a relatively short follow-up (one-month), compared to previous spatial neglect rehabilitation trials (e.g., Longley et al., 2022; Rossit et al., 2019; Ten Brink et al., 2017). Unfortunately a longer follow-up period was not feasible within the project timeframe, but would better capture any persisting effects of tested interventions (Bowen et al., 2013).

The outcome measures could have been expanded to include other aspects of post-stroke consequences which may impact engagement in rehabilitation (e.g., apathy; Tay et al., 2021). These outcomes were originally included in the study protocol but were removed to reduce study visit times during the COVID-19 pandemic. Including additional questionnaires (e.g., mood measures) could inform interpretation of quantitative (e.g., adherence) and qualitative (e.g., interview) data to better assess the usability of c-SIGHT. Additional measures of post-stroke effects could help understand specific barriers to use of c-SIGHT within different groups of stroke survivors (e.g., is low mood or apathy associated with lower adherence rates/drop-outs?).

In retrospect, interviews with intervention delivery staff (e.g., Longley et al., 2022) could have explored acceptability amongst clinicians and identified potential barriers and facilitators of implementing c-SIGHT. This, alongside participant interview data, would also provide feedback to inform future development/refinements of c-SIGHT to improve implementation.

Finally, aspects of feasibility (e.g., recruitment) are limited in their generalisability to inform future studies due to the extraordinary effects of the COVID-19 pandemic. In other words, the recruitment figures in the present study may not accurately reflect recruitment outside of a pandemic. Although, given the variation that exists in post-acute stroke services within the United Kingdom (SSNAP, 2021), recruitment strategy and NHS site recruitment numbers are likely to vary between regions. Even within the same region (East Anglia) recruitment within different NHS organisations and settings was highly variable depending on resources available (e.g., research time, staff numbers). Nonetheless, the recommendations proposed below based on the lessons learnt during this study could be useful to inform other similar studies.

4.4.2 Recommendations

Recommendations based on the current findings are summarised in **Table 4.12.** The recommendations here could be useful to inform research questions, design, methods, and reporting of similar studies. Using previous knowledge (e.g., recommendations) is important to reduce research waste (Grainger, Bolam, Stewart, & Nilsen, 2020). The recommendations provided here are particularly valuable since, to the best of our knowledge, this is the first randomised controlled trial investigating the use of a home-based, computerised rehabilitation tool for spatial neglect post-stroke.

4.4.3 Conclusion

The present findings suggest that it is feasible to train NHS staff to set-up and train participants to use a computerised telerehabilitation tool for spatial neglect in stroke survivors' homes. However, the COVID-19 pandemic posed a significant challenge in running this trial and affected key feasibility outcomes, such as recruitment. The small sample size from low recruitment and drop-out rates (e.g., in the attentional control group) negatively affected the power and generalisability of the current findings. Further review of these aspects of the trial design are warranted before informing a subsequent trial investigating the efficacy of c-SIGHT in a larger sample. These findings demonstrate the value of feasibility studies and their role in reducing research waste through understanding whether a trial design and intervention are suitable before moving onto larger studies (Morgan et al., 2018).

Feedback from our sample of stroke survivors suggest that c-SIGHT was acceptable to use at home, but adherence to the prescribed dosage was low. For this reason, further refinements of the system are required to address both technical and practical barriers to use identified here. Finally, we found some preliminary evidence (albeit in a small sample) of improvements in visual search in extrapersonal space after using c-SIGHT (active intervention). This is a novel finding and warrants further investigation. Despite the trial's limitations and challenges due to the COVID-19 pandemic, the findings and recommendations are useful in informing the design of future trials delivering a home-based intervention for stroke survivors with spatial neglect (or indeed other post-stroke consequence).

Table 4.12. Recommendations based on the current findings to inform similar future trials.

Aspect of trial	Recommendation
Recruitment	Consider NHS site capacity (e.g., resources, staff time) in assessing the number of sites needed to reach target. Use feasibility reports before inviting sites (e.g., number of patients with condition seen at site). Consider using community-based stroke services to reduce attrition rates (e.g., participants consent after discharged home). Routinely use expression of interest to identify eligible participants at acute stroke sites and obtain consent post-discharge as close to study activities as possible to reduce chance of drop-outs.
Eligibility criteria	Use the Pragmatic-Explanatory Continuum Indicator Summary 2 Wheel (Loudon et al., 2015) to guide eligibility choices. For instance, if a pragmatic approach is taken, keep eligibility criteria broad to better reflect the stroke population (e.g., inclusion of previous neurological conditions, cognitive impairments, no capacity to consent). Assess the practical considerations of the intervention (e.g., space, staff time) to consider whether participants in a care home should be excluded.
Allocation	Computerised allocation system using minimisation to balance groups. Additional strata used for minimisation (i.e., include more than two categories of neglect severity, e.g., very severe, severe, mild/suspected) to balance groups.
Blinding	Computerised allocation system with automated emails communicating directly with NHS delivery staff.
Intervention (e.g., delivery, system refinements)	Clearer instruction to participants to prevent them moving/packing-up equipment until delivery staff are present to perform monitoring checks. Reduce space required by modifying equipment used to measure adherence (e.g., replace Microsoft Kinect Sensor). Consider using a waitlist design to overcome ethical issues and drop-outs within the control group. See **Table 4.11** for participant suggestions.
Design	Use an intention-to-treat approach to reduce missing data and smaller final sample sizes. Use the Pragmatic-Explanatory Continuum Indicator Summary 2 Wheel (Loudon et al., 2015) to guide trial design to align with study aims.
Outcome measures	Observational ADL assessments. Measurement of post-stroke consequences (e.g., mood, apathy) which may impact engagement with the rehabilitation intervention. Longer and/or more follow-up(s) (e.g., 4-month; Rossit et al., 2019).
Implementation evaluation	Interviews with intervention staff delivery to assess potential barriers of implementation of intervention.

5. General Discussion

Overall, the studies presented within this thesis aimed to investigate the use of technology in the assessment and rehabilitation of spatial neglect. It first set out to demonstrate the capabilities of a computerised tool (CENT) in assessing visuospatial attention in healthy adults in extrapersonal (far) space. Following these results and collection of normative data, CENT was used to detect spatial neglect post-stroke in extrapersonal space – something which is not commonly assessed in both research and clinical practice. The subsequent, and final empirical chapter aimed to establish the feasibility of a two-armed randomised controlled trial using a novel computerised version of SIGHT (c-SIGHT) in stroke survivors' homes. This chapter also investigate the potential effects of c-SIGHT and used qualitative work to evaluate the usability of c-SIGHT to inform future development. Akin to the first two chapters, the final chapter posed to demonstrate the capabilities of technology when applied to an existing rehabilitation intervention. Specifically, how enhancing an intervention with a computer-based programme and motion sensor could facilitate self-administration at home (without the presence of a therapist) and asynchronous monitoring of user adherence, respectively. Below is a discussion of the main findings of each chapter.

5.1 Chapter 1: Aging effects on extrapersonal (far-space) attention

Data from 179 healthy adults aged between 18 and 94 years old (mean age = 49.29 years old) offered novel findings that visuospatial attention tasks (cancellation, line bisection) in far-space are sensitive to aging. Specifically, performance significantly declined in healthy adults over the age of 60 years old. The variables showing this age-related decline in visuospatial attention would not be detected without the use of a computerised test (e.g., CENT). The data also provided normative information to inform the detection of attentional deficits in clinical populations (e.g., stroke survivors). Providing age-graded normative data on variables known to be affected by age reduces the chance of false positives in diagnosing attentional deficits.

Older age was associated with slower processing speeds (i.e., task duration) on both the cancellation (visual search) and line bisection task. This finding replicated robust findings of slower processing speeds in older adults (Benjamins et al., 2019; Hommel et al., 2004; Müller-Oehring et al., 2013; Potter et al., 2012; Tamura & Sato, 2020; Warren et al., 2008). However, the findings here show that the aging effect in processing speeds generalises to extrapersonal space. Interestingly, older age was associated with poorer search organisation and efficiency in extrapersonal space, which could reflect a decline in processing speeds (i.e., making searches slower, ergo less efficient) and difficulty with inhibitory control (i.e., selecting targets amongst distractors becomes more difficult). Aging effects aside, the sample of healthy adults performed relatively inefficient searches. Therefore, this variable alone should not be used to determine whether an individual has attentional deficits (Benjamins et al., 2019).

Overall, healthy adults displayed a preference or 'over-attendance' to the left side of space (pseudoneglect). The leftward spatial bias was consistent between both the cancellation and line bisection tasks. For example, performance in the line bisection task revealed an age-resistant leftward bias. In other words, healthy adults – irrespective of age - marked the middle of lines to the left of the true midpoint. A similar effect was found in the cancellation task; 89% of the sample begun their search on the left and were faster at searching for targets on the left side. This finding lends support to the theory that spatial processing is dominant within the right hemisphere (Cicek, Deouell & Knight, 2009), and why spatial neglect (or inattention) is typically more severe following damage to the right hemisphere (Li & Malhotra, 2015).

Other aspects of performance were associated between the two tasks. Longer line bisection task time was associated with poorer search speed and quality of search. Associations in performance between cancellation and line bisection tasks in extrapersonal space has theoretical implications within the literature as it suggests that these two might measure similar aspects of attention - something that has long been debated (Ferber & Karnath, 2001; Keller et al., 2005; Molenberghs & Sale, 2011).

Finally, males were unexpectedly faster at searching for targets (but not more accurate) compared to females. This is a novel finding which has not been previously reported in visual search in extrapersonal space. Some theories offer to explain these findings (e.g., hemisphere asymmetry between sexes, evolutionary theories; Eals & Silverman, 1994; English et al., 2021; Stancey & Turner, 2010; Stoet, 2011), but more research is required to consider the role of personality factors (e.g., impulsivity; Riley et al., 2016) which were not measured here.

This study demonstrated the benefits of using a computer-based assessment (CENT). Specifically, CENT revealed interesting age-related effects of attention in extrapersonal space using variables (e.g., search organisation, efficiency) which would not be possible to measure using standard paper-and-pencil neuropsychological attention assessments. CENT's administration is arguably superior to previous methods of visual search tasks in extrapersonal space which have relied on manual proxy responses (e.g., participant uses a laser pointer and the experiment then records the response) and provided limited performance metrics, such as overall accuracy, re-cancellations or starting position (Berti et al., 2002; Buxbaum et al., 2012; Van der Stoep et al., 2013). The findings from Chapter 1 add knowledge to the scarce literature on assessing visuospatial attention in far-space. Understanding how healthy adults perform on attention tasks has implications in the accurate diagnosis of (underreported) attentional problems (e.g., spatial neglect) in extrapersonal space in clinical populations.

5.2 Chapter 2: Assessing spatial neglect in extrapersonal space after stroke

In a group of 57 stroke survivors, CENT identified 18 cases of neglect in extrapersonal space which would otherwise have gone undetected. Importantly, CENT's cancellation task had excellent diagnostic accuracy, sensitivity, and validity compared to the widely used, validated paper-and-pencil neglect tests. CENT also showed high agreement with these same tasks performed in peripersonal space. In fact, it is possible that accuracy scores in the CENT cancellation task better reflected quality-of-life since it was the only variable which significantly correlated with self-reported recovery post-stroke.

Consistent with previous literature (Bowen et al., 1999; Hammerbeck et al., 2019; Longley et al., 2022; Moore et al., 2021; Puig-Pijoan et al., 2018; Ringman et al., 2004; Rowe et al., 2019), 35% of the sample had peripersonal neglect in at least one validated paper-and-pencil neglect test (e.g., cancellation, line bisection task). Overall, it was more common for peripersonal and extrapersonal neglect to co-occur together than for one subtype to appear in isolation. Overall cancellation tasks (both paper-and-pencil/peripersonal and CENT/extrapersonal) were more sensitive in detecting cases of neglect compared to line bisection. However, there were more cases of neglect detected using the line bisection task in peripersonal versus extrapersonal space. These findings support the recommendation of the use of cancellation tasks in rapid neglect screening (Moore et al., 2022). But also have theoretical implications in the debate as to whether line bisection and cancellation task do or do not measure similar aspects of attention, since many stroke survivors who were impaired on the cancellation task were not impaired on the line bisection task (in both peripersonal and extrapersonal space).

This study could be the first to explicitly report (or indeed measure) allocentric neglect in extrapersonal space. There was a dissociation between ego- and allocentric neglect in both peripersonal and extrapersonal space. However, no stroke survivor had both subtypes in extrapersonal space. It is possible that the heterogeneity within the sample may have contributed to this since most of the stroke survivors had mild rather than severe neglect. Despite this, there were some paradoxical neglect behaviours which could be cases of ipsilesional neglect (previously observed in line bisection; Williamson et al., 2018) or showcase learned compensatory strategies (i.e., consciously searching on the neglected side) in chronic stroke survivors.

Finally, the study identified three variables which represented neglect-specific attentional deficits: cancellation accuracy score, re-cancellations, and quality of search. It seems these attentional parameters reflect neglect behaviour, such as the inability to detect targets in the neglect side of space (resulting in low accuracy), in turn affecting the efficiency of the visual search (quality of search). It also highlights the non-lateralised attentional deficits in spatial working memory (leading to re-cancellations) which occur with spatial neglect. Crucially, the study informed us which attentional parameters (search speed, longer processing speeds, errors) were not neglect specific, and therefore should *not* be used in isolation to determine the presence of neglect. Search organisation should not be used to determine attentional deficits (such as spatial neglect) post-stroke since there was a high variance in search organisation which was relatively poor across both stroke survivors and age-matched controls. This is consistent with both Chapter 1 and previous research (e.g., Benjamins et al., 2019).

It is likely that limitations in the data analyses used (i.e., grouping left and right neglect together) explained why lateralised variables (asymmetry time score, ego- and allocentric score, line bisection) were not found to be neglect specific. This appears to be a contradiction of the ‘core’ neglect deficit which would usually result in a lateralised bias (e.g., over attendance to the non-neglected side). Ultimately, CENT performance needs to be explored in a larger group of stroke survivors with analyses grouped by side of lesion/neglected space.

Crucially, using a computerised assessment facilitated the measurement of additional attentional parameters which have given us insight into which variables should or should not be used to inform diagnosis of neglect. In light of the promising psychometric properties of CENT (particularly the cancellation task), it could be used alongside other assessments to form part of a comprehensive neglect assessment battery to detect extrapersonal neglect (which often goes undetected). Since some variables were indicative of attentional deficits (e.g., processing speed) CENT could also be applied to detecting attentional deficits (e.g., other than spatial neglect) post-stroke. Finally, given the poor prognosis of neglect (Chen et al., 2015; Gillen et al., 2005; Hammerbeck et al., 2019; Jehkonen et al., 2006), assessing multiple subtypes (e.g., ego-, allocentric, extrapersonal neglect) using CENT could inform rehabilitation strategies to focus on specific impairments.

5.3 Chapter 3: A feasibility RCT of c-SIGHT post-stroke

Using a randomised controlled trial (RCT) design, this chapter presented preliminary evidence that it was feasible for NHS staff (e.g., research, clinical staff) to set-up and train participants to use a home-based, computerised rehabilitation intervention (c-SIGHT) for spatial neglect post-stroke. Moreover, stroke survivors with spatial neglect were able to self-administer c-SIGHT without the presence of a therapist. To the best of our knowledge, this is the first study to investigate the feasibility of a RCT using a computerised rehabilitation intervention for spatial neglect at home.

The COVID-19 pandemic caused significant barriers to the feasibility of the trial. Specifically, it negatively impacted recruitment to the study, both through delaying the opening of the study and reduction in NHS staff capacity to screen and consent stroke survivors. Recruitment was the largest risk to the statistical power and generalisability of the study findings. The final sample was significantly smaller (n = 7) than the target sample size (n = 46). High exclusion and drop-out rates (in the control group) also contributed to the small, final sample size. Further review of aspects of the trial design are needed before considering progressing to a subsequent trial. This includes review of eligibility criteria (informed by whether the trial is pragmatic or explanatory; Loudon et al., 2015; Roland & Torgerson, 1998) to reduce high exclusions rates, and consideration of recruitment from community-based stroke services only (rather than acute settings). The latter approach may be more effective in retaining participants by obtaining consent once participants are discharged home (and as close to study activities as possible). For example, a systematic review of recruitment methods used in 512 stroke rehabilitation RCTs found that recruiting stroke survivors from the community was the most effective strategy: 48% of stroke survivors screened in the community enrolled on the study, versus 27% screened in an acute setting (McGill et al., 2020). Additionally, stroke survivors in the chronic stage (over 6 months post-stroke) were also more likely to join an RCT compared to those in the acute stage (less than a month post-stroke; McGill et al., 2020).

Finally, review of the trial design may be required to reduce the drop-out during the intervention phase. Here, there was a high (50%) attrition rate within the control group. One study also reported a higher drop-out rate in their control group, which used a sham device (wrist watch) during limb activation therapy in stroke survivors with spatial neglect (Fong et al., 2013). The most reported reason for withdrawal was ‘lost interest’ (Fong et al., 2013). Within the present study, based on participant feedback, the high drop-out rate was likely due to a lack of understanding of the purpose of the control group exercises. Although previous studies using the same exercises did not report high attrition rates (Harvey et al., 2003; Rossit et al., 2019). Thus, future investigations may consider reviewing the attentional control exercises or modifying the trial design (e.g., use an intention-to-treat or waitlist design; Aycock et al., 2018).

A number of other aspects of the trial were successful and are recommended for similar trials going forward. Allocation using minimisation was successful, and reduced the heterogeneity between groups. Additionally, the blinding procedures used here were also successful. These aspects addressed limitations within the literature in which studies of interventions for spatial neglect often have a high risk of methodological bias (Bowen et al., 2013; Longley et al., 2021).

Importantly, stroke survivors with spatial neglect were able to use c-SIGHT independently at home (i.e., without a therapist/researcher). This is a novel finding given that, according to the current published literature, the majority of interventions for spatial neglect (including computerised tools) are still primarily used in a clinical setting with the assistance/supervision of a therapist/researcher (Svaerke et al., 2019). However, the variance in adherence rates and participant feedback suggests that further refinement of c-SIGHT is required. These refinements would address the technical (e.g., robotic voice, motion sensor sensitivity) and practical (e.g., space requirements) barriers and increase the usability of c-SIGHT.

Consistent with previous studies using (non-computerised) SIGHT (Harvey et al., 2003; Rossit et al., 2019), there was preliminary evidence of the positive effects of c-SIGHT. Of particular interest was that participants in the intervention group (c-SIGHT 1) displayed an improvement in their visual search (ability to find more targets, search organisation and efficiency) in extrapersonal space. The results have theoretical implications since they suggest that c-SIGHT (an *allocentric* based intervention carried out in peripersonal space) produced improvements in *egocentric* (e.g., visual search) tasks in extrapersonal space. In other words, c-SIGHT may be capable of producing therapeutic effects generalising to extrapersonal space and could potentially be used to rehabilitate this subtype of neglect. Interestingly, there was no improvement in allocentric based tasks (line bisection), which has been reported in previous studies (Rossit et al., 2019). These are novel findings since the majority of studies investigating interventions for spatial neglect do not include a specific measure of neglect symptoms in extrapersonal space. Though these results are based on a very small sample and lacks statistical power (no statistical tests were performed), these results warrant further investigation in a larger sample.

Overall, the findings from Chapter 3 demonstrate the value of feasibility studies in providing recommendations to inform future studies, in turn reducing research waste (Grainger et al., 2020; Morgan et al., 2018). Revision of a trial design is not uncommon; one review found that 32 of 60 trials made changes to the trial design (e.g., recruitment) in subsequent trials (McDonald et al., 2006). Sharing knowledge and recommendations (**Table 4.12)** from a novel study of this kind is critical to increasing the success of future studies (e.g., development of an intervention for spatial neglect), and societal impact (e.g., producing findings with real-life implications; Morgan et al., 2018).

5.4 Thesis limitations and future directions

The sample (overall and sub-group) sizes across the chapters affected the analyses used and generalisability of the results. Specifically, the smaller sample sizes in the older age groups in Chapter 1 (e.g., 80-94 years old) meant that some normative cut-off values were not produced. The overall sample size in Chapter 2 was sufficient for the analyses used, but it was not possible to run sub-group analyses (e.g., per side of lesion). Running these analyses would help isolate neglect versus hemisphere specific attentional deficits (Ten Brink et al., 2016, 2020; Van der Stoep et al., 2013) to aid interpretation of CENT performance (and ultimately diagnosis of neglect symptoms in far-space). Finally, the final sample size in Chapter 3 was a significant limitation in generalising the results. Although the aim of a feasibility trial is not to investigate efficacy, the current sample size meant that no statistical tests could be run to formally explore the potential effects of c-SIGHT. Unfortunately, the sample size in the feasibility trial contributed to the similarly small and underpowered sample sizes within the literature (Bowen et al., 2013; Longley et al., 2021), including those investigating computerised tools (Laver et al., 2017). This is problematic as it increases the chance of false positives in concluding whether an intervention is effective (Faber & Fonseca, 2014).

NHS capacity and staff work-loads were significantly affected during the COVID-19 pandemic (Thornton, 2020; YouGov, 2021), which directly affected recruitment to non-COVID-19 related trials nationally (van Dorn, 2020). Even outside of a pandemic, poor recruitment is common in clinical trials (e.g., 31% of trials achieve their target sample size without an extension; McDonald et al., 2006). The challenges of recruiting stroke survivors with spatial neglect to RCT (e.g., Chapter 3) represent similar challenges felt within the stroke rehabilitation research community. Recruitment to stroke rehabilitation trials is challenging. A review found that a median of 1.5 participants were recruited to stroke rehabilitation RCTs per month (per recruitment site; McGill et al., 2020). Recruitment rates were also significantly higher for rehabilitation trials aiming to improve overall disability or leg function post-stroke, compared to those targeting vision or cognition (McGill et al., 2020). Compared to other diseases, recruitment to cancer and drug trials has been more successful (McDonald et al., 2006). Perhaps this is related to the fact that research funding is comparatively lower for stroke (£48 per stroke survivor) versus cancer (£241 per person with cancer; Stroke Association, 2019). Historically, cancer has had the infrastructure (e.g., NHS networks) to facilitate integration of cancer research into clinical practice (McDonald et al., 2006). Though it seems things are changing; since the National Institute of Health Research (NIHR) was established in 2005, there is now a dedicated stroke speciality group which has helped recruit over 173,232 participants since 2015 (National Institute of Health Research, 2023).

Given that we know that recruitment to stroke rehabilitation studies is challenging - but more effective within the community - perhaps efforts should be made to centralise recruitment strategies for researchers (e.g., via national research databases). The NIHR's national 'Be Part of Research' (bepartofresearch.nihr.ac.uk) exists to help patients and public find studies for many diseases, however there is currently no national stroke specific research platform or database. Databases in other disease areas (i.e., Join Dementia Research; joindementiaresearch.nihr.ac.uk) facilitate the recruitment of participants to dementia research without relying on NHS resources (time, staff). For example, Join Dementia Research currently have over 60,000 people registered, with nearly 75,000 participants joined a study (joindementiaresearch.nihr.ac.uk). The resources – and financial cost - required to set-up, design, manage and govern a database of this kind (e.g., consent to contact for research) would be large, however systems could be put in place on regional, or indeed institutional levels to delegate these roles and streamline recruitment. For example, an institutional database could facilitate access to participants and save resources (and reduce research waste) by preventing recruitment procedures being replicated by different studies and researchers. A collaborative approach with open communication and transparency of studies, could mean that stroke survivors consenting to join a database may be eligible for multiple studies for different post-stroke consequences.

The next limitation of the thesis is the lack of lesion-symptom mapping analyses. These analyses were not feasible given the delays to the project caused by COVID-19. However, clinical brain scans were extracted for all stroke survivors recruited to both Chapter 2 and 3.

Performing lesion-symptom analyses to investigate the neural anatomical substrates associated with extrapersonal neglect (or indeed general attentional deficits) in Chapter 2 could have added valuable data as to whether peripersonal and extrapersonal neglect are anatomically dissociable. Research into understanding the neural underpinnings of neglect in extrapersonal space is currently lacking: there are only two studies using lesion-symptom mapping to investigate the neural underpinnings of neglect in different spatial regions, and of those, no consensus could be established (Moore et al., 2023). From a theoretical perspective, these analyses could have facilitated investigations as to whether lesions in ventral and/or dorsal visual processing streams are associated with deficits in extrapersonal and/or peripersonal space, respectively (Aimola et al., 2012; Van der Stoep et al., 2013). By doing so, the two-stream visual processing hypothesis (Goodale & Milner, 1992) could be applied to investigate whether there is a preferential bias for dorsal stream processing visual information in peripersonal space as it is in within 'actionable' space (Lane et al., 2013). Similarly, lesion-symptom mapping could be applied to participants in Chapter 3 to investigate whether lesions locations were associated with more/less improvements after using c-SIGHT. Ultimately, applying lesion-symptom analyses to the data reported in this thesis has the potential to inform both assessment and rehabilitation of spatial neglect post-stroke.

Fortunately, elements of this research (Chapter 3 recruitment) are ongoing, so it is hoped that further analyses (e.g., lesion-symptom mapping) could be carried out in future. Data collected and code written as part of thesis will also be (or already is, e.g., Chapter 1) open access for future analyses. Fortunately, research has shown that voxel-based lesion-symptom mapping using routine clinical (e.g., CT) brain scans to investigate the neural anatomical substrates of cognitive domains (e.g., attention) is possible (Moore & Demeyere, 2022). Using routine scans means that we can 'capitalise on clinical data' (Moore & Demeyere,

2022) and save funding which is needed to collect research neuroimaging data – costing up to £470 per MRI scan (British Heart Foundation, 2022).

The penultimate limitation of the work presented in this thesis is the limited assessment of the implementation of the computerised tools used. Although fidelity and acceptability of c-SIGHT was explored in Chapter 3, interviews with NHS delivery staff would have been useful in understanding the potential barriers to use of a computerised rehabilitation tool in clinical practice. This data would also add to the evaluation of usability to improve system functionality (Cavedoni et al., 2022).

No implementation evaluation was planned or carried out for CENT since the psychometric properties (e.g., diagnostic accuracy) were not yet known. These evaluations could be carried out now that Chapter 2 has demonstrated the utility of CENT. Given that there is currently no routine test for extrapersonal neglect in clinical practice, CENT could be used in both community and acute settings to form part of a comprehensive battery of post-stroke assessments. Using a computerised test provides additional attentional parameters to inform diagnosis and rehabilitation, as well as reducing time in calculating performance scores. Before this is possible however, further work is needed to establish the feasibility of using CENT in various healthcare settings. Previous qualitative work with clinicians has identified barriers associated with equipment needed to deliver a computerised (e.g., virtual reality) assessment for spatial neglect (Ogourtsova et al., 2017). More specifically, 11 occupational therapists reported that cost, space, and training requirements would be barriers to use of a computerised assessment in clinical practice (Ogourtsova et al., 2017). With this in mind, it is likely that some modifications may be required to make CENT more accessible for use in clinical settings. Particularly since CENT requires the participant – or patient – to be sat at a distance (ideally 170cm) from the screen presenting the CENT. Based on Chapter 2, we know that it is feasible to use CENT in *most* of the participants' homes, but there were occasions when it was not possible due to limited space. Modifications might include making use of existing equipment within clinical settings (e.g., a wireless mouse) rather than purchasing the Vive equipment used here which can cost up to £1,000. This would address barriers surrounding cost, simplify set-up, and training needs.

Ultimately, conducting further work on the implementation of both computerised tools (CENT and c-SIGHT) hopes to increase the chance of adoption into clinical practice (Ogourtsova et al., 2017). Increasing the transparency in how interventions are delivered in RCTs using standardised reporting (e.g., TiDier checklist used here; Hoffmann et al., 2014) will be essential in facilitating future implementation (e.g., replication by researchers, clinicians), and hopes to reduce the translational gap between research and practice (Rudd et al., 2020).

Finally, due to limitations discussed – particularly the small and underpowered final sample size in feasibility RCT – further work is needed to investigate the efficacy of c-SIGHT. Efforts were made to ensure that the feasibility RCT (e.g., quadruple blinding, sample size estimates, CONSORT reporting) improved upon the current quality of the literature investigating interventions for spatial neglect (Longley et al., 2021). Considering the impact of spatial neglect on stroke survivor's recovery (Chen et al., 2015) and family (e.g., informal carers; Chen et al., 2017), an effective treatment is needed. However, improving upon the current quality of the evidence (e.g., reviewed by Bowen et al., 2013; Longley et al., 2021) requires using more rigorous methods and reporting (Longley et al., 2021). RCTs – deemed the 'gold standard' design – are time intensive and expensive (Hariton & Locascio, 2018), particularly traditional parallel-group designs (The Adaptive Platform Trials Coalition, 2019). One review found that the mean time between beginning a traditional trial (including feasibility/pilot studies) to final results was 8 years and funding for full RCTs was up to £2.1 million (Morgan et al., 2018).

Innovative trial design, such as adaptive platform trials facilitate testing multiple interventions simultaneously for a specific condition (The Adaptive Platform Trials Coalition, 2019). Bayesian statistical models are used for randomisation, whereby participants are allocated to one intervention arm which is performing superiorly over interventions in other arms of the same trial (The Adaptive Platform Trials Coalition, 2019). These models enable the trial to become adaptive by using 'within-trial learning' (using information learnt *during* the trial, rather than after it has ended; The Adaptive Platform Trials Coalition, 2019). For example, interventions which appear not to be as effective can be terminated or participants may be moved from one arm to another. Moreover, stratification can be used to allocate subtypes within conditions (e.g., stroke) into intervention and control arms to allow for the inspection of the sub-group specific intervention effects (The Adaptive Platform Trials Coalition, 2019). This could be promising in the development of 'patient-centred precision medicine' (The Adaptive Platform Trials Coalition, 2019) and useful if applied to spatial neglect given its number of subtypes (e.g., manifesting in spatial regions, reference frames and sensory modalities).

Comparing multiple interventions in one 'master protocol' is more efficient as it saves significant time compared to running separate, serial intervention trials (Gold et al., 2022; The Adaptive Platform Trials Coalition, 2019). See **Appendix G** for an illustrative comparison (Gold et al., 2022). However, elements of these designs are complex (e.g., obtaining informed consent, statistical techniques) and obtaining funding for these trials can be difficult as they do not often have a fixed timeline or sample size (The Adaptive Platform Trials Coalition, 2019). Despite these challenges and considerations, these efforts may be worthwhile since features of these designs (e.g., 'within-trial learning', moving participants into different intervention arms) can help obtain more statistical power with fewer participants (The Adaptive Platform Trials Coalition, 2019). This could be particularly useful given the frequently limited sample sizes reported in the current spatial neglect (computerised and non-computerised) rehabilitation literature (Longley et al., 2021). A collaborative approach would be required in order to consider using an adaptive platform trial design to evaluate the efficacy of interventions for spatial neglect. To date, adaptive platform trial designs mostly use pharmaceutical interventions for cancer, flu and Alzheimer's disease (The Adaptive Platform Trials Coalition, 2019), and there are currently no adaptive platform trial stroke studies registered on ClinicalTrials.gov. There is scope to use these designs with behavioural interventions and increasing the efficiency of the research by directly comparing multiple interventions simultaneously (Gold et al., 2022). This would be advantageous for efficiently investigating rehabilitation techniques for spatial neglect, though careful considerations are required to prevent contamination of one intervention to another if participants are moved across multiple arms (Longley et al., 2021). Particularly since washout periods for some behavioural interventions are not known and effects from some interventions have been reported to last for months (e.g., SIGHT; Rossit et al., 2019).

5.5 Final remarks

This thesis demonstrates the utility, capabilities and feasibility of a computerised assessment and rehabilitation tool for spatial neglect post-stroke. The computerised assessment (CENT) contributes to the scarce knowledge of healthy aging (and sex) effects of visuospatial attention in extrapersonal space. It also demonstrates its capabilities in detecting rates of spatial neglect within extrapersonal space, which would otherwise go undetected post-stroke. This added knowledge (and computerised assessment) has practical applications in forming a comprehensive assessment of spatial neglect after stroke, in both research and clinical practice. Findings from the feasibility study contribute practical recommendations for future spatial neglect rehabilitation trials, as well as understanding that a computerised, home-based intervention can be used by stroke survivors with spatial neglect post-stroke. Ultimately, this thesis demonstrates the usefulness of technology in detecting spatial neglect and delivering rehabilitation to stroke survivors at home. Both aim to better support and improve people's lives after stroke.

6. References

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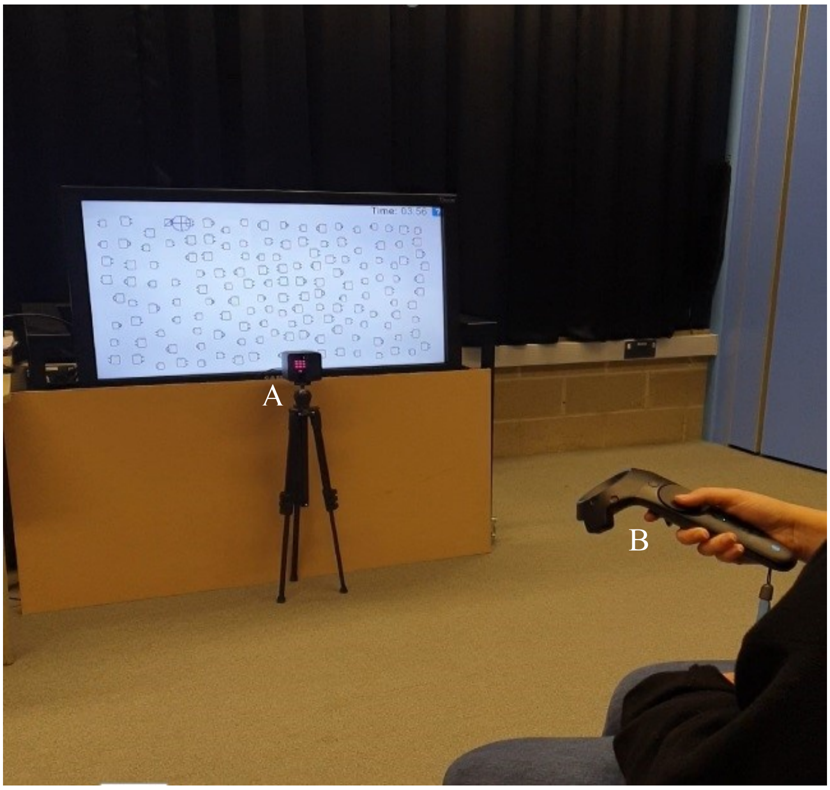
7. Appendices

7.1 Appendix A: Example set-up of CENT completion in Chapter 1.

CENT Cancellation task example set-up



For both tasks: participants were seated approximately 170cm away from the television, with their midsagittal plane in line with the centre of the television.

A. HTC Vive base station placed on a tripod underneath the television and in line with the middle of participants' bodies.

B. Wireless HTC Vive controller to click on stimuli.

CENT Line bisection task example set-up

7.2 Appendix B: Rates of neglect impairments in peripersonal and extrapersonal space.

Appendix Table A. Table to show percentage (N) of stroke survivors (n= 57) showing an impairment in cancellation and line bisection task(s) in peripersonal, extrapersonal space or both.

	Peripersonal	Extrapersonal	Both
Cancellation	28.07% (16)	28.07% (16)	17.54% (10)
Line bisection	22.81% (13)	8.77% (5)	8.77% (5)
Cancellation only	12.28% (7)	22.81% (13)	
Line bisection only	7.02% (4)	3.51% (2)	
Both	15.79% (9)	5.26% (3)	
Total	35.08% (20)	31.58% (18)	

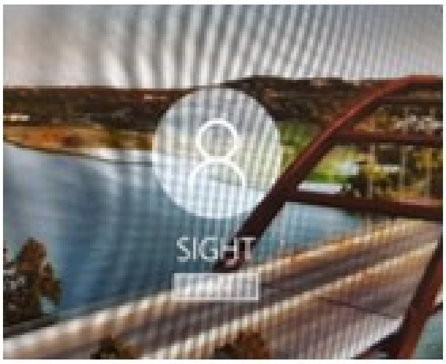
Notes: Extrapersonal tests are those included in CENT (cancellation, line bisection). Tests in peripersonal space include the paper-and-pencil based cancellation (Star cancellation, OCS Cancellation task; Wilson et al., 1987; Demeyere et al., 2015) and line bisection (e.g., Rossit et al., 2012).

7.3 Appendix C: Participant step-by-step c-SIGHT instructions.

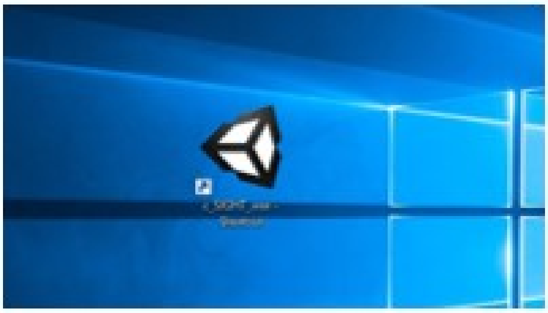
c-SIGHT Start-up Instructions

1. Turn on laptop

2. Sign in to user: SIGHT. There is no password

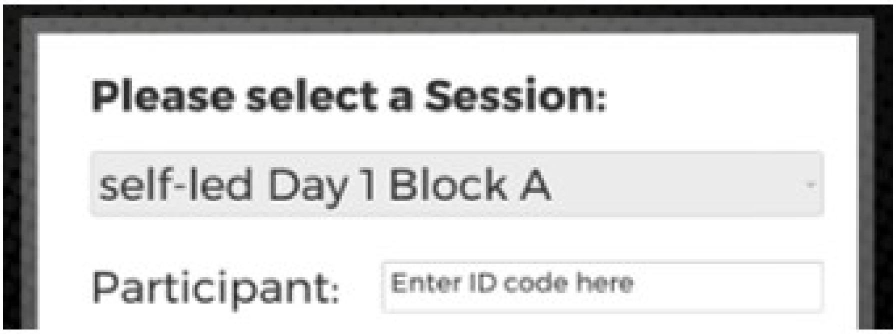


3. Click on c-SIGHT icon on the desktop

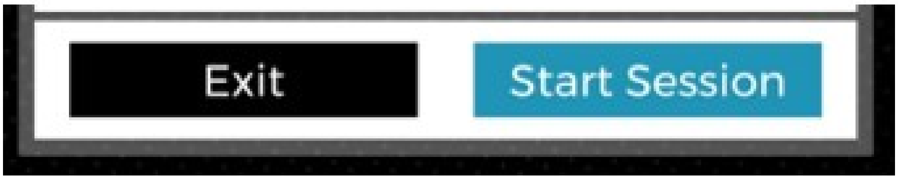


c-SIGHT start-up instructions Version 1.0 17/03/2020 IRAS number: 275001
1

4. Check the right day and session is showing. If it isn't click the correct one from the drop-down menu



5. Click start to begin, or exit to close c-SIGHT



Note: If you need to stop while using c-SIGHT, press the 'Esc' key

7.4 Appendix D: CONSORT 2010 checklist (Schulz et al., 2010) and c-SIGHT Template for Intervention Description and Replication (TIDier) checklist (Hoffmann et al., 2014).

CONSORT 2010 checklist (Schulz et al., 2010)

		Reporting Item	Page Number
Title and Abstract			
Title	#1a	Identification as a randomized trial in the title.	129
Abstract	#1b	Structured summary of trial design, methods, results, and conclusions	N/A
Introduction			
Background and objectives	#2a	Scientific background and explanation of rationale	135
Background and objectives	#2b	Specific objectives or hypothesis	136
Methods			
Trial design	#3a	Description of trial design (such as parallel, factorial) including allocation ratio.	136
Trial design	#3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	158
Participants	#4a	Eligibility criteria for participants	139
Participants	#4b	Settings and locations where the data were collected	137
Interventions	#5	The experimental and control interventions for each group with sufficient details to allow replication, including how and when they were actually administered	144
Outcomes	#6a	Completely defined prespecified primary and secondary outcome	152

		measures, including how and when they were assessed	
Outcomes	#6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	#7a	How sample size was determined.	140
Sample size	#7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomization - Sequence generation	#8a	Method used to generate the random allocation sequence.	144
Randomization - Sequence generation	#8b	Type of randomization; details of any restriction (such as blocking and block size)	144
Randomization - Allocation concealment mechanism	#9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	144
Randomization - Implementation	#10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to interventions	144
Blinding	#11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how.	144
Blinding	#11b	If relevant, description of the similarity of interventions	144
Statistical methods	#12a	Statistical methods used to compare groups for primary and secondary outcomes	154

Statistical methods	#12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	154
Results			
Participant flow diagram (strongly recommended)	#13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	156
Participant flow	#13b	For each group, losses and exclusions after randomization, together with reason	156
Recruitment	#14a	Dates defining the periods of recruitment and follow-up	157
Recruitment	#14b	Why the trial ended or was stopped	158
Baseline data	#15	A table showing baseline demographic and clinical characteristics for each group	162 & 163
Numbers analysed	#16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	156
Outcomes and estimation	#17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	169
Outcomes and estimation	#17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	#18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N/A

Harms	#19	All important harms or unintended effects in each group (For specific guidance see CONSORT for harms)	168
Discussion			
Limitations	#20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	191
Generalisability	#21	Generalisability (external validity, applicability) of the trial findings	191
Interpretation	#22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	183
Registration	#23	Registration number and name of trial registry	136
Other information			
Protocol	#24	Where the full trial protocol can be accessed, if available	137
Funding	#25	Sources of funding and other support (such as supply of drugs), role of funders	137

TIDieR
Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located ** Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	135	______________
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	131	______________
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	147	______________
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	144	______________
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	148	______________
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	149	______________
	WHERE		

7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	145	______________
	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	138	______________
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	147	______________
	MODIFICATIONS		
10.ǂ	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	N/A	______________
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	149, 151, 152	______________
12.ǂ	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	165-167	______________

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).
ǂ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

7.5 Appendix E: Fidelity checklist adapted from Powers et al. (2022).

Participant ID:

		Evidence?	Source
	Stage 1: Equipment Set-up		
Core	Laptop positioned in-front of participant (i.e., able to view screen)	YES	CRF
Core	Motion sensor positioned infront, in view and in-line with participant's midline	NO	Photograph
Core	Training mat used reflecting use of unimpaired arm	NOT DELIVERABLE	Video
Core	Training mat positioned infront of participant (flat, secured to table)		Correspondence
Core	Three rods (red, blue, green) positioned on table infront of participant		
Core	Wireless mouse connected to laptop and positioned on table infront of participant		
Core	Motion sensor connected to laptop and detecting participant repetitions		
Core	Participant shown how to launch c-SIGHT		

Stage 1: Equipment Set-up	
Core	
Evidence	1
No Evidence	1
Not Deliverable	1
Fidelity score (%)	12.50

		Evidence?	Source
	Stage 2: Intervention training		
Core	Participant positioned with middle of body in line with hand printed on the mat		
Core	Participant following correct instructions according to group allocation		
Core	Participant using unimpaired arm		
Core	Participant lifting rod with pincer grip		
Core	Participant lifting to shoulder height to trigger bling		
Core	Participant places rod on mat after each lift		
Core	Participant able to click mouse to trigger next trial		
Core	Participant trained how to carry out c-SIGHT (according to group allocation)		
Core	Completed Day 1 Block A session while c-SIGHT trial staff present		

Stage 2: Intervention training	
Core	
Evidence	0
No Evidence	0
Not Deliverable	0
Fidelity score (%)	0.00

		Evidence?	Source
	Stage 3: Telephone check-in		
Core	Telephone call completed		

Stage 3: Telephone check-in	
Core	
Evidence	0
No Evidence	0
Not Deliverable	0
Fidelity score (%)	0.00

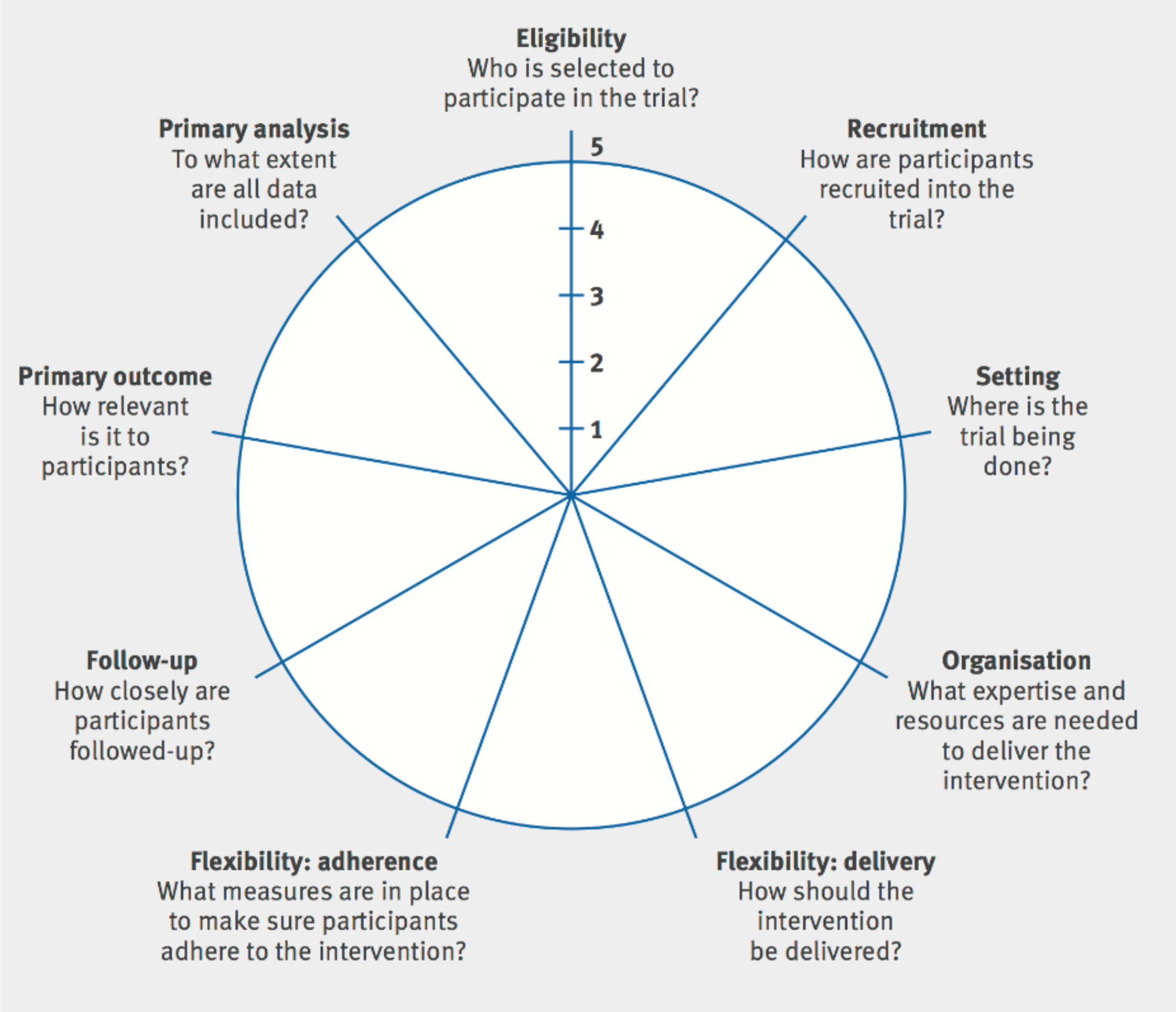
		Evidence?	Source
	Stage 4: Equipment collection		
Core	Day 10 Block B completed with participant		
Core	Laptop positioned in-front of participant (i.e., able to view screen)		
Core	Motion sensor positioned infront, in view and in-line with participant's midline		
Core	Training mat positioned infront of participant		
Core	Participant using unimpaired arm		
Core	Training mat positioned infront of participant (flat, secured to table)		
Core	Participant positioned with middle of body in line with hand printed on the mat		
Core	Three rods (red, blue, green) positioned on table infront of participant		
Core	Wireless mouse connected to laptop and positioned on table infront of participant		
Core	Motion sensor connected to laptop and detecting participant repetitions		
Core	Participant positioned with middle of body in line with hand printed on the mat		
Core	Participant following correct instructions according to group allocation		
Core	Participant lifting rod with pincer grip		
Core	Participant lifting to shoulder height to trigger bling		
Core	Participant places rod on mat after each lift		
Core	Participant able to click mouse to trigger next trial		
Core	Equipment collected		

Stage 4: Equipment collection	
Core	
Evidence	0
No Evidence	0
Not Deliverable	0
Fidelity score (%)	0.00

Total fidelity score (core components only)	Fidelity score (%)
Stage 1: Equipment Set-up	12.50
Stage 2: Intervention training	0.00
Stage 3: Telephone check-in	0.00
Stage 4: Equipment collection	0.00

Notes:

7.6 Appendix F: The Pragmatic-Explanatory Continuum Indicator Summary 2 Wheel (Loudon et al., 2015).



7.7 Appendix G: Figure showing a "Comparison of traditional clinical trials and a platform trial for five behavioural interventions" from Gold et al., (2022).

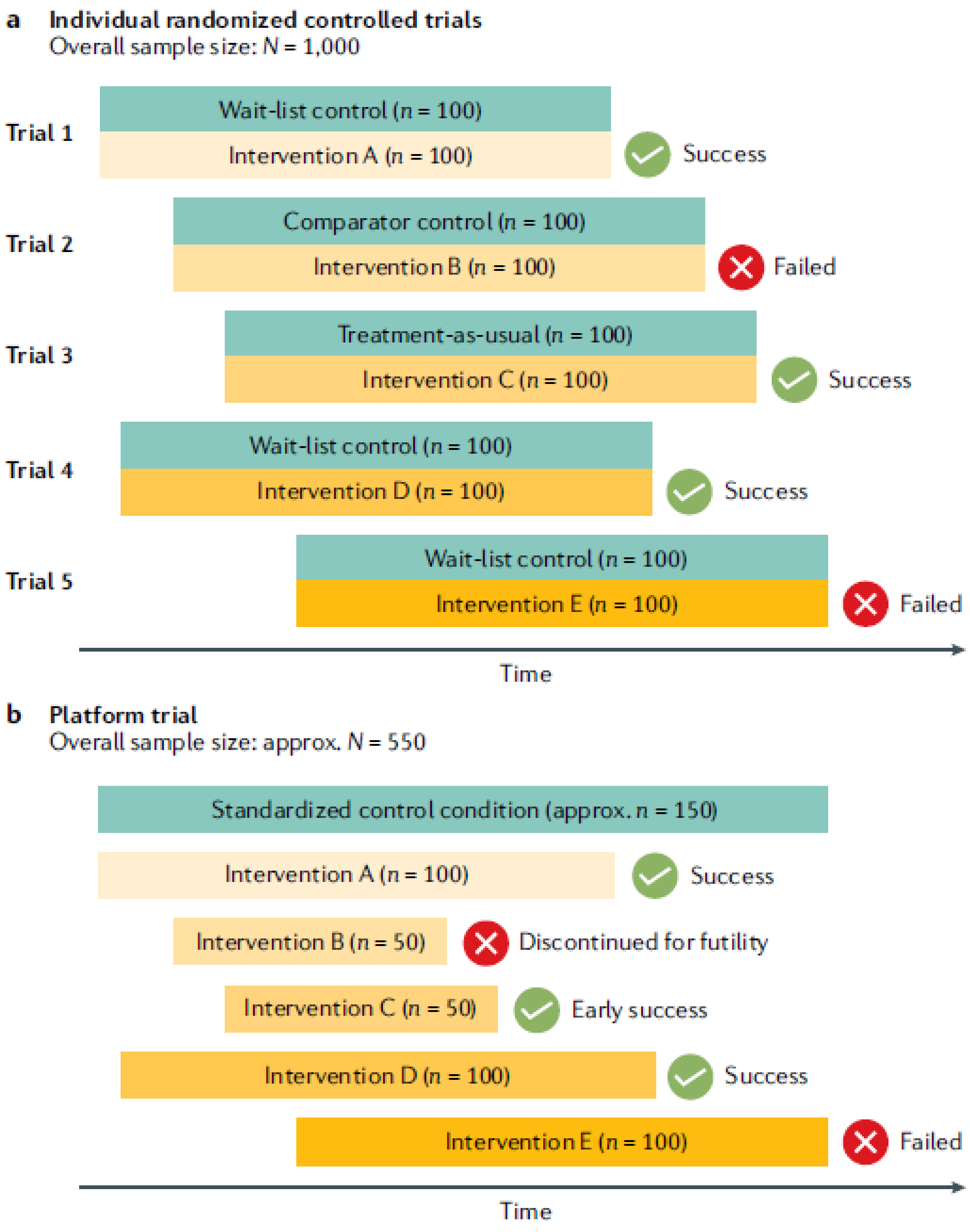


Fig. 1 | **Comparison of traditional clinical trials and a platform trial for five behavioural interventions. a** | In a traditional approach, independently run randomized controlled trials each test one experimental intervention. **b** | In a platform trial, a shared infrastructure is used to test several treatments against a shared control condition. New treatment arms can be added or discontinued over time. This approach uses resources more efficiently because the overall sample size, and the number of participants in control conditions, are lower (assuming equal effect sizes in both scenarios).