Investigation of Virtual Reality as a new model of delivery for evidence-based stroke rehabilitation

Fiona Ellis

Doctor of Philosophy

Faculty of Medicine and Healthcare

University of East Anglia, Norwich UK

September 2020

ABSTRACT

Virtual reality-aided exercise-based training has shown promise for post-stroke upper limb motor recovery in the home. Robust studies are needed to develop evidence-based guidelines and facilitate uptake in clinical practice. Thus, a three-phase mixed methods design was used to (I) identify if VR can drive neural recovery, (II) incorporate end-users into the refinement of a device and (III) provide a robust feasibility study within the home to inform a future clinical efficacy trial.

Phase I was a systematic review that demonstrated there is insufficient robust data to identify neurophysiological changes correlated with or accompanying a reduction in motor impairment, in response to VR. The four included studies reported a varying impact of VR on motor recovery and were of poor quality. Thus, revealing the need for research to address the mechanisms by which VR potentially drives motor recovery, and for more robust initial investigations to guide the development of clinical trials.

Phase II incorporated the views of ten stroke survivors, seven informal carers and nine clinicians into the refinement of a virtual reality device. Demonstrations of the Virtualrehab platform and a small home-trial confirmed the need for a low-cost non-immersive VR device that can deliver personalised home-based therapy. The end-users provided key recommendations for the next iteration of the device; in order to facilitate acceptability, usability and uptake of such technology.

Phase III investigated the feasibility of delivering upper limb therapy via VR, within the home of eleven stroke survivors. The 12-week intervention demonstrated that this mode of delivery was feasible and acceptable to stroke survivors; of note was the 87.5% therapy adherence. The results identified practical challenges for delivering and investigating VR within the home; particularly recommendations for collecting neural and behavioural outcomes. Thus, providing results to inform a future dose-optimisation study and then a clinical efficacy trial.

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ACKNOWLEDGEMENTS

A sincere thank you to my supervisors, Professor Valerie Pomeroy, Dr Nicola Hancock and Dr Niamh Kennedy; for their support with every hurdle of this project, the knowledge and skills I have learned from you all have laid the foundation for my career.

To my colleagues in ABIRA and the PhD office, thank you for always putting a smile on my face and lending your expertise; especially to Liz, who always offered guidance and help.

This research would not have been possible without my participants. Thank you for welcoming me into your lives, homes and the effort you gave.

I will always treasure the friendships I have made, especially Catarina, who always had my corner.

I will forever be thankful to my parents, who have never faltered in showing support and love for all my endeavours. You both have given me the inspiration and strength to get this far in life.

To Matt, I cannot fully express how grateful I am for your support over the years. You deserve an award for living with me through four years of a PhD and were always there for every deadline, success and failure; you always supported me and never let me give up.

A last thank you to my cats whose demands for food at five am were never swayed by deadlines or sleep deprivation.

DISSEMINATION

Manuscripts awaiting editorial review

Submitted to the journal of Physiotherapy, August 2020: **Ellis, F**., Hancock, N., Kennedy, N., Pomeroy, VM. *Neurophysiological changes accompanying reduction in upper limb motor impairments in response to exercise-based virtual rehabilitation after stroke: systematic review.*

Submitted to the journal of Neurorehabilitation and Neural Repair, August 2020: **Ellis, F**., Hancock, N., Kennedy, N., Clark, A., Wells, J., Chandler, E., Payne D., Pomeroy, VM. *Consideration-of-concept of the VirtualRehab platform for delivery of upper limb rehabilitation at home for people late after stroke.*

Conference presentations

Oral and poster presentation - Association of Chartered Physiotherapists in Neurology, 2018. (Abstract in Appendix 2E). Title: Neural correlates of motor impairment response to virtual reality-aided exercise-based training after stroke: a systematic review. Authors: **Ellis, F**., Hancock, N., Kennedy, N., Pomeroy, VM.

Poster presentation - Second International Congress on NeuroRehabilitation and Neural Repair, 2017. (Abstract in Appendix 1E). Title: Investigating the usability and feasibility of a virtual reality stroke rehabilitation tool. Authors: **Ellis, F**., Hancock, N., Kennedy, N., Pomeroy, VM.

This abstract was also presented at:

- Oral presentation – University of East Anglia Healthcare Sciences Research Festival, 2017.
- Oral presentation - University of East Anglia Faculty of Medicine and Healthcare Sciences Postgraduate Research Conference, 2017.– 1st prize.

Other presentations

Norwich Science Festival 2017 – oral presentation and workshop. Title: Virtualrehab and stroke. (Lanyard given to members of the public, Virtualrehab and stroke workshop specific in Appendix 3E).

1 INTRODUCTION

1.1 INTRODUCTION TO THE THESIS

Strokes are a leading cause of disability worldwide; there are approximately 1.2 million survivors currently in the United Kingdom (UK) and around 100,000 incidences occurring annually (Stroke Association, 2018). The survival rate is predicted to rise 120% by 2035, coupled with a 60% increase in the incidence rate; potentially costing the National Health Services (NHS) £75 billion a year (King *et al.*, 2020). It is clear that stroke provides an ever-increasing strain on healthcare services.

An upper limb motor impairment affects approximately 70 to 80% of survivors, with a poor rate for full functional recovery and challenges in delivering the recommended evidence-based therapy (Tinham, 2008; Bernhardt *et al.*, 2017; Clarke *et al.*, 2018). The use of Virtual Reality (VR) to deliver upper limb therapy within the home has shown promise in overcoming challenges and reducing impairment (Laver *et al.*, 2017). Presently, there is a distinct lack of uptake in clinical practice and recommendations cannot be made due to the poor methodological quality of the evidence; further work is also required to understand the mechanisms by which VR might drive motor recovery (Hughes *et al.*, 2014; Langan *et al.*, 2018; Chen *et al.*, 2019; Levin, 2020). There is also a need to report challenges faced when researching VR interventions within the home-environment, to develop robust future clinical trials (Threapleton, Drummond and Standen, 2016).

Hence this thesis presents three studies addressing the following research aim:

To investigate the delivery of exercise-based upper limb stroke rehabilitation via virtual reality within the home

The thesis comprises of nine chapters:

- Chapter one is an introduction and overview of stroke, upper limb motor impairments, challenges with rehabilitation, and the promise of technology-based rehabilitation aids, specifically virtual reality devices.
- Chapter two provides the thesis research questions and aims.
- Chapter three details the virtual reality equipment used in this thesis, namely, the Virtualrehab platform.
- Chapter four outlines the methodological underpinnings of the thesis, detailing the multiphase mixed methods approach undertaken to address the research aim.
- Chapter five is a systematic review carried out to determine if there is evidence that neurophysiological changes are correlated with, or accompany, a reduction in motor impairment, in response to virtual reality-aided exercise-based training.
- Chapter six describes a user refinement study that focussed on incorporating the views of end-users on using and refining the Virtualrehab platform.
- Chapter seven details the quantitative components of a feasibility study that delivered a 12-week exercise-based intervention via the Virtualrehab platform within the home environment.
- Chapter eight details the qualitative components of the feasibility study, exploring stroke survivors' experiences with participation and the Virtualrehab platform.
- Chapter nine discusses the three studies in the context of the literature, the strengths and limitations of the thesis, future directions for research and ends with concluding remarks.

1.2 STROKE

This section explores the impact of strokes, both on the individual and society; in order to highlight the importance of identifying and implementing effective rehabilitation strategies.

A stroke ensues when the blood supply to the brain is interrupted, leading to cell death within minutes. Approximately 85% of strokes are caused by an ischaemic attack, where a blockage cuts off the blood supply. The remainder occurs when a blood vessel bursts, leading to a haemorrhagic stroke, either on the surface (subarachnoid) or within (intracerebral) the brain (Bowen, James and Young, 2016; Khaku, Hegazy and Tadi, 2019).

Strokes are a leading cause of death worldwide with more than 100,000 occurring annually, and on average, 38,000 deaths, in the United Kingdom (UK). Fortunately, advances in medicines are improving survival rates, with around 1.2 million survivors in the UK (Stroke Association, 2018). Although the survival rate is predicted to rise, 120% by 2035, the overall stroke incidence rate is expected to increase by 60% over the same timeframe (King *et al.*, 2020).

Several factors are contributing to this growth in stroke incidences, including the increasing population, and a surge in unhealthy sedentary lifestyles (Tinham, 2008; Bowen, James and Young, 2016). For example, poor diets

have left one in seven individuals with high blood pressure, a contributing factor in half of all strokes in the UK (National Institute for Health and Care Excellence, 2019). Several factors, both modifiable and unmodifiable, can severely increase the risk of stroke, all of which are rising in an ageing population. Modifiable factors under the individual's control, such as weight, smoking and drug use, can potentially be mitigated through lifestyle improvements. This cannot be said for unmodifiable factors which are beyond the person's control, such as family medical history, sex and age (O'Donnell *et al.*, 2010).

It is clear that the number of strokes and subsequent survivors needing care are rising and this is placing an increasing strain on society, particularly on the UK's National Healthcare Services (NHS). Strokes cost approximately £26 billion each year, with around 60% covered by unpaid/informal carers. Overall costs are predicted to increase to £75 billion by 2035, typically spread across:

- Healthcare, prevention and treatment;
- Social care;
- Unpaid/informal contributions from family and friends;
- Productivity losses due to leaving or interrupting employment (Patel *et al.*, 2017; King *et al.*, 2020).

A potential means to lower the overall costs of strokes is through facilitating the recovery of survivors with rehabilitation. Unfortunately, the heterogeneous nature of strokes provides a challenge for prescribing appropriate therapies. The impact of the disease depends on the brain area affected, and the extent of the damage (Ward, 2017). Strokes are a leading cause of disability in the UK; two-thirds of survivors leave hospital impacted in one of the common areas (i.e. motor, verbal, physical, cognitive) and often with chronic fatigue which can limit their ability to carry out optimal doses of therapy (Adamson, Beswick and Ebrahim, 2004; Bowen, James and Young, 2016).

Stroke survivors identify upper limb weakness as one of the most challenging impairments due to its impact on their quality of life (Stroke Association, 2018). The upper limb is used for many functional activities during the day (i.e. eating, dressing). These tasks require sequences of complex movements integrating appropriate muscular group activations and sensorimotor coordination (Miranda *et al.*, 2018). Recovery of the upper limb is vital for survivors' quality of life, independence and psychological well-being (Barker and Brauer, 2005; Nichols-Larsen *et al.*, 2005; Morris *et al.*, 2013). Upper limb weakness affects approximately 70 to 80% of survivors, with a poor rate of full functional recovery (Tinham, 2008; Bernhardt *et al.*, 2017). Thus, identifying effective treatments for upper limb motor impairments is a key priority for research, as suggested by stroke survivors, carers and clinicians (Pollock, St George, *et al.*, 2014; Bowen, James and Young, 2016).

It is challenging to provide appropriate treatment plans that account for the complexities of upper limb motor impairments which are not static, often changing as recovery proceeds (Bernhardt *et al.*, 2017). Thus, targeted therapies need to evolve and adapt, especially with the simultaneous presentation of impairments (i.e. an arm weakness may still be present after spasticity occurs). Clinicians need to know which underlying impairment to treat first and become adaptive when others are uncovered, or develop (Raghavan, 2015). To provide appropriately targeted treatments, a clear understanding of the underlying impairments and mechanisms involved in recovery is required (Bernhardt *et al.*, 2017).

1.3 UPPER LIMB MOTOR IMPAIRMENTS: UNDERLYING MECHANISMS OF MOTOR RECOVERY

It is essential to understand the dynamics that drive motor recovery in order to provide effective, tailored therapy (Boyd *et al.*, 2017). The term 'recovery' can be understood in two ways: as the change of an outcome between two or more timepoints, or the underlying mechanisms of improvement in terms of behavioural restitution, or compensation strategies (explained in full below) (Bernhardt *et al.*, 2017). The following section explores the functional consequences of upper limb impairments and mechanisms of motor recovery following a stroke, in order to understand the theoretical underpinnings of upper limb motor rehabilitation.

Upper limb impairments lead to several functional consequences that impact potential motor recovery (Raghavan, 2015). Stroke survivors commonly experience weakness, paresis, chronic central pain and neuronal hypersensitivity (deafferentation) in the affected arm, all of which can increase the use of the less paretic arm (Taub *et al.,* 1994). This often leads to 'recovery' through 'compensatory' strategies whereby the survivor uses alternative approaches to successfully complete tasks than those carried out before the stroke (for example, using their mouth and less affected hand to open a packet) (Cortes *et al.,* 2017). While compensation is a successful strategy when the prognosis for neural recovery is poor, such movements are often inefficient, can cause pain and lead to 'learned non-use' of the more paretic arm (Cirstea and Levin, 2007). This can carry on beyond the resolution of the initial cause, which prevents functional improvements from being translated to increased use in daily life (Gamble *et al.,* 2002). Stroke survivors often develop such compensatory hyper reliance on the less paretic side or other maladaptive behaviour strategies, in order to carry out daily activities despite their impairments (Roby-Brami *et al.,* 2003; Kischka and Wade, 2004). Unfortunately, the efficient nature of motor compensations can prevent the more paretic side from recovering 'normal' motor patterns of daily activities, thereby limiting the final functional outcome (Takeuchi and Izumi, 2012).

These ‘compensatory strategies’ have been well documented in the upper limb, specifically reaching and grasping tasks (Levin, Kleim and Wolf, 2009). For example, in a small-sample of stroke participants, the severity of muscle weakness and impairment contributed to compensatory muscle recruitment strategies to complete a reaching task (McCrea, Eng and Hodgson, 2005). Another study demonstrated shoulder trunk flexion and compensated elbow extension when reaching (Cirstea and Levin, 2000). Further, stroke survivors trying to grasp an object showed forearm pronation and wrist flexion, rather than the neutral position and wrist extension seen in healthy participants (Raghavan *et al.*, 2010). This evidence showed that ‘compensatory’ strategies could lead to poor accuracy, and reinforce the abnormal movement, otherwise known as ‘maladaptive behaviour’.

Stroke rehabilitation must take into account this ‘learned non-use’ and ‘maladaptive behaviour’ to provide tailored therapy for an optimal functional outcome. Thus, in rehabilitation, the aim is to discourage ‘compensation’ and facilitate neural ‘restitution’ (Bernhardt *et al.*, 2017). Neural restitution refers to the re-establishment of movement behaviours that were used before the stroke through the restoration of neural components (Bernhardt *et al.*, 2017). This so-called "true recovery" requires neuroplastic change, the alteration of nerve structure and function in response to experience and system demands (Pekna, Pekny and Nilsson, 2012). Structural changes resulting in neural repair are believed to result in a better recovery of movement than changes in neuronal networks whereby secondary areas become the main locus of

movement (i.e. areas which usually only assist the primary brain area responsible for a particular function) (Bernhardt *et al.*, 2017).

As restitution has the potential to lead to a better recovery, interventions that exploit neural plasticity are considered to be the most effective (Alia *et al.*, 2017). Neural plasticity is the process of re-organising neural connectivity from experience or practice. As we age the rate of plasticity decreases, but damage to the brain produces a heightened amount to facilitate spontaneous biological recovery of the damaged functions (Kwakkel, Kollen and Lindeman, 2004). Spontaneous biological recovery refers to behavioural improvements without treatment. This occurs during a window of heightened recovery in the early post-stroke stage. The duration varies across neural systems, but spontaneous motor recovery is often claimed to occur between weeks and months for the upper limb (Nakayama *et al.*, 1994; Bernhardt *et al.*, 2017).

Thus, the goal of rehabilitation is to facilitate neural plasticity and aim for restitution of motor function. Rehabilitation for the upper limb utilises mechanisms of recovery and advocates for tasks that are repetitive, intensive, functional and goal-orientated to drive neural reorganisation (Ward, 2017; Bernhardt, Hayward, *et al.*, 2019).

1.4 REHABILITATION FOR UPPER LIMB MOTOR IMPAIRMENTS

The underlying mechanisms of neural recovery are clear, and it is known that high dosages of therapy support greater functional improvement (Boyd et al., 2017). The exact dose and potential for an individual's recovery are still unclear; however, evidence-based guidelines for stroke rehabilitation have been proposed (Boyd et al., 2017; Lohse, Lang, & Boyd, 2014). This section details these recommendations, the challenges in following them and in providing optimal therapy for stroke survivors.

Evidence-based guidelines recommend at least 45 minutes, five days a week of functional exercise-based rehabilitation (Bowen, James and Young, 2016). In order to drive long term neuroplastic changes, this goal must be met and exceeded (Ward, 2017). Physical training needs to be functional, repetitive, long-lasting, challenging, intensive, salient and motivating to maximise sensorimotor recovery after brain lesions (Kleim and Jones, 2008).

Unfortunately, there are significant challenges in delivering this level of therapy in clinical practice. Time allocated for face-to-face therapist contact is substantially lower in the UK than in other European countries (De Wit *et al.*, 2006). Although this report is over a decade old, recent studies have shown that face-to-face challenges are complex, still apparent and interfere with carrying out the guidelines (Clarke *et al.*, 2018). Further, national audits have raised concern over the low level of therapy being received by patients

within the hospital and in the community, approximately half of the recommended dose (Bowen, James and Young, 2016).

Numerous explanations have been proposed relating to why the recommendations often cannot be carried out (Clarke *et al.*, 2018). Two key issues have been identified as a lack of resources for clinicians and challenges in therapy adherence. There is an apparent lack of resources available to carry out evidence-based guidelines, and this affects the amount of therapy that can be delivered within inpatient and outpatient rehabilitation settings. Stroke clinicians and audits have reported constraints such as limited time, personnel or resources (Clarke *et al.*, 2018). Further, a lack of funding has impacted the number of resources available for therapists to cope with overstrained caseloads (Juckett *et al.*, 2020). Stroke clinicians also argue that keeping appraised of recent findings is challenging, and thus they lack awareness of the evidence. They often struggle to find an appropriate time to review new research and transfer it from trial to clinical setting (Lynch, Chesworth and Connell, 2018; Eng *et al.*, 2019). For example, understanding the potential of a patient's recovery and then tailoring therapy to their needs is time-extensive and challenging, especially with the lack of agreement in the literature around optimal approaches and biomarkers of stroke recovery (Boyd *et al.*, 2017). Alongside the challenges clinicians face in delivering therapy guidelines, there is a distinct lack of adherence by stroke survivors (Stroke Association, 2018).

Stroke survivors have identified key challenges to adherence such as a lack of support, feedback, confidence and boredom; with one in four experiencing significant fatigue leaving subsequent travel to appointments as an arduous task (Coetzee *et al.*, 2008; Jurkiewicz, Marzolini and Oh, 2011; Lerdal *et al.*, 2012; Simpson *et al.*, 2020). An inconsistent patient-centred approach to rehabilitation is also suggested as affecting adherence; it is clear that recovery is more effective when survivors have a voice in therapeutic decision-making (Rosewilliam, Roskell and Pandyan, 2011; Chen, Xiao and De Bellis, 2016; Sadler *et al.*, 2017; Satink *et al.*, 2018). Finally, the repetitive intensive nature of functional exercise-based rehabilitation can reduce motivation and increase the risk of the challenges mentioned above.

Novel rehabilitation strategies are required to alleviate the strain felt by stroke clinicians, to produce efficient, effective therapy programmes with robust evidence that accounts for the 'real-life' pragmatic barriers of implementing stroke therapy. In order to increase adherence to such therapy, stroke survivors need to be involved in developing their rehabilitation. Attempting to address these challenges has driven research towards investigating technology-based interventions to augment therapy.

1.5 DELIVERING REHABILITATION VIA TECHNOLOGY

This section explores the common categories adopted in 'technology-based' rehabilitation, with a focus on their strengths and limitations in addressing the challenges of delivering upper limb stroke therapy. Rapid innovations in technology have led to increased accessibility and availability. Thus, its applicability in healthcare has increased, and there is a wide range of devices on offer. Table 1 provides an overview of these devices.

Table 1: Overview of common technology-based rehabilitation devices

Common technology-based rehabilitation	Description	Potential Benefits	Potential Limitations
Robotic devices (Zhang *et al.*, 2011; Bertani *et al.*, 2017)	• Custom-built to aid movement. • They generate a wide range of forces, for active flexion and extension range of movement, and motions for training. • They are known either as exoskeletons, which determine the kinematic configuration of the joints; or end-effectors, robotic arms that extort force on the distal part of the limb. • They are often used to augment manual rehabilitation provided by clinicians with automated motor assistance.	• They can provide intensive repetitive training, theoretically facilitating neuroplasticity. • They can record accurate measures of dose and performance. • Independent training requiring less supervision can be used instead of manual facilitated training given by the therapist, which could save treatment time.	• They can be difficult to deploy in the home environment as they require large spaces, and the forces they generate in an unsupervised environment has potential safety concerns. • They often require a certain amount of technical proficiency. • They can be expensive to develop, deploy and maintain, estimated around $35,000 to $75,000, often requiring customised builds. • The motor function gains are similar to conventional therapy outcomes.
Games (Chen *et al.*, 2019)	• Games can be used to deliver repetitive exercise-based rehabilitation. • There are commercially available systems and software packages (e.g. the Wii Sports (Nintendo, Kyoto, Japan).	• They can provide intensive repetitive training, theoretically facilitating neuroplasticity. • They can enhance adherence through motivating and engaging tasks when delivering repetitive exercises.	• Commercial games may lack sufficient guidance on positioning and movements for accurate therapeutic purposes. • Tailored games usually require adaptions from other technologies (i.e. robotics) to

Common technology-based rehabilitation	Description	Potential Benefits	Potential Limitations
	• There are also tailored gaming software packages, that have been developed specifically for rehabilitation purposes (usually integrating movement sensors or robotic devices for effective detection and tracking).	• They have shown to be acceptable in the home, particularly in order to overcome transport difficulties. • Commercial gaming devices could provide affordable and accessible home-based rehabilitation.	accurately track and guide, which additionally incurs their limitations. They also require further technical training and learning for adoption in practice. • Commercial games can have hidden costs and liabilities, such as insurance, privacy and security.
Telerehabilitation (Appleby *et al.*, 2019; Laver *et al.*, 2020)	• Telephone and video conferencing connect therapists with patients in the home, where they can observe movement when the patient executes tasks.	• Has the potential to reduce the duration of hospitalisation and costs. • Can be beneficial for those with transport difficulties or who depend on caregivers for travel.	• They often require a certain amount of technical proficiency. • They are dependent on a strong internet connection. • There is the possibility of less face-to-face, patient-clinician interactions. • Policies need to be in place relating to costs, privacy, liability and security.

Common technology-based rehabilitation	Description	Potential Benefits	Potential Limitations
Sensors (Chen *et al.*, 2019)	• They are used to measure patients' movements and provide feedback. • They can include both motion and physiological sensors.	• The data collected can be beneficial for remote monitoring.	• Validation of the accuracy of such sensors is required in the home environment.
Tablets, mobile apps (Pugliese *et al.*, 2018)	• Mobiles and tablets are used to provide commercially available therapy programmes.	• Commercially available and relatively affordable.	• Post-stroke impairments may be a barrier to use, such as motor or visual difficulty.
Virtual reality (Laver *et al.*, 2017)	• Provides a virtual environment that replicates the physical world. • The devices can offer customised and commercially available therapy programmes.	• A controlled and safe environment where real-life tasks can be carried out without the consequence from mistakes in real-world situations (i.e. using the kettle) • Often uses sensors and games in the devices - incurring their benefits.	• The validation of clinical outcomes, particularly for commercial programmes not designed for rehabilitation, is needed. • The sensor feedback argued to be key to neural plasticity and motor recovery, which can potentially be reduced with virtual environments. • If sensors and games are used, then their limitations could be incurred.

There are several promising technology-based rehabilitation options, each with potential benefits and limitations. Key challenges in delivering optimal upper limb motor rehabilitation within NHS services include a lack of resources, time and adherence (Clarke *et al.*, 2018). Thus, the optimal technology approach must incorporate affordable, accurate, motivating, challenging, accessible factors with the ability to tailor and securely monitor patients remotely (Chen *et al.*, 2019).

Robotics can provide repetitive functional training with recorded dosages and tailored progressions, however, the devices currently on offer are expensive and often inaccessible due to the space requirements in the home. A more affordable, accessible and easily deliverable approach is through the use of commercial and tailored games. Unfortunately, the lack of guidance and accurate monitoring is problematic; they also often require other technology-devices (i.e. robotics) which accrues additional limitations (Chen *et al.*, 2019).

It is clear that telerehabilitation (providing clinician-patient contact virtually) can offer efficient use of resources, such as clinician time, with remote monitoring of patients (Chen *et al.*, 2019). Aspects of this approach are beneficial but require practicalities, such as consistent internet services which limit the applicability in rural areas (Appleby *et al.*, 2019; Laver *et al.*, 2020). Furthermore, the use of tablets, often associated with telerehabilitation, is

useful but limited for those with motor and visual difficulties (Pugliese *et al.*, 2018). Overall, the reliability of measurements and customisation of these approaches are problematic (Chen *et al.*, 2019).

The technology mentioned above has the potential for stroke rehabilitation. However, Virtual Reality (VR) can incorporate the advantageous features from other technology approaches; thus, it is a promising means of delivering repetitive intensive functional upper limb therapy. For example, VR devices can combine games, sensors, remote monitoring abilities and potentially provide affordable, accessible, accurate, motivating and challenging rehabilitation (Laver *et al.*, 2017). However, VR also has limitations that need considering, and, all technology approaches have barriers to development and implementation within the complex home environment (i.e. practical challenges, technical challenges and social context considerations) (Threapleton, Drummond and Standen, 2016). It is important to consider the variations of VR devices and critically appraise the evidence for delivering therapy via virtual reality within the home.

1.6 DELIVERING STROKE REHABILITATION VIA VIRTUAL REALITY DEVICES

This section provides an overview of Virtual Reality (VR) focussing on common terminology and devices used. The general public often misunderstands the term 'virtual reality'; it encompasses a wide range of different devices with various hardware and software components. A commonly used definition in research is:

> Use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real-world objects and events
>
> (Weiss and Katz, 2004, p. 7)

Virtual reality gaming systems use technology to generate life-like environments in which users can practice tasks and movements in real-time (Laver *et al.*, 2017). Each virtual environment can provide users with visual and auditory feedback to varying levels of 'immersion'. Immersion relates to how 'real' the user perceives an environment to be, as opposed to reality; VR can be categorised as either full, semi or non-immersive (Rose, Nam and Chen, 2018).

Fully immersive systems generate virtual environments with surround sound, auditory and haptic feedback, using visual display units (i.e. curved screens, head-mounted displays or bodysuits) (Rose, Nam and Chen, 2018). These

systems are credited with inducing a high sense of ‘immersion’ or presence in the virtual world, but they require considerable space, cost and complex maintenance needs (Pallavicini, Pepe and Minissi, 2019). In particular, there have been initial reports of falling risks or nausea (i.e. cybersickness) induced in users, a particular concern for stroke survivors (Weech, Kenny and Barnett-Cowan, 2019). In contrast, semi or non-immersive systems typically present the virtual environment on a screen, and interaction occurs through movement sensors (Smith *et al.*, 2012). These devices typically require smaller space, lower costs and have reported fewer side-effects; they are currently a popular choice for rehabilitation (Subramanian, Cross and Hirschhauser, 2020).

Virtual reality systems are also developed from either commercially available devices (e.g. videogame equipment) or are custom built. Lohse and colleagues (2014) systematically compared commercial versus custom virtual reality equipment and found no significant difference between the two, across 26 trials. It was noted that the commercially developed devices were advantageous for potential implementation into stroke rehabilitation due to the competitive pricing strategy in the gaming industry (Lohse *et al.*, 2014). Recently, researchers have reviewed the commonly used types of platform: out of 125 published studies, two-thirds used commercially available platforms; commonly used systems included the Nintendo Wii (Nintendo, Kyoto, Japan) and Microsoft Xbox One (Microsoft, Washington, United States). The majority of systems included sensors to track movement (i.e.

accelerometers or Kinect V2 cameras (Microsoft, Washington, United States)) (Subramanian, Cross and Hirschhauser, 2020).

It is clear that virtual reality devices have the potential to address the challenges in delivering optimal stroke therapy within the home environment. However, it is important to consider the quality of evidence regarding the use of VR for stroke therapy.

1.7 THE QUALITY OF EVIDENCE REGARDING THE USE OF VIRTUAL REALITY REHABILITATION, TARGETING UPPER LIMB MOTOR IMPAIRMENTS

For more than a decade, studies have reported initial reductions of upper limb motor impairments, when delivering therapy via virtual reality (Laver *et al.*, 2017). This section provides a critique of the evidence underlying the use of virtual reality for upper limb stroke rehabilitation within the home.

Virtual rehabilitation is considered to facilitate treatment adherence and promote high dosages of functional exercise-based movements when compared with conventional or no therapy. This is a repeated message reported in systematic reviews ranging from 2011 to 2019, particularly throughout the Cochrane updates by Laver and colleagues (Henderson, Korner-Bitensky and Levin, 2007; Mumford and Wilson, 2009; Laver *et al.*, 2011, 2015, 2017; Lohse, Lang and Boyd, 2014; Aramaki *et al.*, 2019;

Valkenborghs *et al.*, 2019; Maier *et al.*, 2019; Rohrbach, Chicklis and Levac, 2019; Subramanian *et al.*, 2019).

Unfortunately, recommendations cannot be made for clinical guidelines due to the poor quality of evidence reported (Laver *et al.*, 2017). There are consistent methodological weaknesses in the form of small heterogeneous samples, high risk of bias, variety of outcome measures, differing equipment and protocols.

This prevalence of poor-quality research is still evident when considering a more recent systematic review. A 2019 review reported moderate effect sizes on upper limb function (standardised mean difference with a random-effects model was used), compared to conventional therapy, in chronic stroke survivors (effect size = 0.431; $p \leq 0.001$; confidence intervals = 0.424 to 0.537) (Lee, Park and Park, 2019). However, the small number of studies (n = 21) included a wide range of devices and training procedures, once more limiting the applicability of the findings.

Promising publications came in 2020 from two systematic reviews with meta-analyses that reported strong methodologically sound evidence. They both used the PEDro score, which was developed by the Physiotherapy Evidence Database and is a valid measure of clinical trial quality (high, 6 to 10; fair, 4

to 5; and poor ≤ 3) (de Morton, 2009). The first review included 27 Randomised Controlled Trials (RCTs) with 1,094 participants, and a PEDro score of 6.29 (high), in their findings (Mekbib *et al.*, 2020). The other review included 20 studies with 874 participants and found a PEDro score of 6.25 (high) (Domínguez-Téllez *et al.*, 2020). The findings from each review showed a significant impact on Upper Limb (UL) functional impairment, during the subacute phase with 15 or more hours of therapy (Mekbib *et al.*, 2020) and significantly improved Upper Extremity Fugl-Meyer Assessment scores (FMA-UE) (Domínguez-Téllez *et al.*, 2020). It appears that these reviews not only further support the initial promising findings of virtual rehabilitation but suggest that the methodological quality has improved in recent trials.

It is important to consider the limitations of the reviews themselves, in light of the potential impact on the evidence base for virtual stroke rehabilitation. The 2020 reviews included studies with an intervention group (using virtual reality therapy) and a control group (using conventional therapy), as the other reviews have done. Unfortunately, of the 27 RCTs included in Mekbib and colleagues analysis, six of the studies combined virtual reality with conventional therapy in their intervention group. In addition, the included studies did not match the therapy frequency, intensity or dose between conditions. That is also a limitation of Domínguez-Téllez and colleagues meta-analysis, they included virtual reality interventions combined with various conventional therapies and occasionally robotic devices. Thus, it is

not surprising that the results highlighted a significantly reduced motor impairment when comparing virtual reality interventions combined with conventional therapy, often with higher dosages than the control groups.

There were also similar methodological limitations in the included studies within the 2020 reviews, as those reported in the last decade. The reviews reported a heterogenous stroke population, in terms of the impact site, time since onset, sex and age. Current recommendations promote categorising patients by their stroke recovery biomarkers; although challenging to carry out, it can increase the robustness of evidence and our understanding of potential treatment response (Boyd *et al.*, 2017). It is also important to report appropriate outcome measures and procedures; this has been a challenge highlighted by all the reviews above. Often, the studies vary in terms of data reported (i.e. missing participant drop-out information) and can use different versions of the same outcome scale or measuring units.

To this Researcher's (author of the thesis) knowledge, reviews investigating virtual stroke rehabilitation have no agreed categorisation system for the devices and procedures included; for example, these can range in terms of immersion, saliency and feedback. These aspects can crucially affect the engagement and motor learning undertaken in such interventions (Chen *et al.*, 2019; Subramanian, Cross and Hirschhauser, 2020).

Overall, the effect of virtual reality on upper limb motor impairment is promising, although there is a lot unknown. For example, the 'active ingredients' of VR need further investigating, such as the underlying mechanisms, optimal doses and procedures (Laver *et al.*, 2017). Thus, there is a need for larger robust trials that investigate the effect of VR therapies and identify changes in different groups of stroke survivors (i.e. acute v chronic). Unfortunately, developing robust interventions is a complex process and often fails to translate into clinical practice (Dobkin, 2009; Stroke Association, 2018; Juckett *et al.*, 2020). It is clear that further investigation into delivering upper limb motor rehabilitation via virtual reality is required.

Although robust investigations are important, they also need to identify the underlying mechanisms involved in the changes seen in motor impairment, in response to virtual rehabilitation. Several proposed components are thought to work together, such as intensive, motivating therapy through exercise games and stimulation of motor learning.

1.8 PROPOSED UNDERLYING MECHANISMS OF DELIVERING UPPER LIMB REHABILITATION VIA VIRTUAL REALITY

This section explores the evidence for proposed underlying mechanisms of motor impairment reduction, in response to therapy delivered via virtual reality devices. There has been some investigation of the underlying mechanisms of change (i.e. cortical reorganisation) of virtual reality therapy (Pollock, Farmer, *et al.*, 2014). However, the evidence base appears modest

in terms of examining the impact virtual reality has on the facilitation of neuroplasticity. It is also difficult to investigate strokes due to the heterogeneity of patients, lesion site and functional impairments.

Although the area has 'modest' evidence, the updated Cochrane review has stated that "Neuroimaging findings are guiding the development of Virtual Reality" (Laver *et al.*, 2017). Exploring the limited research in the area revealed the underlying neural mechanisms had been investigated by outcomes derived from methods such as Transcranial Magnetic Stimulation (TMS) and Functional Magnetic Resonance Imaging (fMRI). Preliminary findings from two studies indicated that neural activation was dominant in the contralesional motor cortex before an intervention. At the outcome measurement time point, the activation appeared to shift to the ipsilesional motor cortex (Jang *et al.*, 2005; You *et al.*, 2005). This potentially demonstrates cortical reorganisation in response to the VR intervention. However, the VR devices, intervention and control procedures differed, with small sample sizes and only one study included a measure of motor impairment (Jang *et al.*, 2005); without which it is unclear if the neural change is reflective of true recovery.

Additionally, another study found the combination of a robotic-hybrid virtual reality intervention with conventional therapy, produced more post spinal excitability, suggestive of peripheral nerve changes following this hybrid VR

(Saleh *et al.*, 2017). This initial evidence appears to suggest that VR devices could potentially facilitate changes in cortical and spinal excitability, demonstrating cortical reorganisation. However, this evidence is of minimal quality and includes variable protocols, outcomes, devices and heterogeneous participants. Further, is that the devices are accompanied by another therapy aid (i.e. robotics), which can interfere with identifying the 'active' mechanisms of VR. In addition to this Researcher's knowledge, there has been no attempt to systematically synthesise the evidence of neural changes accompanying reduction of motor impairment, nor reporting on the quality of such research.

The use of theoretical underpinnings and small trials to guide the development of such complex interventions is concerning; therapies must be guided by robust, large trials that evidence the underlying neurophysiological mechanisms of change (Pomeroy and Tallis, 2000). It should also be noted that one of the drivers for end-users (i.e. stroke survivors, informal carers and clinicians) accepting technology are devices accompanied by high-quality evidence (Demers, Chan Chun Kong and Levin, 2019).

Further improvements in stroke rehabilitation are promised by promoting motor recovery; the goal is to limit compensatory behaviour (Boyd *et al.*, 2017). Therefore, despite the promising indications of motor impairment

reduction in response to VR; in order to understand its applicability in stroke rehabilitation, it must be clear if such therapy can drive neural recovery.

The difficulty in translating evidence into clinical recommendations is not a new message in the area of virtual stroke rehabilitation; as evidenced by the reviews mentioned above urging for stronger trial designs to be carried out, to continue the 'translational research pipeline'. Robust research findings are required to inform the successful delivery of rehabilitation into practice (Walker *et al.*, 2013; Lynch, Chesworth and Connell, 2018). Growing frustration with the lack of progress is prompting careful consideration of how stroke recovery treatment trials are designed and conducted; a focus of the third theme proposed for the second stroke recovery and rehabilitation roundtable (Bernhardt, Borschmann, *et al.*, 2019).

This section identified a clear need to understand the neurophysiological changes underlying reduction of motor impairment in response to therapy delivered via VR. In addition, investigations into virtual stroke rehabilitation require robust initial trials to determine the optimal design and procedures of larger RCTs. In order to design such an initial investigation, consideration must be given to the end-users (i.e. stroke survivors, carers and clinicians) views on engaging, developing and investigating such technology.

1.9 HOME-BASED VIRTUAL REALITY FOR STROKE REHABILITATION

Virtual Reality (as defined in section 1.6) has been shown as a promising mode of delivering therapy within the home, with the potential to address some of the main challenges in stroke rehabilitation. For example, travelling to and from clinics adds burden and can be tiring for stroke survivors and their families, with 45% of survivors reporting feelings of abandonment when they leave the hospital (Stroke Association, 2018). Providing therapy via virtual reality within the home environment has been indicated by end-users as potentially alleviating such issues. It is important to consider their views in order to facilitate the acceptance of such technology. This section details the drivers reported by end-users to engage with virtual reality home-based therapy. It also includes results from a wealth of research investigating home-based virtual rehabilitation solution for stroke.

The delivery of upper limb rehabilitation via virtual reality within the home has been proposed to increase adherence to high dosages of functional exercise-based tasks. The potential challenging nature of technology-based rehabilitation may address the 'boredom' reported by stroke survivors with other ways of delivering therapy (Pallesen *et al.*, 2018; Demers, Chan Chun Kong and Levin, 2019; Warland *et al.*, 2019). The addition of challenging, rewarding and modifiable features could increase the enjoyment of therapy, facilitate adherence and enhance the potential for motor learning, thus, motor recovery (Levin, Weiss and Keshner, 2015; Laver *et al.*, 2017). The systems

also provide a safe environment which allows clinicians to maintain stimulus control, delivery and measurement (Schultheis and Rizzo, 2001). These potential benefits can help promote rehabilitation autonomy, an important aspect for stroke survivors, and help the provision of repetitive intensive functional tasks to drive neuroplastic changes required for upper limb motor recovery (Brunner *et al.*, 2016; Levin, 2020). Further, virtual reality could offer a way to deliver therapy with the efficient use of resources and therapist time (Turolla *et al.*, 2013). For example, an increase in therapist contact time is often seen as one of the main benefits of telerehabilitation and technology-based devices that offer clinician oversight (Loureiro *et al.*, 2011; Viñas-Diz and Sobrido-Prieto, 2016; Chua and Kuah, 2017; Chen *et al.*, 2019).

A recent systematic review investigating the types and crucial design features of technology-based rehabilitation found it was vital to include external and internal motivational aspects to facilitate adherence (Chen *et al.*, 2019). External motivation features can include gamified exercises, adaptive difficulty levels and tailoring the therapy plan to individual functional ability. Internal motivation, meanwhile, can include providing feedback, tailoring rehabilitation goals and increasing the length and duration of sessions. These potentially provide entertaining, fun experiences that adapt to the survivor as they progress.

The potential benefits of delivering stroke rehabilitation within the home are clear. There is a wealth of research providing promising results of using technology-based solutions within the home, for various stroke impairments such as the upper limb (Dodakian *et al.*, 2017; Bernocchi *et al.*, 2018; Cramer *et al.*, 2019; Warland *et al.*, 2019; Ghorbel *et al.*, 2020; Qiu *et al.*, 2020). The type of virtual reality solution used varies from robotic gloves (Bernocchi *et al.*, 2018), to the LEAP hand motion sensor (Qiu *et al.*, 2020) and hands-free systems such as the Microsoft Kinect (Bai and Song, 2019; Ghorbel *et al.*, 2020); all of which demonstrated promising feasible results in small pilot trials (Burridge *et al.*, 2017; Warland *et al.*, 2019). The adherence within the home has been particularly promising at 97.9% over four weeks of daily upper-limb therapy (Dodakian *et al.*, 2017). In addition, other functional impairments such as lower limb weaknesses have shown promise with virtual therapy delivered within the home following the user's input (Howes *et al.*, 2019). The promise of home-based virtual rehabilitation has also been shown in larger trials. A randomized, assessor-blinded, noninferiority clinical trial of 124 adults following a stroke, telerehabilitation showed comparable efficacy to traditional in-clinic rehabilitation for improving function (Cramer *et al.*, 2019). However, the aforementioned studies did not provide a cost-analysis of carrying out therapy within the home. When comparing virtual home-based rehabilitation with conventional outpatient rehabilitation the cost-effectiveness was comparable (Chen *et al.*, 2017; Allen *et al.*, 2019). Finally this promise is continuing to be investigated in published protocols (Kilbride *et al.*, 2018; Stephenson *et al.*, 2020). It is clear that the use of virtual

reality for home-based stroke rehabilitation is an area of strong research interest with promising initial findings.

This section showed the potential of VR as an engaging, motivating method of therapy delivery in the home; however, despite its promise, there is a distinct lack of uptake of such devices in clinical practice (Glegg and Levac, 2018; Levin, 2020). The challenges of developing and researching VR for stroke therapy needs to be considered in order to facilitate integration into NHS stroke services.

1.10 DEVELOPING AND INVESTIGATING VIRTUAL REALITY DEVICES FOR UPPER LIMB MOTOR IMPAIRMENT

There is clear potential for delivering upper limb motor rehabilitation via virtual reality within the home. Firstly, it could be used to combat resource constraints felt by the NHS and allow therapists to prescribe home-based exercises with remote monitoring and updating capabilities. Secondly, the engaging, motivating and personalised environment could facilitate patient's adherence to their intensive repetitive programmes. Despite the promise and ever-increasing interest in research, there is a clear lack of uptake in clinical practice (Glegg and Levac, 2018; Levin, 2020). The following section details key challenges that have been proposed when implementing VR research into clinical practice. Firstly, the societal perception of age correlating with technology ability is discussed, followed by the crucial need to include end-

users in the development of technology-based rehabilitation devices. Finally, insights into the challenges of conducting and reporting research into delivering therapy via VR within the home environment is considered.

1.10.1 The societal perception of age as a barrier to technology engagement

There is a societal perception that age is a barrier to engaging with technology (Mitzner *et al.,* 2017). This perception can affect stroke survivors and informal carers interest in virtual rehabilitation devices and the therapist's willingness to utilise technology, potentially explaining some of the challenges with uptake. This conflict between societal views and older adults opinions on technology is not a new challenge in technology-based rehabilitation research.

Often the 'digital divide', those who do not engage in technology are at risk of being left behind, is cited as the main challenge for the uptake of older adults with technology (Mitzner *et al.,* 2010). In 2018 over half of adult internet non-users (never used or it had been more than three months) were over the age of 75; however, the UK's office for national statistics shows this generational divide is narrowing (Serafino, 2019). This is important for stroke research as the average age for survivors in the UK is 72 (men) and 78 (women) (Bowen, James and Young, 2016); with the rate of stroke in those aged 45 and above expected to rise 59% in the next 20 years (King *et al.,*

2020). However, researchers and end-users argue that if the technology device is affordable, accessible and usable, then it can be accepted into stroke survivors lives, regardless of age and previous experience (Balsam *et al.*, 2013). One study, in particular, found that age was not correlated with the frequency of use of home-based VR gaming interventions (Standen *et al.*, 2015); while several studies reporting older adults found gamification of their rehabilitation enjoyable (Casserly and Baer, 2014; Wingham *et al.*, 2015; Threapleton *et al.*, 2017). Thus, it is clear that the usability and acceptability of technology-based rehabilitation devices are dependent on incorporating end-users into their development.

1.10.2 The importance of end-users in developing and researching technology-based rehabilitation devices, following a user-centred design approach.

Often rehabilitation devices within the home require patients and carers to operate the system. It is crucial that end-users can engage in such systems with appropriate support to ensure frustrating technical barriers are overcome (Chen *et al.*, 2019). For example, stroke survivors have reported practical challenges such as technical reliability of the equipment, space it requires and time to set-up, as key barriers to acceptance; thus, it is important to consider the individuals' lifestyle and that of other members of their household (Donoso Brown *et al.*, 2015; Proffitt and Lange, 2015; Glegg and Levac, 2017). In addition, clinicians' voices are required to understand the key issues they consider when choosing and implementing therapeutic aids;

for example, those that are time-consuming, difficult, unreliable and costly are unlikely to be used in practice (Threapleton, Drummond and Standen, 2016). Thus, any technology system proposed for rehabilitative purposes must be deemed usable by the end-users; within this thesis, usability is defined as:

> "The extent to which a system, product or service can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use."
>
> (Organizacion Internacional de Normatizacion - ISO, 2018)

The involvement of end-users in rehabilitation technology development is known as the User-Centred Design approach (UCD) (Jankowski *et al.*, 2017). The iterative design process incorporates end-users (i.e. patients, family members and clinicians) into the design and testing of a system (Proffitt *et al.*, 2019). The UCD framework depicted in Figure 1 has been used with prior virtual rehabilitation systems and aligns with guidelines that recommend involving users early in the development (Egglestone *et al.*, 2009; Tsekleves *et al.*, 2016; Ivanova *et al.*, 2017; Lopes *et al.*, 2018; Howes *et al.*, 2019; Warland *et al.*, 2019; Wentink *et al.*, 2019; Fong *et al.*, 2020).

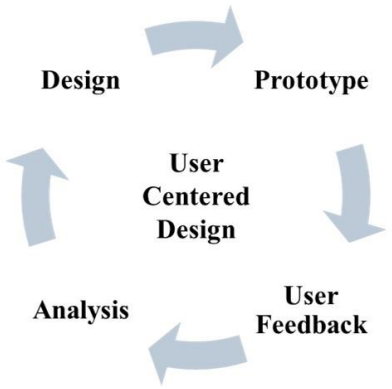
The flexibility of the framework allows researchers to incorporate users at the most appropriate points in the system development. This involvement ranges from individual or group discussions with service users, from development until the implementation of the system. In particular, one project consulted

service users in scoping meetings during the early stages of development and with an initial prototype of an active computer gaming system for strength and balance (Howes *et al.*, 2019). This allowed them to gather safety, usability, acceptability information via group feedback and specific outcome measures (i.e. the System Usability Scale (Brooke, 1996)). Other projects have followed this initial iterative feedback of a prototype with extended testing periods; for example, clinicians used an upper limb rehabilitation robotic device for six weeks, followed by group discussions (Fong *et al.*, 2020). The UCD approach is a common practice in developing virtual rehabilitation systems. Additionally, future trials continue to incorporate this approach in their design to facilitate the systems' usability (Stephenson *et al.*, 2020).

In addition to understanding the usability of a system, it is equally important to identify how end-users would engage with the system in different environments and situations; to identify features that need further development to facilitate future implementation. A person-based approach (Yardley *et al.*, 2015) allows for such in-depth understanding to be gathered. For example, the users view on the planned behaviour change the system aims to elicit and if their view differs due to prior experiences; alongside the barriers and facilitators of delivering rehabilitation in such a manner, in various environments. These results can be used to plan interventions and the further development work which is required. Thus, combining person-based and UCD approaches are recommended when developing technology-based

healthcare interventions (Yardley *et al.*, 2015); to improve the acceptability of interventions and the implementation of systems from the end-user perspective.

Figure 1: The User Centered Design framework adapted from (Proffitt et al., 2019)



The UCD and person-centred approaches have been argued to be of equal importance as efficacy information, for the acceptance of such interventions into practice (Mountain *et al.*, 2010). Thus, any investigation of delivering upper limb rehabilitation within the home via a virtual reality device must incorporate the end-users. In addition to the promise such inclusion has on facilitating the uptake of devices, home-based research's practical challenges need to be considered to provide robust implementable evidence.

1.10.3 The practical challenges of research in using technology within the home

One of the main challenges in implementing research findings into clinical practice is the lack of consideration and reporting of challenges with published home-based research (Threapleton, Drummond and Standen, 2016). For example, research often provides insufficient detail on equipment installation, set-up, acceptability in the home environment and any key issues encountered. Delivering interventions within the home environment, to heterogeneous patients and those relatively inexperienced with technology, is complex and challenging. The home environment cannot be controlled, monitored or recorded easily; there are aspects of the participants' lives, such as family and friends, that cannot be changed or anticipated. Thus, there is a unique set of challenges in researching VR within the home and translating this evidence into meaningful changes for clinical practice. For example, recruitment, equipment, training, adherence, monitoring, safety and carrying out appropriate assessments are all challenging in the home environment. Initial investigations must be carried out to identify and mitigate these practical issues to improve the quality of future RCTs that will ultimately inform the efficacy and effectiveness of VR for upper limb motor rehabilitation.

1.11 CONCLUSION

This introduction chapter has established the ever-increasing demand stroke has on healthcare services. To meet this demand, research has focused on technology-based devices as a mode to deliver stroke rehabilitation that promotes behavioural restitution. There is initial promise in using virtual reality devices for rehabilitation to reduce motor impairment. These devices can offer an engaging, motivating environment that could facilitate therapy adherence. Further, they have the potential to alleviate resource and time restraints on stroke clinicians and allow them remote oversight of home-based therapy. Unfortunately, recommendations have not been made as the evidence is of poor methodological quality, with varying protocols, procedures and outcomes. In addition, there is a clear need to understand the potential neural mechanisms of change in response to a reduction of motor impairment. Finally, despite the ever-increasing interest in research and the wealth of VR devices on offer, there is a clear lack of uptake in clinical practice. Therefore, robust reporting is required with staged preliminary trials and the inclusion of end-users at every possible point. These gaps highlighted an opportunity for this thesis to investigate the following research aim:

To investigate the delivery of exercise-based upper limb stroke rehabilitation via virtual reality within the home

2 STATEMENT OF AIMS

The introduction chapter has established the need:

To investigate the delivery of exercise-based upper limb stroke rehabilitation via virtual reality within the home

This research aim arose from the following gaps in the evidence base:

Despite the promising indications of motor impairment reduction in response to Virtual Reality (VR), in order to understand its applicability in stroke rehabilitation, it must be clear if such therapy can drive neural recovery. There have been suggestions of 'modest' evidence but to date no systematic synthesis.

Gap 1. There is a clear need to systematically synthesise the evidence of neurophysiological changes which are correlated with, or accompany a reduction in motor impairment, in response to virtual reality-aided exercise-based training.

Even with the promise of initial motor impairment reductions in response to therapy delivered via VR, there are reported challenges and a lack of uptake in clinical practice. For example, researchers have identified insufficient time to gain familiarity, inadequate user instructions and a lack of user involvement in all stages of the technology's development (Demain *et al.*, 2013; van Ommeren *et al.*, 2018; Nguyen *et al.*, 2019). Thus, including stroke survivors, their informal carers, and clinicians in technology development might enhance the likelihood that it will meet the requirements of intended

users (Hochstenbach-Waelen and Seelen, 2012; Balsam *et al.*, 2013; Nasr *et al.*, 2016; Glegg and Levac, 2017).

Gap 2: There is a need to include end-users in the development of virtual reality devices to improve their usability and acceptability.

Finally investigating the delivery of rehabilitation via VR is complex, often the practicalities and specific challenges of the home environment are not reported; which has limited the applicability of evidence into clinical practice (Threapleton, Drummond and Standen, 2016). This complex set of developmental considerations requires a staged approach starting with a proof-of-concept feasibility trial.

Gap 3. There is a need to investigate the feasibility of delivering therapy via a virtual reality device in stroke survivors homes, to provide proof-of-concept for a dose-finding study and further clinical trial.

In order to address the research gaps, three research questions have been devised that required a three-phased mixed-method approach (described in chapter four).

2.1 RESEARCH QUESTION 1

Is there evidence that neurophysiological changes are correlated with, or accompany, reduction in motor impairment, in response to virtual reality-aided exercise-based training?

To answer the first research question, phase I aimed to:

Aim 1a: Determine the neurophysiological correlates of upper limb motor impairment response to virtual reality aided exercise-based training following a stroke.

If insufficient evidence was found to answer research aim 1a, a subsidiary aim was devised.

Aim 1a.2: Determine if there is evidence that an improvement of motor impairment occurs alongside change in neurophysiological measures.

The first research question was investigated in phase I of this thesis, via a systematic review (chapter five).

2.2 RESEARCH QUESTION 2

What are the views of end-users on using and refining virtual reality-aided exercise-based training for stroke rehabilitation?

To answer the second research question, phase II aimed to:

Aim 2a: Explore the usability and acceptability of a virtual reality system (the Virtualrehab platform) for delivery of home-based stroke rehabilitation.

Aim 2b: Inform the development of future iterations of the device via user feedback and experience.

The second research question was investigated in phase II of this thesis, using a qualitative study that incorporated the voice of end-users into the next iteration of the Virtualrehab platform (chapter six).

2.3 RESEARCH QUESTION 3

How feasible is virtual reality-aided exercise-based training as a mode to deliver upper limb stroke rehabilitation within the home?

To answer the third research question, phase III aimed to:

Aim 3a: Determine the feasibility of delivering exercise-based upper limb stroke rehabilitation within the home via the Virtualrehab platform.

The specific research objectives were to:

1. Establish the process for recruitment of stroke survivors to a subsequent Randomised Control Trial (RCT) when they have been discharged from NHS specialist stroke services;
2. Explore adherence (number of more paretic upper limb repetitions) of stroke survivors to the 'prescribed' use of the Virtualrehab platform;
3. Assess the viability of the researcher adjusting the 'prescribed' training programme over time;
4. Evaluate the technical reliability of the Virtualrehab platform;
5. Test the viability of collecting neuromechanical and behavioural data in the home;
6. To assess the viability of using randomised length of baselines and repeated measures during the intervention period to inform a subsequent dose-optimisation study;
7. Estimate changes in paretic upper limb functional ability and motor impairment and neural measures;

8. Ascertain the acceptability of home-based task-orientated upper limb training via non-immersive virtual reality to stroke survivors in their own homes;
9. Establish the acceptability of participation in the study.

The third research question was investigated with a convergent parallel mixed-methods feasibility study, consisting of a series of replicated single-case studies following an AB design and 1:1 interviews (chapters seven and eight).

3 THE VIRTUAL REALITY EQUIPMENT: VIRTUALREHAB PLATFORM

Phase II and III used an exercise-based virtual rehabilitation system called the Virtualrehab platform. The following chapter provides an overview of the developer (the industrial collaborator) and the platform's components. All images relating to the Virtualrehab platform were obtained from the industrial collaborator (permission in appendix A).

3.1 INDUSTRIAL COLLABORATOR

Evolv Rehabilitation Technologies (Evolv, Basauri, Spain) manufactures technology-based medical devices; the company part-funded the PhD studentship of the Researcher (author of the thesis), provided access to the Virtualrehab platform's software and offered on-going technical support for phase II and III.

The Virtualrehab platform was developed by an interdisciplinary team of engineers and software designers before the start of the thesis work. The platform was designed to deliver tailored full-body physical rehabilitation via exercises and exercise-based games (termed exergames) with additional assessment options to track changes in Active Range of Motion (AROM) over time. The platform has achieved a Conformité Européene (CE) marking and is proposed to offer therapy within the home environment, while also allowing therapists remote monitoring and updating of their patients'

rehabilitation plans. According to definitions from prior published research (chapter 1, section 1.6), the platform would be labelled as a 'customised non-immersive' virtual reality device.

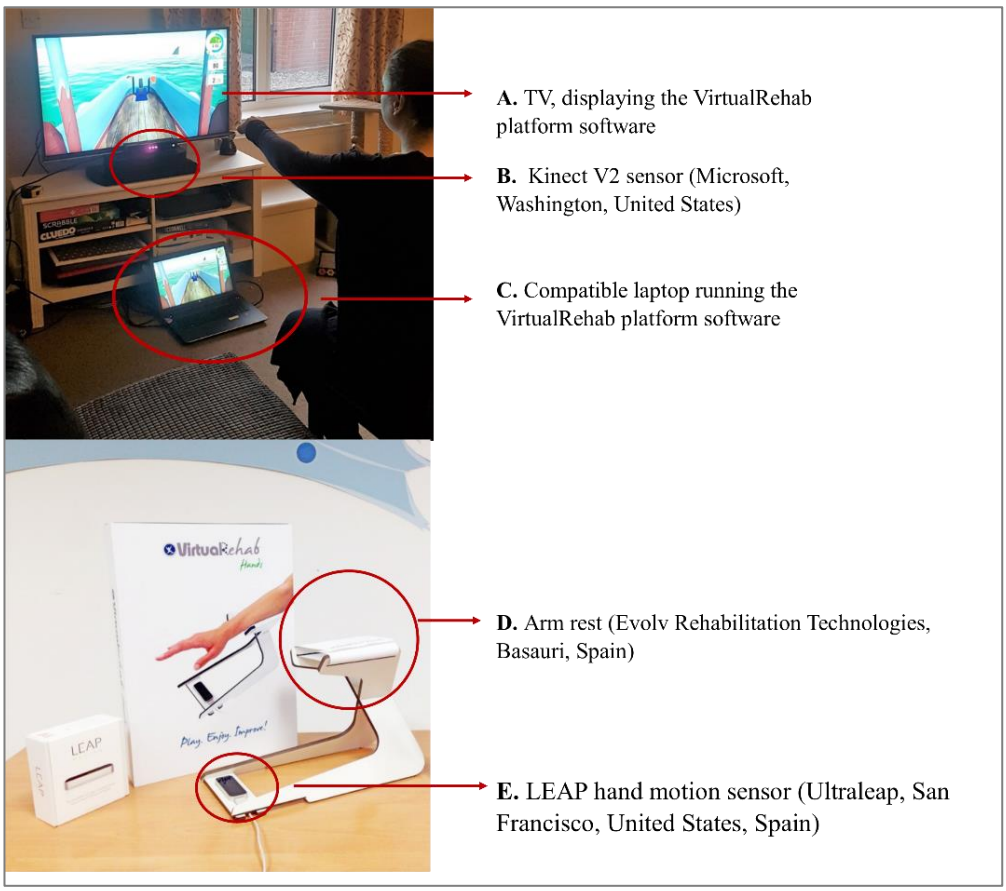
3.2 HARDWARE COMPONENTS

The Virtualrehab platform hardware was composed of three main pieces of equipment:

- The Kinect V2 sensor (Microsoft, Washington, United States);
- The LEAP hand motion sensor (Ultraleap, San Francisco, United States);
- The computer and associated cables required to run the software.

The following section describes each component of the hardware, and an example set-up is shown in Figure 2.

Figure 2: Example set up of the Virtualrehab platform hardware components



3.2.1 The Kinect V2 sensor

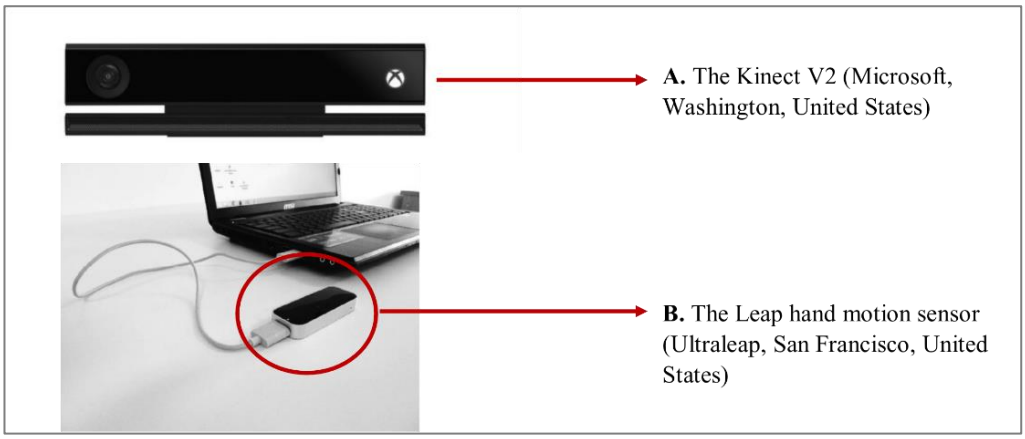
The Kinect V2 (Microsoft, Washington, United States) uses a camera sensor to track three dimensional (3D) objects in the real world and translate them to an onscreen avatar simultaneously (Figure 3). The camera contains a depth sensor with an infrared projector that can be adjusted to detect near (seated) or far (standing) movements. The camera detects up to 25 skeletal joints per individual as anatomical landmarks, in order to replicate movements (e.g. the shoulders, spine). The Kinect V2 (Microsoft, Washington, United States) manufacturing stopped in October 2017; multiple devices were obtained by

the University of East Anglia (UEA) Movement and Exercise Laboratory (MovExLab) for use in this thesis.

3.2.2 The LEAP hand motion sensor

The LEAP hand motion sensor (Ultraleap, San Francisco, United States) uses an infrared camera to track finer motor movements of the hand (Figure 3). The Virtualrehab platform offers hand-specific rehabilitation using this sensor. The individuals' arm must be held above the sensor, which is challenging for those with upper limb paresis. Thus, the industrial collaborator designed an armrest to support paretic arms (Figure 1D). The industrial collaborator provided one LEAP hand motion sensor (Ultraleap, San Francisco, United States) and armrest to use in the thesis. Phase I of this thesis found the hand-specific rehabilitation component required further development for the sensor to detect paretic hands, common to stroke survivors requiring such rehabilitation. Thus, obtaining any additional LEAP hand motion sensors (Ultraleap, San Francisco, United States) was not required, as this part of the Virtualrehab platform was not used in phase III.

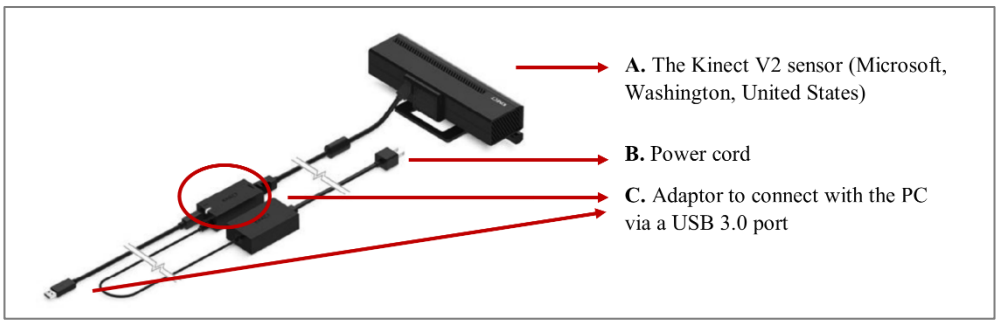
Figure 3: The Kinect V2 and Leap hand motion sensor



3.2.3 Compatible computer with associated cables

The Kinect V2 (Microsoft, Washington, United States) was not compatible with computers without an additional adaptor cable (Figure 4). In addition, an HDMI/VGA cable was required to connect the laptop to the TV screen.

Figure 4: The Kinect V2 adaptor cables



The Virtualrehab platform software required specific computer hardware components to run optimally (correct for the 2017 version).

- **Processor:** Intel Core i5 4460 for desktops or Intel Core i5 4200H for laptops.
- **Graphics card:** The Nvidia GeForce GT 740 for desktops or Nvidia GeForce GT 840M for laptops.
- **RAM:** 4GB or higher.

In addition, a USB 3.0 port was required to run the Kinect V2 sensor (Microsoft, Washington, United States) software through the computer which needed to run Windows Eight operating system (Microsoft, Washington, United States) or above. One appropriate laptop was obtained for phase I and five more for phase II (i.e. five laptops used in participants home for the intervention and one for the Researcher to manage the therapy plans).

3.3 SOFTWARE COMPONENTS

The Virtualrehab platform offers three software modules to create tailored rehabilitation plans, known as Assessment, Exercise and Exergames. There is also a 'therapy editor' where the rehabilitation plans are created, monitored and updated. The platform remotely records adherence (number of repetitions prescribed and recorded). All terminology concerning the Virtualrehab platform's software was named by the industrial collaborator (i.e. the exercise module includes a shoulder 'flexion' movement).

3.3.1 The therapy editor

The therapy editor was created to provide stroke clinicians with a method of creating, monitoring and adjusting tailored therapy plans. The number of repetitions, targets for movements, time given to complete and 'difficulty' was adjustable for each individual (Figure 5 and Figure 6). It should be noted that the levels of 'difficulty' were created and labelled by the industrial collaborator. The therapy editor also allows access to the 'statistics' (data captured by the device, available in an excel format) which reported the number of movements and successful tasks carried out with a score given (created by the industrial collaborator) and day/time the session was completed. To update the plan, a remote internet connection was required.

Figure 5: Example of the 'therapy editor', a display shown to clinicians of the prescribed exergames for their patient

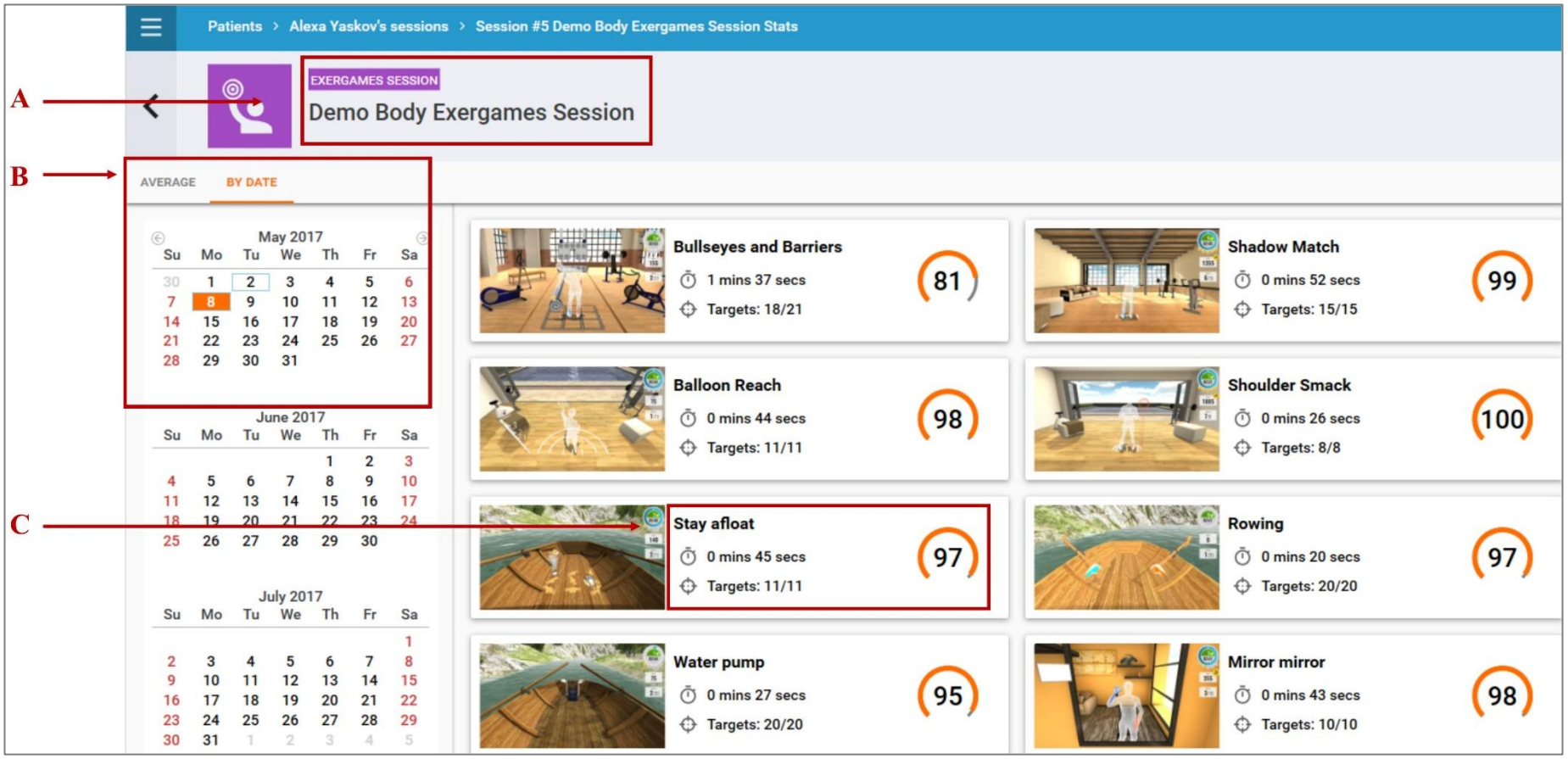


Figure 4 legend

A. The exergames prescribed to a patient are shown all together, with summary performance statistics. It should be noted that all prescribed exercises are shown in a similar display but on a separate option in the software.

B. The summary performance statistics can be displayed by 'date' (as in the example, the days with completed sessions are highlighted in blue, the clinician can select the day and display the results of the patients performance – in the example the 8th May, 2017 is selected and the results of that session shown), or by 'average' (where the average preliminary results of all completed days are shown).

C. Each prescribed exergame shows a summary performance statistic, the full data can be shown by selecting the individual exergame (explained further in figure 5). The time spent carrying out the targets (repetitions) is given in minutes and seconds followed by the number of targets (repetitions) correctly completed by the patient, finally the accuracy achieved for each target (repetition) is shown as a percentage to the right of the time and completed targets (repetitions).

Figure 6: Example of the ‘therapy editor’, the display shown to clinicians when tailoring their patients exergame session

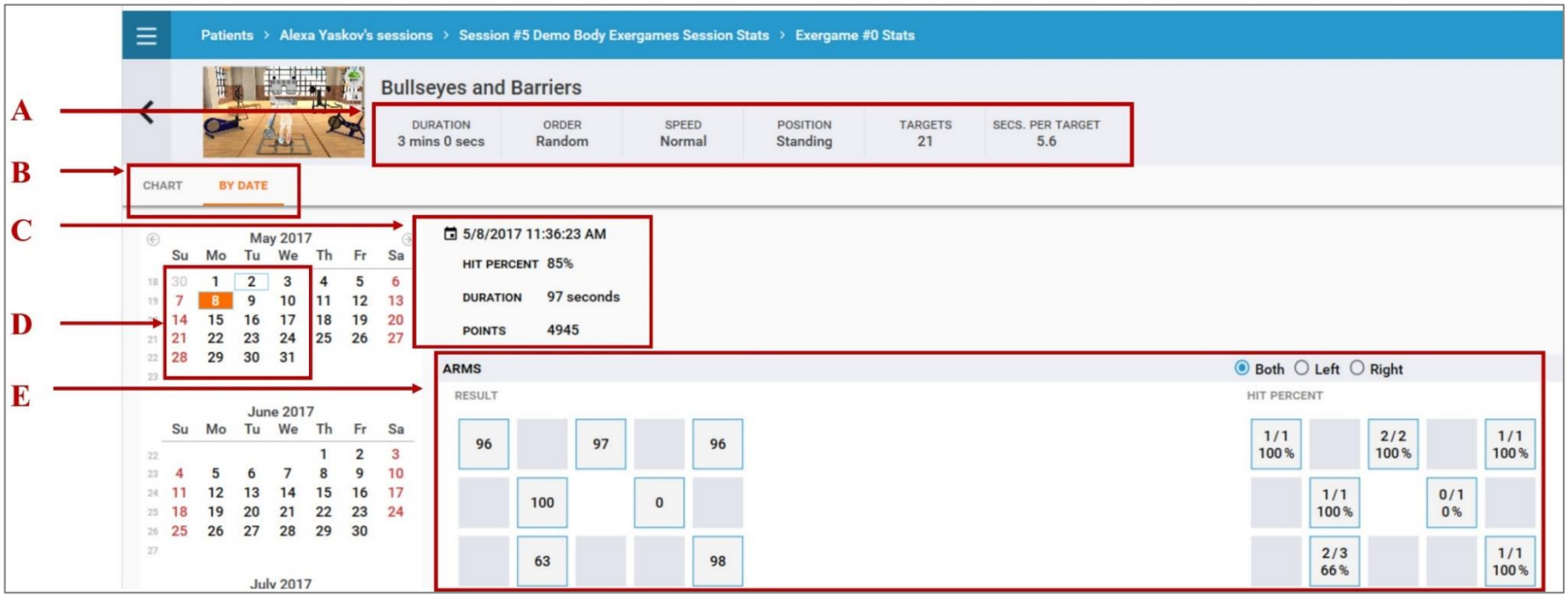


Figure 6 legend

A. A summary of the exercise or exergame is shown at the top of the screen:

- Duration: Once the clinician has planned the number of targets (repetitions) and time allowed for each target, the longest time the exercise/exergame will run for is shown.
- Order: The targets (repetitions) are assigned to appear either randomly or in the order the clinician chose (i.e. left arm, then right arm, then right leg).
- Speed: The clinician can choose how fast the next target (repetition) appears following the completion of the previous one, allowing a rest period for the client.
- Position: The individual can complete the exercise/exergame standing or seated.
- Targets (repetitions): the total number of targets (repetitions) selected for the exercise/exergame.
- Seconds per target (repetition): the time chosen by the clinician for each target (repetition) to be completed within.

B. The results from previous sessions can be displayed as demonstrated or downloaded in an excel form.

C. A summary of the results from the selected session displayed with the date and time it was completed. The hit percentage describes the percentage of correction repetitions carried out. The duration details the total time spent carrying out the movements and points refers to the participants score from the session (note. These scores were created by the industrial collaborator).

D. The calendar displays the days participants completed the sessions, highlighted in blue.

E. The repetition targets could be selected and results from the prior session displayed. The grey boxes display the possible positions and those highlighted in blue indicate the ones selected, the results depict the percentage of completed repetitions.

3.3.2 The Assessment Module

The Assessment module was designed to provide stroke clinicians with information on patients Active Range Of Motion (AROM) (0 to 170 degrees for the upper limb); alongside a specific option for detecting hand movements with the LEAP hand motion sensor (Ultraleap, San Francisco, United States). The industrial collaborator adapted the movements from traditional physiotherapy exercises (i.e. shoulder abduction). The Acquired Brain Injury Alliance research team (ABIRA) (that the Researcher was part of) provided feedback from physiotherapists on the movements, to the industrial collaborator. Throughout phase II the Researcher collated information for the industrial collaborator; challenges were identified (i.e. the programmed range of movement that the sensors would determine as a 'correct movement' did not allow for the variation typical of stroke survivors). For example, abnormal trunk movement would not be recognised by the platform, and thus, such users could not carry out the therapy plans.

However, the adjustments to this module were not completed in time for phase III; thus, the 'assessment' module was not used. In addition, phase II also demonstrated that the LEAP hand motion sensor (Ultraleap, San Francisco, United States) required more adjustments to detect paretic hand movements successfully; thus the hand-specific assessment, exercise and exergames tasks were not used in phase III.

3.3.3 The Exercise Module

The Virtualrehab exercise module included tasks based on traditional physiotherapy exercises to provide motor function training, the below list examples of the exercise tasks offered.

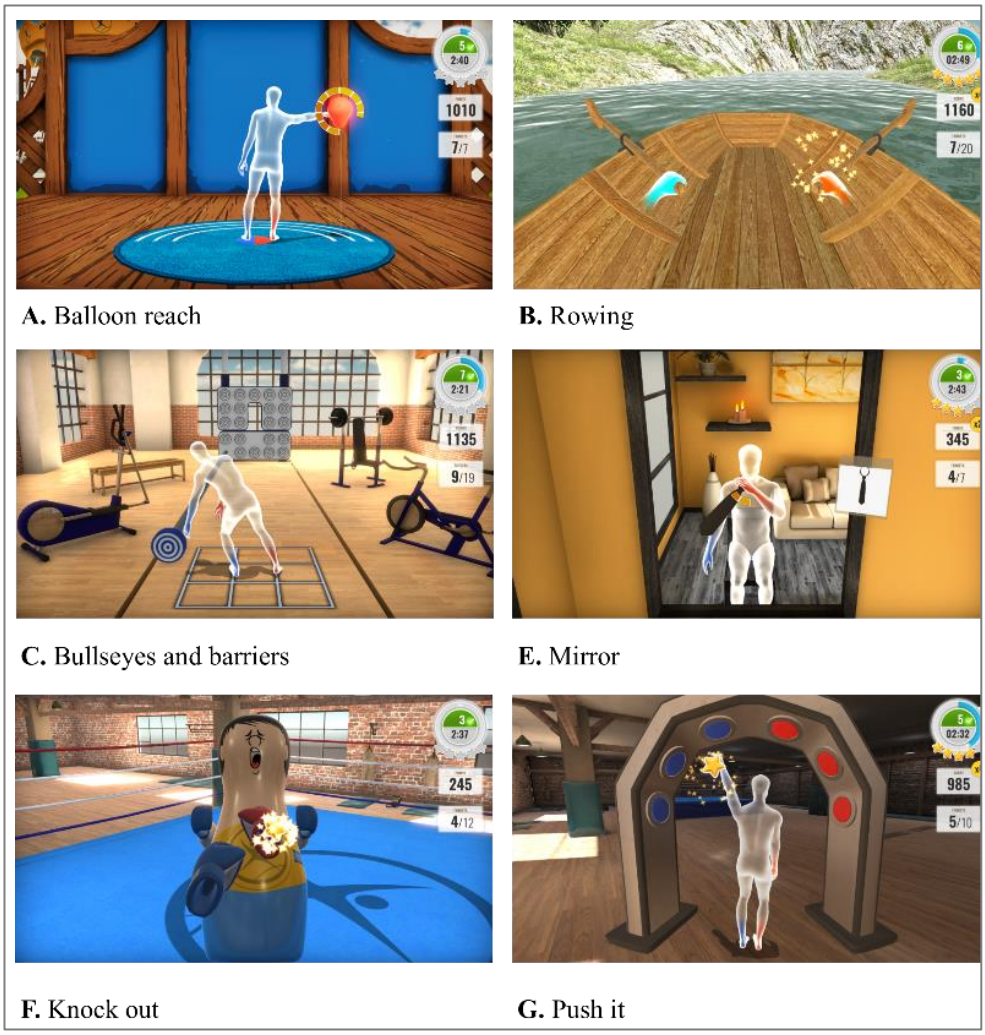
- Shoulder abduction;
- Shoulder flexion;
- Elbow extension and flexion;
- Leaning forward;
- Sit to stand;
- Knee bends;
- Shoulder Extension;
- Reaching forward in sitting;
- Bilateral shoulder external rotation;
- Hip abductor strengthening.

3.3.4 The Exergames module

The term exergame is a portmanteau, linguistic blend of words, of ‘exercise’ and ‘game’ used for games that provide a form of exercise. The exergame module included gaming activities that contain functional strengthening and range of motion exercises (an example of the graphics is shown in Figure 7). Throughout the thesis, the exergame module was updated, the following lists examples of the exergames used for full-body therapy.

- **Knock out:** A boxing game scenario that engaged both upper limbs.
- **Rowing:** Mimicking a rowing action to move the virtual boat down the river.
- **Weightlifting:** Bilateral upper limb movements to virtually lift a weight bar into various positions.
- **Sit to stand:** Moving from a seated position to standing.
- **Sit step reach:** In addition to standing, one leg is used to step forward, while one arm reaches out to a virtual target.
- **Balloon reach:** Virtual balloons were placed at varying distances on either side of the participant's avatar. The goal was to reach out in front/or to the side to touch each virtual balloon.
- **Reach with shoulders:** The user must intercept the balloons which appear on-screen using their shoulders.
- **Water pump:** A virtual sinking boat required water to be pumped out—this required contralateral arm movements.
- **Bullseyes and barriers:** A virtual layout sent a randomised pattern of either a bullseye (e.g. a target for the hand to virtually touch) and barriers (e.g. a virtual step which required the knee to lift to clear).
- **Fit into a figure:** The user ensured the avatar shape (aligned with their body) matches the various shape shown on the screen.
- **Push it:** Participants were asked to push virtual targets away from their body in a smooth movement.
- **In the Kitchen:** A virtual kitchen layout required participants to identify the target item (i.e. apple) on a shelf and then place it on the virtual countertop.
- **Mirror:** A virtual mirror reflected the participants' avatar, items appeared related to typical dressing activities (i.e. glasses, gloves) and the participant needed to place the item on the appropriate highlighted part of the body of the avatar.
- **Plug the holes in a boat:** The user only saw the position of their hands - they have to cover the holes that appear in the boat.

Figure 7: Example of the Virtualrehab platform exergame graphics



A. Balloon reach **B.** Rowing

C. Bullseyes and barriers **E.** Mirror

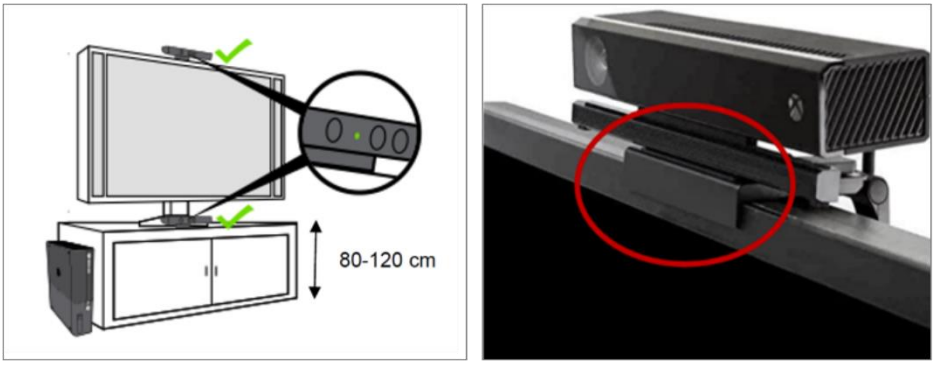
F. Knock out **G.** Push it

3.4 SET-UP REQUIREMENTS WITHIN THE HOME

The industrial collaborator provided a manual, detailing the specific set-up requirements (adapted from recommendations used with the Kinect V2 sensor (Microsoft, Washington, United States)); this was to ensure the optimal use of the Virtualrehab platform in the home environment. The following summarises information given by the industrial collaborator. It should be noted that these requirements were adapted for each individual's home environment the equipment was set-up in, during the studies reported in this thesis.

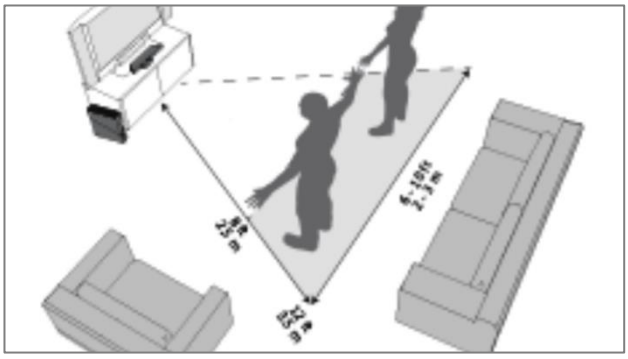
The sensor required a certain height to optimally capture the anatomical landmarks, to ensure this was reached in each home environment; a clip was obtained to attach the sensor to the TV (Figure 8).

Figure 8: Kinect V2 set-up required for the home environment



The user required approximately six foot of space, with adequate room for their full range of movement to safely use the platform (Figure 9).

Figure 9: The optimal distance for set-up



Other environmental factors that needed to be considered, included:

- Limiting other light sources which could interfere with the sensors (i.e. sunlight, mirrors and floors with shine);
- Ensuring that all the anatomical landmarks were in the sensors field of view (i.e. no animals or children, no furniture – aside from supportive equipment).

For appropriate set-up within the home environment, a tape measure was required to ascertain the distance from the device to where the participant would be standing or sitting. Overall, participants needed to be at least one metre tall, ensure they wore appropriate clothes (i.e. avoid baggy or shiny clothes), ensure their feet were touching the floor.

3.5 ITERATIVE DEVELOPMENT

Phase II and III of the work reported in this thesis were undertaken in part to provide end-user and Researcher feedback to the industrial collaborator; a research diary was used to record challenges throughout the thesis period.

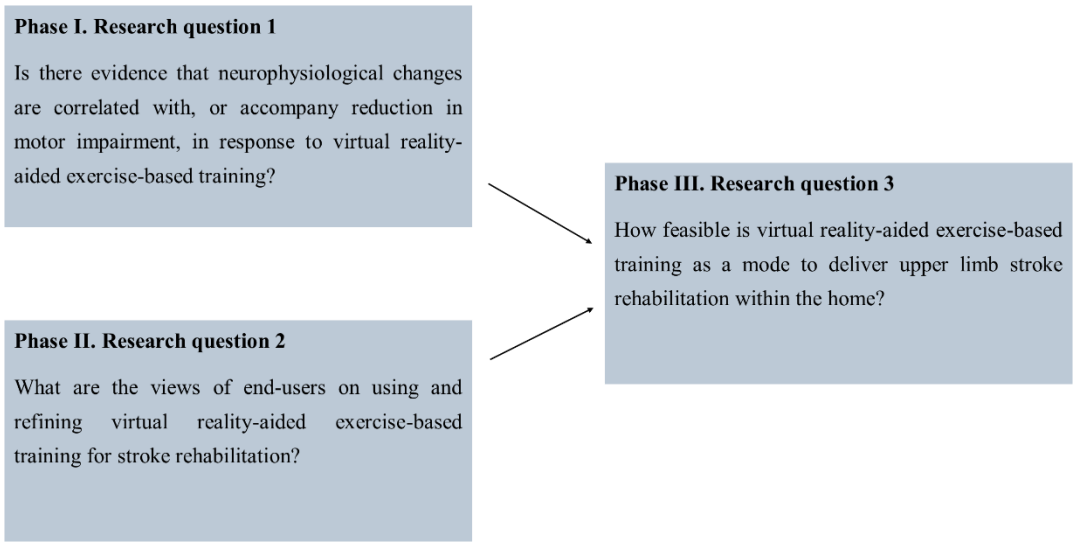
4 METHODOLOGICAL FRAMEWORK

A rigorous methodological approach is essential for replicable, robust and implementable evidence (Walker *et al.*, 2017). The following chapter justifies the multiphase mixed-methodology framework that was used to address the overarching research aim:

To investigate the delivery of exercise-based upper limb stroke rehabilitation via virtual reality within the home

To appropriately explore the aim, three phases of work were designed (Figure 10).

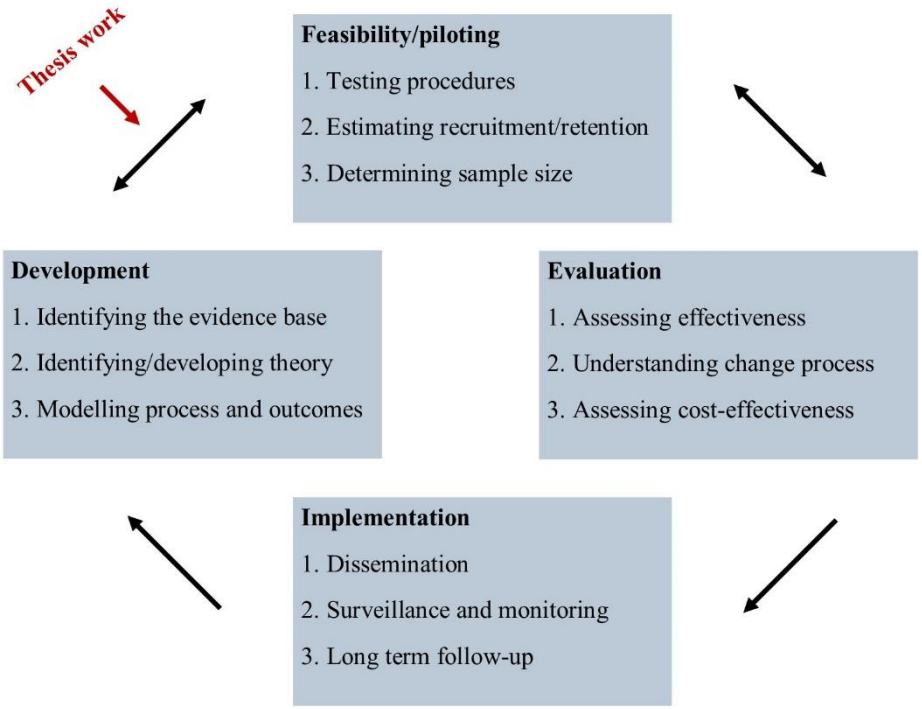
Figure 10: The phases of work addressing the overarching thesis aim



4.1 METHODOLOGICAL UNDERPINNINGS TO THE THESIS

The research reported in this thesis falls under the scope of a complex intervention as it involves a heterogeneous stroke population, multi-faceted healthcare system and tailored rehabilitation technology. Thus, the methodological underpinnings are first guided by the Medical Research Council's (MRC) Framework for Complex Interventions (Figure 11). It is important to note that the progression from 'development' to 'implementation' requires a systematic multi-phased approach (Craig *et al.*, 2008).

Figure 11: The MRC Framework for Complex Interventions, from development to implementation (Craig et al., 2008, p. 8), with a note of where the thesis work falls in this framework.



The thesis focused on refining a potential virtual rehabilitation tool and investigating its use within the community, rather than 'evaluating' or 'implementing' an intervention. Therefore, the work falls between the 'development' and 'feasibility' stages of the MRC Framework for Complex Interventions (as indicated in Figure 11). Researching complex interventions for stroke rehabilitation is known to be challenging. Stroke is a heterogeneous disease, with recovery highly dependent on the brain regions involved in the infarct (Regenhardt *et al.*, 2020). Interventions require a targeted, individual approach built from a robust understanding of the numerous mechanisms involved (i.e. biomarkers of motor recovery, time after stroke) (Boyd *et al.*, 2017). Hence, translating stroke research into meaningful, implemented clinical practice is a complicated process, and often unsuccessful (Dobkin, 2009; Stroke Association, 2018; Juckett *et al.*, 2020).

It can be challenging to bridge the gap between feasibility/pilot studies to large, robust trials and finally, clinical rehabilitation guidelines and practice. In order to facilitate the process of designing successful clinical trials, recommendations have been developed for conducting higher quality initial investigations (i.e. pilot, feasibility studies) (Dobkin, 2009). Thus, the thesis development was also informed by stage one (consideration-of-concept trials) and stage two (development-of-concept trials), taken from the progressive staging of pilot studies to improve phase three trials for motor interventions (Dobkin, 2009). The above framework guided this thesis in order to progress the evidence-pathway appropriately.

4.2 A MIXED METHODS RESEARCH APPROACH

Healthcare research is inherently complex and must account for the nuances of real-world investigations (i.e. uncontrollable human factors; outside therapeutic influences; diverseness of the study population) (Bradshaw, Atkinson and Doody, 2017; Greenhalgh and Papoutsi, 2018; Juckett *et al.*, 2020). Furthermore, delivering stroke rehabilitation via technology includes many additional factors (i.e. challenges with technology and intricacies of home-based therapy).

In order to account for the complex factors involved, a mixed-methods approach was deemed appropriate. The design offers a more comprehensive interpretation of the phenomena, than either qualitative or quantitative alone (Tashakkori and Creswell, 2007). The combination of such methodologies is often seen to be 'complementary', overcoming the weaknesses inherent in both processes (Creswell, 2014; Hafsa, 2020).

The qualitative methodology offers an inductive process to explore the lived experiences of individuals undertaking or working with stroke rehabilitation. However, despite the in-depth wealth of information gained, the small samples sizes limit the generalisability of interpretation. Furthermore, the diverse nature of the stroke population is difficult to account for, and thus small samples can limit the effectiveness of interventions in real-world clinical settings (VanderKaay *et al.*, 2018).

On the other hand, quantitative methodologies utilise large representative samples to investigate phenomena empirically. These methods are essential in understanding the underlying mechanisms of change that interventions can produce, allowing for a targeted therapy that can facilitate behavioural restitution. However, acceptability and clinical uptake of interventions cannot be fully explored without the experiences of those involved (Tariq and Woodman, 2013).

The integration of both qualitative and quantitative findings is key to providing a 'holistic' in-depth view of all the factors within a phenomenon (Hafsa, 2020). It is also important to include person-centred rehabilitation and co-development, as these are known to be at the centre of facilitating the uptake of stroke therapy (Bowen, James and Young, 2016; Kulnik *et al.*, 2019). There are numerous potential benefits of collaborating with the end-user in research, including insights into how therapy delivery could be optimised as well as improving retention, recruitment to research and adherence to therapies (Kerr *et al.*, 2018; Wentink *et al.*, 2019; Kübler, Nijboer and Kleih, 2020).

Thus, it is necessary to utilise a mixed-methodology research approach in order to produce robust evidence that has the potential to improve stroke rehabilitation, with both empirical findings and the lived experiences of those involved (Bowen, James and Young, 2016).

The mixed-methodology research approach used in this thesis is defined as:

> Collecting, analysing, and mixing both quantitative and qualitative data in a single study or a series of studies.
>
> (Creswell and Clark, 2007, p. 2)

The philosophical assumptions of a mixed-methods approach are founded in pragmatism (Cherryholmes, 1992; Shaw, Connelly and Zecevic, 2010; Creswell, 2014), defined as:

> A paradigm that debunks concepts such as 'truth' and 'reality' and focuses instead on 'what works' as the truth regarding the research question under investigation.
>
> (Tashakkori and Teddlie, 2003, p. 713)

A pragmatism approach offers researchers flexibility in terms of the methods, techniques and procedures utilised in combination, to provide a comprehensive view of the research question. It allows for a holistic understanding of the research problem; particularly in light of the complexities of healthcare research (Creswell, 2014).

A mixed-method approach is required to provide robust evidence and facilitate the uptake of stroke rehabilitation technologies; a multi-faceted approach long advocated for in research (Craig *et al.*, 2008; Creswell, 2014). It is also vital to include the voice of those who would benefit from such research. This approach is recommended at all stages and notably advocated by the MRC's Framework for Complex Interventions (Craig *et al.*, 2008).

4.2.1 Identification of the mixed-methods research approach

Identifying which mixed-method research approach to use is a complex, flexible process, that differs depending on several factors such as the research aims, population investigated, and procedures involved. The decision of which approach to use in this thesis was guided by the key principles put forth by Creswell and colleagues. There are four key principles and decisions to consider when choosing an appropriate mixed-methods design (Creswell and Plano-Clark, 2011). The full process used to decide the mixed-methods approach adopted in this thesis is outlined in Table 2.

Table 2: Key principles considered in identifying the appropriate mixed methodology for the thesis

Principle	Description of principle	Relevance for thesis work
A mixed methods research design can be fixed and/or emergent	**Fixed**: QUAL and QUAN methods are predetermined before the study conduction. **Emergent**: QUAL or QUAN methods are added during the study to overcome challenges with the original methods used. **Both:** Both fixed and emergent designs can be used to aid complex intervention development.	The overarching framework of the thesis followed a **fixed approach**, incorporating both QUAL and QUAN within the planning of the phases. However, during the conduction of each study (phase of the thesis) aspects of an **emergent approach** was required to overcome any challenges in the planned methodologies.
Identifying an approach to the mixed methods research design	**Typology-based approach**: Choosing a mixed-method classification based upon an existing design and adapting it to the study's purpose and research questions. **Dynamic-based approach**: Choosing components from different mixed method designs that fit the study's purpose and research questions.	A **typology-based approach** was chosen to answer this overarching thesis aim (chapter two). This was used as a guide for developing the overarching thesis research design, and its components were adapted to the research purpose.

Principle	Description of principle	Relevance for thesis work
Level of interaction between the components (QUAN and QUAL)	**Independent**: The QUAN and QUAL components are kept separate throughout the study research questions, data collection and analysis. The only point at which mixing occurs is the overall interpretation at the end of the study. **Interactive**: The QUAN and QUAL components are used to build upon each other throughout the study research questions, data collection and analysis.	Within the three work phases for this thesis, the components are **independent** and were mixed at the point of interpretation, including the overall discussion addressing the overarching research aim.
The priority of the components (QUAN and QUAL)	**Equal priority**: Both QUAN and QUAL components have equal priority in answering the research aim. **Quantitative priority**: The QUAN components takes overall priority within the research study. **Qualitative priority**: The QUAL components take overall priority within the research study.	Overall, the components have **equal priority** within this thesis in order to achieve the overarching aim. Phase I of the thesis only incorporates QUAN components (chapter four). Whereas Phase II, the QUAL components is the priority as dictated by the research question (chapter six). Finally, in phase III, both components have equal priority as is appropriate for the research objectives (chapter seven and eight).

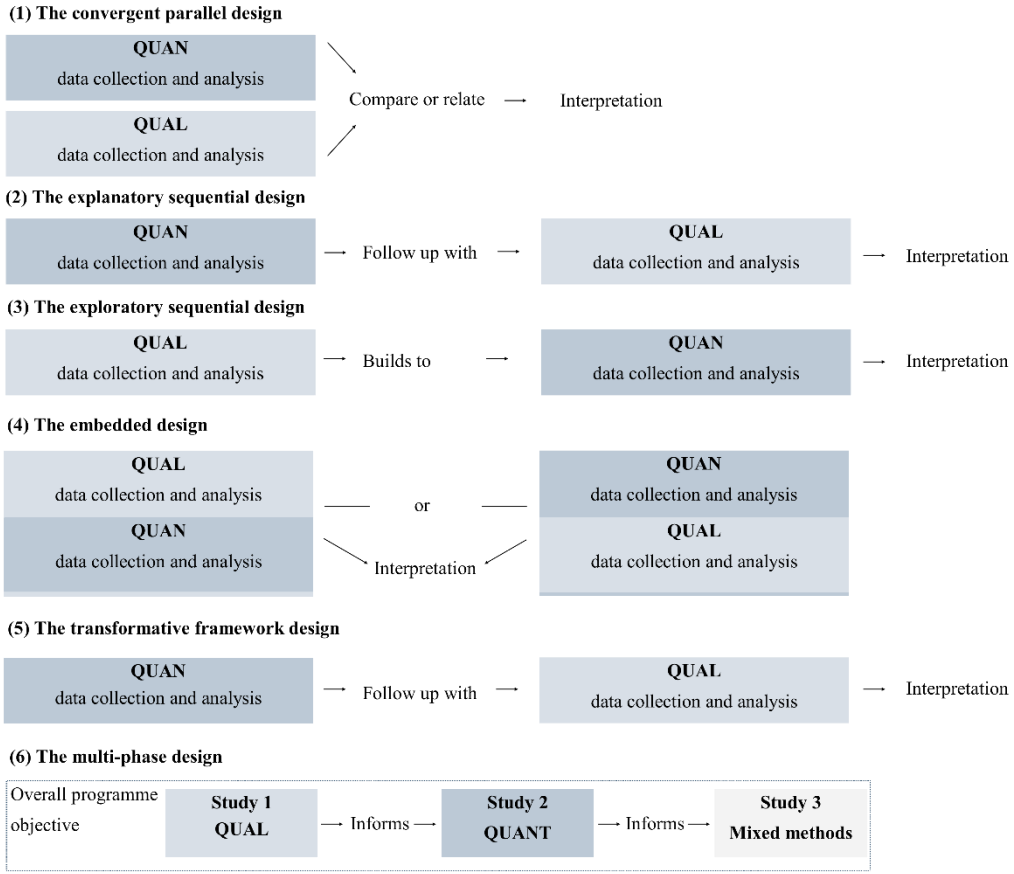
Principle	Description of principle	Relevance for thesis work
The timing of the components	**Concurrent**: QUAN and QUAL are used parallel and independently. **Sequential**: One method precedes the other, influencing the other. **Multiphase combination timing:** A series of QUAN and QUAL phases are used to answer an overall research aim, the exact combination of which is dependent on the research question.	The most appropriate timing to address the overarching thesis aim is a **multiphase combination timing**.

NB. QUAN, quantitative; **QUAL,** qualitative

After considering the key principles, the mixed-methods approach was both a fixed and emergent design. It also utilises a typology-based approach with independent interaction between each component. The results of each method are mixed at the point of interpretation and given equal priority. Finally, a multiphase combination timing was most appropriate for the three phases developed, to answer the overarching thesis aim.

Once the design principles have been decided, the exact mixed-methodology framework needs to be considered. There are traditionally six main designs (Figure 12). It should be noted that each research discipline will have variations in the design, and the process is flexible. Typically, the flexibility of applying the frameworks are guided by the research aims (Creswell and Plano-Clark, 2011). Each of the six main mixed-method designs has strengths and weaknesses, with guidance on implementation in research. For the thesis overarching research aim, we regarded a multiphase mixed-method design appropriate.

Figure 12: Diagrams of the six-common mixed-methods designs (QUAN, quantitative methods; QUAL, qualitative methods), adapted from (Creswell and Plano-Clark, 2011, pp. 69–70 fig 3.2)



4.2.2 The multiphase mixed-method design

The multiphase mixed-method design provides an overarching methodological framework that calls for a set of incremental research questions to address the overall research aim (Creswell, 2014). The factors detailed in this chapter led to the choice of framework. Overall, a single mixed-method study would not address the overarching research aim. This project was also supported by a multi-disciplinary research team, with experience in such programmes (i.e. the supervisory team; additional colleagues from the Acquired Brain Injury Research Alliance (ABIRA) and the industrial collaborator). The team had the resources and funding to support the Researcher (author of the thesis) in carrying out the different phases. This included access to a wide range of expertise in stroke rehabilitation, physiotherapy, technology rehabilitation and both qualitative and quantitative methods. It is also important to consider the philosophical assumptions behind the design, as discussed earlier; a pragmatic approach is appropriate for the research aim. This assumption is also recommended for multiphase mixed methods research projects (Creswell, 2014). Finally, the systematic phased approach of this design has been advocated by MRC's Framework for Complex Interventions (Craig *et al.*, 2008).

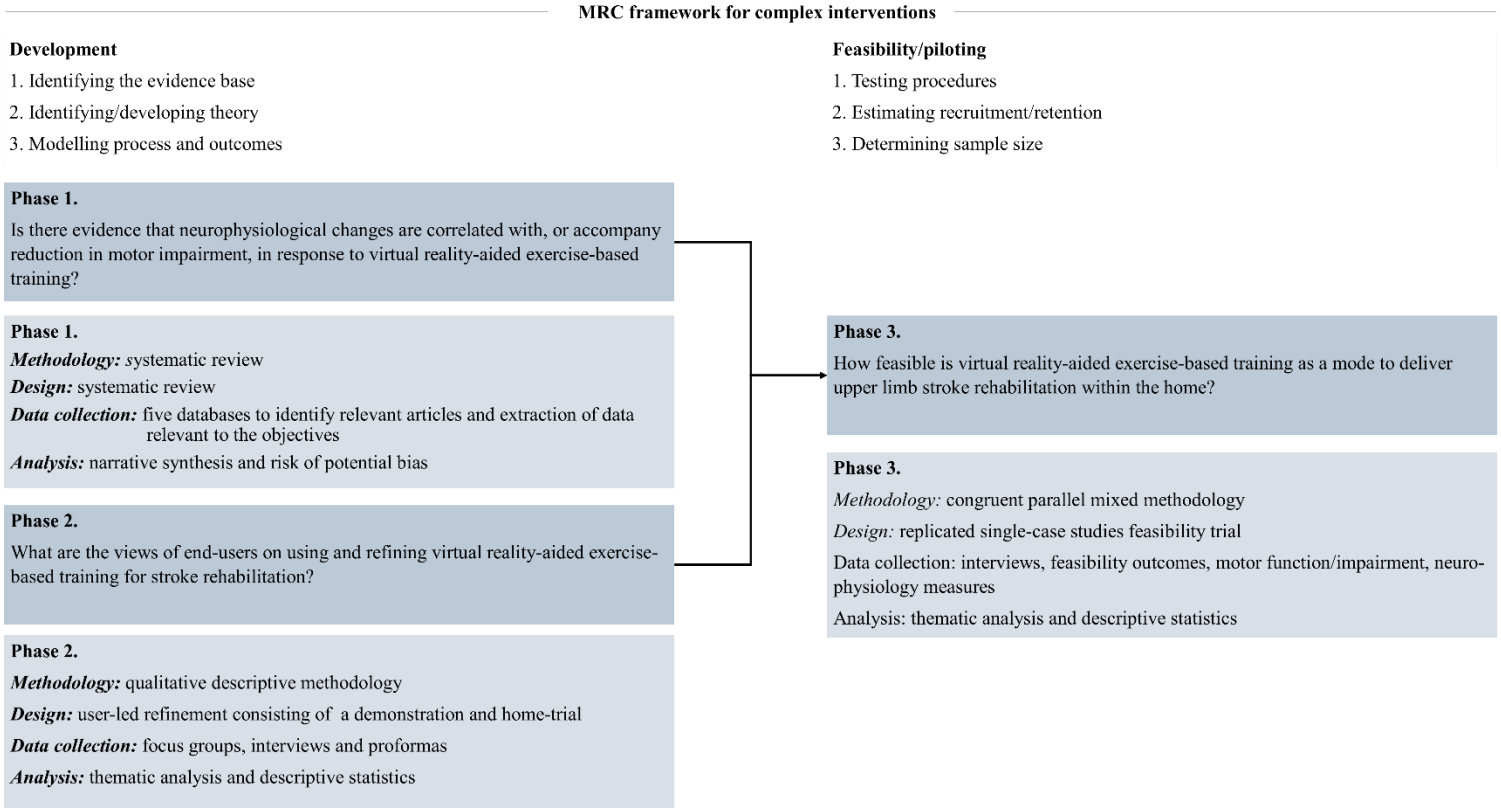
It is important to acknowledge the strengths and challenges of the chosen methodological design. The complexity of the intervention and the subsequent need to investigate a diverse population in the community requires a flexible approach. This design allows for a series of interconnected research

questions to be explored in an adaptable, pragmatic way. Indeed, this design provides an overall framework for the multiple studies required. This design presents several challenges that are relevant to the thesis's research aim. It is important to anticipate and account for the challenges associated with each study (phase) of the project. This is apparent when considering the resources and time required to conduct multiple studies over several years. For example, each methodology requires different ethical and recruitment procedures; if a phase is dependent upon the completion of a prior one, any challenges can produce an accumulative effect. The time over which such projects are carried out is also challenging when working with a fast-paced evolving industry such as technology; adaptions are required for potential changes in the equipment required.

4.2.3 Operationalisation of the mixed-methods design within the thesis

The mixed-method design was used to address the overarching thesis research aim via a series of interconnected studies. Each study consists of specific research aims, questions and methods that contribute to the overall program of inquiry. This framework was utilised within the thesis in three phases (Figure 13). Phase I consisted of systematic quantitative synthesis of the evidence base (chapter five); phase II involved developing a qualitative descriptive design (chapter six); and in phase III, a convergent parallel mixed-methods approach was implemented (chapter seven and eight). The results of all three phases are integrated into a discussion to address the overall research aim (chapter nine).

Figure 13: Diagram of how the multiphase mixed-methodology research design, following the MRC framework for complex interventions, was operationalised within the thesis



4.3 CONCLUSIONS

This chapter has justified and detailed the multiphase mixed methodology framework used to answer the thesis research aim and associated research questions/objectives. The thesis consists of three phases, aligned with the 'development' and 'feasibility' stages of the MRC's Framework for Complex Interventions (Craig *et al.*, 2008) and informed by the progressive staging of pilot studies to improve phase three trials for motor interventions (Dobkin, 2009).

5 PHASE I: NEUROPHYSIOLOGICAL CHANGES ACCOMPANYING A REDUCTION IN UPPER LIMB MOTOR IMPAIRMENTS IN RESPONSE TO EXERCISE-BASED VIRTUAL REHABILITATION AFTER A STROKE

5.1 INTRODUCTION

Phase I addressed the first research question (chapter 2, section 2.1):

Is there evidence that neurophysiological changes are correlated with, or accompany reduction in motor impairment, in response to virtual reality-aided exercise-based training?

The research question was investigated through a systematic review of the literature, aligning with the 'development' stage of the Medical Research Council's (MRC) Framework for Complex Interventions (Craig *et al.*, 2008).

The following chapter presents the systematic review's research objectives, methods, results and discussion.

5.2 RESEARCH AIMS

To answer the first research question, phase I aimed to:

Aim 1a: Determine the neurophysiological correlates of upper limb motor impairment response to virtual reality aided exercise-based training following a stroke.

The above research aim was devised to establish if Virtual Reality (VR) can drive neural recovery. As a recent Cochrane review noted that there was a limited number of studies investigating the underlying neural mechanisms (Laver *et al.*, 2017), if insufficient evidence was found to answer research aim 1a, a subsidiary research aim was proposed 1a.2.

Aim 1a.2: Determine if there is evidence that an improvement of motor impairment occurs alongside change in neurophysiological measures

5.3 METHODS

5.3.1 Design

This study followed a systematic review design, conducted according to the Cochrane Collaboration guidelines (Higgins, 2015). The systematic review's protocol can be found on the Prospero database, registration number: CRD42017071312. Three reviewers worked independently, using pre-prepared proformas to (a) identify eligible studies, (b) assess the potential risk of bias and (c) extract data. Disagreements were resolved through referral to the full text, with a fourth reviewer arbitrating if an agreement could not be reached.

5.3.2 Searching for studies

The search strategy was developed in collaboration with a research librarian. Eight online databases were searched from their inception to August 2020:

- MEDLINE via Ovid;
- Allied and Complementary Medicine Database (AMED);
- Excerpta Medica dataBASE (EMBASE);
- PubMed Central (PMC);
- Cochrane Library (COCHRANE);
- The Cumulative Index to Nursing and Allied Health Literature (CINHAL);
- ProQuest Dissertations and Theses (PROQUEST);
- Open Grey Europe (OPEN GREY).

The search combined MeSH and non-MeSH terms. The example search strategy provided in Table 3 was used for MEDLINE and adapted as appropriate for other databases (Appendix 1B). In addition, the reference lists of eligible articles were hand searched for potential studies not identified in the databases.

Table 3: The search strategy used to search the MEDLINE via Ovid database as an example of electronic searches

Participant (title and abstract only)	Stroke survivors OR stroke patients OR cerebrovascular accident OR stroke OR CVA OR stroke rehabilitation
Intervention (title and abstract only)	Virtual reality rehabilitation OR VR OR telerehabilitation OR telehealth OR computer rehabilitation OR technology rehabilitation OR user-computer interface
Outcome (full text)	Electromyography OR EMG OR Electroencephalography OR EEG OR M-waves OR H-reflex OR Functional electrical stimulation OR FES OR peripheral stimulation OR electrical stimulation OR Biomechanic* OR TMS OR Trans Magnetic Stimulation OR Evoked potential OR non-invasive brain stimulation (NBS) OR Functional Magnetic Resonance Imaging OR FMRI OR SMRI OR MR imag* OR MR scan OR magnetic resonance scan OR structural adj2 MR* OR volum adj2 OR MR OR vMRI OR MRI OR Diffusion tensor imaging OR DTI OR BOLD OR Tomography OR X-ray computed OR computer adj3 tomograph OR Positron Emission Tomography OR Magneto-encephalography OR MEG OR Neural correlate OR neurophysiological measure OR cortical reorgani* OR MEP OR PET OR CAT OR CT
Limits	English Language, human, full text.

NB. Each search row was combined using the command 'AND'

5.3.3 Eligibility Criteria

Types of studies

All experimental study designs were included if they investigated an experimental and a control condition before and after the provision of a VR intervention (defined in subsection – types of intervention).

Types of participants

Participants were at least 18 years old and had an upper limb motor impairment at any time point after a stroke. Studies were excluded if they investigated participants who had a diagnosis of a neurological condition in addition to the stroke.

Types of intervention

Studies were eligible if they included virtual reality exercise-based interventions designed to reduce motor impairment and used an electronic screen. All virtual reality devices were included, ranging from immersive (i.e. using headsets) to non-immersive (i.e. real-time movement replicated via an onscreen avatar). However, studies that investigated virtual reality combined with another rehabilitation technology (e.g. a robotic arm device) were excluded.

Types of measures

Studies were eligible if they reported measures of motor impairment (i.e. Upper Extremity Fugl-Meyer, Biomechanical variables) and neural measures (i.e. Electromyography (EMG), Transcranial Magnetic Stimulation (TMS), functional Magnetic Resonance Imaging (fMRI) – derived measures).

5.3.4 Assessment of potential risk of bias

The Cochrane Risk of Bias tool (CROB) was used to measure methodological weaknesses in the design or execution of the included studies; which can increase the risk of bias, influence the validity of the findings and lead to an overestimate or underestimate of the intervention's effect (Higgins *et al.*, 2011; Higgins, 2015). Each study was individually evaluated according to the criteria by the Researcher, in consultation with the review team.

The CROB tool was designed to assess Randomised Control Trials (RCTs), known as the gold standard research design for assessing interventions. Systematic reviews and meta-analysis of RCTs are used to synthesise the evidence-base to guide recommendations for clinical practice; for example, prior reviews of virtual reality for stroke rehabilitation have used the CROB tool to assess RCTs (Laver *et al.*, 2017).

The tool was used to assess the Non-Randomised Studies (NRS) included in the systematic review. Although it was not developed with these designs in mind, it has been argued that a comprehensive assessment of the evidence requires an in-depth understanding of both RCTs and NRS designs (Saturni *et al.*, 2014; Bothwell *et al.*, 2016). It is known that RCTs investigating complex health care interventions are difficult to implement into clinical practice because of the methodological weaknesses, not only inherent in the larger trials but in the initial investigations that are used to develop RCTs (i.e. non-randomised small pilot or proof-of-concept studies) (Walker *et al.*, 2013;

Lynch, Chesworth and Connell, 2018). It is clear that these initial NRS need to be held to the same scrutiny as the 'gold standard' trial designs (Dobkin, 2009).

There were two other risks of bias tools considered for the systematic review. Firstly, the Cochrane collaboration released a CROB for NRS in 2016 (ROBINS-I) (Sterne *et al.*, 2016); this was during the development of the systematic review and had not been widely used, or assessed, at the time and thus was not utilised. Secondly, the Downs and Black ROB tool was considered (Downs and Black, 1998). It was determined that the tool would not allow for an in-depth review of the methodological quality for the multiple trial designs included; potentially underestimating the risk of bias. A more in-depth investigation was required; hence the Cochrane RoB tool was chosen.

5.3.5 Data extracted

At the baseline point for included studies, the data extracted were: the number of participants in experimental and control condition; age; time since the stroke; and the values for motor and neural impairment. For each included study, the intervention characteristics extracted were the: number of weeks; number of sessions; duration of each session; device details and training task. At the outcome point for included studies, the data extracted were: the number of participants in each condition; time since baseline; and the values for motor and neural impairment. If data was not available within the publications, then the authors were contacted for the data required.

5.3.6 Synthesis

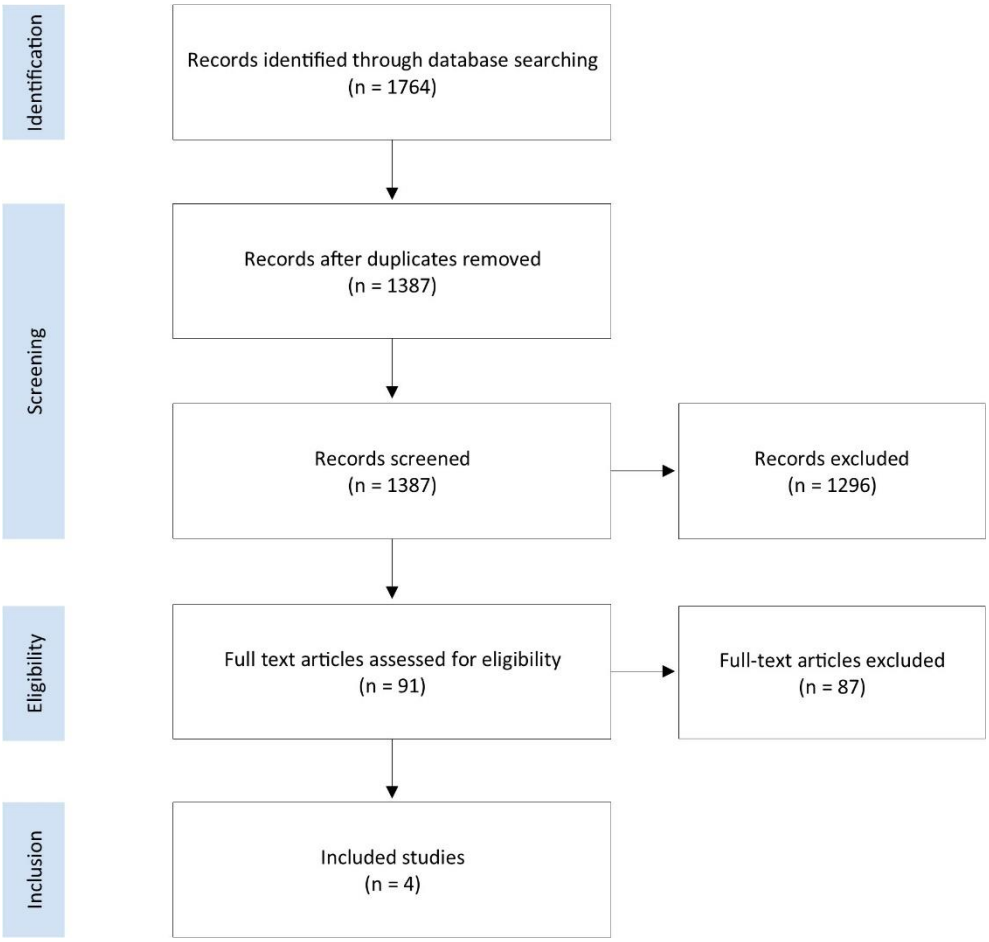
A meta-analysis was not possible because of the heterogeneity in participants, interventions and outcome measures. A narrative synthesis was, therefore undertaken to address the research aims.

5.4 RESULTS

5.4.1 Identification of studies

The PRISMA flowchart is provided in Figure 14. Initially, 1764 records were identified from the electronic searches. Removal of duplicates left 1387 records, of which 1296 were excluded. Consequently, 91 full-text articles were screened for eligibility. No additional records were identified from searching the reference lists of eligible full-text articles. Four articles met the eligibility criteria (Jang *et al.*, 2005; Carey *et al.*, 2007; Donoso Brown *et al.*, 2014; Ballester *et al.*, 2017). The main reasons for records to be excluded were a lack of neurophysiological outcome measures, using virtual reality combined with another intervention, and no control condition.

Figure 14: Prisma diagram of searches and identification of included studies in this review.



NB. The percentage of full-text articles under each exclusion criteria

- No neurophysiological outcome measure (75%);
- No Virtual Reality intervention (44%);
- A diagnosis of other neurological condition (5% reported; 60% did not report this);
- No pre/-post control group (46%);
- No clinical measure of motor impairment (37%);
- No upper limb motor impairment (31%);
- No diagnosis of stroke (24%);
- Not an experimental study design (20%);
- Not adult participants, 18+ (20%);
- No pre/-post-intervention group (19%);
- Not written in English (18%);
- Other reasons: 5% were protocols; 12% did not have an available full text.

5.4.2 Characteristics of included studies

Participant characteristics are displayed in Table 4, Table 5.

5.4.2.1 Types of studies

The four included studies had different experimental designs:

- parallel-group controlled trial (Ballester *et al.*, 2017);
- randomised cross-over trial (Carey *et al.*, 2007);
- single-group repeated measures study, with the control phase preceding the intervention phase (Donoso Brown *et al.*, 2014);
- pre/post-test randomised controlled design (Jang *et al.*, 2005).

Table 4: Characteristics of included studies and participants at baseline, part 1

Study reference	**Number of participants**		**Age, years.** (mean ± standard deviation, unless otherwise stated)		**S**ex (female: male)		**Time since stroke, years.** (mean ± standard deviation)	
	VR	**Ctrl**	**VR**	**Ctrl**	**VR**	**Ctrl**	**VR**	**Ctrl**
Ballester et al. 2017	17	18	65.1 ± 10.3	61.8 ± 12.9	8: 9	11: 6	2.9 ± 2.1	2.2 ± 1.2
Carey et al. 2007	10	10	65.9 ± 7.4	65.9 ± 7.4	9: 1	6: 4	3.5 ± 2.0	2.9 ± 2.2
Jang et al. 2005	5	5	54.5 ± SE 5.3	54.5 ± SE 5.3	3: 2	3: 2	13.8 ± 3.6	3.4 ± 2.2
Donoso Brown et al. 2014	9[a]		59.9 ± 8.9[a]		4:5[a]		7.2 ± 7.9[a]	

N.B. SE, Standard Error; a, repeated measures design, participants took part in both intervention and control conditions.

Table 5: Characteristics of included studies and participants at baseline, part 2

Study reference	**More paretic side** (Left: Right)		**Type** (Haemorrhagic: Ischemic); **Location of stroke lesion** (R, right; L, left)	
	VR	**Ctrl**	**VR**	**Ctrl**
Ballester et al. 2017	11: 6	9: 9	6: 11; Location not reported.	6: 12; Location not reported.
Carey et al. 2007	5: 5	8: 2	Type not reported; Cortical (5); Subcortical (5)	Type not reported; Cortical (3); Subcortical (7).
Jang et al. 2005	Not reported	Not reported	2: 3 Thalamic (R =1, L=1); Cortical (R=1, L=0); Corona Radiate (R=1, L=1)	2: 3 Thalamic: R=1, L=1; Corona Radiate: R=1, L=2.
Donoso Brown et al. 2014	6: 3[a]		Type not reported Unknown = 4; Brainstem = 2; Basal Ganglia = 1; Frontal = 1; Parietal/Frontal = 1.	

NB. a, repeated measures design, participants took part in both intervention and control conditions.

5.4.2.2 Participants

The included studies reported baseline characteristics data on a total of 74 participants, 32 for the intervention and 33 for the control condition, with an additional nine participants who took part in both conditions in a repeated measures design. The mean ages of all participants were: 62.35 (standard deviation = 10.5) years and similar for those in the virtual reality conditions, 62.67 (standard deviation = 9.41) years, and the control conditions 61.39 (standard deviation = 10.42) years. The mean times since stroke onset were: 4.22 (standard deviation = 4.63) years for all participants, 5.45 (standard deviation = 5.66) years for participants in the intervention condition and 3.82 (standard deviation = 4.69) years for participants in the control condition.

The severity of motor impairment at baseline ranged from moderate to severe, according to the included studies criteria and confirmed by data collected at baseline (i.e. passive paretic hand extension-flexion (Carey *et al.*, 2007), Upper Extremity Fugl-Meyer (UE-FMA) scores (Jang *et al.*, 2005; Ballester *et al.*, 2017), paretic finger and elbow Active Range Of Movement (AROM) (Donoso Brown *et al.*, 2014)).

5.4.2.3 Virtual Reality intervention equipment and procedures

A variety of equipment was used for the Virtual Reality intervention conditions (Table 6). All included studies used a computer and screen in their set-ups (Jang *et al.*, 2005; Carey *et al.*, 2007; Donoso Brown *et al.*, 2014; Ballester *et al.*, 2017). Three included studies used types of data collection gloves (Jang *et al.*, 2005; Carey *et al.*, 2007; Ballester *et al.*, 2017). One study used surface Electromyography (sEMG) to map Upper Extremity (UE) movements (Donoso Brown *et al.*, 2014). The tasks engaged upper limb movements that were tailored and customised for individuals. Planned amounts (doses) of the intervention varied between studies, with only one reporting the actual dose provided (fidelity) (Donoso Brown *et al.*, 2014).

Table 6: Included studies details of Virtual Reality intervention equipment and procedures

Study reference	VR intervention procedures				Control intervention procedure		
	Equipment	**Task**	**Dose**	**Fidelity**	**Task**	**Dose**	**Fidelity**
Carey et al. 2007	Computer with customized software. Data gloves containing custom-made electro goniometers, each with 2 potentiometers capturing (extension/flexion movement at the index MP joint and the wrist). First-person perspective, with real-time hand movements, translated on-screen (joint movement, represented through voltage collected at 100hz).	Target: Flexion/ extension with the index finger and wrist to complete waveforms appearing on the computer. Game: The screen showed a target waveform and tracking response from the participants. Tailored: Knowledge of results via an accuracy score with text	2 weeks 10 sessions, 120 mins each Paretic side for 90% of the training.	Not reported	Target: Flexion/ extension with the index finger and wrist. Game: screen displaying a sweeping cursor, but no target is shown or feedback provided	2 weeks 10 sessions, 120 mins each.	Not reported

Study reference	VR intervention procedures				Control intervention procedure		
	Equipment	**Task**	**Dose**	**Fidelity**	**Task**	**Dose**	**Fidelity**
		instructions on how to improve.					
Ballester et al. 2017	Computer with customized software. Camera to capture UE movement (trunk movements were filtered out). Data gloves equipped with bend sensors capturing finger flexion and extension. First-person perspective, with real-time movement, translated on-screen	Target: Bilateral reaching movements with wrist and fingers flexion/extension. Game: Interception and grasping of virtual spheres. Tailored: Performance ratio (successful trials over total trials) was kept above 0.6 and below 0.8. Customized: Trajectories	3 weeks 15 sessions, 30 mins each Equally split between each hand	Not reported	Target: Mimic the VR-intervention movements. Game: Stacking/un-stacking of plastic cups with right and left hand consecutively.	3 weeks 15 sessions, 30 mins each	Not reported

Study reference	VR intervention procedures				Control intervention procedure		
	Equipment	**Task**	**Dose**	**Fidelity**	**Task**	**Dose**	**Fidelity**
		(differing hand and grasp motions); velocity.					
Jang et al. 2005	Computer with customized software. Camera to capture UE movement Data gloves for movement capture. First-person perspective, with real-time movement, translated on-screen.	Target: Reaching, lifting and grasping motor skills (i.e. hand soccer). Game: Combination of custom games, such as bide-ball; soccer. Tailored: created and overseen by therapists.	4 weeks 20 sessions, 60 mins each	Not reported	No therapy	No therapy	No therapy

Study reference	VR intervention procedures				Control intervention procedure		
	Equipment	**Task**	**Dose**	**Fidelity**	**Task**	**Dose**	**Fidelity**
		Customised: speed, angles and lifting force for each game. Feedback: error rate, speed, direction, joint position and resistive force feedback.					
Donoso Brown et al. 2014	Computer with customized software. To detect movements, sEMG used for the wrist flexor carpi radialis and extensor digitorium communis movements.	Target: Controlled the aim, using their affected upper extremity and launched the ball by clicking a button using the less affected hand	4 weeks 5 days per week; up to 45 (mins, per day) or a total	Sessions: mean = 16.8 standard deviation = 7.0; Hours: mean 11.9, Standard deviation 5.8	No therapy	No therapy	No therapy

Study reference	VR intervention procedures				Control intervention procedure		
	Equipment	**Task**	**Dose**	**Fidelity**	**Task**	**Dose**	**Fidelity**
			of 45	Only recorded			
	First-person perspective, with real-time movement, translated on-screen	Game: Peggle - Participants attempt to clear the board of orange pegs by identifying the correct angle to launch a ball to eliminate pegs. Tailored: software converted muscle activity into movements used to control the game. Sensitivity can be adjusted to detect very low levels of activations	hours a week. .	sessions that lasted more than 5 minutes One participant carried out the intervention at the research lab instead of their home.			

Study reference	VR intervention procedures				Control intervention procedure		
	Equipment	Task	Dose	Fidelity	Task	Dose	Fidelity
		Customized: Conversion was adjusted as needed to facilitate challenging but successful gameplay.					

5.4.2.4 Control condition procedures

The control conditions differed across the included studies. In two studies, the control condition was no therapy (Jang *et al.*, 2005; Donoso Brown *et al.*, 2014). In the other two studies, the control condition was a comparator task designed to mimic the movements of the virtual reality intervention tasks but without the replication of the participants' real-time movements (Carey *et al.*, 2007; Ballester *et al.*, 2017). Planned doses for control conditions matched those for intervention conditions.

5.4.2.5 Time points for assessment of outcomes

Data collection points varied between the included studies (Table 7). All studies collected data pre and post the intervention period for both conditions (Jang *et al.*, 2005; Carey *et al.*, 2007; Donoso Brown *et al.*, 2014; Ballester *et al.*, 2017). One study also measured both conditions three weeks into the 12-week intervention period (Ballester *et al.*, 2017). One study included a three-month post-intervention follow-up collection point for the VR-condition to check for retention of any changes acquired (Carey *et al.*, 2007). In one study, an additional time point was needed for one participant due to their schedule requiring an eight-week intervention period instead of the intended five (Donoso Brown *et al.*, 2014).

Table 7: Neurophysiological and motor impairment data measurement points in the included studies.

Study timepoint	**Included study reference**							
	Ballester et al. 2017		Carey et al. 2007		Donoso Brown et al. 2014[c]		Jang et al. 2005	
	NP	**MI**	**NP**	**MI**	**NP**	**MI**	**NP**	**MI**
Day 1					✓	✓	✓	✓
Day 10	✓	✓	✓[a]	✓[a]				
Day 15			✓[b]	✓[b]				
Day 28		✓						
Day 56					✓	✓	✓	✓
Day 84					✓[d]	✓[d]		
Day 91	✓	✓						

[a]: Only the control group received a crossover test after 10 days

[b.] Only the virtual reality group received a follow-up test 3 months post-test

[c.] Day 1 measures were beginning of control phase and day 28 measures were the end of the control phase

[d]: One participant undertook outcome measures at day 112

NP, neurophysiological measure; **MI**, motor impairment measure

5.4.2.6 Motor impairment outcome measures

The motor impairment outcome measures varied across the included studies (Table 8). Only two included studies used the same measure, namely the Fugl-Meyer Upper Extremity (FM-UE) scores, to determine the severity of motor impairment (Jang *et al.*, 2005; Ballester *et al.*, 2017).

Table 8: Data reported in included studies, motor impairment measures

Study ID	Motor impairment outcome measure	Number of participants reported to have completed the measure	
		Experimental	Control
Ballester et al. 2017	(1) Ashworth proximal and distal scores. (2) Fugl-Meyer. (3) Grip force (procedural details not reported). (4) MRC proximal and distal scores. (2) Finger flexion/extension (calculated from bend sensors in gloves (ranging from 0 to 1 to indicate maximal and minimal metacarpal angles), averaged across all fingers on the paretic hand during an active movement).	17	18
Jang et al. 2005	(1) Fugl-Meyer Upper Extremity scores	5	NR
Donoso Brown et al. 2014	(1) Active range of motion (wrist extensor) during pick-up a cup task (movement with the wrist for maximum extension and flexion (supported at forearm), an average of 5 attempts - the absolute value of the wrist angle from start of movement minus the maximum of the wrist extension completed during the trial). (2) maximum elbow extension (deg) during a pickup a cup task (calculated from the vector dot product of 2-line segments formed by the shoulder to the elbow marker and the elbow marker to the average position of the 2 wrist markers). (3) number of movement segments from the hand marker during a pickup a cup task	VR and C: 8	

Study ID	Motor impairment outcome measure	Number of participants reported to have completed the measure	
		Experimental	Control
	(The hand marker velocity peaks were defined as the difference between the first the local min and max velocity, and the next max velocity that was >20mm/s occurring at least 150miliseconds after the prior peak, the number of velocity peaks meeting that criteria were the number of movement segments). (4) Reach time during pickup cup task (the time from the start of movement (when the third metacarpal of the hand is greater than 2% of the max velocity of the hand marker) until the cup was moved a min of 2mm from its starting position during the trial). (5) maximum trunk displacement during a pickup a cup task (Displacement of the trunk from the starting position in millimetres).		
Carey et al. 2007	(1) Active range of motion for the finger (deg) (electro goniometer attached to the more paretic hand, with the potentiometer centred on the MP joint of the index finger. To determine the range of motion, participants made a fist, followed by the maximum extension of the index finger. This movement was held at the peak of each motion for approximately 3s; a voltage signal was recorded and converted into an angular value (degrees)).	10	10

5.4.2.7 Neurophysiology outcome measures

There was no commonality between the neurophysiological outcome measures used in the included studies (Table 9). Two studies used functional Magnetic Resonance Imaging (fMRI), but within differing anatomical regions of interest, collecting measures such as the laterality index between hemispheres, number of significantly activated voxels or relative volume and intensity index (Jang *et al.*, 2005; Carey *et al.*, 2007). One included study used Transcranial Magnetic Stimulation (TMS) to collect measures (e.g. Motor Evoked Potentials (MEPs)) from the Abductor Pollicis Brevis (ABP) and Extensor Carpi Radialis (ECR) muscles (Ballester *et al.*, 2017). Finally, one study used surface Electromyography (sEMG) to measures the co-contraction of wrist flexors and extensors (Donoso Brown *et al.*, 2014).

Table 9: Data reported in included studies, neurophysiological outcome measures

Study reference	**Neurophysiological outcome measure**		**Number of participants reported to have completed the measure**	
			Experimental	**Control**
Ballester et al. 2017	TMS derived measures (the cortical motor areas representing the APB and ECR in M1, for both hemispheres).	(1) Stimulation Efficacy (greatest value in the 80th percentile of Motor Evoked Potentials, divided by the maximum stimulation intensity). (2) Centroid location of the cortical motor areas.	14	3
Jang et al. 2005	fMRI derived measures (Anatomical regions: the bilaterally predefined regions of interest (ROIs), including the primary sensorimotor cortex (SM1), the premotor cortex (PMC), and the supplementary motor area (SMA)).	(1) Laterality index: (the laterality index ranged from 1.0 (all contralateral activation) to –1.0 (all ipsilateral activation)). (2) the number of significantly activated voxels.	5	5
Donoso Brown et al. 2014	sEMG derived measures	(1) Maximum Voluntary Contractions (MVCs).	*VR and C: Extensor = 8, flexor = 7	

Study reference	Neurophysiological outcome measure		Number of participants reported to have completed the measure	
			Experimental	Control
	(more paretic wrist flexor carpi radialis and extensor digitorum communis used for MVCs in a pregame maximum flex or extend 3 trials, each for 10-seconds).			
Carey et al. 2007	FMRI derived measures (Anatomical regions*:* primary motor area (M1), supplementary motor area (SMA), premotor cortex (PMC) in each hemisphere. The primary somatosensory area (S1) including the grey matter comprising the entire postcentral gyrus).	(1) laterality index (Volumes of activation for each anatomical region was compared between hemisphere.) (2) relative volume (voxels activated when surpassed threshold of a false determination rate of less than 0.01. The total number of active voxels.) (3) intensity index	10	10

Study reference	Neurophysiological outcome measure	Number of participants reported to have completed the measure	
		Experimental	Control
	(change in BOLD signal intensity during active movement versus rest).		

NB. *Only 8 participants had usable motion analysis data and only 6 had usable sEMG data

5.4.2.8 Risk of potential bias

All of the included studies were assessed as having a high risk of potential bias (Table 10). The number of potential participants approached during recruitment was unclear, as well as the number and reasons for attrition; one study accounted for the loss of a participant but not the other three who withdrew (Ballester *et al.*, 2017). There also appeared to be poor reporting of all included outcome measures; several described in the methods were not detailed in the results or the discussion (Jang *et al.*, 2005; Carey *et al.*, 2007; Donoso Brown *et al.*, 2014; Ballester *et al.*, 2017). Additionally, such outcomes were not carried out by blinded assessors (Jang *et al.*, 2005; Carey *et al.*, 2007; Donoso Brown *et al.*, 2014; Ballester *et al.*, 2017).

When considering the intervention allocation and related risk of bias, we acknowledge that the nature of Virtual Reality leads to challenges when carrying out appropriate blinding. One study (Jang *et al.*, 2005) ensured that intervention allocation was carried out by a team member who was unaware of the baseline characteristics. The other studies did not describe this in sufficient detail (Carey *et al.*, 2007; Donoso Brown *et al.*, 2014; Ballester *et al.*, 2017). Similar challenges would not affect random sequence generation (selection bias), but this revealed a high risk of bias. Two studies did not clarify how allocation sequences were generated (Jang *et al.*, 2005; Carey *et al.*, 2007). One (Ballester *et al.*, 2017) detailed their stratified block randomisation methods, while another (Donoso Brown *et al.*, 2014) used repeated measures and as such, randomisation was not appropriate. Half of the studies (Carey *et al.*, 2007; Ballester *et al.*, 2017) had a high probability

of reporting bias; for instance, one (Ballester *et al.*, 2017) published study differed from the clinical trial retrospectively published in terms of the primary outcomes.

Table 10: Potential risk of bias assessed with the Cochrane tool

Study reference	Random sequence generation (selection bias)	Allocation concealment	Selective reporting (reporting bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)
Ballester et al. 2017	+	?	-	-	-	-
Carey et al. 2007	?	-	-	-	-	-
Donoso Brown et al. 2014	-	-	+	-	-	-
Jang et al. 2005	?	-	+	-	?	-

Key.

+ Low risk of bias

? Unclear risk of bias

- High risk of bias

5.4.3 Narrative Synthesis of findings in relation to review questions

5.4.3.1 Aim 1a: Determine the neurophysiological correlates of upper limb motor impairment response to virtual reality aided exercise-based training following a stroke

The published reports of the included studies did not provide data on the correlation between neurophysiological and motor impairment changes in response to virtual-reality exercise-based training after stroke. Authors of the included papers were contacted, and of the three who responded, the appropriate raw data was not available; thus, correlations could not be calculated. Research aim 1a could, therefore, not be addressed.

5.4.3.2 Aim 1a.2: Determine if there is evidence that an improvement of motor impairment occurs alongside a change in neurophysiological measures

Two of the four included studies found an improvement in motor impairment and a change in neurophysiology measures (Carey *et al.*, 2007; Ballester *et al.*, 2017) (Table 11). There was a reported improvement in the more paretic fingers flexion and extension ($p = 0.01$), alongside an increase in the stimulation efficacy within the ipsilesional hemisphere for the Abductor Pollicis Brevis (APB) ($p < .01$) and the Extensor Carpi Radialis (ECR) ($p = 0.05$) representation within the primary motor cortex (Ballester *et al.*, 2017). This occurred after Virtual Reality (VR) training that engaged bilateral reaching movements with the wrist and fingers flexion/extension. There were no other reported improvements post-intervention within the motor impairment measures (i.e. Ashworth proximal and distal, grip force, Medical Research Council (MRC) proximal and distal and the Fugle-Meyer upper extremity scores). There was also no significant change within the centroid

location of the cortical motor areas producing Motor Evoked Potentials (MEPs) for the ABP and ECR within the primary motor cortex (Ballester *et al.*, 2017). There was a significant change in the active range of motion for the finger (deg) post-VR intervention which engaged the index finger and wrist with flexion and extension movements ($p = 0.004$). This was accompanied by a significant decrease in the relative volume within the ipsilesional Supplementary Motor Area (SMA) anatomical region ($p = 0.008$) (Carey *et al.*, 2007). No other significant changes occurred within the other functional Magnetic Resonance Imaging (fMRI) derived measures (i.e. laterality and intensity index).

The other two included studies showed a significant change within their neurophysiological measures but no improvement in the motor impairment measures. There was a significant increase in the selective activation of the wrist extensor Maximum Voluntary Contractions (MVCs) ($z = -1.992$, $p = 0.046$), but no improvement in motor impairment (i.e. Active range of motion wrist extensor; elbow extension; reach time and maximum trunk displacement) (Donoso Brown *et al.*, 2014). Another included study found a significant increase in the laterality index ($p < 0.05$) and the number of significantly activated voxels ($p = 0.05$) within the ipsilesional hemisphere for the primary Sensory Motor cortex (SM1) anatomical region; however, this was not accompanied by a significant improvement in Fugl-Meyer upper extremity scores after therapy, including reaching, lifting and grasping motor movements (Jang *et al.*, 2005).

Table 11: Measurement values pre/-post Virtual Reality intervention

Study reference	**Motor impairment changes reported**					**Neurophysiological changes reported**				
	measure	**Pre**	**Post**	**Significant change**		**measure**	**Pre**	**Post**	**Significant change**	
Ballester et al. 2017	1. Ashworth proximal	m = 1.24 sd = 1.25	m = 1.18 sd = 1.25	No		1. Stimulation efficacy[1] comparison across hemispheres, APB for the M1	Not reported	Not reported	↑ Ipsilesional	m = 4.17 sd = 9.86 p < .01
	2. Ashworth distal	m = 1.47 sd = 1.51	m = 1.35 sd = 1.19	No		2. Stimulation efficacy[1] comparison across hemispheres, ECR for the M1	Not reported	Not reported	↑ Ipsilesional	m = 5.21 sd = 10.98 p = 0.05
	3. More paretic fingers flexion/extension	Not reported	Not reported	↑ week 2/3	p = 0.01	3. Centroid location of the cortical motor	med = 0.1	med = 0.55	No	

Study reference	Motor impairment changes reported				Neurophysiological changes reported			
	measure	Pre	Post	Significant change	measure	Pre	Post	Significant change
					areas, producing MEPs APB in M1			
	4. Grip force	m = 6.15 sd = 5.04	m = 6.36 sd = 5.82	No	4. Centroid location of the cortical motor areas, producing MEPs ECR in M1	med = 0.72	med = 1.41	No
	5. MRC proximal	m = 3.47 sd = 0.51	m = 3.35 sd = 86.18	No				
	6. MRC distal	m = 2.82	m = 3.12	No				

Study reference	Motor impairment changes reported				Neurophysiological changes reported				
	measure	Pre	Post	Significant change	measure	Pre	Post	Significant change	
		sd = 1.19	sd = 1.05						
	7. Fugl - Meyer	m = 42.94 sd = 14.37	m = 42.77 sd = 15.02	No					
Donoso Brown et al. 2014	1. Active range of motion wrist extensor (deg)	m = 31.6 sd = 17.7	m = 25.4 sd = 17.7	No	1. Maximum Voluntary Contractions (MVCs)	m = 3.47 sd = 5.85	m = 5.84 sd = 9.78	↑ selection activation of the wrist extensor	z = -1.992 p = 0.046
	2. Elbow extension (deg)	m = 96.8, sd = 24.7	m = 95.5, sd = 22.1	No					
	3. Reach time	m = 2.52, sd = 1	m = 95.5, sd = 22.1	No					

Study reference	Motor impairment changes reported					Neurophysiological changes reported				
	measure	Pre	Post	Significant change		measure	Pre	Post	Significant change	
	4. Maximum trunk displacement (mm)	m = 123.22 sd = 65.1	m = 131.7 sd = 49.6	No						
Carey et al. 2007	1. Active range of motion for the finger (deg)	m = 64.5, sd = 10.8	m = 86.5 sd = 8.4	↑ more paretic index finger	p = 0.004	1. Relative volume (fMRI)	Not reported	Not reported	↓ Ipsilesional in the SMA anatomical region	p = 0.008
						2. Laterality index (fMRI)	Not reported	Not reported	No	
						3. Intensity index (fMRI)	Not reported	Not reported	No	
Jang et al. 2005	1. Fugl-Meyer upper extremity	m = 51	m = 58	No		1. Laterality index (fMRI)	m = 0.1 sd = 0.2	m = 0.9 se = 0.1	↑ ipsilesional	p < 0.05

Study reference	Motor impairment changes reported				Neurophysiological changes reported				
	measure	Pre	Post	Significant change	measure	Pre	Post	Significant change	
		sd = 7.12	sd = 6.25					in the SM1 anatomical region	
					2, Number of significantly activated voxels	m = 57.8 se = 27.2	m = 4.4 sd = 4.4	↑ Ipsilesional in the SM1 anatomical region	p = 0.05

NB. 1. The stimulation efficacy was determined as the greatest value in the 80th percentile of Motor Evoked Potentials (MEPs); divided by the maximum stimulation intensity

m = mean; **sd** = standard deviation; **med** = median; **se** = standard error.

ABP = abductor pollicis longus muscle; **ECR** = Extensor Carpi Radialis; **M1** = primary motor cortex; **SM1** = Sensorimotor cortex

MEPs = Motor Evoked Potentials; **fMRI** = functional magnetic resonance imaging

5.5 DISCUSSION

The systematic review found insufficient data to identify the neurophysiological correlates of change in motor impairment in response to VR training for the upper limb after a stroke (aim 1a). Of the four included studies, two found a change in motor impairment and a neurophysiology change in response to an exercise-based virtual reality intervention (aim 1a.2). However, across the four studies, many measures of motor impairment and neurophysiology showed no change between pre-intervention and post-intervention time points. Consequently, this systematic review demonstrates that there is insufficient robust data to provide an understanding of the neurophysiological changes underlying reduction in motor impairment in response to VR exercise-based intervention.

The findings of this review are in broad agreement with conclusions seen in other reviews in that there appears an initial change in motor impairment in response to therapy delivered via virtual reality devices (Henderson, Korner-Bitensky and Levin, 2007; Mumford and Wilson, 2009; Laver *et al.*, 2012, 2017; Chen *et al.*, 2015; Aramaki *et al.*, 2019; Maier *et al.*, 2019; Rohrbach, Chicklis and Levac, 2019; Subramanian *et al.*, 2019; Valkenborghs *et al.*, 2019). The findings included in these reviews have been noted to be steering the development work for virtual stroke rehabilitation devices (Laver *et al.*, 2017; Maier, Ballester and Verschure, 2019). This promising initial reduction in motor impairment has been used to strengthen the theoretical underpinnings; that functional exercise-based VR training facilitates neural

plasticity and thus reduces motor impairment (Cheung *et al.*, 2014; Levin, Weiss and Keshner, 2015).

Although there is a promising reduction in motor impairment reported within the included studies, it is important to view this in light of their methodological strengths and weaknesses. Importantly, the potential risk of bias of the included studies was high overall. Notably, attrition rates often were not accounted for, and withdrawal reasons not collected. Virtual rehabilitation devices require high levels of usability and acceptability to facilitate integration in healthcare (Demain *et al.*, 2013; Wentink *et al.*, 2019). It is crucial to understand if attrition rates could be due to the device features, therapy procedures or dose to facilitate the end-user experience.

Additionally, the lack of reporting within the included studies hindered the ability to address the aims of the review (i.e. means, standard deviations, effect sizes and confidence intervals were often missing or incomplete). Appropriate reporting is of importance for the replicability and interpretation of such research. Other methodological inconsistencies influence the extent to which the neural correlates found can be interpreted. All the included studies lacked statistical power due to small sample sizes, including one that only completed neural measures on three control condition participants, as opposed to the fourteen in the virtual reality intervention condition (Ballester *et al.*, 2017).

The prior reviews, coupled with this study's findings, conclude with the same recommendation: a need for larger, robust trials to overcome the methodological weaknesses of current evidence (i.e. small samples, lack of reporting and variation in protocols and devices) (Henderson, Korner-Bitensky and Levin, 2007; Mumford and Wilson, 2009; Laver *et al.*, 2012, 2017; Chen *et al.*, 2015; Aramaki *et al.*, 2019; Maier *et al.*, 2019; Rohrbach, Chicklis and Levac, 2019; Subramanian *et al.*, 2019; Valkenborghs *et al.*, 2019). This call for stronger evidence has not changed in the last decade, though the included studies can provide a foundation for further investigative work to be carried out with a rigorous staged approach (Dobkin, 2009; Boyd *et al.*, 2017). This is an important future step to augment the evidence of motor impairment reduction based upon clinical outcome changes that are then used to assume a reflective neural change (Laver *et al.*, 2011). Nevertheless, we argue that there is still a prevalent gap in the evidence base. We cannot know if VR is beneficial for reducing motor impairments until thorough, robust trials investigate the impact on neural physiology and motor impairment.

It is important to interpret these findings in light of the strengths and limitations of this systematic review. The studies included demonstrated heterogeneous results; in part, this could be due to the broad definition of Virtual Reality included in the searches. An appropriate, concise stratification of devices and protocols falling under the umbrella 'Virtual Reality' is required; for example, the differing levels of participant engagement occurring within each device, particularly with the different immersion and participant engagement within each device (Laver *et al.*, 2017; Lee, Park and

Park, 2019). Attempts to gain raw data from the authors of the included studies were unsuccessful, limiting the synthesis to the data reported in the papers. In addition to being applied to non-randomised control trials there are other limitations of the CROB that need to be noted, researchers have criticized that subjective interpretation of the tool, difficulty in assessing selective reporting outcomes, terminological ambiguity (subjective/ objective) and modest inter-observer agreement (Jørgensen *et al.*, 2016). Further, the inclusion of 'unclear' as a category can leave assessors lacking the sufficient information to adequately address bias overall and could influence recommendations for clinical decisions and future studies (Mariano Faggion Jr, 2016; Puljak *et al.*, 2020).

On the other hand, this review did not restrict the literature search by date, or study design, allowing for a comprehensive overview of potentially relevant studies. This was, to our knowledge, the first systematic review that aimed to identify the neurophysiological correlates of changes in upper limb motor impairment in response to VR exercised based interventions. We conclude that there is insufficient evidence to address this research question. There is also an apparent lack of adequately powered studies investigating the relationship between reduction in motor impairment and neurophysiological change.

Future trials investigating the effect of virtual reality intervention on upper limb motor impairments should investigate both clinical outcomes and

correlate these with evidence of reflective neural changes. This should be done with larger, robust and replicable trials with clear reporting. In order to drive the evidence-base forward, the research question proposed in this review needs to be answered in order to conclude if VR drives neural recovery.

6 PHASE II: USER-LED REFINEMENT OF THE VIRTUALREHAB PLATFORM

6.1 INTRODUCTION

Phase II addressed the second research question (chapter 2, section 2.2):

What are the views of end-users on using and refining virtual reality-aided exercise-based training for stroke rehabilitation?

The research question was investigated using a qualitative descriptive study incorporating the voice of end-users into the next iteration of the Virtualrehab platform. This work aligns with the 'development' stage of the Medical Research Council's (MRC) Framework for Complex Interventions (Craig *et al.*, 2008).

The following chapter presents the study's research aims, methods, results and discussion.

6.2 RESEARCH AIMS

To answer the second research question, phase II aimed to:

Aim 2a: Explore the usability and acceptability of a virtual reality system (the Virtualrehab platform) for delivery of home-based stroke rehabilitation.

Aim 2b: Inform the development of future iterations of the device via user feedback and experience.

6.3 METHODS

6.3.1 Design

A Qualitative Descriptive (QD) study design was used, with demonstrations of the Virtualrehab platform (stage one) and a small home-trial (stage two). Full details of the Virtualrehab platform can be found in chapter two. Data was collected from end-users through focus groups, interviews, and questionnaires. The term 'end-users' is used within this thesis to describe those who would potentially incorporate the Virtualrehab platform into their rehabilitation practices; three groups were identified.

1. Stroke Survivors (SS): individuals who have had a self-reported stroke.
2. Informal carers (IC): family and friends who have been part of an individual's stroke journey.
3. Stroke Clinicians (SC): physiotherapists or occupational therapists that have worked in stroke rehabilitation services.

The QD research design was chosen in order to address the research aims and incorporate the end-users voice into the Virtualrehab platform. It is typically utilised in healthcare research where a descriptive understanding is needed for intervention development or improvement to practice (Sandelowski, 2010). The design is appropriate when time and resources are limited (for example, in a PhD research project), or a mixed-methods approach is undertaken (for example, the overarching multi-phase mixed methods framework used in this PhD, described in chapter three). The inductive pragmatic approach has sound methodological and theoretical underpinnings (Sandelowski, 2010; Bradshaw, Atkinson and Doody, 2017). The design allows for flexibility with diverse real-world investigations that the other main approaches cannot provide (i.e. Narrative, Grounded theory, Phenomenology and Ethnography). For example, this flexibility allows for a variety of methods and techniques to be used that may typically be associated with other qualitative approaches, all of which depend on the research question (Neergaard *et al.*, 2009; Sandelowski, 2010; Bradshaw, Atkinson and Doody, 2017).

6.3.2 Ethics

Ethical approval was granted by the University of East Anglia's (UEA) Faculty of Medicine and Health ethics committee; on the 17th of February 2017 (reference 2016/17-27). An amendment was approved on the 16th of March 2017, to include the option of interviewing participants if the recruitment numbers were not suitable for a focus group (i.e. less than three) (O.Nyumba *et al.*, 2018). The approval letters are in Appendix 1C. Potential participants were given at least one week to read the information sheet,

detailing the study's procedures. Any questions were answered via email, phone or in-person. Those interested were invited to the Movement and Exercise Laboratory (MoveExLab) at UEA, where written informed consent was obtained (Appendix 2C and 3C).

Electronic data was stored on a password protected UEA computer, accessible by the researcher and supervisory team only. Physical copies of data were stored in a locked filing cabinet within the Researcher's (author of this thesis) office for the duration of the PhD. The final custodian of data from this study is the primary supervisor.

6.3.3 Participants

6.3.3.1 Sampling

A non-probability purposeful sampling technique was used to identify potential participants from each end-user group. This method is recommended for qualitative investigations in healthcare research and focuses on the characteristics of interest (i.e. each end-user group); as well as those accessible to the research team within the study's time and resources (Neergaard *et al.*, 2009; Bradshaw, Atkinson and Doody, 2017).

Sample size

Stage 1

The intent was to recruit up to ten participants for each end-user group. The pragmatic nature of this research determined the sample size. In-depth data is required from each participant in qualitative studies; as such, the samples tend to be small (Bradshaw, Atkinson and Doody, 2017). Other factors considered

were the small sample sizes and high attrition rates prevalent in similar studies within the Researcher's research group, the Acquired Brain Injury Rehabilitation Alliance (ABIRA). In addition, the rural nature of Norfolk can cause potential participants difficulties organising travel to UEA, and it can be a long fatiguing journey (Leira *et al.*, 2018; Ferreira *et al.*, 2019).

Stage 2

The two-week home trial required a stroke survivor and informal carer dyad. Two dyads were chosen, from stage 1, to complete the two-week trial. It was only possible to complete two dyads because there was only one Virtualrehab platform device available during stage two; which the dyads used consecutively totalling four weeks for completion. The stroke clinicians were considered for this stage of the study, but the time commitment needed was not possible within their work schedules.

6.3.3.2 Recruitment and criteria

The stroke clinicians were recruited from NHS hospitals in Norfolk. Cambridge hospitals were not approached due to their involvement in developing an alternative virtual reality device.

To recruit stroke survivors and their informal carers, stroke support groups in Norfolk and Cambridgeshire were approached. The Researcher contacted the gatekeepers for each group and also gained permission from the East of England Stroke Association area manager. Four support groups responded with interest.

The Researcher visited the support groups to garner interest in participation. During each visit, the Researcher gave a presentation to the entire group, outlining the study's aims and procedure, with laminated pictures of the Virtualrehab platform as an aid. The Researcher then interacted with each person individually, to further explain the study and hand out participant information sheets while answering any questions. From these conversations, similar concerns were highlighted; the main hesitation was on giving views relating to unfamiliar technology (i.e. never used a laptop). The Researcher answered any concerns or questions and reiterated the aim was to develop the Virtualrehab platform to be usable by individuals who were living with the consequence of stroke. The participant criteria used are detailed in Table 12.

Stage one

The support group visits recruited 11 stroke survivors and seven informal carers for the study. Unfortunately, this number was approximately half of the people who indicated an interest in participating; those who could not participate mentioned either being unable to travel to the MoveExLab or not having a suitable date free. In order to optimise the recruitment and anticipate those who could not attend on the day, additional data collection days were included; although it was acknowledged that the number within each focus group would be lower. Therefore, an ethics amendment was obtained to allow for a smaller sample of participants for each data collection day, with potential for 1:1 interviews if the number was lower than three (detailed in 6.3.2).

Table 12. End-user groups inclusion criteria and rationale

End-user group	Criteria	Rationale
Stroke Survivors (SS)	Diagnosis of stroke with an onset at least three months prior.	To ensure participants have preliminary knowledge of typical stroke rehabilitation on offer.
Informal Carer (IC)	A family member or friend that has been part of an individual's stroke journey	To ensure participants understand typical stroke rehabilitation on offer.
Stroke Clinicians (SC)	Physiotherapist or Occupational therapist who is currently involved in stroke rehabilitation	To ensure participants have experience with typical stroke rehabilitation on offer.

Stage two

All stroke survivors and informal carers from stage one were informed about the second stage of the study to identify those interested in participating. As there was one device available, only two dyads (a stroke survivor and an informal carer) could be recruited; this was decided based upon participants availability. Each participant dyad was given the device within their home for two weeks, allowing sufficient time to experience the Virtualrehab platform. After which the next dyad received the device for their home trial.

6.3.4 Procedures

This section details the procedures for stage one and two visualised within the flow diagrams (Figure 15 and Figure 16).

6.3.4.1 Stage one: demonstration of the Virtualrehab platform

End-user groups (stroke survivors and informal carers) attended the UEA MovExLab in small groups, across different days, dependent on their schedules. The Researcher visited the final end-user group (stroke clinicians) at the hospital to minimise the impact on their work.

The participants completed the characteristics questions. Then the Virtualrehab platform (fully detailed in chapter two) was demonstrated for each end-user participant group by the Researcher. The hardware and software components were shown with the potential end-use of the platform explained (i.e. how a therapy plan could be set-up and carried out in practice). Participants were offered a chance to try the platforms exercises and exergames, while the Researcher answered questions. The exercise and exergames trialled were done either seated or standing, dependent on the participants preference and at the 'easiest' level offered (full details on the possible tailoring of the system is explored in chapter two). The demonstrations took between 30 minutes to an hour, dependent on questions and the reliability of the software. Particular to this study, the assessment module and LEAP hand motion sensor (Ultraleap, San Francisco, United States) were unusable in both stages, due to technical errors. The participants then completed the system usability questionnaire. Following which the

participants then took part in discussions with the Researcher (i.e. focus groups and interviews) following a semi-structured topic guide, lasting between 30 minutes to an hour (Table 15). The discussions were carried out in their end-user group; for example, when the stroke survivors discussed their views, their informal carers were in another room having a refreshment break. Laminated pictures of the hardware and software were used, in case participants needed to focus on a specific part of the Virtualrehab platform or remember their earlier thoughts.

6.3.4.2 Stage two: a home-trial

Two dyads completed the second stage of the study, each consisted of a stroke survivor and their informal carer. The Researcher first set up the Virtualrehab platform system in the home of each dyad. The participants were given instructions on how to set-up, use the system and the sessions planned for them were explained in detail. Each stroke survivor was a set a session that included all the exercises (i.e. shoulder abduction) and exergames (i.e. rowing) available (full list is available in section 3.3.3 and 3.3.4, respectively), in order to trial the system. The participants were asked to use the system for at least 30 minutes a day, five days per week, for two weeks; and to trial all exercises and exergames over the two weeks. The participant could choose when to trial each exercise and exergame, and they were given audio recorders and self-reported proformas (i.e. notebooks) to record views of the sessions. At the end of the two weeks, all participants filled in the system usability questionnaire and the Researcher conducted a 1:1 interview with the stroke survivor.

Figure 15: Flow diagram of stage 1

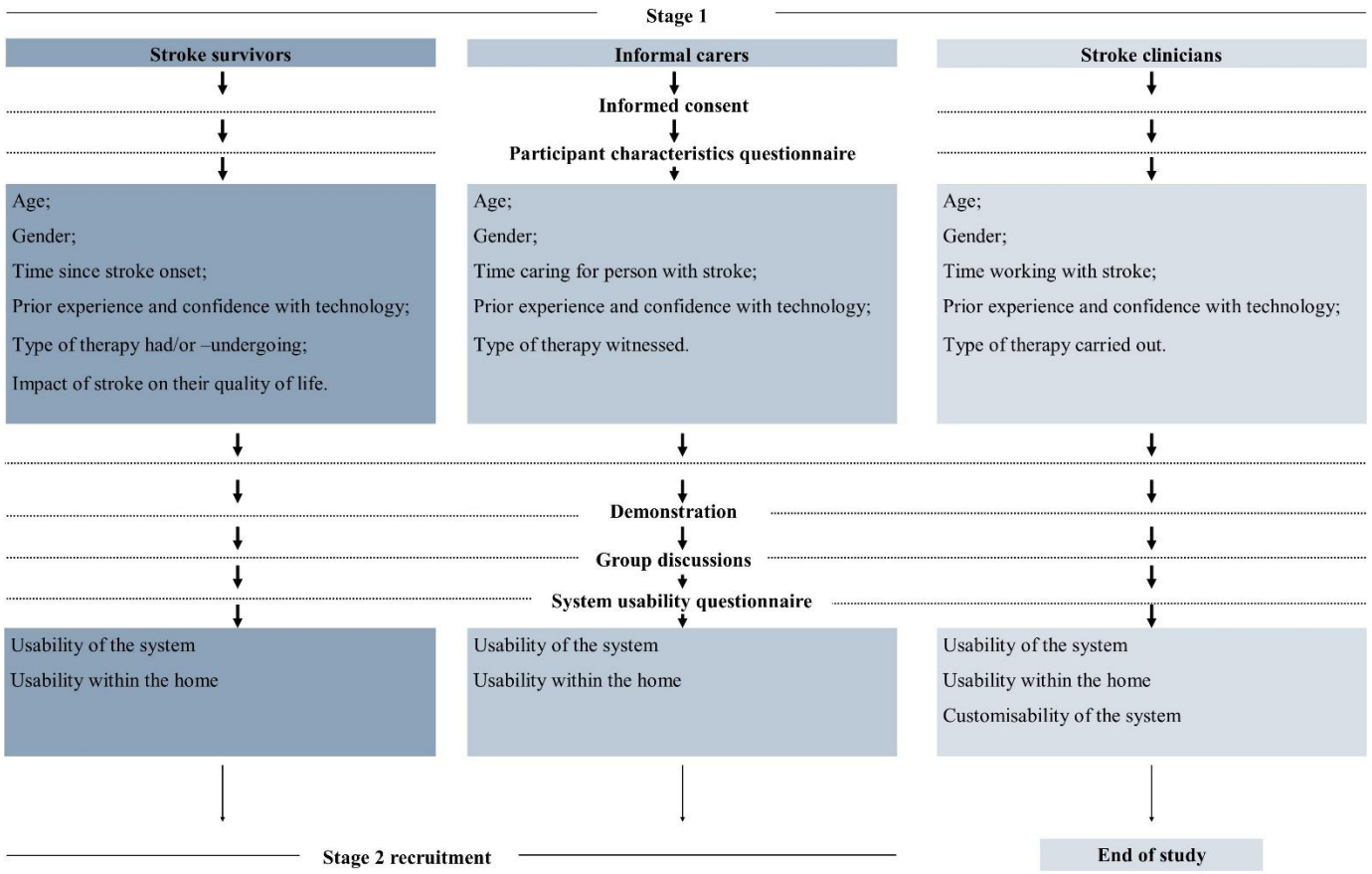
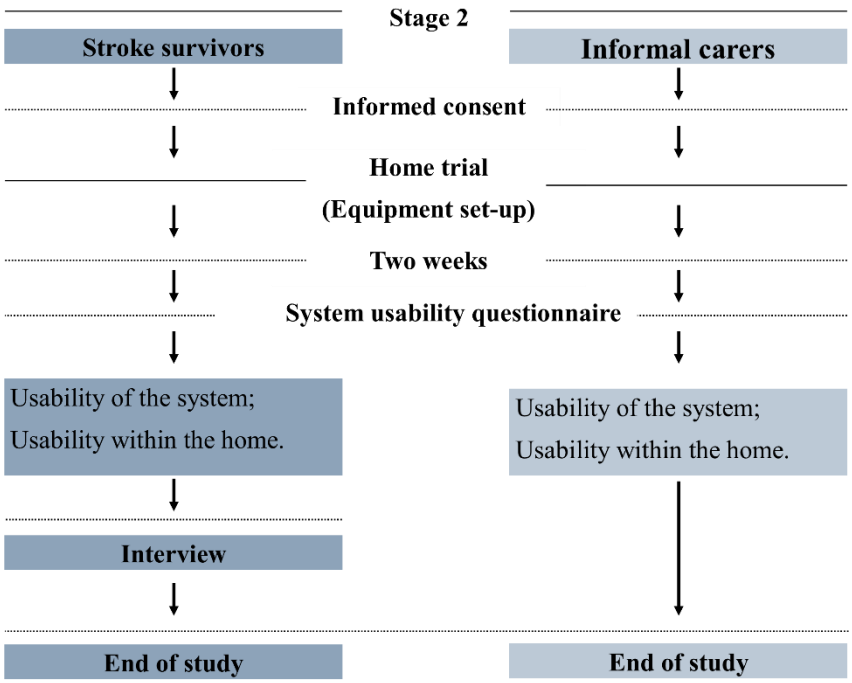


Figure 16: Flow diagram of stage 2



6.3.4.3 Participant characteristics

Participant characteristics were recorded in a proforma before the demonstrations for all end-user groups. Alongside typical characteristics (i.e. age, sex and experience with stroke) (Table 13), their prior experience and confidence with technology were gathered.

Table 13: Participant characteristics collected per group

Participant group	Characteristics collected
Stroke Survivors (SS)	Age; Sex; Prior experience and confidence with technology; Time since stroke; Type of therapy they have/-or are undergoing; Impact of stroke on quality of life.
Informal Carers (IC)	Age; Sex; Prior experience and confidence with technology; Time caring for someone with stroke; Type of therapy they have/-or is witnessing.
Stroke Clinicians (SC)	Age; Sex; Prior experience and confidence with technology; Time working in stroke rehabilitation; Type of therapy they have/-or is carrying out.

Experience and Confidence with technology

Prior experience and confidence in using technology can influence views on the usability and acceptability of devices such as the Virtualrehab platform (Lewis *et al.*, 2011). It is important to understand the potential bias underlying the participant groups when interpreting their qualitative data. Therefore, two specific self-reported questions were created by the Researcher for the study:

(1) how confident are you with using common technology (which shared features needed to use the Virtualrehab platform):

- Mobile phone (specifically touchscreen versions);
- Computers;
- TV;
- Tablets/iPad;
- Wi-fi;
- Internet;
- Email.

A multi-choice answer scale was devised for participants to choose from: 'confident', ‘unsure’, 'unconfident' and 'never used'.

(2) What is your prior experience with technology similar to the Virtualrehab platform:

- The Microsoft Xbox One Kinect;
- The Nintendo Wii;
- Videogames on the computer;
- The PlayStation;
- Games on the mobile.

A multi-choice answer scale was devised for participants to choose from: can use it and set it up; can set it up; can use it; not used it and not heard of it.

The answers were chosen to allow for information on those who had experience with the technical aspects (i.e. setting it up for themselves or other people) and general (i.e. using it after it was set-up by others). This allowed answers to be differentiated between those who had heard of the technology before but not used it and those who had not at all.

Impact of stroke on quality of life

Stroke is known to be heterogeneous in terms of impairments, disability and lasting impact on the quality of life (Boyd *et al.*, 2017). Thus, it is difficult to ensure the inclusion of representative potential user views from the entire stroke population. It is important to identify the characteristics of the individuals' stroke to understand how representative the views are. In addition to the earlier characteristics collected the self-reported impact on the stroke survivors Quality of Life (QoL) was collected. There are several reliable and valid psychometric assessments available to measures QoL. The Stroke Impact Scale (SIS 3) (Duncan *et al.*, 2003a) was deemed most appropriate;

the tool gathers information on how a stroke has impacted their health and lives (Sullivan, 2014). The SIS 3 (Duncan *et al.*, 2003a) is a valid and reliable self-reported scale (Choi *et al.*, 2017). The 59-item instrument measures QoL in eight dimensions. Each is rated on a 5-point Likert scale depending on how 'difficult' the participant perceives completing the activity.

6.3.4.4 System usability questionnaire

The usability of the Virtualrehab platform was explored with a questionnaire developed for this study. It was used to identify areas of improvement and gather views on specific aspects of the platform (research aims 2a and 2b). The questionnaire was made up of the following:

System Usability Scale (SUS)

The 10-item System Usability Scale (SUS) was chosen to provide a subjective assessment of the Virtualrehab platform's usability (Brooke, 1996). This 5-point Likert scale has been used previously in virtual stroke rehabilitation research (Meldrum *et al.*, 2012; Howes *et al.*, 2019; Stephenson *et al.*, 2020; Tuena *et al.*, 2020). It is also able to differentiate between 'usable' and 'unusable' systems with data from small sample sizes. The answers range from 'strongly agree' to 'strongly disagree'. The SUS scale has strong psychometric properties, having been found reliable and valid (Lewis and Sauro, 2009). The scale was kept identical to the original, apart from the term 'system' which was replaced with 'Virtualrehab tool' for clarity (Table 14).

Table 14: System Usability Scale (SUS)

System Usability Scale (SUS 3) (adapted from (Brooke, 1996))
1. I think that I would like to use this Virtualrehab tool frequently.
2. I found the Virtualrehab tool unnecessarily complex.
3. I thought the Virtualrehab tool was easy to use.
4. I think that I would need the support of a technical person to be able to use this Virtualrehab tool.
5. I found the various functions in this Virtualrehab tool were well integrated.
6. I thought there was too much inconsistency in this Virtualrehab tool.
7. I would imagine that most people would learn to use this Virtualrehab tool very quickly.
8. I found the Virtualrehab tool cumbersome to use.
9. I would feel very confident using the Virtualrehab tool.
10. I would need to learn a lot of things before I could get going with this Virtualrehab tool.

Additional usability questions

The Researcher developed these questions for the study. All three end-user groups were asked to consider how 'easily' (easy, unsure, or uneasy) they might incorporate certain aspects of the Virtualrehab platform within the home. Stroke survivors and informal carers answered from their perspectives as if they were attempting to use the device. Stroke clinicians were asked to consider it from the perspective of their patients and their knowledge of prior attempts to incorporate similar rehabilitation devices within the home.

Q: How well do you think you/they could incorporate the tool into the home and use it?

- Find a space for the Virtualrehab platform;
- Connect it to the TV;
- Switch it on;
- Turn it off;
- Navigate through the welcome screens and find the exercise sessions.

Stroke clinicians were also asked additional questions on the therapy editor component of the Virtualrehab platform, with answers ranging from important, unsure, or not important.

Q: How important are the following aspects when considering using this tool?

- Customising a rehabilitation plan?
- Accessing other therapists plans and exercises around the world?
- Tracking the overall progress of your patients (i.e. remotely)?
- Adjusting the rehabilitation plan at any time (i.e. remotely)?
- Measuring physiological improvements?

They were also asked about the variety and functionality of the Virtualrehab platform games and exercises, with answer ranging from satisfied to unsatisfied and neither.

Q: How did the games and exercises appeal in terms of:

- The variety on offer;
- The similarity to current rehabilitation exercises/games;
- The functionality of the movements involved in the exercises/games.

6.3.4.5 Group and individual discussions

To appropriately answer the research aims, group and individual discussions were required. Two methods of collecting this data were used, focus groups and 1:1 interviews, both of which are recommended for qualitative descriptive study designs (Bradshaw, Atkinson and Doody, 2017). Focus groups (typically 4 – 12 people) are built on the notion that group interaction encourages respondents to explore and clarify individual and shared perspectives (Dahlin Ivanoff and Hultberg, 2006). Whereas a semi-structured 1:1 interview explores the experiences of participants and the meanings they attribute to them, in an open in-depth manner.

The primary aim for the first stage of the study was to conduct focus groups; there were two exceptions made pragmatically. The first was when the number of participants on the data collection day did not meet the minimum number recommended for a focus group (i.e. less than three); in this instance 1:1 interviews were conducted (Guest, Namey and McKenna, 2017). The second was when stroke participants requested a 1:1 interview; they expressed this would help the challenges they felt with their communication impairments. Overall, both methods followed the same semi-structured topic guide; which was re-worded, re-ordered or clarified to investigate further topics introduced by the respondents where appropriate (Table 15).

Table 15: The topic guide used in all focus groups and interviews

Semi-structured questions
What did you think of the physical device? (i.e. The Kinect V2 and LEAP hand motion sensors)
What did you think of the exercises and games? (i.e. the software modules)
What did you think of the therapy editor?
How would you feel if this was an additional rehabilitation tool?
What do you think of the technology requirements (i.e. set-up and use)?
Do you feel this can be implemented into stroke rehabilitation?
What benefits or challenges could this potentially have for stroke survivors?
Any further thoughts on the positives and negatives of this new tool?

NB. At the end of each question, a prompt was given to identify potential changes to the platform (research aim 2b)

6.3.5 Data analysis

The following section outlines the data analysis techniques used in the study.

6.3.5.1 Participant characteristics

Descriptive statistics were used to describe the questionnaire responses. The Stroke Impact Scale (SIS) (Duncan *et al.*, 2003a) scores were transformed to gain 'domain' scores out of 100, from the following equation (Mulder and Nijland, 2016).

$$Domain\ score = \left[\frac{mean\ item\ score - 1}{4}\right] * 100$$

There is also an additional question in the SIS 3 (Duncan *et al.*, 2003a) that asks participants to score their perceived recovery on a scale of 0 to 100. An additional physical dimension subscale was also created from the summed strength, hand function, Activities of Daily Living (ADL) domains – to create the SIS-16 (Duncan *et al.*, 2003b).

6.3.5.2 System usability questionnaire

System Usability Scale (SUS)

The SUS raw scores were adjusted as follows (Jordan, 1996):

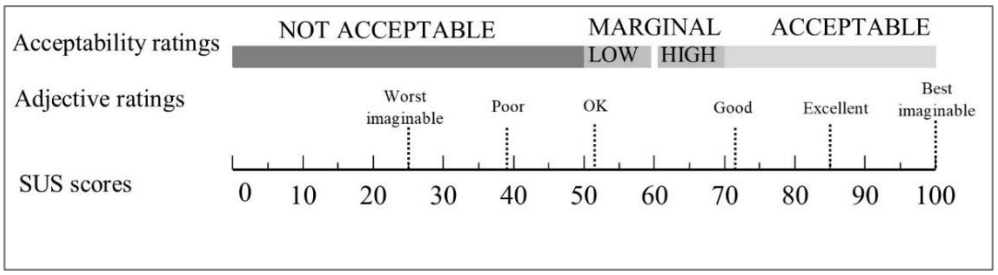
- The even-numbered items (Q2, 4, 6, 7, 10): subtract each response from 5.
- The odd-numbered items (Q1, 3, 5, 7, 9): subtract 1 from each response.
- The converted scores are then summed and multiplied by 2.5: creating an overall ‘adjusted SUS score’ between 0 to 100.

The mean and standard deviation were then calculated from the adjusted SUS scores; the small sample size prevented further inferential statistics.

It is important to note the adjusted SUS scores are not percentages or percentiles and must be interpreted appropriately. Thus, a score of 50 does not indicate the system is "half as good" as one which scored 100, but it indicates serious usability issues that require amending. It has been argued that the SUS adjusted scores should be converted to percentile ranks through a process called normalizing (Lewis and Sauro, 2009). Lewis et al (2009) created a calculator and guide from over 500 SUS studies that convert adjusted scores to percentiles; unfortunately, this study did not have enough resources to purchase this calculator. Thus, it should be noted that as percentiles were not calculated the results of this study cannot be compared with other studies SUS scores.

In the interpretation of the adjusted SUS score a total above 68 is seen as 'above average' (Lewis and Sauro, 2009). Further qualitative context has been created for SUS scores in terms of 'adjective' and 'acceptance' ratings (Bangor, Kortum and Miller, 2008). Other researchers have used Bangor et al (2008) acceptability ratings as a means of interpreting the SUS adjusted scores (shown in Figure 17); this will be also used within this study (Howes et al., 2019; Stephenson et al., 2020).

Figure 17: A comparison of mean System Usability Scale (SUS) scores by, adjective ratings, and the acceptability of the overall adjusted SUS score (from Bangor et al (2008) Figure 13, P592).



Additional usability questions

Percentages were calculated for each end-user group from the results of the additional usability questions created for the study.

6.3.5.3 Discussions within focus groups and interviews

Transcription

An 'intelligent verbatim style' was used, where repetitions, pauses and stuttering were omitted in the transcription. These were not necessary to address the research aims or required for a QD design (Sandelowski, 1994; Halcomb and Davidson, 2006; Davidson, 2009). The participants involved were considered when omitting words; as a stroke can impact communication abilities; potentially leading to repetition, pauses, and stuttering that are not connected to their views. Finally, the discussions were audiotaped; therefore, non-linguistic observations (i.e. facial expressions, intonations and body language) were not available. The Researcher transcribed the discussions following a data management protocol in order to increase content accuracy, transparency, validity and efficiency. The following steps were undertaken:

Step 1. Listen to the recorded audio and consult any notes taken during the discussions;

Step 2. Transcribe using an intelligent verbatim method;

Step 3. Compare the transcription to the audio recording, making alterations or changes as and when needed—repeated as often as required;

Step 4. A Supervisor quality checked a random selection of transcription to increase accuracy.

Finally, to ensure confidentiality, identifiable information was removed by the Researcher. An example of a transcript is shown in Appendix 4C. The transcripts were then imported into NVIVO 11 (QSR International technology and software solutions, Australia), computer software designed to organise qualitative data, facilitating the Researcher's thematic analysis.

Thematic analysis

Once imported, into NVIVO 11 (QSR International technology and software solutions, Australia), the transcripts were analysed with similar codes grouped to identify emerging themes. The analysed focus groups and interviews, per stage, were compared via triangulation. To ensure the trustworthiness of the results a second coder is standard practice for quality checking qualitative data analysis (Nowell *et al.*, 2017). The second coder (a member of the supervisory team) analysed a random selection of the transcripts (two focus groups, two interviews) and then compared with the Researcher. Sources of disagreement were resolved by discussion between the two, or an additional supervisor if required.

The data was analysed following Braun and Clarke's six-stage thematic analysis process (Braun and Clarke, 2006), the following details the steps:

1. Familiarisation of the data;
2. Generating initial codes;
3. Searching for themes;
4. Reviewing the themes;
5. Defining and naming the themes;
6. Producing the report.

In order to answer the research aim 2b - identifying future development directions for the Virtualrehab platform, any emergent changes recommended by participants were coded into a separate theme.

Thematic analysis was chosen to allow the Researcher to stay close to the data and as such, the interpretation would be of low-inference (Neergaard *et al.*, 2009); meaning that different researchers will agree more readily on the same findings, even if they do not choose to present the findings in the same way (Sandelowski, 2010).

Research rigour

It is important to demonstrate rigour in qualitative research to increase the trustworthiness of findings. In order to do so, the Researcher reflected upon their own biases and the effect these may have on the findings, to increase transparency (Nicholas, Clark and Szauter, 2019). In addition, guidance was

taken from Bradshaw (2017) in showing rigour with a QD design – Table 16 described the recommended steps needed to demonstrate rigour.

Table 16: Demonstrating rigour for qualitative description research designs (adapted from Table 2, Bradshaw, 2017)

Steps for demonstration of rigour	**Rigour criteria that each step demonstrates**			
	Credibility	**Confirmability**	**Transferability**	**Dependability**
1. Establish a rapport prior to commencing interviews;	✓			
2. Express compassion and empathy during interviews;	✓			
3. Prolonged engagement with participants throughout the study;	✓			
4. Participants to verify the accuracy of the transcripts (member checking);	✓	✓		
5. Maintaining a reflexive journal;		✓	✓	
6. Establishment of an audit trail describing the study's procedures and processes;		✓		✓
7. Description of participants characteristics;		✓		
8. Findings that represent the data gathered and are not biased by the research, evidenced by the inclusion of direct quotations from participants;		✓		
9. Purposeful sampling is used;			✓	
10. Providing sufficient study details so recreation can occur;			✓	
11. Rich description is shown in the findings;			✓	
12. Account for any changes that occur in the study.				✓

6.4 RESULTS

The following section details the results from both stages of this study according to the appropriate outcome and research question. For the first stage of the study, eight data collection sessions (four focus groups and four interviews) were conducted in total (Table 17). The second stage of the study two dyads (each with one stroke survivor and informal carer) were conducted.

Table 17: Focus groups and interviews details from stage 1

Group (location of data collection)	Participant group	Participants
Group 1 (UEA MovExLab[1])	Informal Carer	n = 2
Group 2 (UEA MovExLab[1])	Informal Carer	n = 3
Group 3 (Support group)	Informal Carer	n = 2
Group 4 (UEA MovExLab[1])	Stroke survivors	n = 3
Group 5 (UEA MovEx Lab[1])	Stroke survivors	n = 1[2]
Group 6 (UEA MovEx Lab[1])	Stroke survivors	n = 1[2]
Group 7 (Support group)	Stroke survivors	n = 6
Group 8 (Hospital)	Stroke clinicians	n = 9

NB. 1 University of East Anglia's Movement and Exercise Physiology Laboratory; 2 Participants requested a 1:1 interview due to self-reported communication challenges

6.4.1 Participant characteristics

Ten stroke survivors, seven informal carers and nine stroke clinicians participated in stage 1 (Table 18). The ages varied for each end-user group: stroke survivors (60 to 82 years); informal carers (46 to 72 years) and stroke clinicians (22 to 52 years). The stroke clinicians group consisted of four occupational therapists and five physiotherapists.

Table 18: Participant characteristics from stage 1

End-user participant group	**Number of participants**	**Age, years (m ± SD)**	**Sex (F; M)**	**Experience with stroke, years (m ± SD)**
Stroke Survivors	11	70.5 ± 7.5	4:7	7.4 ± 4.7
Informal Carers	7	58.6 ± 10.9	4:3	5.36 ± 4.7
Stroke Clinicians	9	31.3 ± 8.6	8:1	7.5 ± 6.8

NB. m, mean; **SD,** standard deviation; **F**, female; **M**, Male

Two dyads were chosen from stage 1 to complete stage 2, each consisting of a stroke survivor and an informal carer within each (Table 19).

Table 19: Participant characteristics from stage 2

Dyad group	**Participant**	**Age, years**	**Sex (F; M)**	**Experience with stroke, years**
1	Stroke survivor	60	F	10
	Informal carer	72	M	10
2	Stroke survivor	82	M	4
	Informal carer	71	F	4

NB. F, female; **M**, Male

Self-reported impact of the participant's stroke

In the first stage of the study, the stroke survivors varied in terms of the self-reported impact of their stroke according to the Stroke Impact Scale (SIS 3) scores (Duncan *et al.*, 2003a); their strength appeared the most affected domain (Table 20).

Table 20: Stroke Impact Scale 3 results from stage 1

Stroke impact score (SIS 3), domain	**Result (m ± SD)**
SIS domain: Strength	35 ± 14.8
SIS domain: Memory and thinking	87.5 ± 15.7
SIS domain: Emotion	66.3 ± 15.5
SIS domain: Communication	94.7 ± 7.4
SIS domain: Activities of Daily Living	84.6 ± 13.8
SIS domain: Mobility	58 ± 26.1
SIS domain: Hand function	64.4 ± 33.9
SIS domain: Participation	71.9 ± 19
SIS-16: Total	257 ± 54.7

NB. m, mean; **SD**, standard deviation

The second stage of the study was carried out with two-stroke survivors who also completed stage 1. They varied in terms of the self-reported impact of their stroke according to the SIS 3 scores (Duncan *et al.*, 2003a). Dyad 1 stroke survivor's hand function was affected and both dyads' appeared strongly affected in the strength domain (Table 21).

Table 21: Stroke Impact Scale 3, results from stage 2

Stroke impact score (SIS 3), domain	Dyad 1, stroke survivor result	Dyad 2, stroke survivor result
SIS domain: Strength	43.75	31.25
SIS domain: Memory and thinking	100	89.29
SIS domain: Emotion	88.89	75
SIS domain: Communication	100	96.43
SIS domain: Activities of Daily Living	75	97.5
SIS domain: Mobility	58.33	94.44
SIS domain: Hand function	35	100
SIS domain: Participation	75	87.5
SIS-16: Total	212.08	323.19

NB. Scores out of 100 for each participant win stage 2, were calculated according to steps outlined in section 6.3.5.1

Self-reported therapy experienced

Only stroke clinicians and stroke survivors provided answers to the question regarding the type of therapy experienced; wherein what constitutes therapy was left as the participants choice (Table 22, lists the 'therapies' shared in response for stroke clinicians and stroke survivors from the first stage). In the second stage of the study, only one participant (Dyad 1) reported currently undergoing ‘hydrotherapy’.

Table 22: Self-reported therapy experienced, stage 1

End-user participant group	'Therapy' experienced, self-reported
Stroke clinicians	Facilitated reaching
	Normal movement
	Active assisted movement
	Mirror-box
	E-stimulation
	Mirror box
	Sensory stimulation/integration
	SAEBO MAS (mobile arm support device)
	Functional tasks
	Neurology physiotherapy
	Hands-on
	Exercise
	Hydrotherapy
	Electrical stimulation
Stroke survivors	Hydrotherapy
	Gym – clinic and home
	Home – personal trainer
	Tai chi
	Swimming
	Walking

Prior experience and confidence with technology

In the first stage of the study, the participants' prior experience and confidence with technology varied. Over half the stroke survivors reported confidence in using technology; however, informal carers and stroke clinicians were more confident in using common technology (shown in Table 23). In particular, over three-quarters of stroke survivors had no reported experience with the Kinect V2 (Microsoft, Washington, United States), the main hardware part of the Virtualrehab platform (Table 24). Over half of the stroke survivors had not experienced any other technology which shared aspects of the Virtualrehab platform. Although informal carers reported more experience with certain technology examples (i.e. computer, mobile and Nintendo Wii (Nintendo, Kyoto, Japan) games), nearly half of the group had no experience with the Kinect V2 (Microsoft, Washington, United States) or PlayStation (Sony Interactive Entertainment, Tokoyo, Japan). The stroke clinicians reported no experience with the Kinect V2 (Microsoft, Washington, United States), but for the other technology examples (i.e. mobile games), a large number of the participant group had experienced them.

Table 23: Confidence in using common technology, stage 1

Technology	End-user participant group	Number of participants (percentage of participant group)			
		confident	unsure	unconfident	never used
Mobile	SS	6 (54.55%)	2 (18.18%)	2 (18.18%)	1 (9.09%)
	IC	6 (85.71%)	1 (14.29%)	0	0
	SC	8 (88.89%)	1 (11.11%)	0	0
Computer	SS	4 (36.36%)	2 (18.18%)	4 (36.36%)	1 (9.09%)
	IC	5 (71.43%)	1 (14.29%)	1 (14.29%)	0
	SC	9 (100%)	0	0	0
TV	SS	8 (72.73%)	2 (18.18%)	1 (9.09%)	0
	IC	6 (85.71%)	1 (14.29%)	0	0
	SC	9 (100%)	0	0	0
Tablet or iPad	SS	5 (45.45%)	2 (18.18%)	2 (18.18%)	2 (18.18%)
	IC	6 (85.71%)	0	1 (14.29%)	0
	SC	8 (88.89%)	1 (11.11%)	0	0
Wi-fi	SS	5 (45.45%)	1 (9.09%)	4 (36.36%)	1 (9.09%)
	IC	5 (83.33%)	1 (16.67%)	0	0
	SC	9 (100%)	0	0	0
Internet	SS	5 (45.45%)	3 (27.27%)	2 (18.18%)	1 (9.09%)
	IC	6 (85.71%)	1 (14.29%)	0	0
	SC	9 (100%)	0	0	0

Technology	End-user participant group	Number of participants (percentage of participant group)			
		confident	unsure	unconfident	never used
Email	SS	7 (63.64%)	1 (9.09%)	2 (18.18%)	1 (9.09%)
	IC	7 (100%)	0	0	0
	SC	9 (100%)	0	0	0

NB. SS, Stroke Survivors; **IC,** Informal Carer; **SC,** Stroke Clinicians

Table 24: Prior experience with technology similar to the Virtualrehab platform, stage 1

Common technology	End-user participant group	Number of participants (percentage of participant group)		
		Experienced	Unsure	Not experienced
Xbox (Kinect V2)	SS	1 (9.09%)	1 (9.09%)	9 (81.82%)
	IC	2 (28.57%)	1 (14.29%)	4 (57.14%)
	SC	0	2 (22.22%)	7 (77.78%)
Wii	SS	2 (18.18%)	2 (18.18%)	7 (63.64%)
	IC	3 (42.86%)	3 (42.86%)	1 (14.29%)
	SC	4 (44.44%)	5 (55.56%)	0
Computer games	SS	2 (18.18%)	3 (27.27%)	6 (54.55%)
	IC	5 (55.56%)	2 (22.22%)	2 (22.22%)
	SC	3 (42.86%)	1 (14.29%)	3 (42.86%)
PlayStation	SS	1 (9.09%)	0	10 (90.91%)
	IC	3 (33.33%)	2 (22.22%)	4 (44.44%)
	SC	2 (28.57%)	2 (28.57%)	3 (42.86%)
Mobile games	SS	2 (18.18%)	1 (9.09%)	8 (72.73%)
	IC	6 (66.67%)	1 (11.11%)	2 (22.22%)
	SC	3 (42.86%)	1 (14.29%)	3 (42.86%)

NB. SS, Stroke Survivors**; IC,** Informal Carer; **SC,** Stroke Clinicians

In the second stage of the study, the participants in Dyad 1 reported confidence in using common technology, while Dyad 2 were unsure about using the computer of TV (Table 25). Whereas, the informal carer in Dyad 1 was confident in their prior experience with technology similar to the Virtualrehab platform (Table 26). The stroke survivor in Dyad 1 was only confident in their prior experience with games on the computer and mobile. Finally, the participants in Dyad 2 were confident in their prior experience.

Table 25: Confidence in using common technology, stage 2

Technology	**Dyad 1**		**Dyad 2**	
	Stroke survivor	**Informal carer**	**Stroke survivor**	**Informal carer**
Mobile	Confident	Confident	Confident	Unsure
Computer	Confident	Confident	Unsure	Unsure
TV	Confident	Confident	Unsure	Unsure
Tablet or iPad	Confident	Confident	Confident	Confident
Wi-Fi	Confident	Confident	Confident	Confident
Internet	Confident	Confident	Confident	Confident
Email	Confident	Confident	Confident	Confident

Table 26: Prior experience with technology similar to the Virtualrehab platform, stage 2

Common technology	**Dyad 1**		**Dyad 2**	
	Stroke survivor	**Informal carer**	**Stroke survivor**	**Informal carer**
Xbox (Kinect V2)	Unconfident	Confident	Unconfident	Unconfident
Wii	Unconfident	Confident	Unconfident	Unsure
Computer games	Confident	Confident	Unconfident	Unconfident
PlayStation	Unconfident	Confident	Unconfident	Unconfident
Mobile games	Confident	Confident	Unconfident	Unconfident

6.4.2 Research rigour

The rigour and subsequent trustworthiness of the qualitative data collected are evidenced in Table 27. In addition, the research team met regularly at all stages of the study to improve the credibility of findings and challenge assumptions.

Although these steps increase rigour, it is also important to consider the bias of the researcher background when considering qualitative data. Their psychology and cognitive neuroscience background with prior experience volunteering in stroke support groups may have influenced the analysis and interpretation of the data. Further, the Researcher carried out the focus groups and interviews, and had built a prior rapport with the participants in the recruiting stage; this coupled with the Researcher’s background and personal characteristics may have influenced the participants' responsiveness to the interviewer.

Table 27: Operationalisation of rigour within the study

Means to support a demonstration of rigour	Operationalised within the study	Rigour demonstrated
1. Establish a rapport prior to commencing interviews;	The Researcher met with the participants before the data collection sessions to establish a rapport and develop a trusting relationship.	Credibility
2. Express compassion and empathy during interviews;	Active listening skills (of which the Researcher is trained in) were employed during the data collection sessions to express compassion and prolong engagement.	Credibility
3. Prolonged engagement with participants throughout the study;		Credibility
4. Participants to verify the accuracy of the transcripts (member checking);	The participants were unable to verify the accuracy of the transcripts due to the potential added participant burden; a summary was given at the end of the data collection sessions to ensure their views were accounted for and understood.	Credibility/confirmability*
5. Maintaining a reflexive journal;	The Researcher kept a reflexive journal that detailed the rationale for and methodological or procedural changes, and personal reflections were recorded.	Confirmability/Transferability
6. Establishment of an audit trail describing the study's procedures and processes;	In addition, an audit trail was kept for all data collection and analysis processes.	Confirmability/Dependability
7. Description of participants characteristics;	The participants' characteristics were described (section 6.4.1).	Confirmability
8. Findings represent the data gathered and are not biased by the research, evidenced by the inclusion of direct quotations from participants;	Direct quotations used from participants, to ensure representativeness of data (section 6.4.3 and 6.4.4).	Confirmability

Means to support a demonstration of rigour	Operationalised within the study	Rigour demonstrated
9. Purposeful sampling is used;	A non-probability purposeful sampling technique was used (section 6.3.3.1).	Transferability
10. Providing sufficient study details so recreation can occur;	Sufficient study details have been provided to allow for recreation (section 6.3).	Transferability
11. Rich description is shown in the findings;	In-depth information (i.e. rich description) was gained from the discussions, shown via the thematic analysis, which addressed the research aims (section 6.4.3 and 6.4.4).	Transferability
12. Account for any changes that occur in the study.	An audit trail was kept to account for any changes within the study (i.e. additional ethics required for 1:1 interview in stage 1).	Dependability

NB. *Despite not checking the transcripts participants found the summaries accounted for their discussions, and thus it can be argued that credibility/confirmability was demonstrated

6.4.3 Research aim 2a: to explore the usability and acceptability of a virtual reality system (Virtualrehab platform) for delivery of home-based stroke rehabilitation

System usability questionnaire

Overall, the SUS scores varied amongst the participant group and study stage, the scores are visualised in Figure 18. In the first stage of the study, the mean SUS total score (out of 100) of all three groups was 57.9 (standard deviation = 15.2) (marginally low). The stroke survivors mean score for the platform was 52.5 (standard deviation = 14.0) (marginally low). The informal carers scored a mean of 75.7 (standard deviation = 9.2) (acceptable) for informal carers, and the stroke clinicians a mean of 50.5 (standard deviation = 7.9) (marginally low) (Table 28). Stroke participants rated the following aspects of the platform the lowest: (4) requiring technical support and (10) feeling the need for training before use. Whereas, the stroke clinicians reported most concerns with: (1) frequent use of the platform and (7) users would adapt to the platform quickly. The informal carers, in general, scored more positively regarding the usability of the platform. Within the second stage of the study, the two dyad's scores varied from 67.5 (marginally high) to 85 (acceptable) (Table 29).

Figure 18: SUS scores visualised for each study stage and participant group (adapted from Bangor et al (2008) figure 13, p. 592).

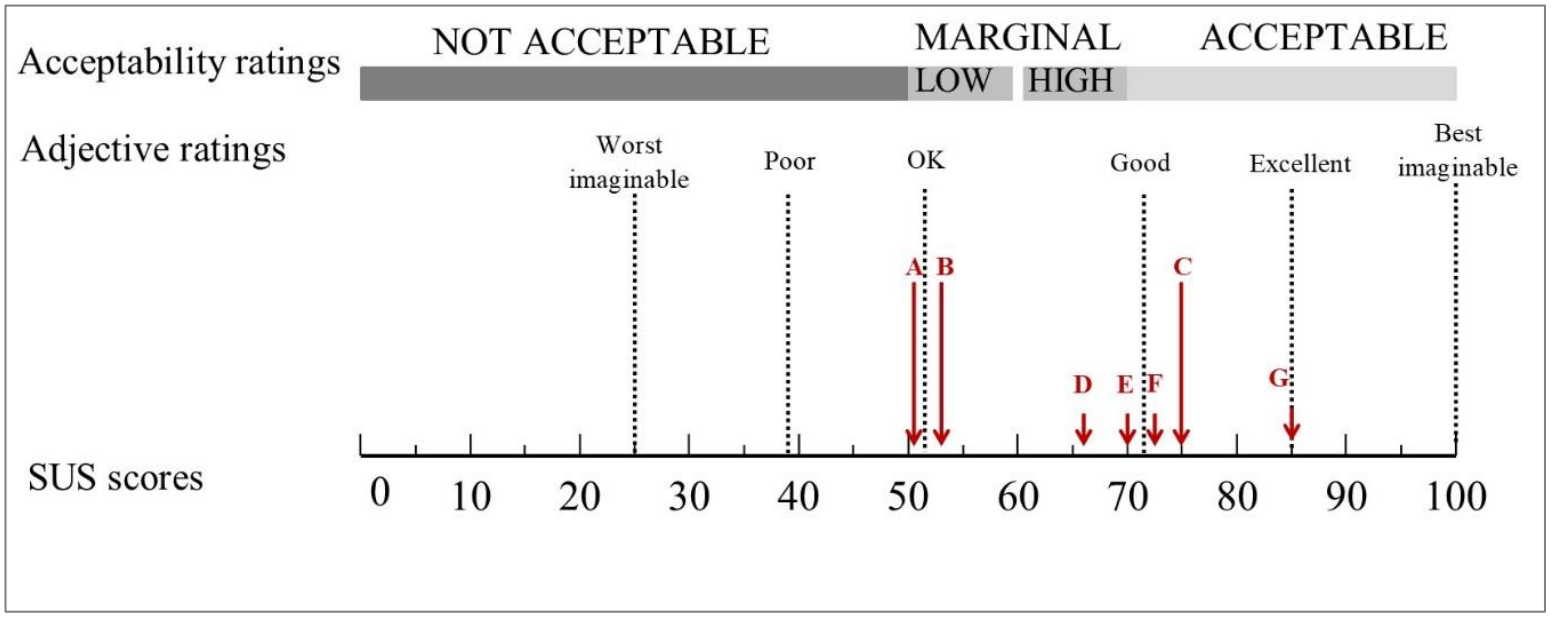


Figure 17 legend

Study stage 1:

- **A** = stroke survivors
- **B** = stroke clinicians
- **C** = informal carers

Study stage 2:

- **D** = Dyad 2 - stroke survivor
- **E** = Dyad 1 - informal carer
- **F** = Dyad 1 - stroke survivor
- **G** = Dyad 2 - informal carer

Table 28: Stroke Usability Scale (SUS adjusted raw scores (m±SD) per question, per participant group, stage 1.

SUS m±SD, per question	Stroke survivors	Informal Carers	Stroke clinicians
1. I think I would like to use this VRP frequently	2.5 ± 0.9	3.7 ± 0.5	1.7 ± 0.7
2. I found the VRP unnecessarily complex	2.0 ± 0.8	2.9 ± 0.5	2.3 ± 0.7
3. I thought the VRP was easy to use	2.2 ± 0.9	3.0 ± 0.6	2.1 ± 0.6
4. I think I would need the support of a technical person to be able to use this VRP.	1.1 ± 0.7	3.0 ± 1.0	2.0 ± 1.0
5. I found the various functions in this VRP were well integrated.	2.5 ± 0.7	3.0 ± 0.6	2.7 ± 0.5
6. I thought there was too much inconsistency in this VRP.	2.2 ± 0.8	2.7 ± 0.5	2.3 ± 0.5
7. I would imagine that most people would learn to use this VRP very quickly.	2.5 ± 0.7	2.9 ± 0.4	1.1 ± 0.8
8. I found the VRP cumbersome to use.	2.3 ± 0.5	3.0 ± 1.0	2.0 ± 0.5
9. I would feel very confident using the VRP.	2.3 ± 0.8	3.4 ± 0.5	2.0 ± 0.7
10. I would need to learn a lot of things before I could get going with this VRP.	1.7 ± 0.9	2.7 ± 0.8	2.0 ± 0.7
Total	52.5 ± 14.0	75.7 ± 9.2	50.5 ± 7.9

NB. m, mean; **SD,** standard deviation, **VRP,** VirtualRehab platform

Table 29: Stroke Usability Scale (SUS adjusted raw scores), stage 2.

Stage 2		**SUS score**
Dyad 1		
	Stroke survivor	72.5
	Informal carer	70
Dyad 2		
	Stroke survivor	67.5
	Informal carer	85

When asked about finding space for the platform in the home, the stroke survivors and informal carers felt this could be done with ease (54.5% stroke survivors, 100%, informal carers) (Table 30). However, the majority of stroke clinicians were unsure if their clients could find space within their home (42.9%). The participants varied in responses when asked about using the platform (i.e. connecting it to the TV, switching it on and off and navigating through the software). The informal carers and stroke clinicians felt connecting the platform to the TV would be easier than stroke survivors (whom only 27.27% felt they could with ease). However, in terms of switching the device on and off over two-thirds of stroke survivors and informal carers participants felt this could be done; the stroke clinicians were less sure that their patients would be able to. Finally, stroke survivors were more unsure of navigating through the software than informal carers, and stroke clinicians believed they would be able to.

Stroke clinicians were also asked how important customising aspects of the Virtualrehab platform therapy was. The clinicians primarily chose 'satisfied' when asked about the variety of content on offer (body-specific - 55.5%; hand specific - 44.4%); the rest were 'unsure'. The majority chose 'unsure' when asked about the functionality of the exercises and exergames (body-specific - 44.4%; hand specific - 55.5%). Overall, the majority (44.4%) were 'satisfied' with the similarity between the platform's content and rehabilitation exercises.

Table 30: System usability questionnaire, specific aspects of the Virtualrehab platform

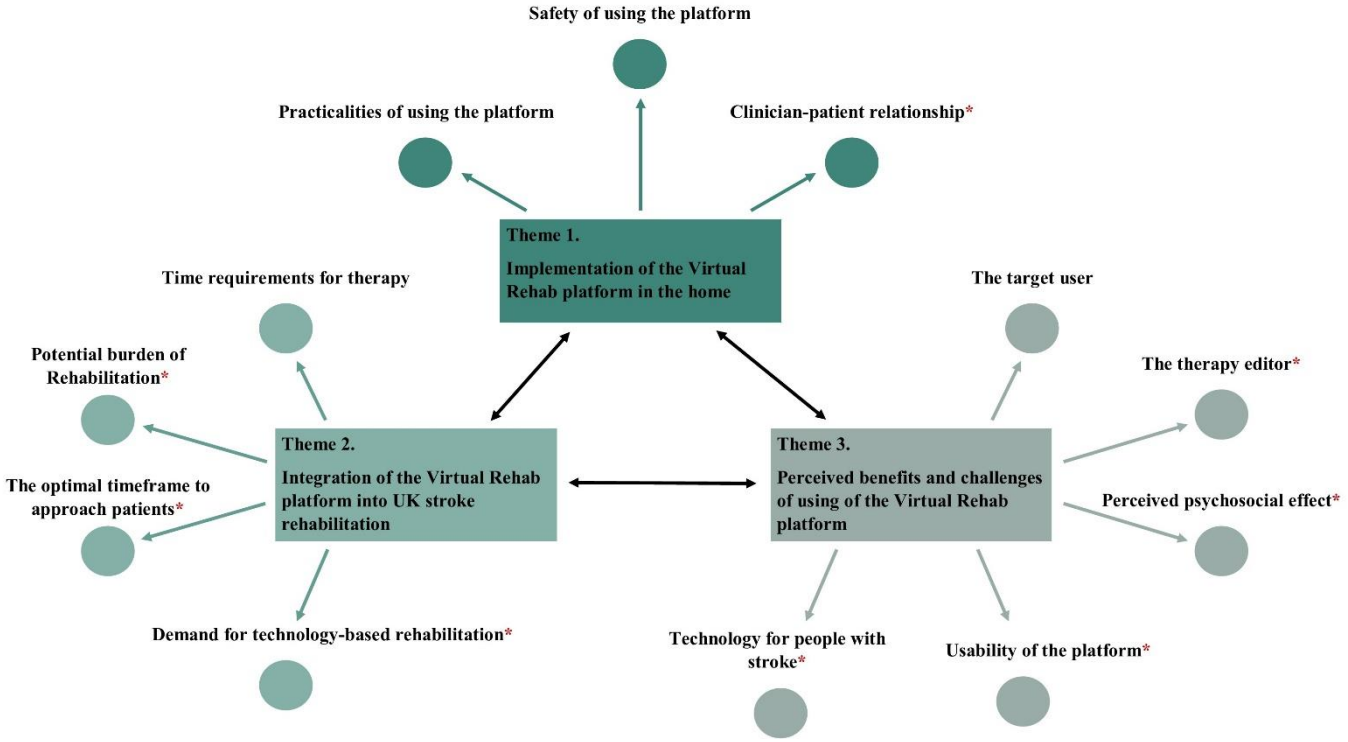
Aspects of using the Virtualrehab platform	End-user participant group	Number of participants (percentage of participant group)		
		Easy	Unsure	Difficult
Find a space for it	SS	6 (54.55%)	4 (36.36%)	1 (9.09%)
	IC	7 (100%)	0	0
	SC	1 (11.11%)	5 (55.56%)	3 (33.33%)
Connect it to the TV	SS	3 (27.27%)	6 (54.55%)	2 (18.18%)
	IC	4 (57.14%)	3 (42.86%)	0
	SC	4 (44.44%)	5 (55.56%)	0
Switch it on	SS	8 (72.73%)	2 (18.18%)	2 (9.09%)
	IC	6 (85.71%)	1 (14.29%)	0
	SC	4 (44.44%)	5 (55.56%)	0
Turn it off	SS	8 (72.73%)	2 (18.18%)	2 (9.09%)
	IC	6 (85.71%)	1 (14.29%)	0
	SC	4 (44.44%)	5 (55.56%)	0
Navigate through the software	SS	4 (36.36%)	4 (36.36%)	3 (27.27%)
	IC	6 (85.71%)	1 (14.29%)	0
	SC	3 (33.33%)	5 (55.56%)	1 (11.11%)

NB. SS, Stroke Survivors**; IC,** Informal Carer; **SC,** Stroke Clinicians

Group and individual discussions

The group and individual discussions from stage 1 and 2 of the study revealed three themes with related subthemes, answering research aim 2a (displayed in a thematic map, Figure 19).

Figure 19: Thematic map, for research aim 2a



* Stage 2 of the study themes

The differences in themes arising between the end-user group and study stages are shown in Table 31.

Table 31: End-user participant group thematic difference amongst study stages

Theme	Subtheme	Stroke survivors		Informal carers	Stroke clinicians
		Stage 1	Stage 2		
Theme 1. Implementation of the Virtualrehab platform in the home					
	(a) Therapist-patient relationship	✓		✓	✓
	(b) practicalities of using the platform	✓	✓	✓	✓
	(c) Safety of using the platform			✓	✓
Theme 2. Integration of the Virtualrehab platform into UK stroke rehabilitation					
	(a) Demand for technology-based rehabilitation	✓	✓	✓	
	(b) the optimal timeframe to approach patients	✓	✓	✓	
	(c) Time requirements for therapy				✓
	(d) Potential burden of rehabilitation	✓	✓	✓	✓
Theme 3. Perceived benefits and challenges of using the Virtualrehab platform					
	(a) the target user			✓	✓
	(b) the therapy editor	✓	✓	✓	✓
	(c) Perceived psychosocial effect		✓	✓	
	(d) Technology for stroke survivors	✓	✓	✓	✓
	(e) usability of the platform	✓	✓	✓	✓

6.4.3.1 Theme 1. Implementation of the Virtualrehab platform in the home (Table 32)

The therapist-patient relationship was highlighted as an important part of rehabilitation: promoting safety, trust and motivation. Participants worried about losing the '*human touch*' element if virtual reality systems replaced therapists. Stroke survivors and informal carers suggested the platform should be a tool for therapists, not independent of them. Stroke clinicians viewed the use of the platform positively, especially the ability to record '*incorrect*' movements potentially highlighting compensation.

The use of the platform within the home was seen as a potential way to increase therapy access. Indeed, stroke survivors reported wanting less travel and more privacy, suggesting advantages to conducting therapy within the home. They also felt that the *'offline'* version would help in areas with poor internet connectivity (the Virtualrehab platform sessions could run without an internet connection; the data recorded is saved until either an internet connection is created or the therapist laptop directly downloads the data). Although stroke clinicians felt the home could be beneficial for therapy, they worried about potentially cluttered environments. The informal carers felt the platform's design was less intrusive than rehabilitation technology they had experience with previously. Although it should be noted, they did not report much experience with prior technology.

Table 32: Subthemes from the implementation of the Virtualrehab platform in a domestic setting

Subtheme	Illustrative quote	Participant group
(a) clinician-patient relationship		
	Whereas a computer can't hold my hand.	Stroke survivor, stage 1
	I think it's also somebody else coming in and it's a watchful eye. It's a backup for me.	Informal carer, stage 1
	I am not sure how great the machine will pick up all the other movements. I think if the patients doing it we would almost have to see the patients doing it, to make sure they are doing the movement correctly.	Stroke clinician, stage 1
(b) practicalities of using the platform		
	I think in your home, you can do it when you want, without being watched.	Stroke survivor, stage 1
	It would be a godsend if there is very little physio involved if you live in a place with little transport and the carer does not drive.	Informal carer, stage 1
	A lot of houses can be quite cluttered	Stroke clinician, stage 1
	Depends on what must be done	Stroke survivor, Interviews, stage 1
	It was not intrusive or anything […] it's easy to work around	Stroke survivor, stage 2
(c) Safety of using the platform		

Subtheme	Illustrative quote	Participant group
	I think it's different doing it in person than doing it in your own home. You have your own time limits in your home […] you are maybe tired or anything, then you can sort of stop any time […] I think it is a comfortable setting anyway in your own home	Informal carer, stage 1
	Ensuring that they are going to be safe if we leave them doing the exercise	Stroke clinician, stage 1

6.4.3.2 Theme 2. Integration of the Virtualrehab platform into UK stroke rehabilitation (Table 33)

Participants considered that integrating technology-based therapy aids into UK stroke rehabilitation had potential; particularly in areas where there was limited, or inconsistent therapist contact time. Stroke survivors felt aids, such as the platform, should be offered as soon as possible but, with support in place to facilitate acceptance.

Stroke clinicians felt that the platform's usability is key to ensuring there is no further burden on the friends and family of stroke survivors. They reported that, in their experience, learning similar systems can reduce treatment time. Informal carers also felt that the platform's design needed to facilitate autonomous rehabilitation to lessen their burden; with clear instructions and technical support for an acceptable system.

Table 33: Subthemes from the integration of the Virtualrehab platform into the UK stroke rehabilitation pathway

Subtheme	Illustrative quote	Participant group
(a) Demand for technology-based rehabilitation		
	We would fit it in, it's a priority in our lives isn't really.	Stroke survivor, stage 1
	She actually feels she is doing something rather than something is being done to her.	Informal carer, stage 1
	I'd like to see it become a normal part of rehab. I do think it would be a benefit.	Stroke survivor, stage 2
(b) the optimal timeframe to approach patients		
	As soon as possible. If it's going to improve their situation.	Stroke survivor, stage 1
	Introduce at the right time, not pushed too soon. Be mindful of the mental impact of a stroke.	Informal carer, stage 1
	As soon as possible. Because it comes from that period of adjustment when all the emotions come, it makes you feel you are not left, I had good input but then there was a period where I went and had therapy.	Stroke survivor, stage 2

Subtheme	Illustrative quote	Participant group
(c) Time requirements for therapy		
	Someone else would need to be quite well trained in order to able to set-it-up quickly and then to get the patient in and it all to be ready, it would be quite frustrating and that could actually be a treatment time in itself.	Stroke clinicians, stage 1
(d) Potential burden of rehabilitation		
	Someone has to do that. I want to burden my partner less, not more. So it'd be best for me if it was set-up, fixed and left static. I mean we have a Wii at home and that is set-up, fixed and static.	Stroke survivor, stage 1
	I was getting frustrated, every time [identifying information removed] was given exercises or homework to do. It was oh help him do this, help him do that and I just thought I don't have enough hours in the day, to help him do the things he has been told, never mind the things to get by and we have to. In that sense this feels good, the way I have seen it today, he could, I could help him get the thing on and going and none of it made me feel he would need me there, obviously I would keep an eye initially but he could possibly do some on his own. That would be a relief.	Informal carer, stage 1

Subtheme	Illustrative quote	Participant group
	Then you have to rely on someone else to help them set it all up, almost carrying it out and moving them really, whether that's carers or family.	Stroke clinicians, stage 1

6.4.3.3 Theme 3. Perceived benefits and challenges of using the Virtualrehab platform (Table 34)

Stroke survivors felt the variety of exercises and games available offered a challenging and enjoyable environment. This was also a benefit for informal carers; they noted that recording progress over time might help stroke survivors to see improvements. Therapists praised the ability of the platform's therapy editor to individualise plans for each stroke survivor. The usability of the platform's software was appreciated by all participants praising the visual design and module content. In particular, the ability to identify wrong movements was praised by stroke survivors. However, participants felt the format of the instructions needed to consider stroke deficits (i.e. audio and written). The main potential challenges identified was the durability, reliability and accuracy of the equipment. Stroke survivors worried about unreliable equipment affecting motivation. Stroke clinicians reported previous experience with unreliable home-based technology led to frustration and additional maintenance or replacement costs. They were also concerned that family members using the equipment would interfere with the data collected.

Stroke survivors acknowledged a personal lack of computer literacy but felt, with the right instruction, they could confidently use the platform. In contrast, informal carers and stroke clinicians felt that computer-based technology could be confusing for stroke survivors. Overall, participants agreed that if using the platform and therapy programmes was easy (e.g. starting with just one action), then it would be acceptable.

Table 34: Subthemes from the perceived benefits and challenges of using the Virtualrehab platform

Subtheme	Illustrative quote	Participant group
(a) the target user		
	Yea because it is a unique thing, you can't say well your stroke will make your body and your brain do this because everyone's is quite unique. So, if it's tailored to your own personal situation it's very good.	Informal carer, stage 1
	It is sometimes easy for us to develop an exercise programme for higher-level patients it is the lower level patients that we want to be more successful with.	Stroke clinician stage 1
(b) the therapy editor		
	I think the therapists has got to be involved in that anyway. As you progress. Because you could end up not knowing what you are doing otherwise couldn't you?	Stroke survivor, stage 1
	It was good that you could set different ranges and targets. Again the schedule for exercises. It is good you can check up on what they are doing. That is useful feedback.	Stroke clinician, stage 1
	I think the stroke rehabilitation team would be quite good, with their input. They would know what the stroke patients need.	Stroke survivor, stage 2
(c) Perceived psychosocial effect		
	I just think motivation is quite hard as they do tend to have a lot of depression understandable. So anything that could make it a little bit fun and not too difficult, that they can't do it.	Informal carer, stage 1

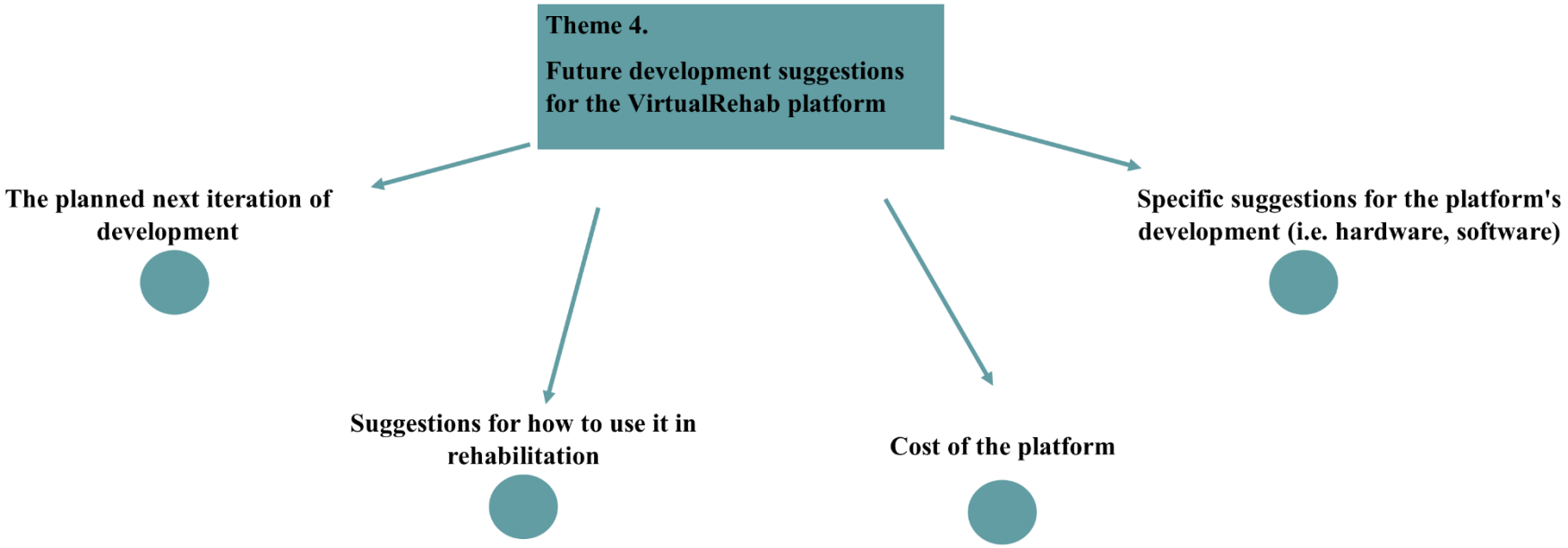
Subtheme	Illustrative quote	Participant group
	Anything that is enjoyable, so perhaps like [identifying information removed] said you can play with someone else or compete with someone else, your carer, your friend, your relative or another stroke, link up with another victim or stroke victim it might be someone you buddied up with someone say in Australia, for example, that would be quite a good motivation, it would help reconnect with society	
	Confidence building, when you suddenly realise that yes I can do something with this hand, do something with my arm. A lot of people just kind of think it does not work, when in fact if they just used it they could see the benefit.	Stroke survivor, stage 2
(d) Technology for stroke survivors		
	Well if it's all set-up for you and you just have to plug it in and switch it on.	Stroke survivor, stage 1
	I don't think they can cope with technology quite honestly. Once they have had a stroke, that's just my opinion, from what I have seen.	Informal carer, stage 1
	Just IT skills in the older generation because they are not actually that big, but it's just the setting up.	Stroke clinician, stage 1
	It (the hardware) fitted in fine, it's just a pity it didn't work properly	Stroke survivor, stage 2
(e) usability of the platform		

Subtheme	Illustrative quote	Participant group
	As a stroke patient if you like that is the way we think, because it's I don't know if you agree with me [referring to other respondents] but it seems we don't want to get to complicated with things we are trying to do in our lives. We know we are trying to normalise it a little bit. So I think if you are going have to re-set something all the time. Then it presents a problem to us I think	Stroke survivor, stage 1
	I think there could be, if they don't understand it. It's very important how its set-up and that they have the time to get used to it, if they are not computer literate. I think it's a motivator, if its handled right and the clients ready for it	Informal carer, stage 1
	It just needs to be as easy and simple as possible and for them to press start [talking over each other] not like those with pages and loads of different steps, yea it will just make them confused [agreement for several other participants]. Simple as possible to get them to where it needs to be, to start their programme.	Stroke clinician, stage 1
	I found it very good actually. One of the things that impressed me was that if, when you are doing the exercises. If the movement isn't correct then it comes up in a red line to show you are in the wrong position. Even the graphics come up on the screen telling you are in a wrong movement, your backs wrong or whatever. I think that's great, that's one thing I really like about it. But maybe put it into writing, say move your foot to the right, for someone who is not as good at correcting their movement.	Stroke survivor, stage 2

6.4.4 Research aim 2b: to inform the development of future iterations of the device

Four main areas for future development were identified from the group discussions and interviews from stage 1 and 2 (Figure 20).

Figure 20: Thematic map, for research aim 2b



6.4.4.1 Theme 4. Future developments for the Virtualrehab platform (Table 35)

Stroke survivors and informal carers emphasised portability for the next iteration of the Virtualrehab platform. Participants felt a portable (i.e. briefcase-style) platform, light enough to be used one-handed, would facilitate autonomy and privacy within the home. Specific improvements to the hardware and software of the platform were suggested to facilitate its usability and acceptability. Stroke survivors felt slow in-depth instructions should be included; both audio and written for different stroke-related impairments, e.g. hemianopia. Stroke clinicians suggested adding more daily living activities; they also wanted to see real-time feedback from their patients to facilitate collaborative therapy design. All participants felt the platform should offer personalised and motivating feedback. Costs of the Virtualrehab platform were discussed; stroke survivors felt being able to trial or rent the platform from stroke units or charities could improve access. Nevertheless, stroke clinicians and informal carers were concerned that such avenues might not have the resources, especially with the 'hidden costs' such as damage updating and the need for therapist oversight. Social and competitive factors were focussed on within the discussions. Stroke survivors felt playing with family may lessen the isolation that is sometimes felt and help people' reconnect with society'. They, including informal carers, felt a multiplayer option (for family, support groups or online communities) could offer companionship, potentially increasing motivation and thus adherence to rehabilitation.

Table 35: Subthemes from future development suggestions for the Virtualrehab platform

Subtheme	Illustrative quote	Participant group
(a) the planned next iteration of development		
	That would be good because it would not necessarily be in the main room. It could be somewhere quiet where you could concentrate on what you want to do.	Informal carers, stage 1
(b) Cost of the platform		
	Me personally I think it's priceless, I really do. I think its brilliant	Stroke survivor, stage 1
	Ultimately it's a tool that cuts down on man power, stops the physio having to go to site, although it is an expensive bit of kit to buy and develop it ultimately it is saving a lot of man power time, but as you say the NHS is not an unlimited pot of money	Informal carer, stage 1
	Well our department would not be able to afford it, you have upkeep and maintenance costs.	Stroke clinicians, stage 1
	I think if stroke organisations bought the packages and hired them out to members.	Stroke surviviors, stage 2
(c) Specific suggestions for the platform's development (i.e. hardware, software)		

Subtheme	Illustrative quote	Participant group
	I would benefit from some kind of motivational thing you know. On the Wii it says 'you haven't been back to the Wii for 7 days, get your act together' it doesn't say that. But it recognises when you are using it and when you are not. Some kind of motivation like you know, 'keep going, a little bit a day will make a difference', don't give up keep going. Something like that would be really helpful.	Stroke survivors, stage 1
	Some of the games [referring to their experience with the Wii], I know are not for person with strokes, have almost a punitive like when you don't do well it would be disastrous in this context. You know positive, encouraging, or soothing, or neutral	Informal carer, stage 1
	I think the hand thing (LEAP) getting low on the floor, some of the stretching ones you have to be careful of not to overstretch.	Stroke survivors, stage 2
(e) Suggestions for how to use it in rehabilitation		
	One idea I had, something that would involve two people a partnership thing. So I can do it with my partner, because we do on the Wii.	Stroke survivors, stage 1
	I thought of one thing, if there were the technology possible to link to other players, I know [identifying information removed] goes to other person with strokes group. if they met up, they could say oh are you playing, they could use it for motivation for other survivors	Informal carers, stage 1
	I think if you went into stroke groups and did it as a group exercise, might be handy.	Stroke survivor, stage 2

6.5 DISCUSSION

This study found that the Virtualrehab platform was usable and acceptable to end-users (aim 2a). For example, participants found: the wide variety and personalised therapy plans to be acceptable; the home environment enabled convenient private rehabilitation, and the software allowed for potentially motivating and engaging functional training. However, the usability of the platform requires improvement, to enhance the ability of stroke survivors to use it independently, and ensure the technology is durable (i.e. account for equipment failures and support required). The Virtualrehab platform received a low rating for the System Usability Scale by participants, indicating improvements are needed to be seen as acceptable for users. There were also specific improvements identified, including better portability, affordability, software changes to improve acceptability, accommodation for post-stroke impairments (aim 2b). These findings support the potential for delivering stroke rehabilitation via technology within the home (Laver *et al.*, 2011). It should also be noted that participants emphasised such devices should be seen as an aid for therapists, not a replacement. As in previous research, this study found that the instructions for using the platform, and a design that facilitates independent undertaking of therapy were important (van Ommeren *et al.*, 2018).

Participants characteristics and prior experiences with technology are important to highlight possible bias in the results. The majority of the participants reported confidence with using common technology, although

the stroke survivors were less likely to; which could influence their views on utilising the platform within stroke rehabilitation. It is important to note that the diverse experience may influence the groups' discussions on the platform.

Impact of the findings for the iterative development of the platform

A series of recommendations arose from the end-user groups (research aim 2b) for the next iteration of the Virtualrehab platform.

- **Specific training and technical support:** appropriate support and instruction need to be given and available throughout the platforms use.
- **Portability:** the platform needs to be portable in an accessible way for one-limb transport.
- **Cost:** it is essential to focus on costing the platform in a way that increases its availability to everyone.
- **Feedback:** it was recommended that further detailed feedback is given to motivate users and also allow them to track their improvement. It was emphasised this feedback must be positive, due to fluctuations in stroke recovery.
- **Community:** it was suggested that a community could be built into the platform, allowing solo players to interact or engage with other users.
- **Safety:** measures need to be in place to ensure the safety of the user and limit the burden to family and friends.
- **Therapist interaction:** further therapist interaction abilities were advised.

- **Evidence:** users would be more inclined to utilise the platform if there was robust evidence of potential rehabilitation benefits.
- **Instructions:** the ability to tailor the instructions and interact aspects of the software of the platform to different potential stroke impacts (i.e. visual, hearing) could allow for more potential users.
- **Time:** ensuring the training and use of the platform did not add more therapist burden.
- **Reliability:** ensuring the reliability and longevity of such devices.

The recommendations from the three participant groups and two dyads were summarised in a report for Evolv Rehabilitation Technologies (Evolv, Basauri, Spain) to incorporate into the next iteration of the Virtualrehab platform. Some of these changes were completed prior to phase III of this thesis, others are currently in progress. The software was altered to allow for slower movements to ensure the participants could follow the exercise and understand the feedback given. In addition, several updates to the software improved the reliability and prevented the problems prior versions saw, such as freezing and losing the data; this helped to lower the number of technical challenges the participants faced.

Strengths and limitations of the study

The inclusion of three end-user groups was a key strength of the study and further demonstrates the importance of the users' voice in the development of rehabilitation devices. This study also highlights the Virtualrehab platform's potential for delivering stroke rehabilitation within the home. The next step is to investigate the potential therapeutic benefits of using the next iteration of the Virtualrehab platform for the delivery of evidence-based physical therapy to stroke survivors in their home setting.

The limitations of this study are acknowledged, specifically the small sample size in each end-user group; the goal was to recruit a larger sample for stage one. The first stage of the study asked participants to discuss the platform prospectively following only one brief demonstration. There was a lack of exposure to the system that limits the usability information gained. In stage 2, only two dyads trialled the platform which limited the diverseness of the participants and thus the information gathered. They also used the platform for only two weeks and were not prescribed a training plan, rather asked to use all available software components. Due to these limitations more extensive home testing, using additional dyads should have been completed in order to strengthen the study reported in phase III. Finally, as the virtual reality system was the Virtualrehab platform, there needs to be caution when generalising the findings to other systems.

6.6 CONCLUSIONS

Phase II of this thesis demonstrated the usability and acceptability of the Virtualrehab platform and incorporated end-users' views into the refinement of the Virtualrehab platform. Stroke survivors, informal carers and clinicians recommended key hardware and software usability changes. Further, this phase of work reported in the thesis underlined the development of phase III, an initial investigation into the feasibility of delivering exercise-based virtual rehabilitation within the home. Finally, the findings from this study were summarised in an internal report sent to the industrial collaborator for use in the next stage of Virtualrehab's platform development.

7 PHASE III: FEASIBILITY OF DELIVERING EXERCISE-BASED UPPER LIMB STROKE REHABILITATION WITHIN THE HOME VIA THE VIRTUALREHAB PLATFORM

7.1 INTRODUCTION

Phase III addressed the third research question (chapter two, section 2.3):

How feasible is virtual reality-aided exercise-based training as a mode to deliver upper limb stroke rehabilitation within the home?

The research question was investigated with a convergent parallel mixed-methods feasibility study consisting of a series of replicated single-case studies, with a 12-week intervention period and two interviews. This work aligns with the 'development', 'feasibility' and 'piloting' stages of the Medical Research Councils' (MRC) Framework for Complex Interventions (Craig *et al.*, 2008); also the study provides a 'consideration of concept' investigation (Dobkin, 2009; Bernhardt, Hayward, *et al.*, 2019). If evidence of feasibility/concept is found, then the next step will be to identify optimal therapeutic dose as a precursor to a clinical efficacy trial.

The following chapter presents the study's methods, results and discussion for the quantitative components (research objectives one to seven, section 7.2). The qualitative details (research objectives eight and nine) are reported in chapter eight.

7.2 RESEARCH AIMS

To answer the third research question, phase III aimed to:

Aim 3a: Determine the feasibility of delivering exercise-based upper limb stroke rehabilitation within the home via the Virtualrehab platform.

The specific research objectives were to:

1. Establish the process for recruitment of stroke survivors to a subsequent Randomised Control Trial (RCT) when they have been discharged from NHS specialist stroke services;
2. Explore adherence (number of more paretic upper limb repetitions) of stroke survivors to the 'prescribed' use of the Virtualrehab platform;
3. Assess the viability of the researcher adjusting the 'prescribed' training programme over time;
4. Evaluate the technical reliability of the Virtualrehab platform;
5. Test the viability of collecting neuromechanical and behavioural data in the home;
6. To assess the viability of using randomised length of baselines and repeated measures during the intervention period to inform a subsequent dose-optimisation study;
7. Estimate changes in paretic upper limb functional ability and motor impairment and neural measures;
8. Ascertain the acceptability of home-based task-orientated upper limb training via non-immersive virtual reality to stroke survivors in their own homes;
9. Establish the acceptability of participation in the study.

7.3 METHODS

7.3.1 Design

A convergent parallel mixed-methods feasibility study was conducted using a series of replicated single-cases following an AB design; with 1:1 interviews after the control and intervention periods. The justification for a convergent parallel mixed-methods study is detailed in section 4.2.3. A feasibility design was chosen to answer the question 'can the study be done' before the next steps leading to a clinical efficacy trial can be carried out.

7.3.1.1 The quantitative component

The quantitative component consisted of replicated single case studies following an AB design. A group of stroke survivors completed both phases, a no therapy control period (A) and 12-week intervention (B). During the A, control phase, stroke participants completed a measurement battery before and after. The control phase was randomised between one to four weeks. Following this, the B, intervention phase, was carried out where stroke participants completed an exercise-based virtual reality therapy programme, alongside weekly measures in the home; with a measurement battery at the end of the intervention period.

The use of replicated single case studies is applicable when: investigating a novel intervention (i.e. virtual reality); when obtaining multiple sets of equipment is challenging; with heterogenous subjects acting as their own controls. The design has the potential for a nuanced, empirically rich holistic account of the phenomena within each participant (Krasny-Pacini and Evans,

2018). Further, the feasibility of this design, with its randomised control period (A), required investigating before a dose-optimisation study can be developed (objective six).

Finally, a group of healthy individuals were recruited to provide standardised normative neural scores. The neural measures are not directly comparable between research settings because of variations in equipment used and the exact instructions provided to participants. It is important to provide normative values from these measures conducted with healthy participants, to compare with the stroke participants.

7.3.1.2 The qualitative component

The qualitative component involved descriptive semi-structured interviews conducted with the stroke participants at the end of phases A and B. Full details are in chapter eight.

7.3.2 Ethics

The following section details the approvals obtained for the study, and subsequent ethical consideration for data management and procedures carried out.

7.3.2.1 Approvals

Ethical approval was obtained from the NHS, specifically, the National Research Ethics Services (NRES) committee in London, Surrey (4th May 2018) and the Health Research Authority (HRA) (13th June 2018) (Appendix 1D to 3D). The Integrated Research Application System (IRAS) project ID is

233548, with reference number 18/LO/0562. Adoption to the National Institute for Health Research (NIHR) portfolio was declined as the industry funding obtained for the project was not via a peer-reviewed process (7th June 2018).

7.3.2.2 Data management

All data was handled as per the European Union's General Data Protection Regulation (GDPR) guidelines (European Union, 2016). The electronic data was kept on a secure password-protected University of East Anglia (UEA) database, accessible only to the research team. Data collected off-campus was stored in a locked folder, with electronic data on an encrypted USB and transferred to a locked filing cabinet within the Researcher's (author of the thesis) office or the secure database at the first opportunity. Contact details were stored securely, accessible only by the Researcher. If at any point during the study, contact with participants was unsuccessful, the Researcher attempted two more times; if no contact was made, the participant was recorded as lost to follow-up and withdrawn from the study.

7.3.2.3 Procedures

The Researcher visited the homes of stroke survivors interested and screened for eligibility (detailed in section 7.3.3.3). The healthy participants were screened via the phone, email or in-person at the UEA Movement and Exercise Laboratory (MovExLab) (section 7.3.3.3). If eligible, written informed consent was obtained, and a unique participant identification number assigned (VRXX, stroke participant group; HXX, healthy participant group).

The outcome measures have been used in prior research investigating upper limb motor impairment rehabilitation following a stroke (Lang *et al.*, 2013; Liu *et al.*, 2013; Budhota *et al.*, 2016; Demers and Levin, 2017; Klein *et al.*, 2018). However, it should be noted that the measurement battery had not been carried out in a home environment and formed the rationale for objective 5 (testing the viability of collecting such data within the home).

The Researcher undertook the appropriate health and safety training required for working within the MovExLab, including first aid, fire safety, moving and handling, accident reporting policies, cleaning and storage of equipment. When working within the home, risk assessments were carried out, and lone worker policies followed. The Researcher ensured their whereabouts were known at all times when travelling, by car, to participants' homes.

The Virtualrehab platform (described in chapter three) required physical activity; this was explained clearly to potential participants, and that they would be encouraged to only carry out movements within their abilities. Potential participants were screened to ensure that there was no contraindication to the level of exercise required.

7.3.3 Participants

The following section details the sampling, sample size, recruitment and criteria within this study for the stroke and healthy participant groups.

7.3.3.1 Sampling

A non-probability convenience sampling method was used to undertake this feasibility work. The method allows for recruitment from accessible areas within the study's time and resources. For the stroke participants, prior similar research within UEA often used a stroke rehabilitation unit from an NHS hospital as the recruitment site (i.e. six-month stroke review team). There are limitations to this method; the capacity to undertake multiple stroke rehabilitation projects is limited – at the time of recruitment, the local teams could not accommodate another study. The other challenge comes from sampling in a rural area, where recruitment and retention rates are typically low (Leira *et al.*, 2018; Ferreira *et al.*, 2019). Finally, the number of patients passing through such a recruitment site with the characteristics required at any given time is unpredictable (Stinear *et al.*, 2020).

A different recruitment approach was undertaken for this study and as a possible additional resource for future trials within the Acquired Brain Injury Rehabilitation Alliance (ABIRA). Thus, those within the community under the care of charge of NHS General Practices (GPs) were considered (objective 1).

7.3.3.2 Sample size

Formal sample size calculations are not required for feasibility trials, although appropriate justification is still important (Billingham, Whitehead and Julious, 2013). Healthcare feasibility research guidelines recommend 30 participants split between the control and experimental groups (Lancaster, Dodd and Williamson, 2004; Arain *et al.*, 2010; Billingham, Whitehead and Julious, 2013). These guidelines were used as a starting point to identify an appropriate sample size. The resources and time accessibility were also considered; five sets of the Virtualrehab platform were procured for the study. The equipment available limited recruitment, as each set potentially would be used for up to four months, per participant. Finally, the recruitment and retention rate of prior research reported within this thesis (phase II, chapter six) and carried out in the ABIRA research group, also guided the sample size.

Stroke participants

Following the points made above, the study aimed to recruit 15 stroke participants, each acting as their control due to the replicated single-case study AB design.

Healthy participants

Healthy participants were required to complete the neural measures. Once more, the practicalities were considered in terms of time and resource availability (i.e. Lab schedule, Researcher's time). The aim was to recruit ten healthy participants, an achievable and suitable amount for the research objectives.

7.3.3.3 Recruitment and criteria

Stroke participants

The following inclusion criteria were used to recruit stroke survivors appropriate to the research objectives (a, g), those who could potentially use the Virtualrehab platform's equipment successfully in their home environment (c to f) and had the potential to show motor impairment changes following such the intervention (c) (Table 36).

Table 36: The stroke participants inclusion criteria

	Criteria	**Rationale**
A	At least six months after a stroke.	To be within the chronic phase of recovery.
B	A score of at least 19/33 on the Motricity Index (Collin and Wade, 1990) elbow flexion and shoulder abduction section.	To ensure responsiveness from the Virtualrehab platform.
C	While also being unable to complete the Nine Hole Peg Test (9HPT) (Kellor *et al.*, 1971) in 50 seconds or less with the contra-lesional (more paretic) upper limb.	To ensure an adequate level of motor impairment of which such exercise movements would be prescribed in typical therapy.
D	Able to use the contralesional upper limb for drinking from a cup, before the onset of the index stroke.	To ensure appropriate motor function existed before the stroke.
E	Have an appropriate space in their home for the Virtualrehab platform's.	To ensure the safe and appropriate set-up to detect movement.
F	Able to play the Virtualrehab 'boxing game' with their ipsilesional upper limb (less paretic).	To indicate the ability to follow instructions relevant to the Virtualrehab platform.
G	Fit to participate in the exercise-based training programme as assessed by a resting heart rate of 90 beats per minute or less and a systolic blood pressure of 140mmHg or less.	Determined by recommendations from the NHS blood pressure general guide (high is systolic of greater than 140) and the British heart foundation as a resting heartbeat of 100 or higher (90 was chosen for caution) (*Your heart rate | BHF*, no date; NHS, 2016)

NB. Participants also needed to be adults (18+), able to provide informed consent.

Stroke survivors were recruited through GP practices within a 25-mile radius of the UEA MovExLab. This radius was chosen to limit the potential burden of travel on participants. The following recruitment method was chosen to avoid any potential participant being inappropriately approached by the research team, for example, if medically unwell, in emotional distress or if they did not want to be approached by a researcher.

1 The Researcher advertised the study through an email newsletter sent to research-active GP practices;
2 Those interested contacted the Researcher, and a meeting was arranged;
3 The Researcher gave the initial screening criteria (a, d, and g) to the research leads within each interested GP practice;
4 The research leads then applied the initial screening criteria to their patient database to obtain a list of potentially eligible individuals;
5 A GP within each practice then confirmed the potential eligibility of the selected individual's records;
6 The research lead then sent invitation packs, containing a recruitment letter, participant information sheet and consent form to the potentially eligible individuals;
7 Potentially eligible individuals who were interested in participation then contacted the Researcher (via phone or email);
8 The Researcher then visited the potentially eligible individuals to carry out the full screening criteria and gain written informed consent;
9 The research leads retained a confidential log of potential participants the invitations were sent to, and one reminder letter was sent to those who had not responded;
10 Once consent was gained, the Researcher contacted the research leads to confirm the participants' stroke diagnosis and identify the time since stroke onset.

Potential participants were given an information sheet with at least 24 hours to read it fully and consider any questions about the project. Subsequent questions were answered via email, telephone conversation or in-person. All the participant forms were created from Patient and Public Involvement (PPI) work done in ABIRA and prior trial documents. The forms followed the Stroke Association guidelines for accessible materials, created from their extensive PPI discussions (i.e. recommended font, spacing and image use) (The Stroke Association, 2012).

Healthy participants

A combination of electronic (i.e. news bulletin emails) and physical (i.e. posters) advertisements was used within UEA to recruit healthy individuals into the study. Interested potential participants contacted the Researcher (via phone or email) and received a participant information sheet, with the eligibility criteria:

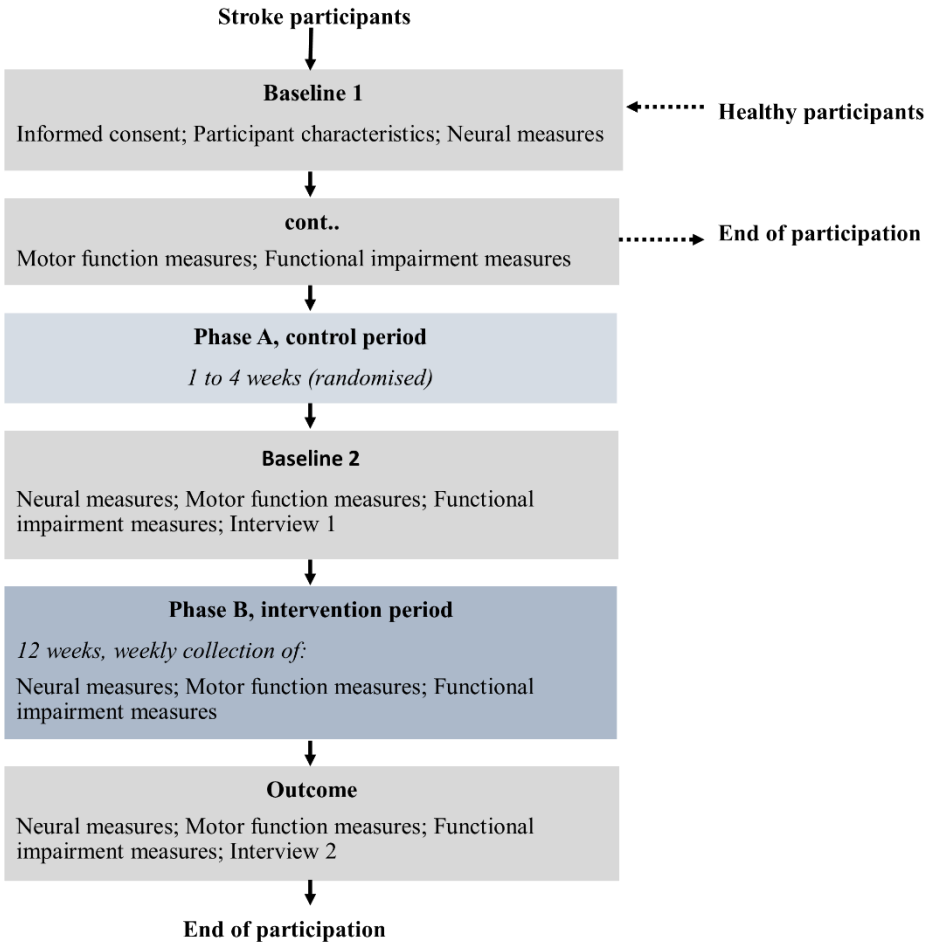
A. 18+
B. No self-reported clinical diagnosis of stroke, epilepsy or other neurological pathology;
C. Able to provide informed consent.

The Researcher assessed eligibility and invited individuals to a data collection session at the UEA MovExLab.

7.3.4 Procedures

This section details the procedures used within this study for both participant groups, visualised within the flow diagram (Figure 21).

Figure 21: Participants procedure flow diagram



7.3.4.1 Stroke participants

Participants attended the UEA MovExLab to begin phase A. Baseline measures one (BL1) were undertaken, and the randomised control period allocated. The control phase A was between one and four weeks. A randomised sequence was used to generate the control phase length for each participant, ensuring an equal spread. An independent administrator concealed the allocation order from the research team in sealed opaque

sequentially numbered envelopes. The envelope was opened at the end of each participants BL1 in order to schedule the next baseline measure appointment (BL2).

The phase B, intervention, lasted for 12 weeks, during which participants undertook weekly measures in their home. These visits also included therapy alteration discussions between the participants and the Researcher; who relayed these to the Research Physiotherapist, before enacting them (full details in section 7.3.4.4). In addition, 1:1 interviews were conducted with participants, by the Researcher, at the end of the control phase (A) and the intervention phase (B).

7.3.4.2 Healthy participants

Participants attended the UEA MovExLab, provided informed consent, completed questions relating to participant characteristics and then to the neural measures.

7.3.4.3 Intervention delivered via the Virtualrehab platform

The Virtualrehab platform hardware and software (described in chapter three) were used to deliver the exercise-based upper limb rehabilitation intervention. The research log captured reported challenges to the Virtualrehab platform's hardware and software (both participant and researcher reported) (objective 4), including if a solution was found and carried out by the Researcher and if necessary, the industry collaborator.

7.3.4.4 The therapy plans

The Virtualrehab platform was set up in the participants home for the intervention phase, B. The Researcher provided training, instructions and ongoing support. If any challenges could not be remediated remotely, then the Researcher made a home visit. The personalised training programme was created by the Researcher, along with a qualified physiotherapist member of the research team (Research Physiotherapist). The programme was a combination of exercises and exergames that targeted the movement challenges of each individual, identified by the Researcher in discussions with the participants. Each participant was asked to undertake their set exercise-based training programme for a minimum of one hour a day, six days a week, for 12 weeks.

The participants were allocated the rowing and the boxing game as a standard element to the therapy programme. In the first week of the intervention period, participants were given a 10-minutes per day, six days a week programme. This allowed them to 'get to grips' with the set-up, use of the Virtualrehab platform; and develop an understanding of the personal exertion needed for such a plan. For the rest of the intervention phase, changes increased in 10-minute increments, per the Research Physiotherapist's advice, to ensure a graduated progression.

The Virtualrehab platform recorded adherence or otherwise to this prescription, the exercises/exergames completed and the number of repetitions (objective 2). However, while the platform records completed sessions, it does not record sessions that are exited early by the participant or due to a software error. To ensure the preservation of the data in case of error, all prescriptions and adjustments were kept in the research log. The information recorded was saved on the Virtualrehab platform and transmitted, without identifiable personal data, to the Researcher. If there was not the appropriate connectivity, the data, without identifiable details, was stored on the Virtualrehab platform and downloaded directly to an encrypted laptop during the Researcher's next visit. The Researcher then met with the Research Physiotherapist (face to face in the early weeks of the intervention) and showed the data on the laptop to discuss the participant-led adjustments. Alternatively, the Researcher emailed the Research Physiotherapist an update on the participant’s progress and requests.

The viability of this participant-led therapy approach, with remote adjustments over time, was assessed from certain factors captured in the research log (objective 3)

- Consideration of the remote adjustments, discussions between Researcher and Research Physiotherapist, and ensuring the participants' views were used in therapy updates.
- Views on changing the programme over time reported throughout the weekly measures.
- The variations of adjustments carried out, with factors that were effective or challenging.
- The content available from the Virtualrehab platform software.

7.3.4.5 Participant characteristics

Participant characteristics were collected during the first baseline session (BL1).

Stroke participant group

- Age;
- Sex;
- Handedness before stroke;
- Time since stroke;
- More paretic side;
- Current therapy undergoing;
- Self-reported impact of the stroke;
- Confidence and experience with technology.

Healthy participant group

- Age;
- Sex;
- Handedness.

Experience and confidence with technology

Stroke participants' prior experiences and confidence with technology were gathered to provide contextual information relating to the qualitative data collected in order to answer research objectives eight and nine. These are described in chapter eight.

Self-reported impact of stroke

Stroke has a known heterogeneous impact, and it is important to understand the variety and severity within a participant sample. Eight self-reported questions were created specifically for this study, covering the following:

1. Physical difficulties;
2. Speech and communication problems;
3. Depression or low mood;
4. Fatigue;
5. Memory;
6. Confusion;
7. Confidence;
8. Motivation.

A multi-choice answer scale was devised for participants to choose from: None, Minor, Moderate, Unsure and Severe.

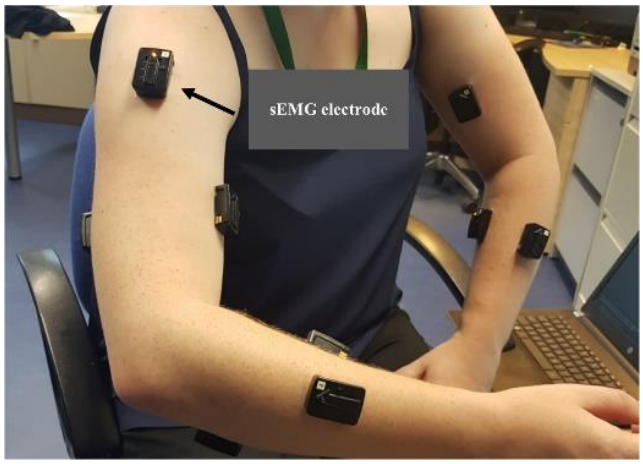
7.3.4.6 Neural measures

After the participant characteristics had been collected, the neural measures were carried out. Participants were shown the equipment, with procedures explained in full and the opportunity to ask additional questions. The following section details the neural measures procedures used throughout this study.

7.3.4.6.1 Equipment

Neural measures were used to detect changes in the neural control of upper limb muscle activity during functional tasks. This study used a 12-sensor surface Electromyography (sEMG) Trigno Wireless Foundation system from Delsys (Delsys, Massachusetts, USA). It is a well-established, safe and painless technique where electrodes are placed on the skin's surface to record muscle activity non-invasively (Figure 22). Data were collected at a sampling rate of 1925.93 Hz; with additional accelerometer data at 148.15Hz.

Figure 22: Demonstration of sEMG sensors placement

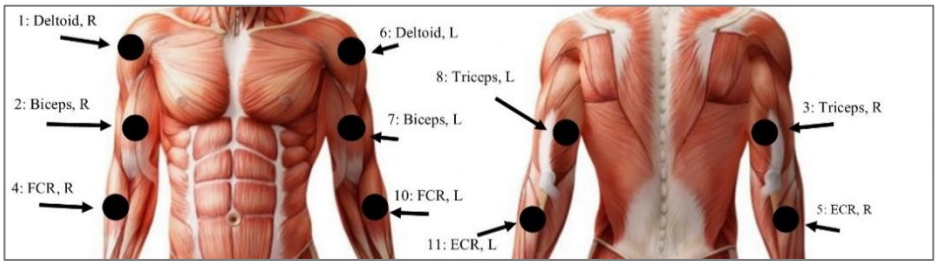


7.3.4.6.2 Muscles of investigation

The following five muscles were chosen as they are essential in everyday functional activities using the upper limbs (i.e. eating, getting dressed). An example of placement can be seen in Figure 23.

1. Deltoid
2. Biceps brachii (Biceps)
3. Triceps brachii (Triceps)
4. Flexor Carpi Radialis (FCR)
5. Extensor Carpi Radialis (ECR)

Figure 23: sEMG sensor placement diagram



7.3.4.6.3 An audible trigger

Previous research within the UEA MovExLab used an integrated trigger delivering a randomised audible 'Go' signal, which automatically marked the movement and neurophysiology data. The trigger was run through Vicon motion capture camera's (Oxford Metrics, Oxford, UK) with integrated sEMG data capturing capabilities. This allowed for movement and neurophysiology data to be time-matched and marked with the 'Go' signal, enabling time to onset to be calculated. Unfortunately, this set-up was tailor-built for the UEA MovExLab and could not be used within the home environment, as required for this study; thus, another trigger method was devised.

Several options were initially considered for the trigger. The Researcher contacted the company who produced the sEMG equipment, Delsys (Delsys, Massachusetts, USA) who offered an additional piece of hardware to deliver a 'Go' signal and mark the subsequent data; however, the price of this was beyond the resources available for the study. A stopwatch method was considered and trialled, but inaccuracies occurred because of delays from the Researcher's physiological reaction times (starting the data recording and the stopwatch) and the inherent software delay between selecting the recording option and the sensors' data collection starting (a random delay of up to a second).

Therefore, the Researcher wrote a series of scripts using the open-source programming language, Python3 (Rossum and Jr, 1995) to provide a randomised (between 10 to 15 seconds) audible 'Go' signal; record the sEMG recording onset, and mark the data accurate to 10 milliseconds (full details in Appendix 4D). This enabled time to onset to be calculated (detailed later in the section). A randomised trigger was used to potentially prevent anticipatory movements and allow for a resting baseline to be collected.

7.3.4.6.4 Procedure: reach-to-cup

A reach-to-cup task was chosen as an everyday functional activity that engages the muscles of interest. The SENIAM procedures outlined for skin preparation and sensor placements were followed within this study (Hermens *et al.*, 2000). The participants' skin was prepared for the sEMG placement using an alcohol wipe. The electrodes were applied to both the more and less paretic upper limbs. Participants were asked to sit comfortably in front of the table, with their trunk and shoulders positioned neutrally. Their arms rested on the table surface with wrists aligned with the edge. The researcher placed the 'cup' (a standardised can of drink) on a template measuring the length of each participant's forearm. Participants were instructed to stay as still as possible until they heard the trigger (an audible beep). Then as quickly as possible, they were instructed to pick up the cup and bring it to their mouth as if to drink, and then place it back on the table and return their arm to the starting position. The less paretic arm was used first, and the trial repeated three times, per arm. If the participant could not grasp the cup or lift it, they were asked to touch the cup to complete the movement and return to the start position.

7.3.4.6.5 Processing and quality checks

The sEMG sensors record electrical currents conducted through the muscle tissue, generated during contractions known as muscle action potentials that represent neuromuscular activities (Reaz, Hussain and Mohd-Yasin, 2006). The resultant signal is typically described in terms of its amplitude and frequency. However, additional 'noise' interferes with the true muscle activity signal. There are two main sources of interference. The first source comprises physiological interferences, typically oils, or lotions on the skin, and in some cases, the amount of subcutaneous fat present. As poor electrode-skin interface increases electrode impedance, standardised skin preparation procedures must be followed. The other main source of interference is from the inherent noise generated from electronic equipment, or even additional equipment in the area (i.e. fridges, phones, laptops). Whilst trialling the neural measures within the UEA MovExLab, there was an unknown electronic interference within the sEMG recorded data. This was surprising as the lab itself is built with electrical shielding, and during data collection sessions, steps are taken to limit the additional noise (i.e. equipment not required is turned off). Upon investigation, the interference was linked with the laptop's battery, while the 'noise' was not detected when running on the charger. It was beyond the scope of this project to identify the reasons behind this. However, the finding allowed for a clearer signal within the data collection. This was particularly useful knowledge for the home, as the Researcher was able to ensure that the laptop charger was always plugged in. Unfortunately, within the home there are unavoidable interferences (i.e. builder equipment, older poorer insulation in houses); the viability of collecting sEMG data in

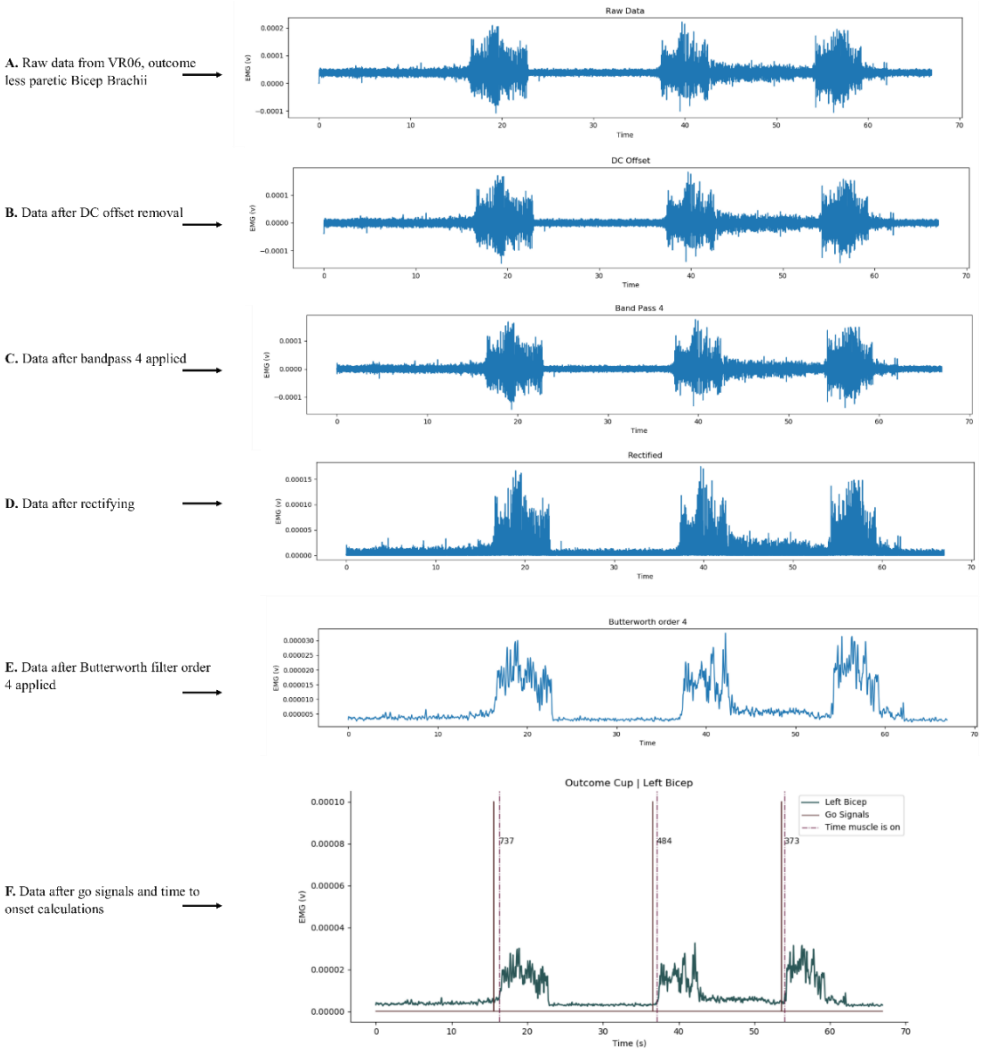
this environment had not been investigated previously and thus was an objective for this study (5).

Overall, to lower the risk of electronic interference, signal checks were carried out before collecting data. Despite measures to limit additional 'noise' on the recorded signal, there are always interferences that cannot be mitigated during data collection. Thus, it is expected and common practice to process sEMG data before deriving the outputs desired. The following describes the steps taking to process the sEMG data from the cup task, using an exemplar from a stroke participant (Figure 24). The raw sEMG data was exported into excel format (A), and the Researcher wrote a processing script using Python3 (Rossum and Jr, 1995). The raw sEMG data first had the DC offset removed (B), then a bandpass four filter was applied (C) followed by rectifying the data (D); a Butterworth order four filter was then applied (E). Finally, the 'Go' signals were calculated and added to the data, followed by a calculation of the time to onset of muscle activity (F).

Calculation of time to onset

Muscle onset time was defined at the point which the EMG envelope exceeded the baseline value for >100ms. The onset threshold was set at three standard deviations above the resting mean; the resting mean (baseline) was the mean of the 500ms immediately before the 'Go' signal (Appendix 5D for formulae).

Figure 24: Example of processing steps applied to sEMG data by Python3 scripts

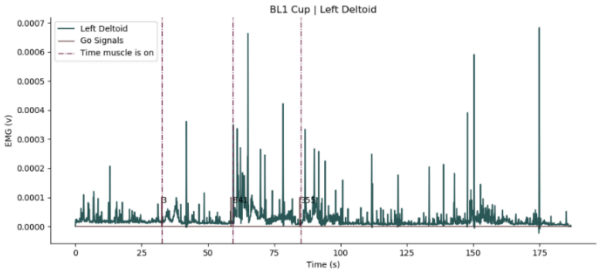


Quality checks to identify valid trials

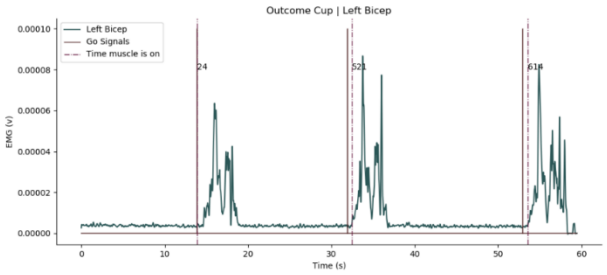
To determine the quality of the data processing, the Researcher and her primary supervisor independently quality checked the stroke and healthy participants' ‘reach to cup’ data. Graphs of the processed data were checked to determine if (1) there was a distinguishable muscle burst; (2) if the ‘Go’ signal calculations were successful (i.e. if there was an error with ‘Go’ signal data collection then the processed data would be missing this information in the graphs). The calculated time to onset values were then checked; if onset occurred before 140ms or after two seconds, then it was determined invalid (except in cases where the stroke survivors' more paretic arm showed consistent onsets above two seconds). A visual example of invalid and valid trials is shown in Figure 25.

Figure 25: Visual examples of invalid and valid trials

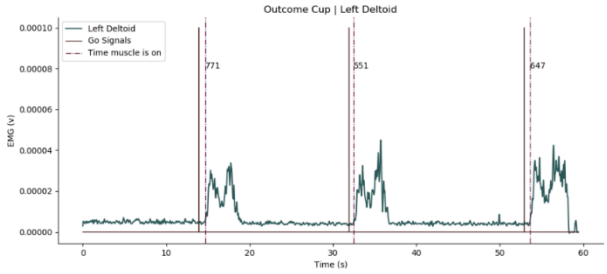
A. Example of three invalid trials due to sEMG noise interference (VR12, Baseline 1, Deltoid)



B. Example of an invalid trial 1 due to erroneous time to onset (VR12—Outcome, Bicep brachii)



C. Example of a valid trials (VR12—Outcome, Deltoid)



7.3.4.7 Functional ability and motor impairment measures

The following section details the measures of functional ability and motor impairment collected from stroke participants; different measures were required for the various data collection points (Table 37). Different measures and procedures were required within the home due to the space available for a standardised protocol to be carried out and to mitigate potential practice effects occurring that could influence outcome measures. The following section details the functional ability measures carried out for the pre/post-intervention carried out in the UEA MovExLab. The details and justification for these measures are as follows.

Table 37: Measures of functional ability and motor impairment

Location data collected	**Points when data collected**	**Functional ability measures**	**Motor impairment measures**
UEA MovExLab	Pre/-post intervention[1]	WMFT	Grip strength via Myometer[2]
Participant's home	Intervention period [3]	ARAT	MI

NB.

1. Baseline 1, 2 and outcome measures;

2. Jamar hydraulic hand dynamometer, Patterson medical;

3. Weekly progress measures during the 12-week intervention period;

UEA MovExLab, University of East Anglia's Movement and Exercise Laboratory;

WMFT, Wolf Motor Function Test (Wolf et al. 2005);

ARAT, Action Reaction Arm Test (Lyle 1981); MI, Motricity Index (Collin and Wade 1990)

7.3.4.7.1 Functional ability measures

The following details the functional ability measures carried out pre/post-intervention period (Wolf Motor Function Test) and within the weekly progress measures during the intervention period (Action Reaction Arm Test).

7.3.4.7.1.1 Pre/post-intervention period, functional ability measures

Functional ability of the upper limb was assessed using the Wolf Motor Function Test (WMFT). The 15-item test quantifies the upper limb movement through timed functional tasks in stroke survivors (Wolf *et al.*, 2005). It measures performance (e.g. strength), time (WMFT-time) and quality of movement through simple and complex functional tasks (e.g. turning a key in a lock) (WMFT-function). The test has been demonstrated to have high internal consistency (coefficient alpha, 0.98); test-retest reliability (intraclass correlation coefficient, 0.94) and concurrent validity, compared with the Action Reaction Arm Test (ARAT) (WMFT score, r = 0.86; timings, r = -0.89) (Nijland *et al.*, 2010). The stability of WMFT scores is also supported by investigations of chronic stroke survivors tested on multiple occasions over time (Morris *et al.*, 2001).

Standardised instructions were followed, set out for the WMFT and used by prior ABIRA research teams (Wolf *et al.*, 2001; Hunter *et al.*, 2018). The participant is seated in an armless chair, head in a neutral position and trunk aligned, to ensure movement effort comes from arm movement only.

The scores were as follows:

Does not attempt with Upper Extremity (UE) being tested

0. UE being tested does not participate functionally; however, an attempt is made to use the UE. In unilateral tasks, the UE not being tested may be used to move the UE being tested.
1. Does attempt but requires the assistance of the UE not being tested for minor readjustments or change of position, or requires more than two attempts to complete, or accomplishes very slowly. In bilateral tasks, the UE being tested may serve only as a helper.
2. Does attempt, but the movement is influenced to some degree by synergy or is performed slowly or with effort.
3. Does attempt; movement is similar to the non-affected side but slightly slower; may lack precision, fine coordination or fluidity.
4. Does attempt, the movement appears to be normal.

The WMFT was not appropriate in the participant's home due to the standardised template size and a requirement for an adjustable table. In addition, using the WMFT over 12 weeks could potentially lead to practice effects influencing the outcomes. Thus, a different measure was required within the participants' homes.

7.3.4.7.1.2 Weekly progress, functional ability measures

The Action Research Arm Test (ARAT) was used to assess upper limb functional ability during the weekly measures (Lyle, 1981). The assessment has demonstrated strong reliability (test-retest reliability, 0.965 – 0.968; inter-rater reliability, 0.996 – 0.998 (McDonnell, 2008)) and validity (compared with the WMFT, as shown above (Chen *et al.*, 2012)).

The 19-item test uses observational methods to measure grasp, grip, pinch and gross arm movement subscales with the following scores:

0 = no movement;

1= movement task is partially performed;

2 = movement task is completed but takes abnormally long;

3 = movement is performed normally.

Standard scoring rules were followed (Lyle, 1981);

- The most challenging task within the subscale is attempted first. If normal movement is achieved, then a score of 3 is awarded and also given to all remaining items within that subscale.
- If the score is between 1 – 2, then the second item within the subscale is tested and the next until the subscale is completed.
- If the score on the most challenging tasks was 0, then the least challenging item is attempted. If the participant scores 0 on this, it is assumed they are unlikely to complete the other items, and the entire subscale is given a score of zero.

The Researcher took the MovExLab ABIRA's standardised ARAT test box, together with a portable table, to ensure the test could be carried out on a stable surface if no table was available within the participant's home. The ABIRA research team trained the Researcher in standard instructions and the scoring above. Participants were seated in a chair with no armrests (also bought by the researcher if none were available), with feedback being given to ensure a neutral head position and the back connecting to the chair. This

was to reduce the opportunity for participants to compensate, such as leaning forward or standing up to complete an item.

7.3.4.7.2 Motor impairment measures

The following section details the motor impairment measures carried out pre/-post (Grip strength) and within the weekly progress measures during the intervention period (Motricity Index).

7.3.4.7.2.1 Pre/post-intervention period, motor impairment measures

In order to assess changes in stroke participants' ability to contract paretic muscles voluntarily, handgrip forces were measured using a Myometer (Jamar hydraulic hand dynamometer, Patterson Medical). This was placed on a stable surface using a standardised upper limb position and standardised instructions. The myometer used has shown both high inter-rater reliability (r = 0.97) and test-retest reliability (r = 0.8) (Mathiowetz *et al.*, 1984). The procedures were adapted from the FAST INdiCATE Trial protocol, of which members of the ABIRA - formed part of the research team (Pomeroy *et al.*, 2014).

Participant position:

- Seated with shoulders abducted and neutrally rotated.
- Elbow flexed at 90^0 with the forearm in a neutral position.
- Wrist between 0 to 30 degrees flexion and between 0 to 15 degrees ulna deviation.
- The Myometer was then set to zero, with the participant's hand comfortably around it at rest. Each value is recorded in Kg.
- The participant performed the test three times per arm.

Participants were instructed and aided to place their hand around the bars at rest. They were instructed to "Squeeze as hard as you can", and repeated this for three trials, per upper limb.

7.3.4.7.2.2 Weekly progress, motor impairment measures

The Motricity Index was used weekly in participants homes to assess motor impairment through measuring upper extremity strength, based upon a 6-point ordinal scale (Demeurisse, Demol and Robaye, 1980; Collin and Wade, 1990). For this study, only the upper limb tests were used: pinch grip; elbow flexion and shoulder abduction, as recommended by the neurology section of the American Physical Therapy Associations stroke taskforce and developed by a panel of research and clinical experts using a modified Delphi process (Sullivan *et al.*, 2013). The test has proven reliability and validity; specifically, relevant for this study procedures were:

- Consistency of scores taken over time by the same researcher, intra-rater reliability (ICC = 0.93; 95% CI = 0.84 to 0.97; $p < 0.001$) (Fayazi *et al.*, 2012). In addition the consensus between ratings from different scorers, is good for the Motricity Index (MI) arm (spearman's rho = 0.88; $p < 0.001$) (Collin and Wade, 1990).
- When compared with chronic stroke survivors over six weeks, the criterion validity was good (Collin and Wade, 1990). Especially compared with the 9-hole peg test, the MI arm was seen as a more sensitive measure for detecting early change (Sunderland *et al.*, 1989).

- Finally, the test has strong concurrent validity between dynamometry measurements of UE and the MI arm score ($r = 0.89$; $p < 0.001$) (Bohannon, 1999).
- In addition, there is good predictive validity of dynamotor measurements and MI arm scores ($r = 0.78$) (Cameron and Bohannon, 2000).

The researcher received training in the measure from experienced physiotherapists within their research group in carrying out the measure with standardised instructions and scoring. The participants were seated in an armless chair to carry out the following measurements.

(1) pinch grip: using a 2.5 cm cube between the thumb and forefinger

- 19 points are given if able to grip cube but not hold it against gravity
- 22 points are given if able to hold cube against gravity but not against a weak pull
- 26 points are given if able to hold the cube against a weak pull, but strength is weaker than normal

(2) elbow flexion from 90° so that the arm touches the shoulder

- 14 points are given if the movement is seen with the elbow out and the arm horizontal

(3) shoulder abduction moving the flexed elbow from off the chest

- 19 points are given when the shoulder is abducted to more than 90° beyond the horizontal against gravity but not against resistance

7.3.5 Data analysis

The following section outlines the data analysis techniques used in the study related to the stated research objectives. All participant characteristics were described with descriptive statistics (i.e. mean, standard deviation and percentages).

7.3.5.1 Research Objective 1. Establish the process for recruitment of stroke survivors to a subsequent Randomised Control Trial (RCT) when they have been discharged from NHS specialist stroke services

The recruitment process was established by detailing the:

- Number of recruitment sites identified;
- Number of potential participants identified at each recruitment site;
- Narratively detailing the process of recruiting through the sites and any challenges needing consideration for future research.

7.3.5.2 Research Objective 2. Explore adherence (number of more paretic upper limb repetitions) of stroke survivors to the 'prescribed' use of the Virtualrehab platform

The following was used to determine adherence to prescribed therapy plans.:

- Number of days prescribed (six per week) in comparison with the number of days the platform recorded use.
- Number of sessions prescribed (one per day, six days a week) compared with the number of sessions the participant completed each day (participants could use the platform multiple times a day if they chose to).

- Number of repetitions prescribed for the more paretic upper limb (i.e. asked to complete, per session) compared with the number completed (calculated from the number of repetitions given for each session, and the number the platform recorded as complete).

7.3.5.3 Research Objective 3. Assess the viability of the researcher adjusting the 'prescribed' training programme over time

Successful and challenging aspects of adjusting the ‘prescribed’ training programme over time were narratively described.

7.3.5.4 Research Objective 4. Evaluate the technical reliability of the Virtualrehab platform

The technical reliability of the Virtualrehab platform was narratively described.

7.3.5.5 Research Objective 5. Test the viability of collecting neuromechanical and behavioural data in the home

The percentage of valid and invalid trials from the neuromechanical and behavioural data within the home, compared to the UEA MovExLab was calculated. The reasons behind invalid trials were narratively described.

7.3.5.6 Research Objective 6. To assess the viability of using randomised length of baselines and repeated measures during the intervention period to inform subsequent study to find the optimum therapeutic dose

The percentage of participants who completed the set duration of the baseline was calculated. The percentage of the total possible measures obtained during the 12-week intervention phase was calculated per measure.

7.3.5.7 Research objective 7. Estimate changes in paretic upper limb functional ability, motor impairment and neural measures

Although it was not possible to measure efficacy in a feasibility trial, initial changes were noted, where possible, in relation to their Minimally Clinical Important Differences (MCID). This was used to show the potential of the intervention to provide a meaningful change to patients.

7.3.5.7.1 Functional ability measures

The following details the data analysis carried out for the functional ability measures carried out pre/post-intervention period (Wolf Motor Function Test) and within the weekly progress measures during the intervention period (Action Reaction Arm Test).

7.3.5.7.1.1 Pre/post-intervention period, functional ability measures

The Wolf Motor Function Test (WMFT) produced two measures, for each measurement point, per participant:

- The performance time (WMFT-time): calculated from the mean performance time across all the function-based tasks.
- The functional ability score (WMFT-function): calculated from the mean scores across all the function-based tasks.

The minimal clinically important difference (MCID) is defined as the threshold of change that provides an improvement in perceived outcomes for patients. The WMFT MCID per item has been defined as the following (Lin *et al.*, 2009):

- The performance time (WMFT-time): 1.5 to 2 seconds;
- The functional ability score (WMFT-function): 0.2 to 0.4 points.

7.3.5.7.1.2 Weekly progress, functional ability measures

The Action Research Arm Test (ARAT) scores per item were summed together to produce an overall score between 0 and 57 points, for each measurement point, per participant. The ARAT has an established anchor-based MCID for chronic stroke derive from approximately 10% of the total range of the scale, 6 points (Alt Murphy, Willén and Sunnerhagen, 2013).

7.3.5.7.2 Motor impairment measures

The following section details the data analysis carried out for the motor impairment measures carried out pre/-post (Grip strength) and within the weekly progress measures during the intervention period (Motricity Index).

7.3.5.7.2.1 Pre/post-intervention period, motor impairment measures

The mean and standard deviation of the three grip strength trials was calculated at the pre/post-intervention measurement points. The Minimally Clinically Important Difference (MCID) in grip strength ranges from 0.04kg to 6.5kg. A recent systematic review recommended changes of 5.0 and 6.5kg as a reasonable estimate of MCID (Bohannon, 2019). Therefore a change of 5.0kg or more was classified as the MCID.

7.3.5.7.2.2 Weekly progress, motor impairment measures

The Motricity Index scores were summed to produce a total arm score (0 to 99), following guidelines established (Collin and Wade, 1990).

> Arm score for each side = SUM (points for the 3 arm tests) + 1 = a score out of 100

To date, a minimal standard of clinically important difference has not been reported. Therefore, the change between MI motor impairment levels was used as an indication of change, although not a clinical one – the scale is shown in Figure 26.

Figure 26: The Motricity Index scores functional impairment levels

MRC grade/ MI level	Pinch grip	Elbow flexion	Shoulder abduction	MI Upper limb total score for each grade
No movement	0	0	0	0
Palpable flicker by no movement	11	9	9	30
Movement but not against gravity	19	14	14	48
Movement but not against gravity	22	19	19	61
Movement against resistance	26	25	25	77
Normal	33	33	33	100

NB. total upper limb score for each grade calculated from the sum of pinch grip, elbow flexion, shoulder abduction plus 1.

7.3.5.7.3 Neural measures pre/post-intervention and weekly progress data

The neural measures were analysed to indicate changes in time to onset (calculation detailed in section 7.3.4.6.5), over time and in comparison, with the healthy group values.

7.4 RESULTS

The following section details the results of the study concerning the stated research objectives.

7.4.1 Participant characteristics

Participants were recruited from five GP practices; with 761 invitation packs sent. Of the 222 interested individuals, the researcher carried out a full criteria screening within the homes of 35 people. Of these, 17 people were eligible for participation and 12 provided informed consent (Figure 27, for full details.). Seven participants completed the study, and their details are shown in a flowchart (Figure 28).

Figure 27: Participant recruitment flow diagram

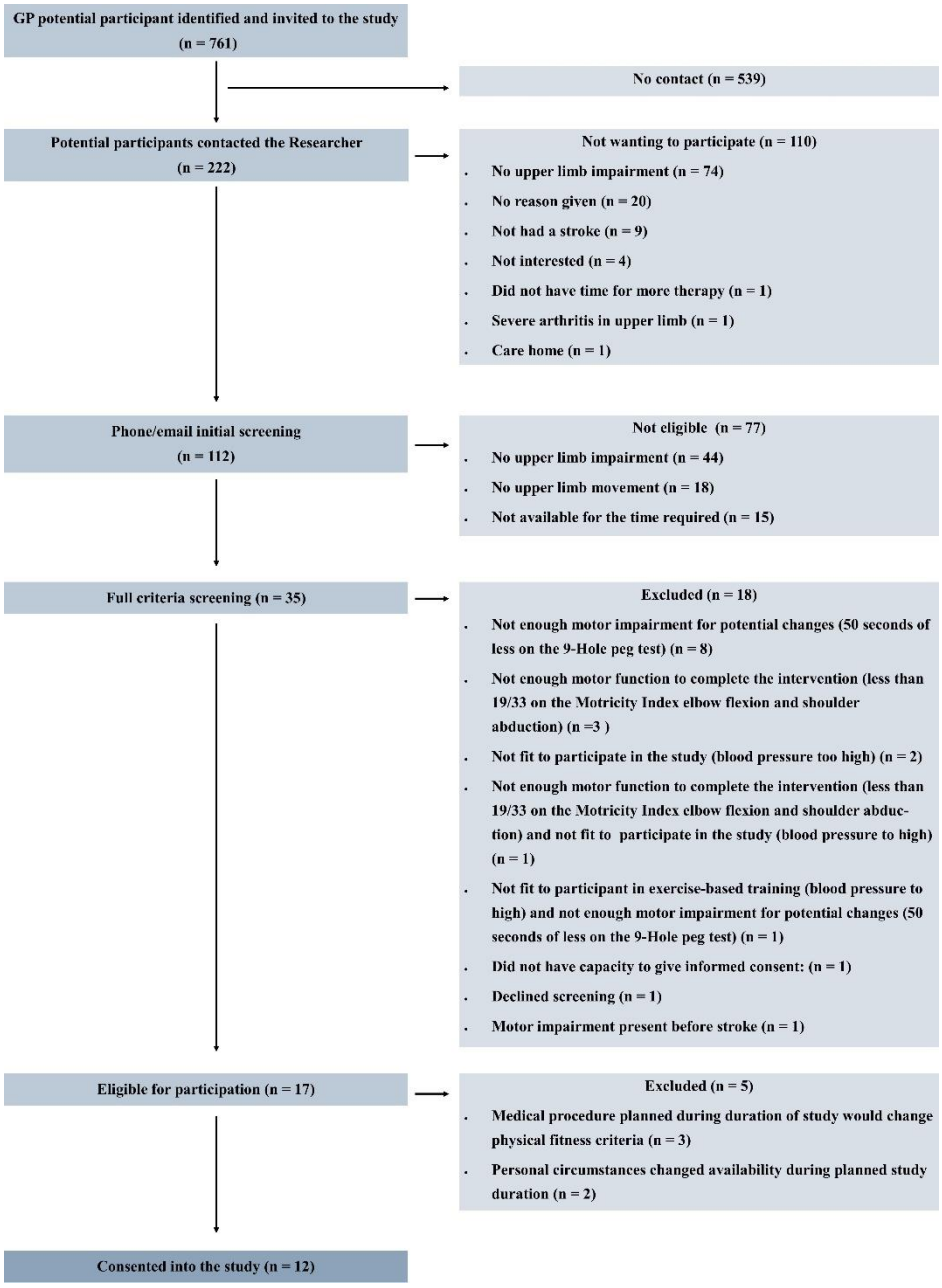
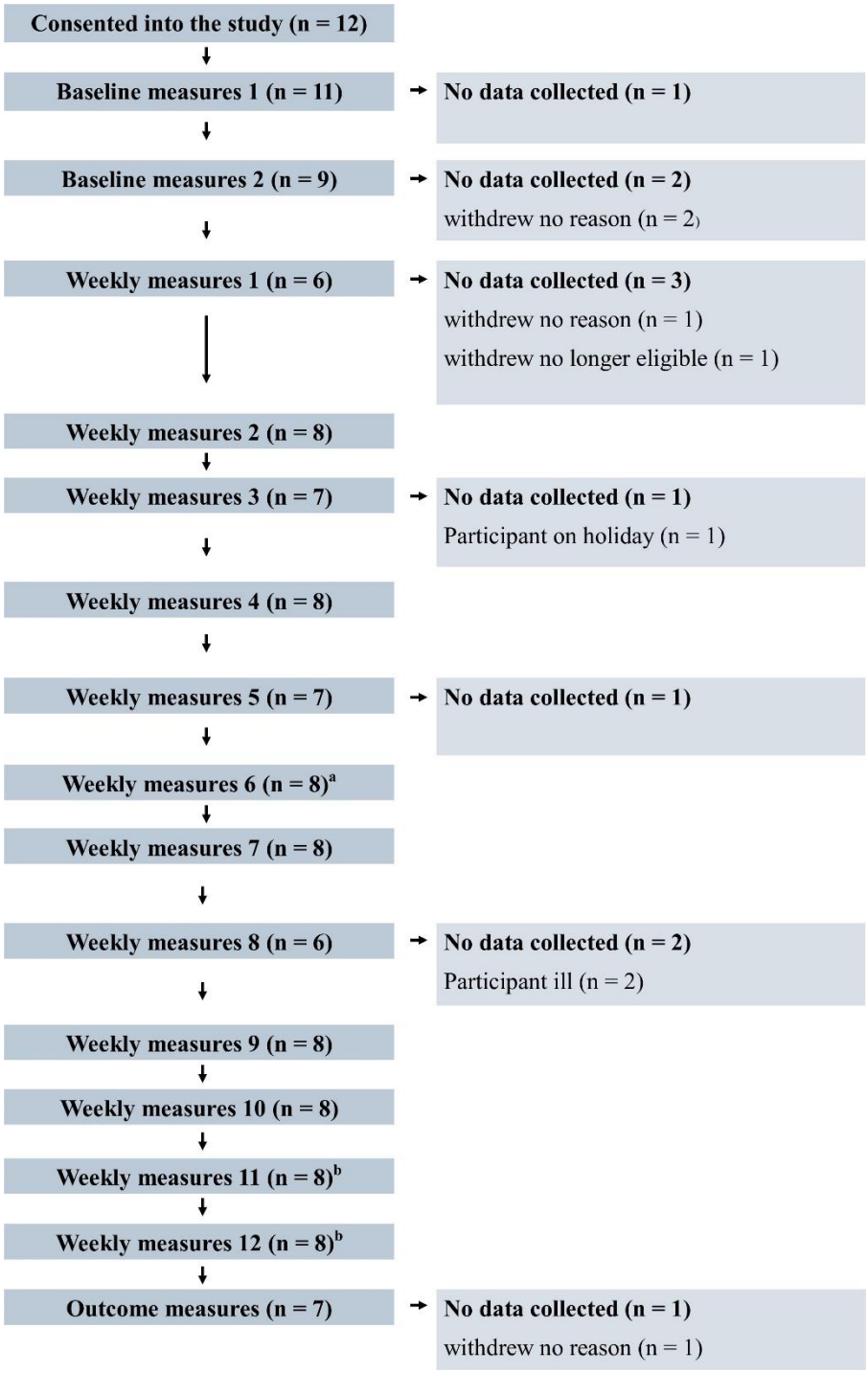


Figure 28: Stroke participant retention



NB. A, participant completed neural measures, but was fatigued and did not wish to complete the motor function and functional impairment measures.
B, participants more paretic arm was fatigued, the motor function and functional impairment measures were not completed.

Of the twelve consented participants, one withdrew before characteristics were collected (VR07), resulting in eleven participants. The stroke participant group consisted of five women and six men, with ages ranging from 53 to 93 (mean = 67.5; standard deviation = 12.6) years. The time since stroke varied from 12 months to almost 72 months (mean = 31.9 months; standard deviation = 22.9 months). Half of the participants' medical records reported that their more paretic side was the right; seven participants had their dominant side affected. Two of the participants were undergoing physiotherapy during the intervention phase, with another having completed self-reported 'exercise sheets' (VR06 and VR09), given by an NHS physiotherapist post-stroke that they retained to complete in their spare time (VR12). The intervention set-up varied amongst the homes; full participant characteristics can be found in Table 38.

Table 38: Stroke participant group characteristics at baseline

ID	Age (years)	Sex	Handedness prior to stroke	More paretic side	Time since stroke (months)	Intervention set-up
VR01	80	F	R	R	20.0	Equipment errors prevented set-up. Withdrew.
VR02	62	M	R	L	63.9	Seated and standing. Chair in a set-position for the duration of the intervention. Required assistance to set-up.
VR03	93	F	R	L	63.4	Withdrew before set-up
VR04	82	F	L	L	70.6	Seated and standing. Chair in a set-position for the duration of the intervention. Required assistance to set-up.
VR05	56	F	R	R	32.4	Seated and standing, laptop on floor. No assistance required to set-up.
VR06	58	M	R	R	13.6	Seated-only, laptop on floor. Required assistance to set-up each time.
VR07	59	m	R	R	17.8	Seated-only, laptop on floor. Required assistance to set-up each time.

ID	Age (years)	Sex	Handedness prior to stroke	More paretic side	Time since stroke (months)	Intervention set-up
VR08	wd	wd	wd	wd	wd	Withdrew before set-up
VR09	53	M	R	L	12.6	Seated and standing, equipment put away after each use due to young children.
VR10	67	F	R	L	27.2	Seated-only, chair in a set-position for the duration of the intervention
VR11	62	M	R	R	10.0	Withdrew before set-up
VR12	71	M	R	R	19.0	Seated-only, laptop within reach and chair in a set-position for the duration of the intervention

NB. F = female, **M** = male. **R** = right, **L** = left. **wd** = withdrew

Table 39: Stroke participants self-reported impact of stroke

Areas of stroke impact	Self-reported impact rating, number of respondents (% of stroke group)				
	Severe	**Moderate**	**Minor**	**None**	**Unsure**
Physical difficulties	4 (50)	3 (37.5)	0 (0)	0 (0)	1 (12.5)
Fatigue	3 (37.5)	2 (25)	2 (25)	0 (0)	1 (12.5)
Speech and communication	1 (12.5)	1 (12.5)	2 (25)	3 (37.5)	1 (12.5)
Confidence	1 (12.5)	4 (50)	1 (12.5)	1 (12.5)	1 (12.5)
Motivation	1 (12.5)	5 (62.5)	0 (0)	1 (12.5)	1 (12.5)
Depression or low mood	0 (0)	4 (50)	0 (0)	3 (37.5)	1 (12.5)
Memory	0 (0)	5 (62.5)	0 (0)	2 (25)	1 (12.5)
Confusion	0 (0)	3 (37.5)	2 (25)	2 (25)	1 (12.5)

Participants were asked to rate the perceived effect their stroke had, within common areas of impact Table 39. The main area stroke participants felt their stroke had impacted physical impairments, with a moderate to severe effect. This was followed by fatigue, rated the second most severe impact by the stroke participant group.

Healthy participants

Ten participants consented into the normative values group. This included six women and four men, with a mean age of 36.9 years (SD = 13.5 years), ranging from 26 to 64 years old (Table 40).

Table 40: Healthy participant group characteristics

ID	Age	Sex	Handedness
H01	36	F	R
H02	33	F	R
H03	27	M	R
H04	64	M	R
H05	59	F	R
H06	35	M	R
H07	32	F	R
H08	26	M	R
H09	31	F	R
H10	26	F	R

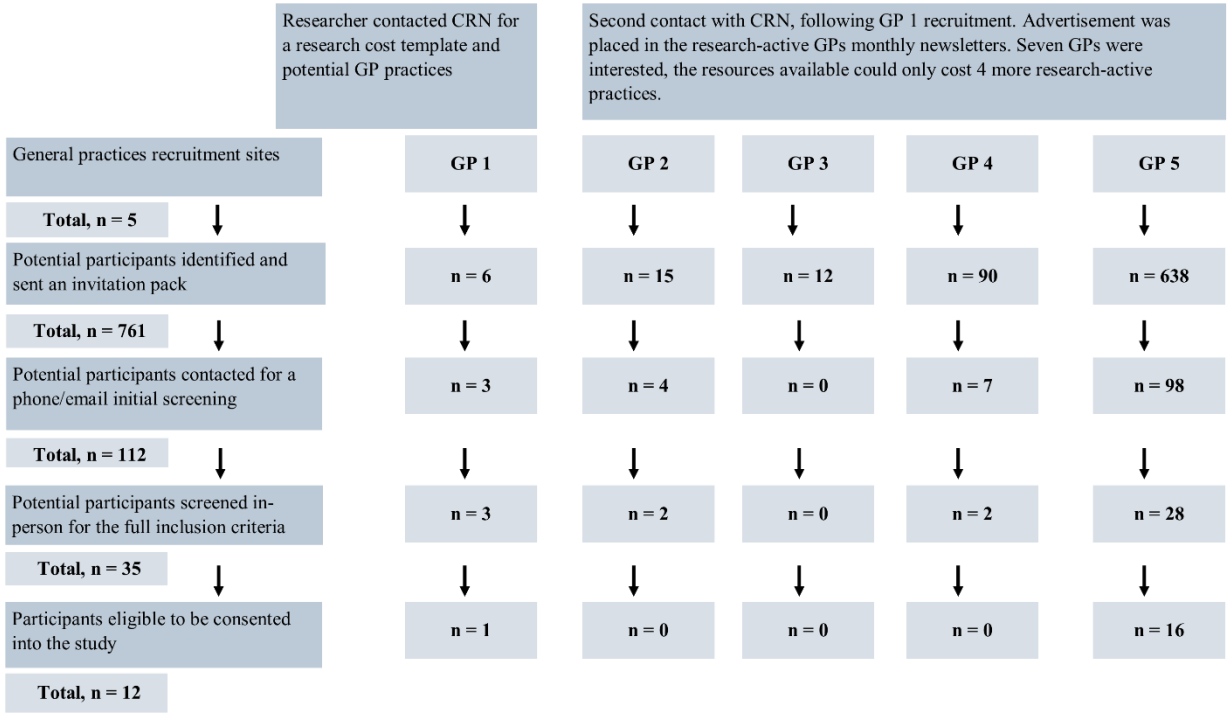
NB. F = female, **M** = male. **R** = right,

7.4.2 Research Objective 1. To establish the process for recruitment of stroke survivors to a subsequent RCT when they have been discharged from NHS specialist stroke services

The process by which participants were recruited from community services was as follows, Figure 29 details the resultant numbers arising from each recruitment site. In order to recruit from the community General Practices (GP), approval was required within the NHS ethics application from the local Clinical Research Network (CRN). The CRN provided approvals, advice, feedback on the protocol and costing templates for setting up recruitment sites within research-active GPs (Figure 27 and Figure 29). The help was limited as the application for adoption onto the NIHR portfolio was unsuccessful, limiting the avenue of the advertisement within the CRN contacts and requiring instead the researcher to manage and provide funding for the GP recruitment sites. Nevertheless, an initial GP practice (GP 1) was approached with the screening criteria (section 7.3.3.3), to pilot the potential recruitment rate from the GP. Four more GPs were then set-up as recruitment sites within a 25-mile radius of UEA. Although further GPs were interested, there was not the scope in the funding to include them. The researcher visited the included GPs and met with their research leads. The project was presented, and details decided: the method of screening the database; procedure for sending invitation packs to potential participants; maintaining a recruitment log; sending relevant details from their medical history and sending reminder invitation packs out. Also, the GPs throughout the study noted that they were fielding enquiries from potential participants who received an invitation pack but did not initially contact the researcher.

As can be seen in Figure 29, the numbers identified from each GP varied, including those screened and consequently consented to participate in the study. One GP practice operated within a network database with three other GP practices; thus, the numbers were considerably higher than the other four included. It should be noted that aside from the small numbers identified within GP 1 to 3, there were other challenges. The database GPs used appeared to lack the sensitivity required to identify potential participants with upper limb impairments, and in some cases, the person contacted had not suffered a stroke. Individuals contacted also reported confusion in the role their GP practice had in the study, which should be clarified if this recruitment method is used in a future trial. Besides, GP 5 was unable to keep a log due to internal challenges, which prevented a reminder invitation pack from being sent out. Finally of note, research-active GPs do not have a standard organisational structure; for example, one practice was smaller than the others and relatively new to supporting research projects. Others varied in terms of if the research contact was a research-nurse, admin or GP. This may be relevant in future trials if more clinical information is required.

Figure 29: GP recruitment site progression



NB. CRN, NIHR Clinical Research Network Eastern; GP, general practice.

7.4.3 Research Objective 2. To explore adherence (number of more paretic upper limb repetitions) of stroke survivors to the 'prescribed' use of the Virtualrehab platform

Eight participants completed the 12-week intervention period (72 prescribed days, 6 per week); Table 41 details participants' adherence to the prescribed number of days and number of repetitions in total during the intervention period. It should be noted that the number of days within the intervention period ranged from 82 to 86 (mean = 85.25; standard deviation = 1.67). This was dependent upon both the participant availability for the equipment set-up (i.e. day 0) and the day each weekly data collection measures were taken on for the following 12 weeks (e.g. Mondays, Tuesdays…).

The number of days the Virtualrehab platform was used varied amongst participants from 33 (VR06) to 78 (VR12); this variation was due to participant schedules and their preferred number of days during the week to use the platform (i.e. VR06 requested a higher number of repetitions per day, but only used the platform a few times a week as opposed to the prescribed six days).

The number of upper limb repetitions prescribed within the stroke participant group ranged from 2, 013 (VR10) to 20,517 (VR06) (mean = 5,515.6; standard deviation = 6,180.4). This variation was also due to participants' preference of the repetitions per session and the number of days they wanted to use the platform each week. The number of repetitions completed by the stroke participants within the intervention period ranged from 1, 710 (VR09)

to 9, 377 (VR06) (mean = 3,885.2; standard deviation = 2, 471.8). The adherence rates ranged from 46% (VR06) to 12% (VR10) (visualised in Figure 30). The number of repetitions prescribed increased, in collaboration with the participant, during the intervention period and weekly adherence differed per participant (appendix 20D details the number of repetitions prescribed and completed, per week, per participant). Figure 31 displays the number of repetitions carried out per week, per participant, showing the variation over time for each stroke survivor.

Overall variation is accounted for by:

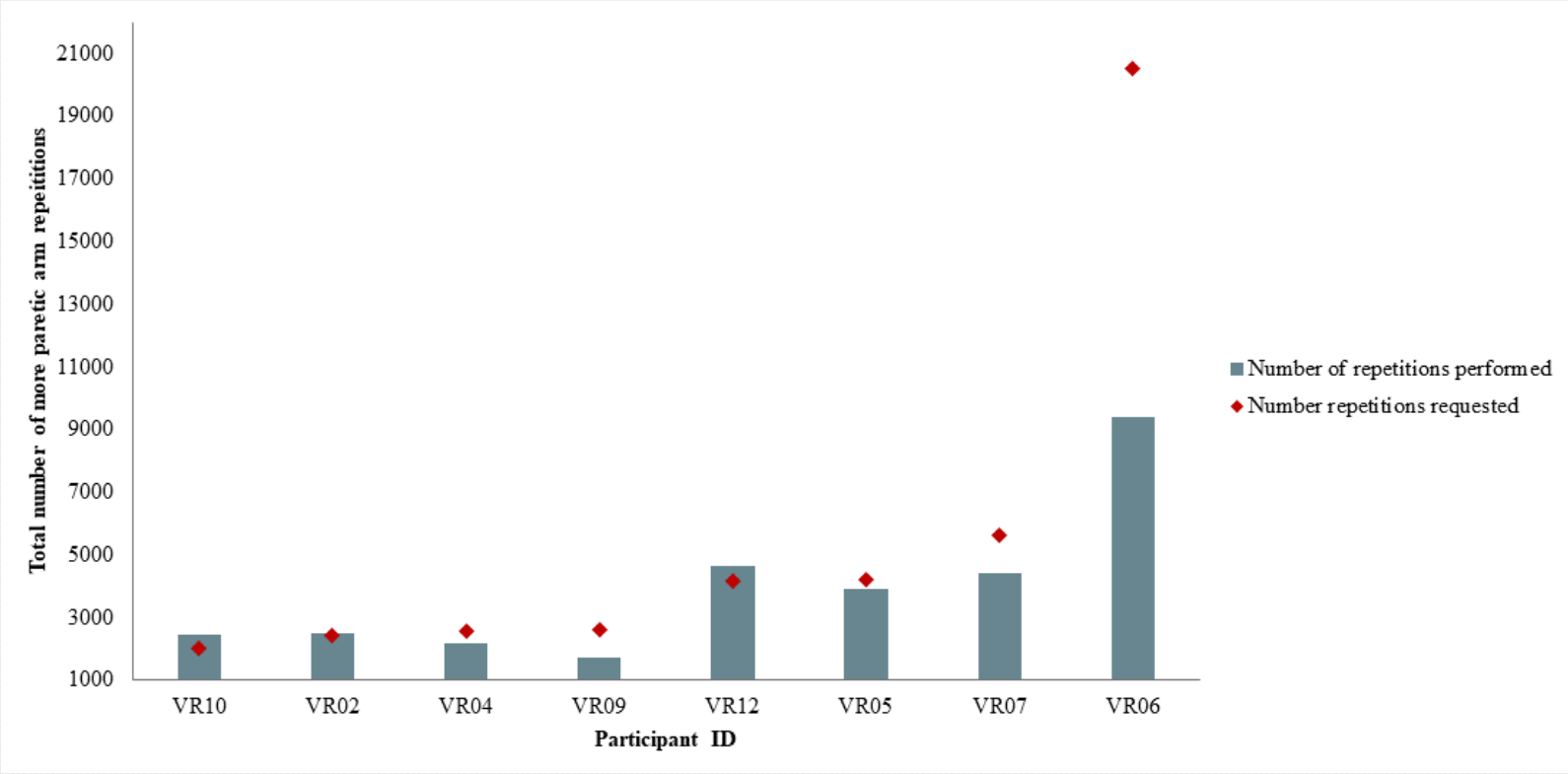
- Participants' schedule (i.e. the number of days they wanted to use the platform each week and their availability over the intervention period);
- Participants' prescription preference (i.e. participants requested number of repetitions differed depending on their preferred number of sessions each week);
- Number of sessions each participant completed, per day (i.e. some participants chose to use the platform multiple times per day);
- Equipment and software errors: these were reported to the Researcher who attempted to fix the issue or contact the industrial collaborator for assistance. Table 41 details these factors and the number of days lost for each participant due to such errors. Further details on equipment reliability challenges are reported in 7.4.6.

Table 41: Stroke participants prescribed therapy

Participant ID	Total days within the intervention period	Prescribed intervention days	Number (%) of days platform used	Number of repetitions requested (more paretic arm)	Number of repetitions performed (more paretic arm)	Fidelity (performed compared to requested) %
VR02	88	72	75 (104)	2447	2478	101
VR04	85	72	60 (83)	2573	2150	84
VR05	85	72	70 (97)	4205	3905	93
VR06	86	72	33 (46)	20517	9377	46
VR07	86	72	56 (78)	5606	4404	79
VR09	82	72	72 (100)	2618	1710	65
VR10	85	72	47 (65)	2013	2442	121
VR12	85	72	78 (108)	4146	4616	111

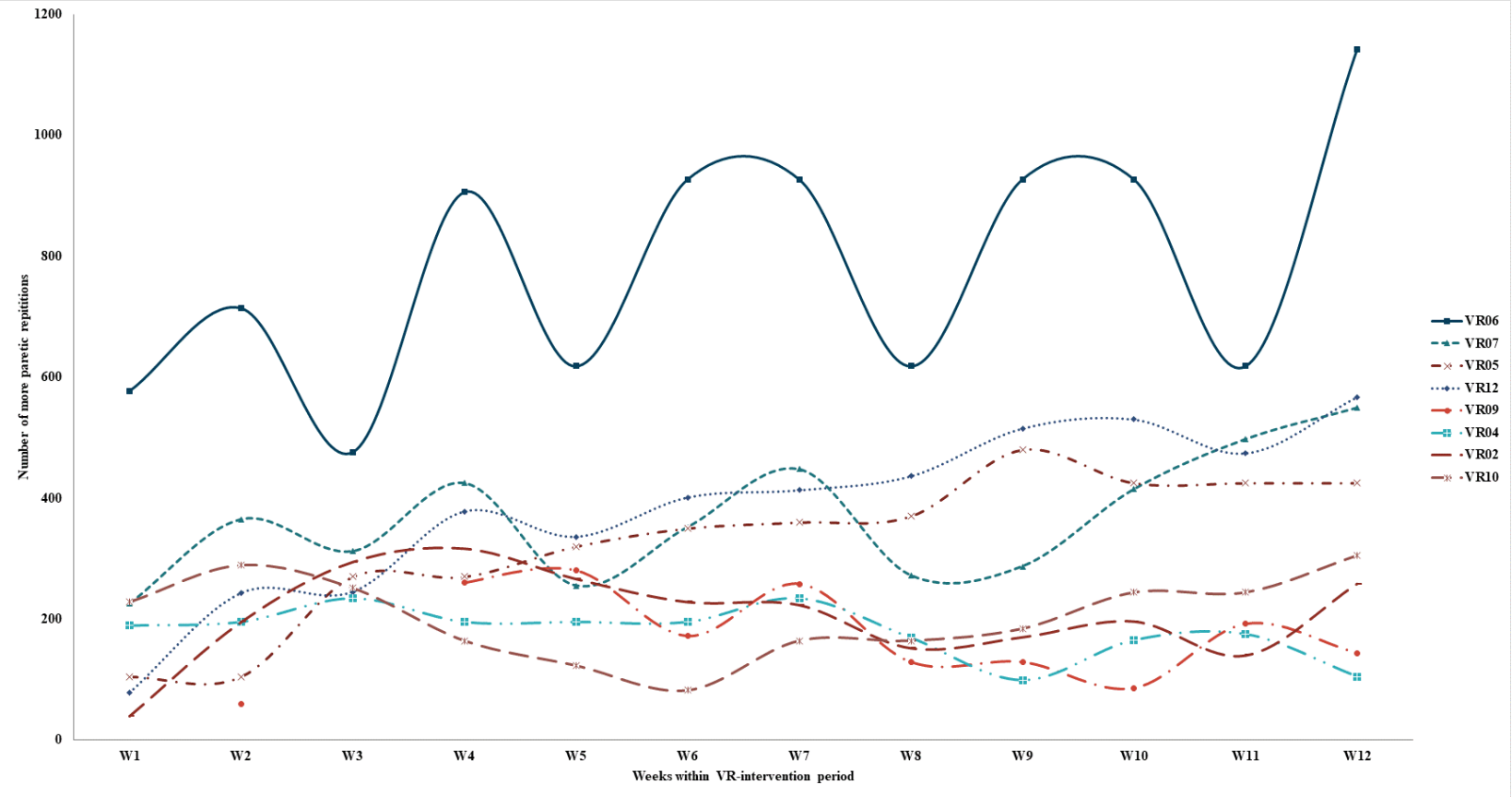
NB. VR01, VR03, VR08 and VR11 withdrew before intervention period begun.

Figure 30: The total adherence during the intervention period to prescribed upper limb more paretic repetitions



NB. Figure is displayed with participants in order of repetitions requested, from least to most. VR01, VR03, VR08 and VR11 withdrew before the intervention period begun**.** VR06 requested a higher number of repetitions per day, but only used the platform a few times a week as opposed to the prescribed six days

Figure 31: Number of more paretic repetitions carried out, by week, during the intervention period



NB. VR01, VR03, VR08 and VR11 withdrew before the intervention period begun

Table 42: Reported factors influencing adherence to the therapy plan

Participant ID	The system did not recognise the starting position	Software froze and data lost	Login problems	Kinect not recognised by the software	Kinect has broken and replaced	Computer software update issues	Virtualrehab platform issues updating therapy plan	Number of days equipment not working in the intervention period
VR02	✓	✓	✓	✓	✓	×	×	7
VR04	×	✓	×	✓	×	✓	×	2
VR05	✓	✓	×	✓	×	×	✓	4
VR06	×	✓	×	✓	×	✓	×	2
VR07	✓	✓	×	✓	✓	×	×	5
VR09	✓	✓	×	×	×	×	×	2
VR10	×	✓	×	×	×	×	×	3
VR12	✓	✓	×	×	×	×	×	2

NB. VR01, VR03, VR08 and VR11 withdrew before the intervention period begun

7.4.4 Research Objective 3. To assess the viability of the researcher adjusting the 'prescribed' training programme over time

The exercises and exergames prescribed per participant are outlined in Table 43. Throughout the intervention period, there were aspects of adjusting the programme that was successful and those that were challenging; these were noted within the research log and are detailed below.

Successful factors

Ability to remotely update the programme: The platform allowed the researcher to adjust the therapy programmes remotely. It also allowed participants to lower the number of repetitions if required quickly. It should be noted that the remote updating was problematic at times; however, this was quickly corrected by the industrial collaborator. This was caused by an update in the software carrying a ‘bug’ in the code, which was identified and corrected.

Record of programme completed: The platform automatically recorded attempts, scores and times for each part of the therapy programme. This allowed the Researcher to monitor participants remotely and update the Research Physiotherapist when changes were requested. Some errors led to some loss of data, but this was mitigated by the participant feedback collected each week and the ability of the Research Physiotherapist to visit the participants home if deemed necessary.

Patient-input into tailored adjustments: Participants were able to tailor their programme, thereby having an active role in the therapy prescription. Throughout the 12-week intervention period, the participants became familiar

with the platform, and their confidence in suggesting changes increased accordingly.

Communication between researcher and research physiotherapist: The Researcher and Research Physiotherapist met weekly for the first month of the intervention period to discuss participants' progress and changes. Towards the end of the intervention period, more adjustments were requested. Communication occurred as and when needed, either in-person, via email or phone calls, both weekly and as required.

Challenging factors

The aim was to prescribe an hour a day, six days a week. Several challenges lowered the prescribed therapy amount throughout the intervention phase.

Limited content available: The Virtualrehab platform was predicted (by the industrial collaborator) to provide enough content for variable therapy plans to use for a maximum of 3 hours a day, six days a week for the 12-weeks. The development of content was delayed, which limited the length of each therapy session and the options available for the participants.

Errors with software: There were several exercises and exergames that contained software errors and were not suitable for the home environment, limiting the therapy prescription. There were exercises and exergames which could not be used within the home environment due to software delays and background influences (i.e. lighting).

Remote oversight: Although the remote abilities of the platform were beneficial, it was limited in one aspect. The lack of physiotherapeutic

oversight during each intervention session led to caution when prescribing therapy. It also created differences in suggested prescription between what the participant felt able to do and what the Researcher and Research Physiotherapist believed appropriate to adjust (i.e. increasing the repetitions by more than 50% was not recommended, to ensure physical safety).

Table 43: Details of exercise-based rehabilitation programme prescribed

Exercise-based virtual rehabilitation therapy software options		**Participant therapy plan, with the level of difficulty (that was categorised by the software developers).**							
		VR02	**VR04**	**VR05**	**VR06**	**VR07**	**VR09**	**VR10**	**VR12**
Exergames (exercise-based movements placed within a virtual game scenario)									
Knock Out	A boxing game scenario engaging both upper limbs	Easy	Easy	Easy	Easy	Easy	Easy	Easy	Easy
Rowing	Mimicking rowing action to move a virtual boat down the river	Easy	Easy	Easy	Easy	Easy	Easy	Easy	Easy
weightlifting	Bilateral upper limb movements to virtually lift a weight bar into various positions (i.e. one hand in front at head level, second underneath at chest level)	Easy	not used	not used	Easy	not used	not used	not used	Easy
Sit to stand	Moving from a real word seated position to standing.	Easy	not used	not used	not used	not used	Easy	not used	not used
Sit step reach	In addition to standing one leg is used to step forward, while one arm reaches out to a virtual target.	Easy	not used	not used	not used	not used	not used	not used	not used
Stay afloat	A virtual boat is sinking requiring a series of holes to be covered virtually with each hand.	Easy	not used	not used	Easy (week 1 to 5);	not used	not used	not used	Easy (week 8 to 10);

Exercise-based virtual rehabilitation therapy software options		**Participant therapy plan, with the level of difficulty (that was categorised by the software developers).**							
		VR02	**VR04**	**VR05**	**VR06**	**VR07**	**VR09**	**VR10**	**VR12**
					Intermediate (week 5 to 12)				Intermediate (week 10 - 12)
Balloon reach	Virtual balloons are placed at varying distances on either side of the participants' avatar. The goal is to reach out in front/or to the side to touch each virtual balloon.	Easy	Easy	Easy	not used	not used	Easy	Easy	Easy
Water pump	A virtual boat required water to be pumped out—this used contralateral arm movements.	Easy	Easy	not used	easy	easy	not used	Easy	Easy
Bullseyes and barriers	A virtual layout sent a randomised pattern of either a bullseye (e.g. a target for the hand to virtually touch) and barriers (e.g. a virtual step which required the knee to lift to clear).	Easy	not used	not used	not used	not used	not used	not used	not used
Push it	Participants were asked to push virtual targets away from their body in a smooth movement.	Easy	not used	not used	not used	not used	not used	not used	not used
In the Kitchen	A virtual kitchen layout required participants to identify the target item	not used	Easy	Easy	not used	Easy	Easy	Easy	Easy

Exercise-based virtual rehabilitation therapy software options		Participant therapy plan, with the level of difficulty (that was categorised by the software developers).							
		VR02	**VR04**	**VR05**	**VR06**	**VR07**	**VR09**	**VR10**	**VR12**
	(i.e. apple) on a shelf and then place it on the virtual countertop.								
Mirror	A virtual mirror reflected the participants' avatar, items appeared related to typical dressing activities (i.e. glasses, gloves) and the participant needed to place the item on the appropriate highlighted part of the body of the avatar.	not used	Easy	Easy	Easy	Easy	Easy	Easy	Easy
Exercises (exercise-based movements depicted by a virtual physiotherapist)									
Shoulder abduction		Easy	Easy	Easy	Easy	Easy	Easy	Easy	not used
Shoulder flexion		Easy	Easy	Easy	Easy	Easy	Easy	Easy	Easy
Elbow flexion and extension		not used	not used	not used	Easy	not used	not used	not used	not used
Knee lifts		Easy	not used	not used	not used	not used	not used	not used	not used
Leaning forward		Easy	not used	not used	not used	not used	not used	not used	not used

NB. VR01, VR03 and VR11 withdrew before intervention prescription

7.4.5 Research Objective 4. To evaluate the technical reliability of the Virtualrehab platform

The research log contained information on the technical reliability challenges of the Virtualrehab platform. The industrial collaborator attempted to solve such problems efficiently and had open communication with the Researcher through the intervention phase. Table 44 identifies the main reliability challenges, the impact they had on the intervention, and the solutions attempted.

Table 44: Technical reliability of the Virtualrehab platform

Virtualrehab platform	Technical reliability	Details	Impact within the thesis	Attempted solutions
Hardware	Manufacturing changes	The Microsoft Kinect V2 is no longer supported through the manufacture.	Shortly before equipment procurement, the manufacture stopped producing Kinects. Second-hand Kinects were purchased, limiting the reliability of the equipment and availability of replacements. Time was lost in the intervention phase, obtaining replacements, also delaying the next group of participants – who were in the control phase.	The industrial collaborator created a new sensor to run the intervention software through. Unfortunately, this was not completed in time for the intervention period.
	Equipment failures	Two of five of the Kinects broke during the intervention phase.	Obtaining replacement caused lost days in the intervention phase and delayed other participants within their control period.	Resources could only procure two additional replacement Kinects.

Virtualrehab platform	Technical reliability	Details	Impact within the thesis	Attempted solutions
		Required cables broke (i.e. HDMI, Kinect to Laptop connectors)	Participants lost time in their intervention phase.	Resources were limited to the amount of supplementary equipment that could be procured.
		Laptop procurement	The supply of laptops was delayed by over a month, thereby delaying the beginning of the intervention phase.	The lab technician communicated with the company until a different, suitable laptop could be obtained. Shortening the potential delay. However, the intervention period was delayed for some participants.
Software	Update challenges	Kinect software	The Microsoft Kinect V2 software update was released during the intervention period. The update was incompatible with the Virtualrehab platform producing an error.	The industrial collaborator provided a solution, where the Virtualrehab platform software code was adapted. This solution was provided quickly, which limited the impact on the

Virtualrehab platform	Technical reliability	Details	Impact within the thesis	Attempted solutions
				participants, although intervention days were lost.
		Laptop software	All updates were turned off on the laptops, to prevent potential inference. However, there was a Windows software update that could not be turned off and interfered with the intervention period.	The researcher returned to the participants' homes as soon as possible to carry out the update, enabling the intervention to continue. For some participants, the researcher was able to talk them through the update steps via the phone. Although for some, intervention days were lost.
		Intervention software	The intervention software was in the process of being refined. The updates caused the software to crash for some participants, losing intervention	The industrial collaborator worked quickly for each software challenge.

Virtualrehab platform	Technical reliability	Details	Impact within the thesis	Attempted solutions
			days before a solution was undertaken.	
Home-set-up	Adaptions required	Required additional hardware for home set-up (i.e. wireless mouse, keyboard)	Each participant home required different set-ups. Participants were unable to use the intervention software from the laptop on the ground. Hence, the need for wireless alternatives.	Wireless alternatives were incorporated to enable the therapy plans to be carried out safely within the home.
	Environmental considerations	The set-up in participants homes varied depending on environmental considerations.	In some participants' homes, the Kinect sensors struggled to identify their starting position. Participants also had differing safety requirements, animals and children that needed to be accounted for.	To ensure starting positions were met, the researcher placed tape on the floor for placing of chairs or participants. The equipment set-up was altered for each participant to ensure safety.
Equipment maintenance	Communication with the industrial collaborator	Communication between the researcher and industrial collaborator was	There were technical challenges that were hard to communicate virtually and delayed attempted	The industrial collaborator resolved challenges as quickly as possible and

Virtualrehab platform	Technical reliability	Details	Impact within the thesis	Attempted solutions
		key to keeping the interventions running.	solutions – in particular, when the error was prevalent in the home environment but not replicable within the industrial collaborators' lab environment.	was available for efficient communication throughout the intervention phase.
	Lone worker safety	The researcher was required to visit the participants' homes when the Virtualrehab platform was not working.	The lone worker policy required the researcher's whereabouts to be known at all times when visiting the participants. This limited the times the researcher could visit participants.	Solutions were primarily attempted via the phone to limit the number of days lost in the intervention period, specifically over the weekends.

7.4.6 Research objective 5. To test the viability of collecting neural and behavioural data in the home.

The viability of collecting neural and behaviour data within the home environment was assessed by the following.

Neural measures

The issues regarding non-valid trials (defined in section 7.3.4.6.5) were grouped into the following when processing the data:

Error with acquiring the Go signal: Recording the Go signal was problematic with the initial lab measurements and participants. This was due to equipment errors with collecting the Go signals: the procedure was new at the time and required refining as challenges became evident. This is shown in the below figures, and once the problems had been solved, there were still trials lost due to Go signal errors, indicating that the process needs careful monitoring and adjustments throughout a study. Overall, the home vs lab environment did not impact the viability of recording the Go signals for the neural data.

sEMG noise interference: Fridges; builders; ambient temperature.

Participant movement error: Trials lost to participant movement error.

Overall, the majority of trials within the lab were valid, with trials lost due to Go signal collection error. Within the home, most participants provided over 50% valid trials. There were substantially more trials lost due to sEMG noise interference; in particular, one participant lost over 50% of trials due to this (Figure 32 and Figure 33)

Figure 32: Validity of neural measures collected in the home vs a lab environment (% of all potential trials)

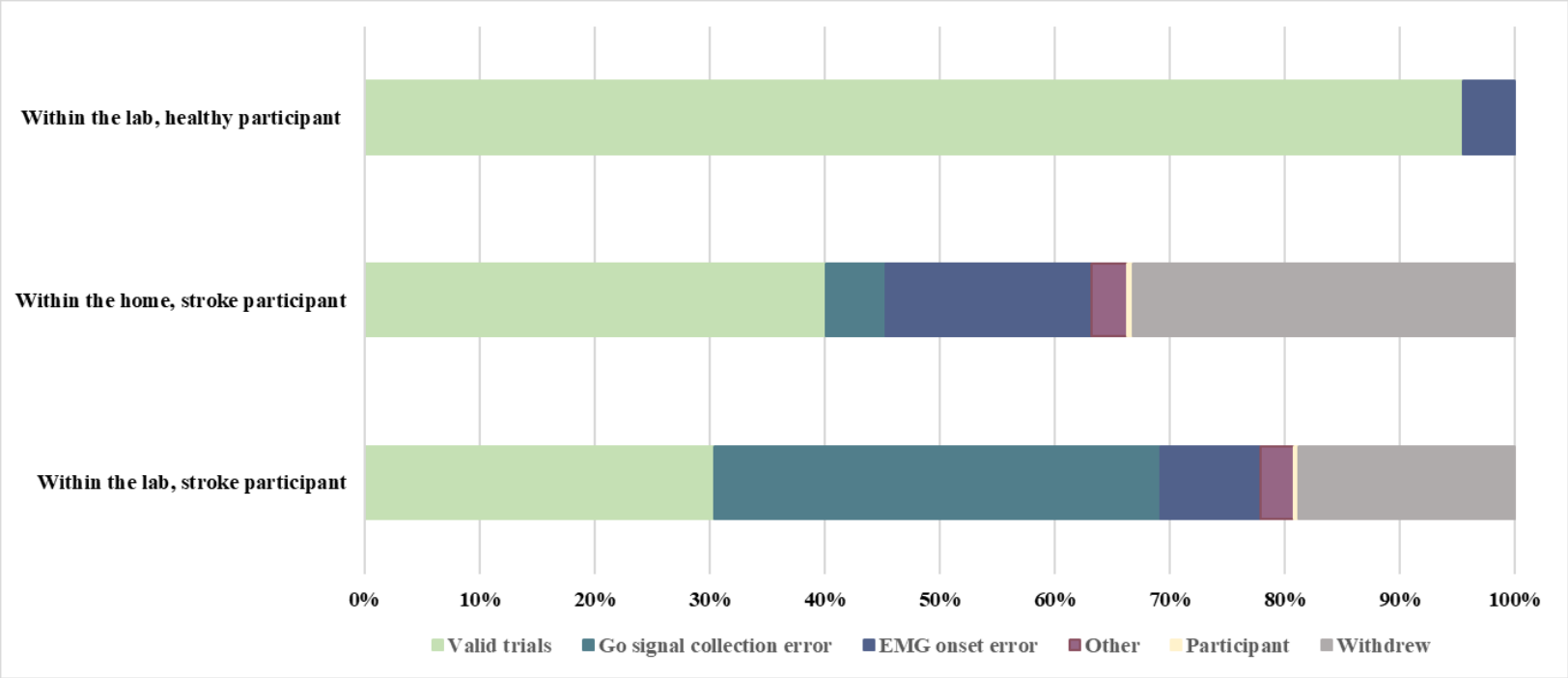
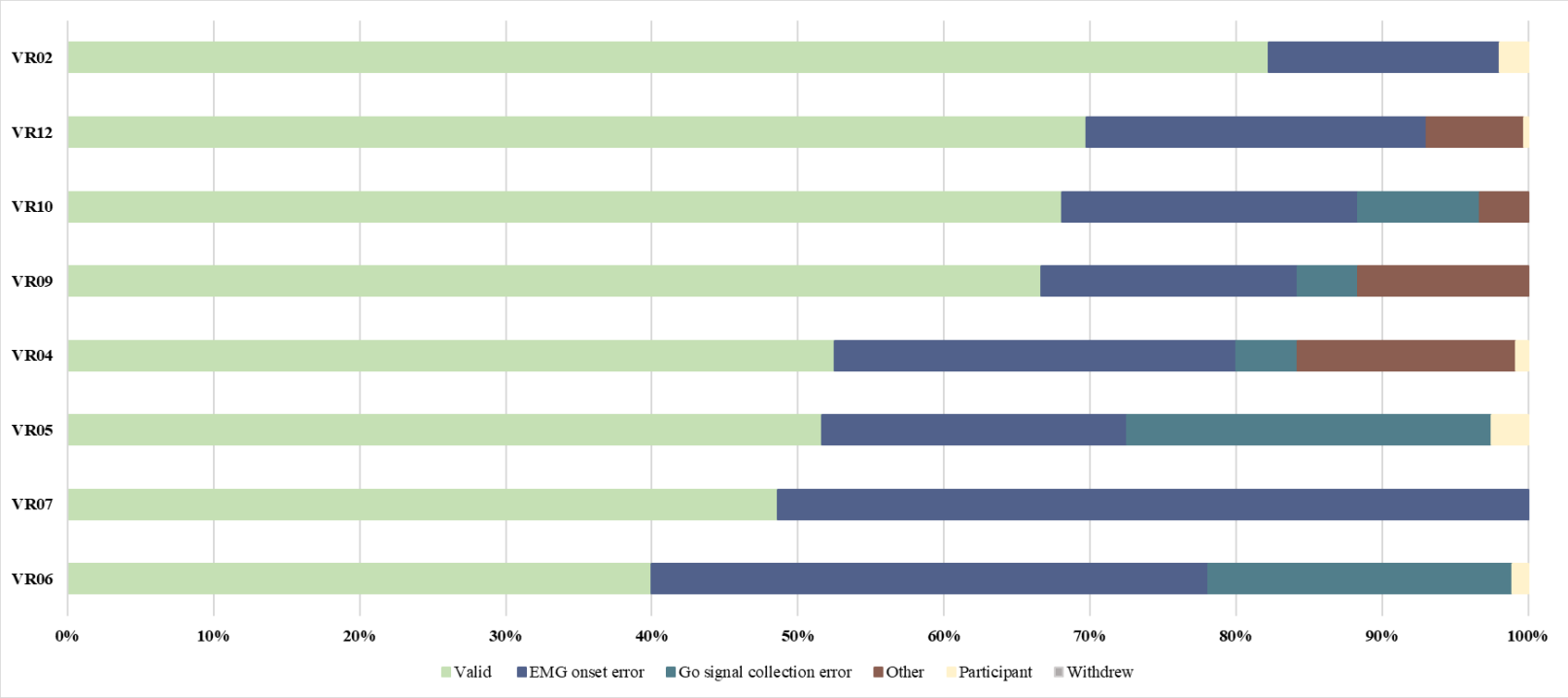


Figure 33: Variations of neural measure validity within the stroke participants home (% of all potential trials)



NB. VR01, VR03 and VR08 withdrew before data collection was carried out in the home

Behavioural data (motor function and functional impairment measures)

The Action-Reaction Arm Test (ARAT) and Motricity Index (MI) were collected weekly within the participants' home. The participant log reflected several practical challenges that needed to be considered and overcome in order to complete the behavioural data collection within the home environment successfully:

1. **The appropriate safe space to carry out the behavioural data collection tasks**

   Each home environment differed in terms of space available and potential obstacles preventing safe measurements; details of such challenges were noted for each participant. For example, in one home it was necessary to ask the participant's family to move furniture/items out of the way for the participant to have full safe movement for the ARAT and MI tasks, and the researcher to observe both sides.

2. **Equipment requirement for standardisation**

   Both behavioural tasks required an armless chair and for participants to be positioned with the table in a standard way, for each data collection week. It was necessary in some cases to bring a portable table and chair in homes where these were not available.

3. **Other environmental considerations**

   There were scheduling conflicts that prevented data collection for some participants, which were not known before the intervention phase began. There were also occasions where the participant was not

feeling able to carry out the behavioural measures on that particular day, for example, post-stroke fatigue. On one occasion, the weather was too hot for the participant to carry out the measures safely, and the decision was made to stop data collection during that time. Finally, children and pets need to be considered when carrying out behavioural measures, for example, the ARAT contains items (i.e. ball) that can be distracting for pets in the area or even potentially dangerous if dropped (i.e. ball bearing) or swallowed. It was necessary for the pets and young children to be removed from the area to ensure their safety.

Overall, half of the participant group completed all 12 behavioural data collection points. The reasons mentioned above are noted in Table 45, depicting the points at which data was not collected.

Table 45: Viability of behavioural data collection within the home environment

Participant ID	Weekly data collection during the intervention phase B											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
VR01	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd
VR02	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
VR03	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd
VR04	✓	✓	✓	✓	✓	I	✓	I	✓	✓	✓	✓
VR05	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
VR06	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
VR07	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
VR08	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd
VR09	H	✓	H	✓	✓	✓	✓	✓	✓	✓	✓	✓
VR10	✓	✓	✓	✓	F	✓	✓	I	✓	✓	✓	✓
VR11	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd
VR12	U	✓	✓	✓	✓	H	✓	✓	✓	✓	✓	✓

✓, completed;

wd, participant withdrew

I, illness preventing participant collecting data that day;

H, holiday, so unavailable for data collection that week;

U, unavailable for data collection that week;

F, fatigued causing data collection to end early

7.4.7 Research Objective 6. To assess the viability of using randomised length of baselines and repeated measures during the intervention period to inform a subsequent dose-optimisation study.

Using replicated single-case studies following an AB design was deemed not appropriate for a subsequent dose-optimisation study. The attempt to randomise participants to their control period (between 1 to 4 weeks) was not possible; randomisation was carried out according to the procedure for only two participants. The baseline periods varied between participants, ranging from 29 to 75 days (mean = 38.7; standard deviation = 14.1 days). The reasons for the unsuccessful randomisation attempts are detailed in Table 46.

Of the repeated measures during the intervention phase, eight participants completed the 12-week intervention phase Figure 28. Four participants completed ARAT and MI measures on ten weeks and four on all 12 weeks. Therefore, for the ARAT and MI scores, 88 of the possible total of 96 (91.7%) were collected. For time to onset of muscle activity, across five muscles in both upper limbs of eight participants, the total possible number of measures was 960. The number of valid measures per participant ranged from 68 of 120 to (56.6%, VR04) to 109 of 120 (90.8%, VR12). For all eight participants, 771 of the total possible 960 measures (80.3%) were collected, eight participants. 76.0% of the possible total for the less paretic upper limb were collected and 78.1% of those possible for the more paretic upper limb.

Finally, it was noted that the aim was to recruit 15 stroke survivors in order to complete a series of replicated single case-studies. There were 17 potential participants eligible for the study, and of these, 12 consented (Figure 27). Of these, three then withdrew before the intervention period began, and seven completed their outcomes. There were scheduling conflicts and illness that prevented participants from completing certain data collection points; for example, one participant was on holiday for two weeks of the intervention period.

Table 46: Details of randomisation within the control phase A

ID	Length of control period (days)	Details of randomisation/lack of randomisation
VR01	29	Randomisation was carried out
VR02	49	Randomisation could not be carried out due to the participants' schedule (they had a family holiday booked in between BL1 and BL2).
VR03	Withdrew	Participant withdrew before BL2.
VR04	30	Randomisation was carried out – Participant was ill on the date of BL2, rescheduling was required.
VR05	35	Randomisation could not be carried out. BL1 was carried out, the participant then had a three-week holiday booked, which the Researcher was informed about at BL1.
VR06	30	Randomisation could not be carried out due to conflicts with (1) participant schedule; (2) lab availability and (3) additional data collection research and a research physiotherapist.
VR07	75	Randomisation could not be carried out due to equipment unavailability (equipment set broke, limiting the number of sets) – the priority was given to ensuring BL2 was measured one week before the intervention period being carried out.
VR08	Withdrew	The participant did not turn up to BL1.

ID	Length of control period (days)	Details of randomisation/lack of randomisation
VR09	36	The participant had separate holiday and family priorities (involving childcare commitments) – these impacted, BL2, equipment set-up, week two and three.
VR10	37	Randomisation could not be carried out due to conflicts with (1) participant schedule; (2) lab availability and (3) additional data collection research and research physiotherapist.
VR11	37	The participant was ill, causing BL2 to be delayed.
VR12	29	Randomisation was attempted – participants schedule caused BL2 to be rescheduled.

7.4.8 Research objective 7. Estimate changes in paretic upper limb functional ability and motor impairment and neural measures

The following details the results from the functional ability, motor impairment and neural measures.

7.4.8.1 Functional ability measures

The following details the results for the functional ability measures carried out pre/post-intervention period (Wolf Motor Function Test) and within the weekly progress measures during the intervention period (Action Reaction Arm Test).

7.4.8.1.1 Pre/post-intervention period, functional ability measures

Seven stroke participants completed a measure of their functional ability (Wolf Motor Function Test, WMFT) pre/-post control and intervention period (table of results in appendix 18D). One participant (VR12) did not reach an MCID in either the mean WMFT-time and WMFT-function (FAS) (Figure 35). Five participants demonstrated an MCID was reached in the (mean) WMFT-time it took to complete each task post-VR intervention (VR02, VR05, VR06, VR07, VR10); two of these also reached an MCID in their WMFT-function (VR07, VR10). One participant reached an MCID in the WMFT-time and WMFT-function between each baseline, but no change post-intervention (VR09).

VR02 time per task reduced by 7 seconds, from baseline two (mean = 58.19; standard deviation = 59.88) to their outcome measures (mean = 51.17; standard deviation = 58.32) (Figure 34). VR05 also reduced their time per task by 26.5 seconds, from baseline two (mean = 90.12; standard deviation = 51.57) to outcome (mean = 63.67; standard deviation = 55.65) (Figure 35). VR06 time per task increased by 1.8 seconds, from baseline two (mean = 6.26; standard deviation = 7.79) to outcome (mean = 8.04; standard deviation = 9.83); it should be noted their time reduced during the control period by 7.3 seconds, from baseline one (mean =13.53; standard deviation = 30.14) to baseline two (mean = 6.26; standard deviation = 7.79) (Figure 36). Further, the above participants did not reach a MCID with their functional activity scores.

VR07 reduced their time per task by 12.1 seconds, from baseline two (mean = 52.69; standard deviation = 57.69) to outcome (mean = 40.61; standard deviation = 51.56) (Figure 36). Their FAS also improved by 0.4 points from baseline two (mean = 2, standard deviation = 1.13) to outcome (mean = 2.4, standard deviation = 1.3). It should be noted that VR07 showed a reduced motor function performance during the control period. Their time increased by 10.2 seconds, baseline one (mean = 42.45; standard deviation = 56.95) to baseline two (mean = 52.69; standard deviation = 57.69) and their FAS reduced by 0.3 points from baseline one (mean = 2.33; standard deviation = 0.98) to baseline two (mean = 2; standard deviation = 1.13). VR10 reduced their time per task by 3.7 seconds (baseline two, mean = 7.47, standard

deviation = 8.88; to outcome, mean = 3.8, standard deviation = 3.78), and their FAS by 1.1 points (baseline two, mean = 3.33, standard deviation = 0.72; to outcome, mean = 4.4, standard deviation = 0.63). Finally, it should be noted VR10 increased their time per task by 0.5 seconds during the control period (baseline one, mean = 7.70, standard deviation = 6.76; to baseline two, mean = 7.47, standard deviation = 8.88).

Figure 34: Pre/post-functional ability, more paretic limb, VR02

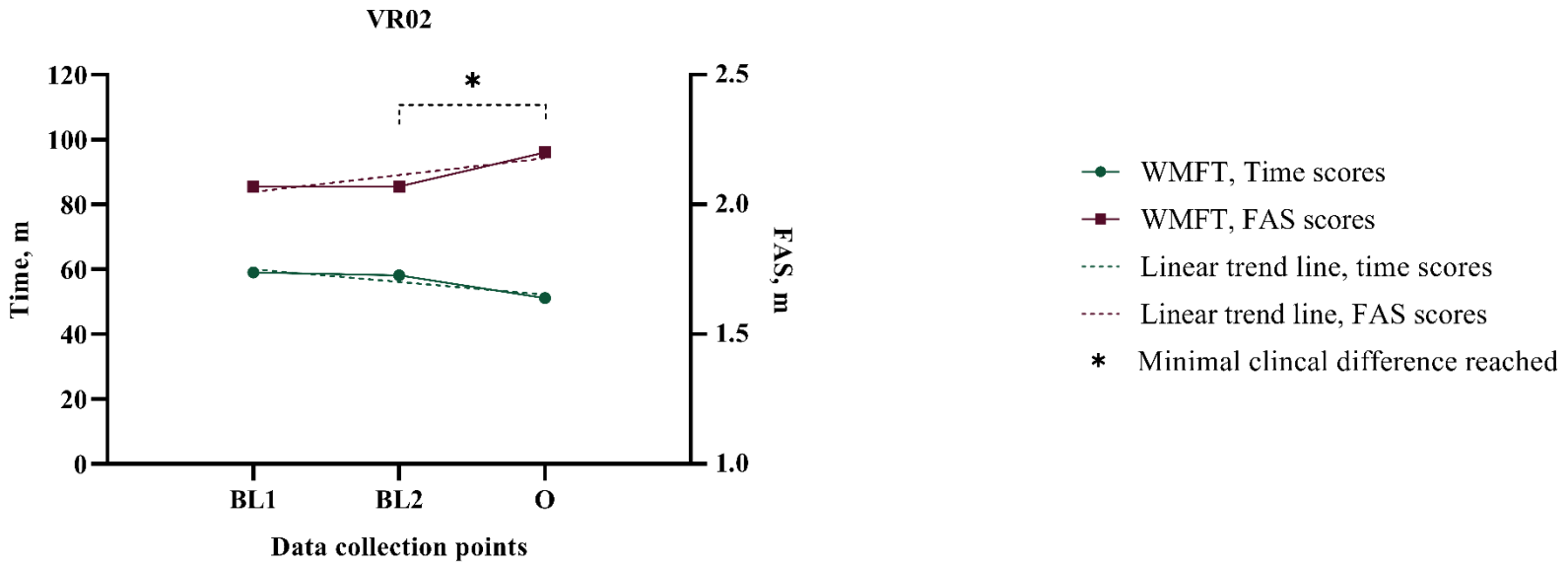


Figure 35: Pre/post-functional ability, more paretic limb, VR05 and VR12

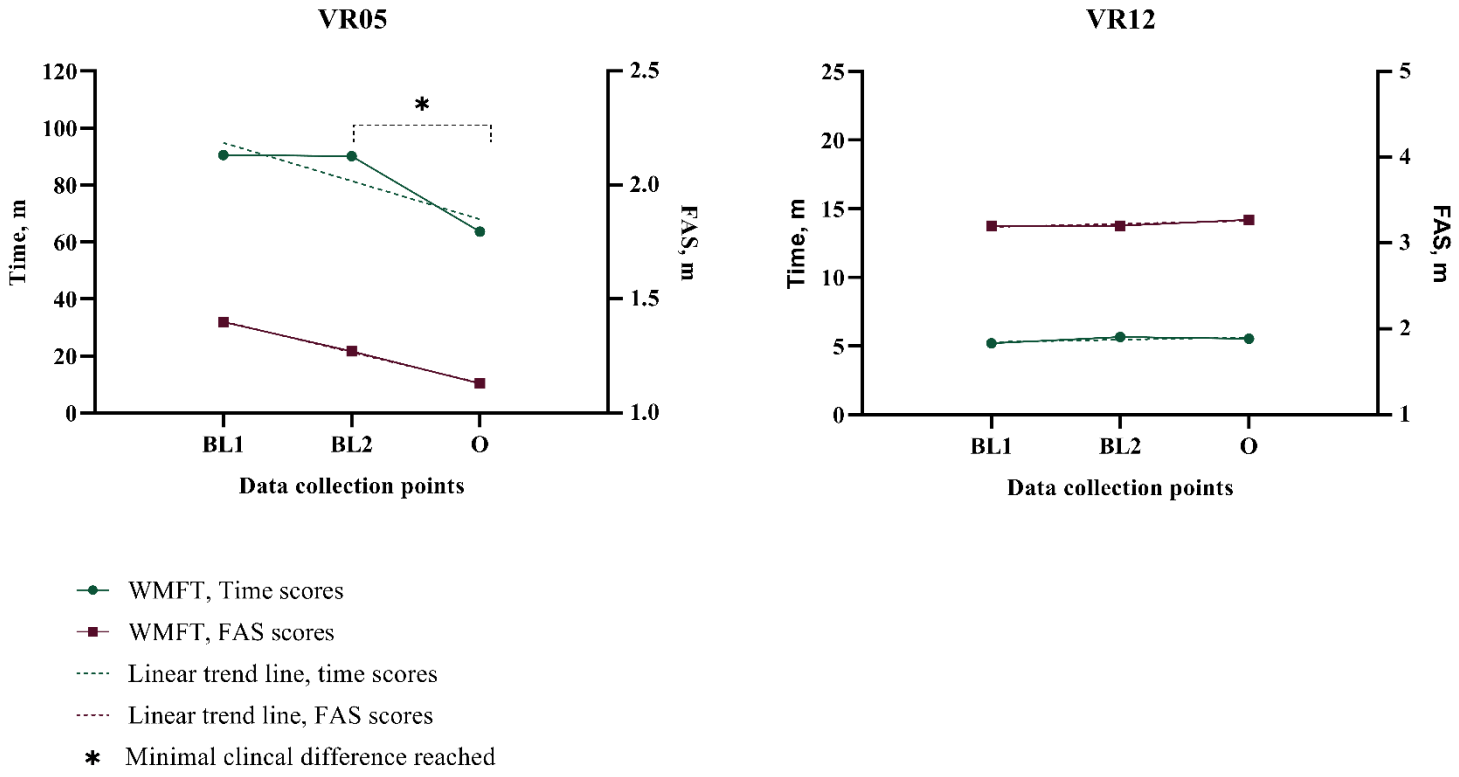


Figure 36: Pre/post-functional ability, more paretic limb, VR06 and VR07

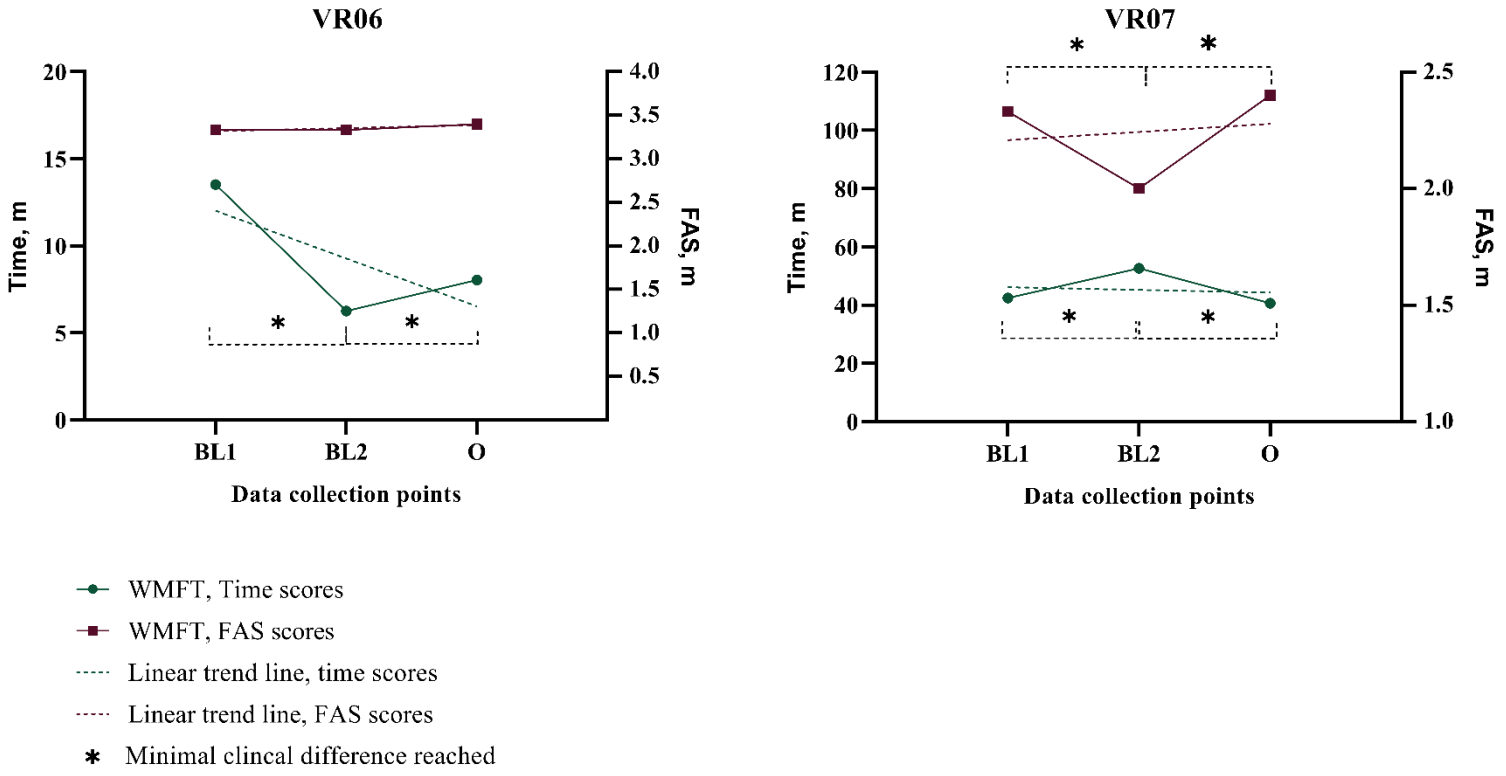
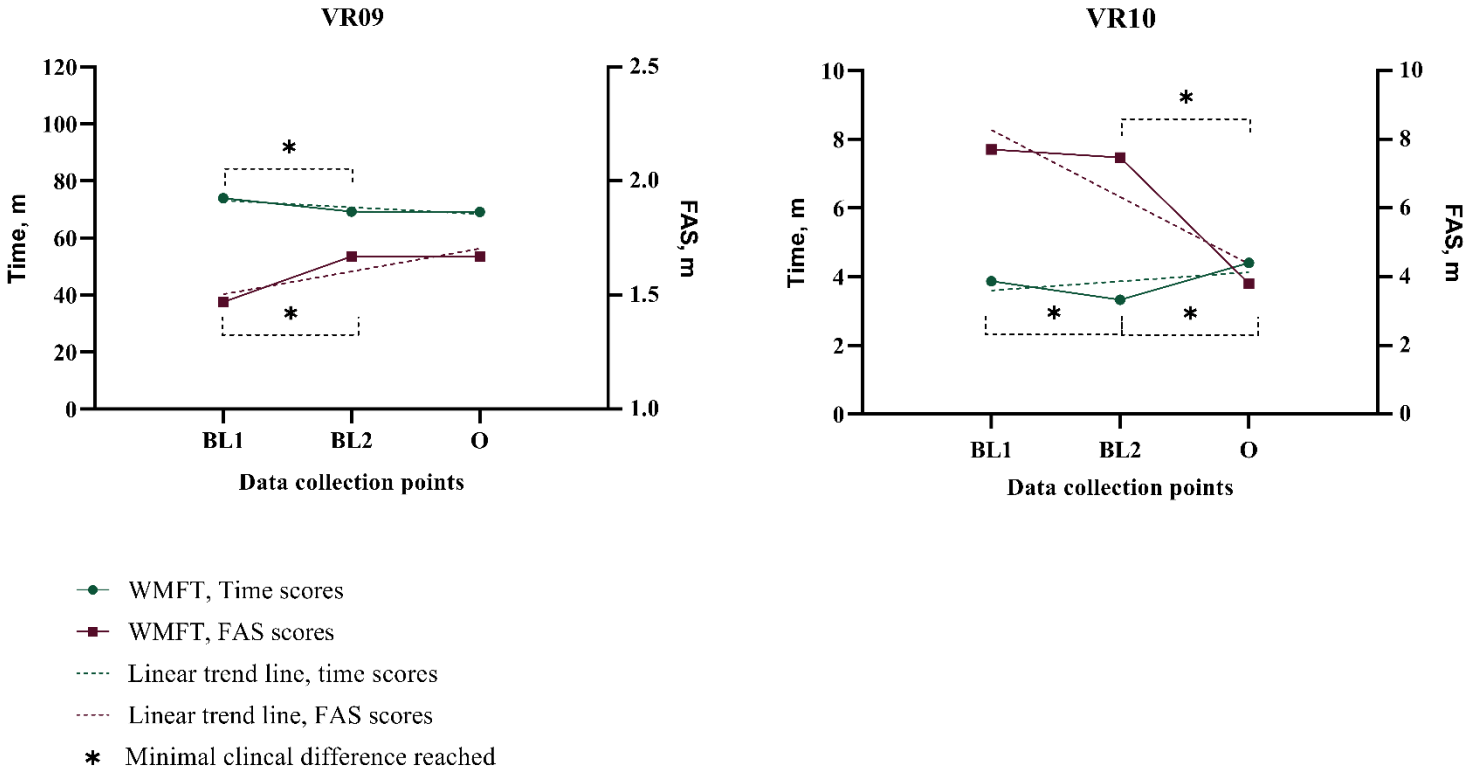


Figure 37: Pre/post-functional ability, more paretic limb VR09 and VR10



7.4.8.1.2 Weekly progress, functional ability measures

Eight participants completed the weekly measures of functional ability during the intervention period, recorded with the ARAT scores (Appendix 19D). Four reached an MCID in an improvement in their scores (VR02, VR04 - Figure 38 and VR06, VR10 - Figure 39). Three participants maintained this change over two weeks (VR02, VR04, VR06), whereas VR10 is unknown as data was not collected the following week. The number of weeks to reach the MCID differed between two and eight. Four did not reach an MCID during the intervention period (VR05, VR07, VR09, VR12) (Figure 40 and Figure 41).

Figure 38: Weekly progress functional ability, more paretic limb VR02 and VR04

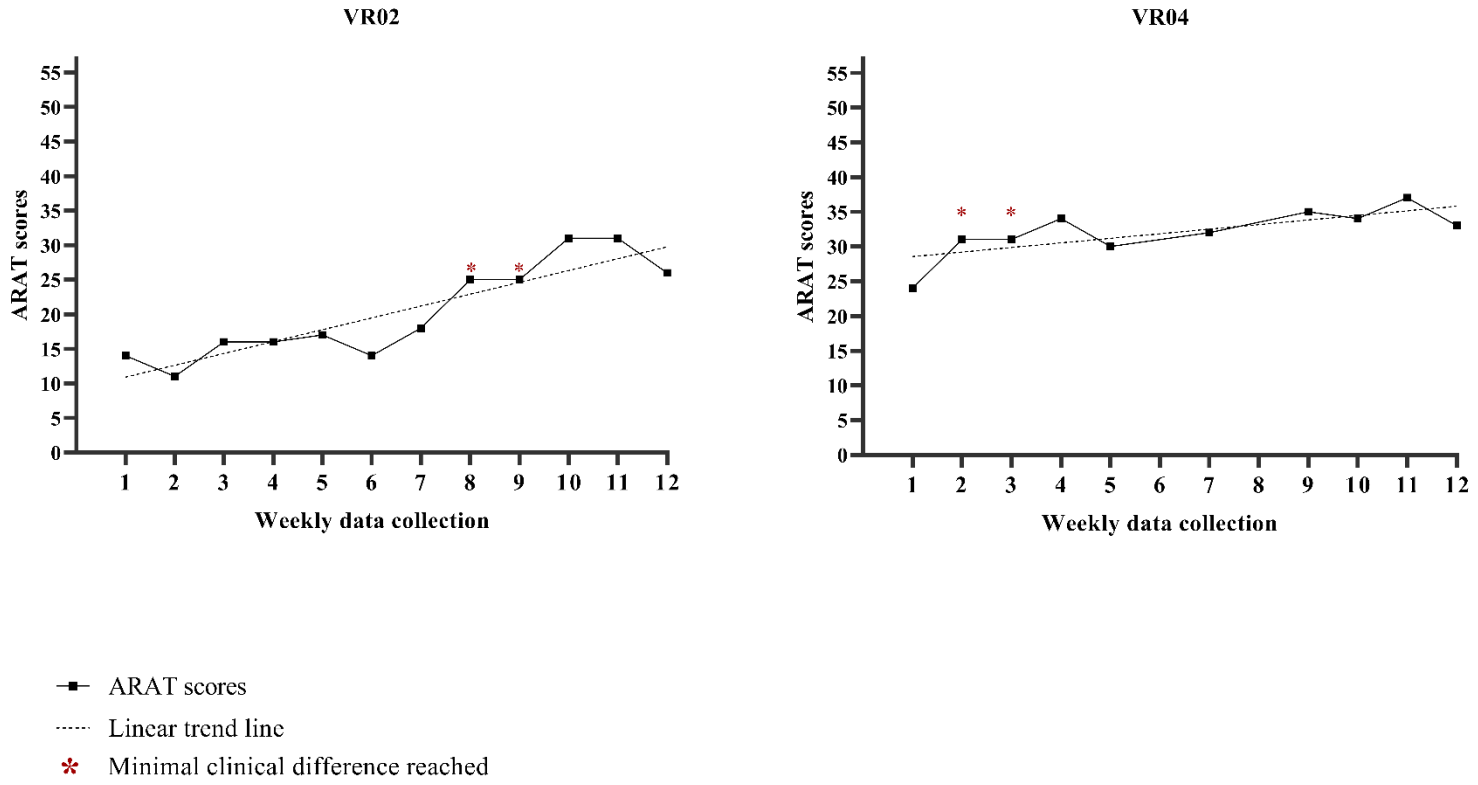


Figure 39: Weekly progress functional ability, more paretic limb, VR06 and VR10

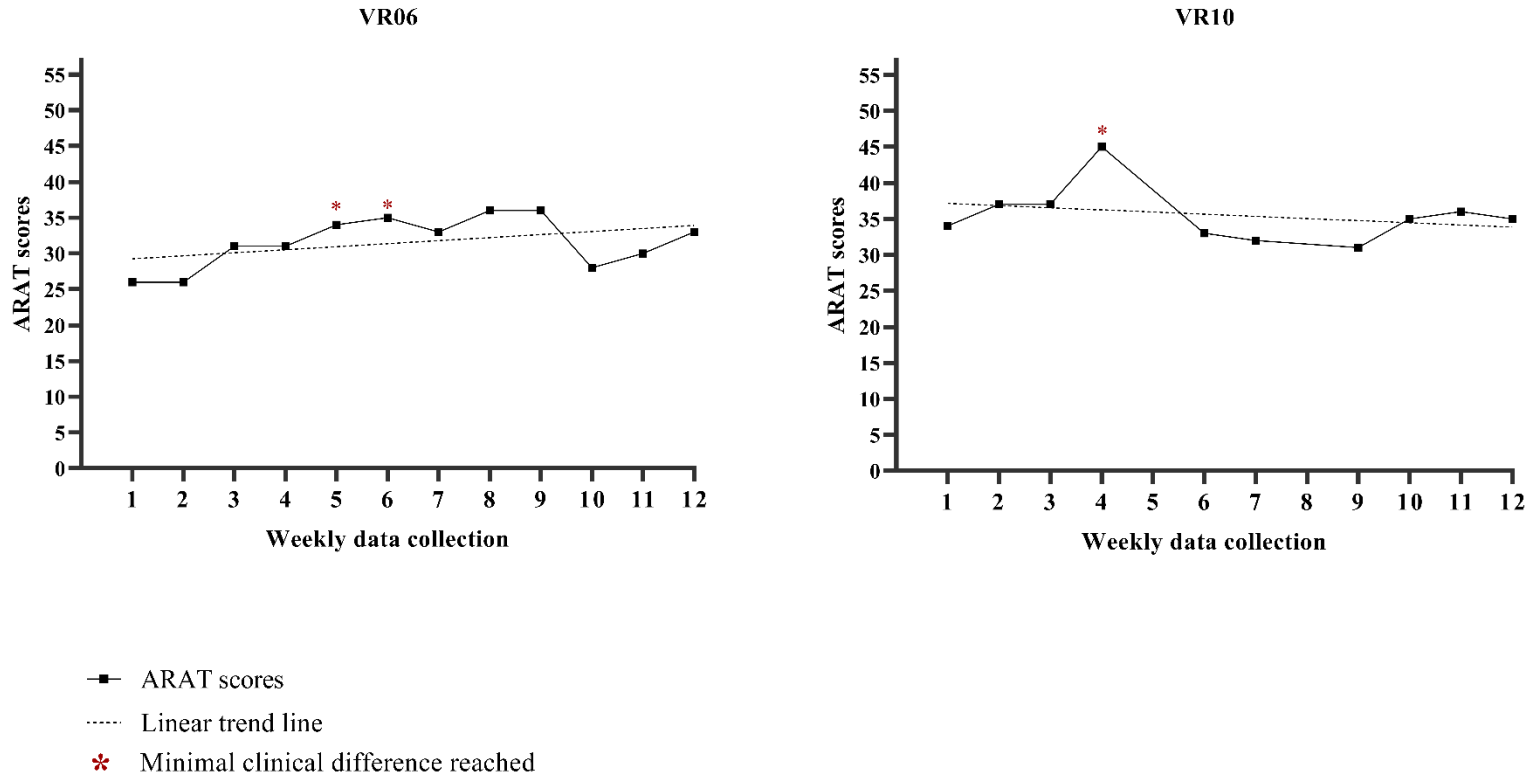


Figure 40: Weekly progress functional ability, more paretic limb, VR05 and VR07

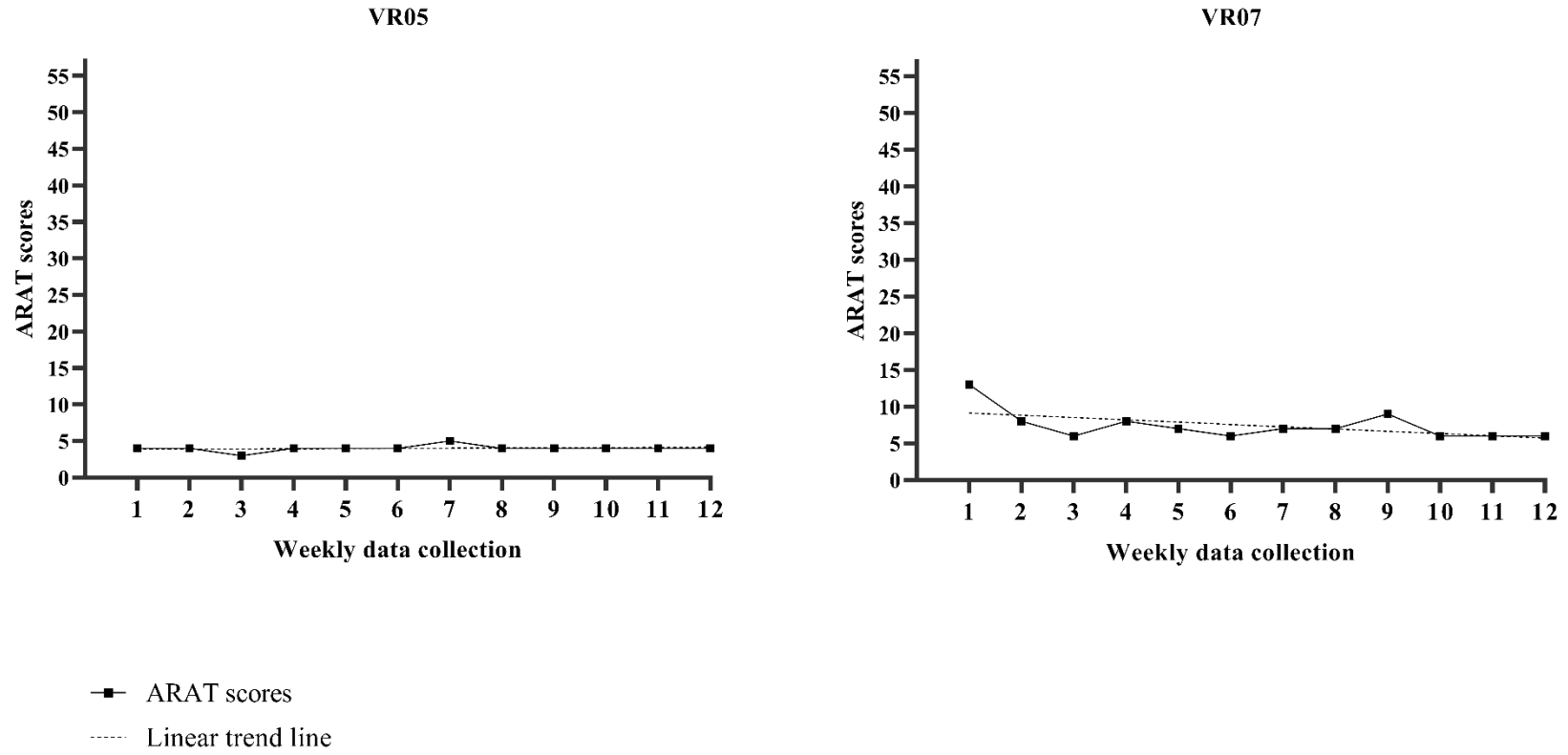
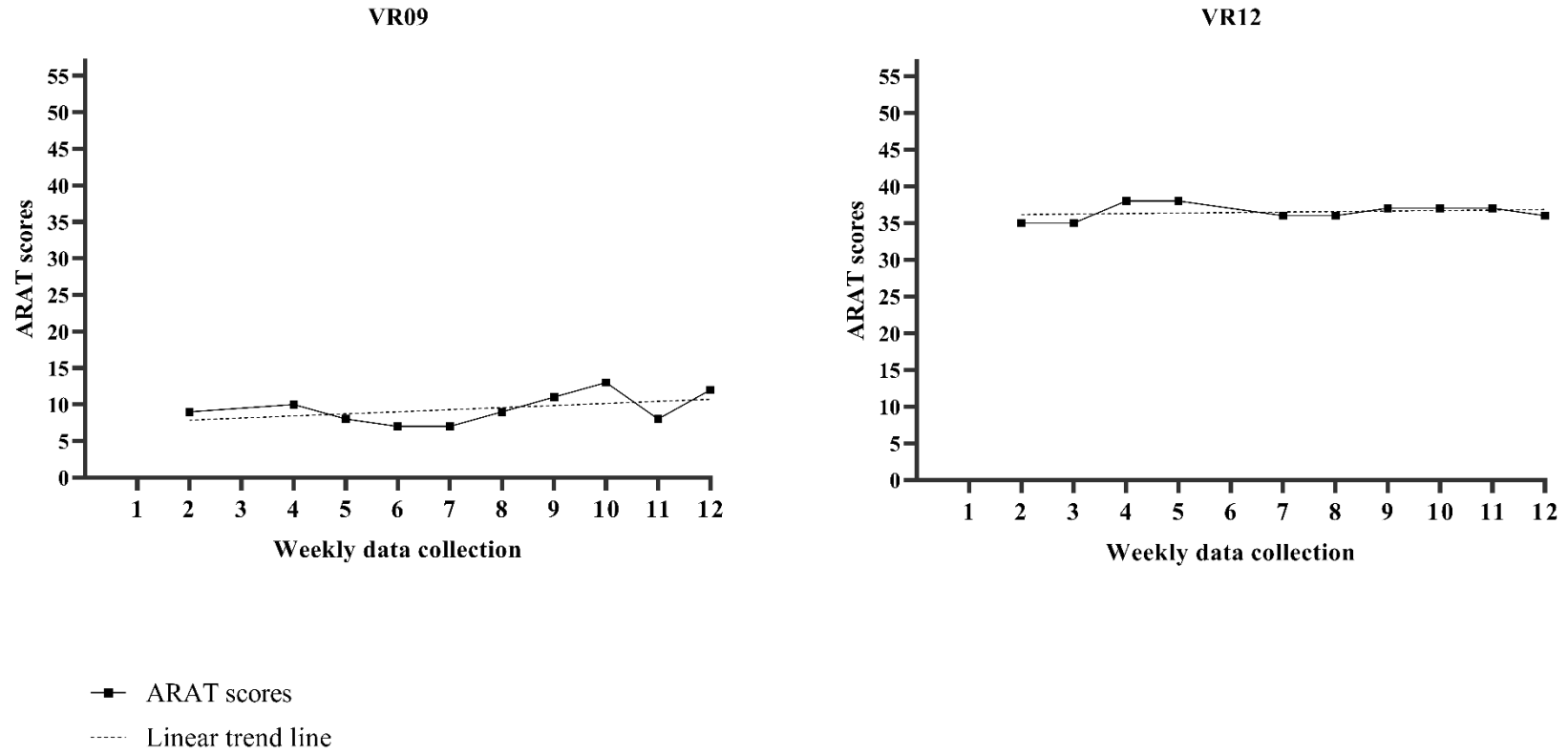


Figure 41: Weekly progress functional ability, more paretic limb, VR09 and VR12



7.4.8.2 Motor impairment measures

The following section details the results from the motor impairment measures carried out pre/-post (Grip strength) and within the weekly progress measures during the intervention period (Motricity Index).

7.4.8.2.1.1 Pre/post-intervention period, motor impairment measures

Seven participants completed the grip strength measures, and two participants reached a change of 5kg or greater in grip strength (VR06 and VR07) (Table 47 for participant scores). VR06 showed a 6.33kg increase between baseline 1 and 2 (the control period) in their more paretic arm, but no change at the outcome; they also showed a decrease of 6kg between pre/post-intervention. VR07 showed a decrease of 6kg between the control period and an increase of 11.67kg post-intervention in their less paretic arm. No other participant showed a change above 5kg in either their less paretic or more paretic arm.

Table 47: Stroke participants, grip strength scores

Participant ID		Baseline one		Baseline two		Outcome		Change over the control period		Change pre/post-intervention	
		LP	**MP**	**LP**	**MP**	**LP**	**MP**	**LP**	**MP**	**LP**	**MP**
VR02	m	17.70	0.01	17.67	0.00	20.00	0.01	-0.03	-0.01	2.33	0.01
	sd	5.11	0.00	1.53	0.00	0.00	0.00				
VR05	m	20.00	1.50	22.07	2.17	21.67	0.42	2.07	0.67	-0.40	-1.75
	sd	2.00	0.00	0.12	0.29	0.58	0.29				
VR06	m	29.00	25.00	33.00	31.33	27.00	26.67	4.00	6.33*	-6.00*	-4.67
	sd	1.00	1.73	3.97	5.69	3.00	1.15				
VR07	m	25.67	2.67	19.67	3.00	31.33	5.00	-6.00*	0.33	11.67*	2.00
	sd	3.21	1.15	2.08	1.73	1.53	3.61				
VR09	m	25.33	0.50	22.00	1.00	21.00	2.00	-3.33	0.50	-1.00	1.00
	sd	3.06	0.50	0.00	0.00	4.58	0.00				
VR10	m	17.33	3.00	15.33	3.58	16.33	5.00	-2.00	0.58	1.00	1.42
	sd	1.15	1.00	3.06	0.72	5.69	1.00				
VR12	m	23.33	3.00	23.33	5.33	24.67	7.33	0.00	2.33	1.33	2.00
	sd	1.53	1.00	1.15	0.58	5.51	1.15				

NB. VR01, VR03, VR04, VR08, VR11 withdrew before outcome measures were taken

LP, less paretic; **MP**, more paretic; **m,** mean; **sd,** standard deviation

***** A change of 5kg or greater was reached

7.4.8.2.1.2 Weekly progress, motor impairment measures

The Motricity Index scores were calculated for each arm, displayed for the stroke participants more paretic arms in Figure 42, Figure 43 and Figure 44 (scores displayed in a table in Appendix 6D). All but one participant scored the maximum (100) for their less paretic arm. The lowest VR06 scored on their less paretic arm was 77, for five weeks (2, 6, 7, 11, 12), and reached 100 in three of the weeks (1, 4, 5). One participant increased between levels in the first week (VR04), showing movement against resistance in their more paretic arm and this was maintained for the 12 weeks. Two participants decreased levels: VR02 (more paretic arm went from moving against resistance to against gravity in the final week 12) and VR10 (started with their more paretic arm moving against resistance, aside from week 9 when it lowered to 'against gravity'; but the scores showed movement again resistance from week ten onwards). Three participants showed various changes during the intervention period. VR05 decreased in week 2 to a palpable flicker and maintained this, aside from in week nine where the more paretic arm moved but not against gravity; this was not maintained the following week. VR09, by contrast, increased to a movement against gravity in week three and maintained this until week 8 when it dropped to movement only, with an overall decreasing trend. While VR07 showed an overall increasing trend, despite a decrease in week 5, in week seven, the more paretic arm went from movement to moving against gravity. Two participants did not change between levels: VR06 maintained movement against resistance for the 12 weeks, while VR12's more paretic arm did not change above a palpable flicker.

Figure 42: Weekly progress, motor impairment, more paretic, VR02, VR04 and VR05

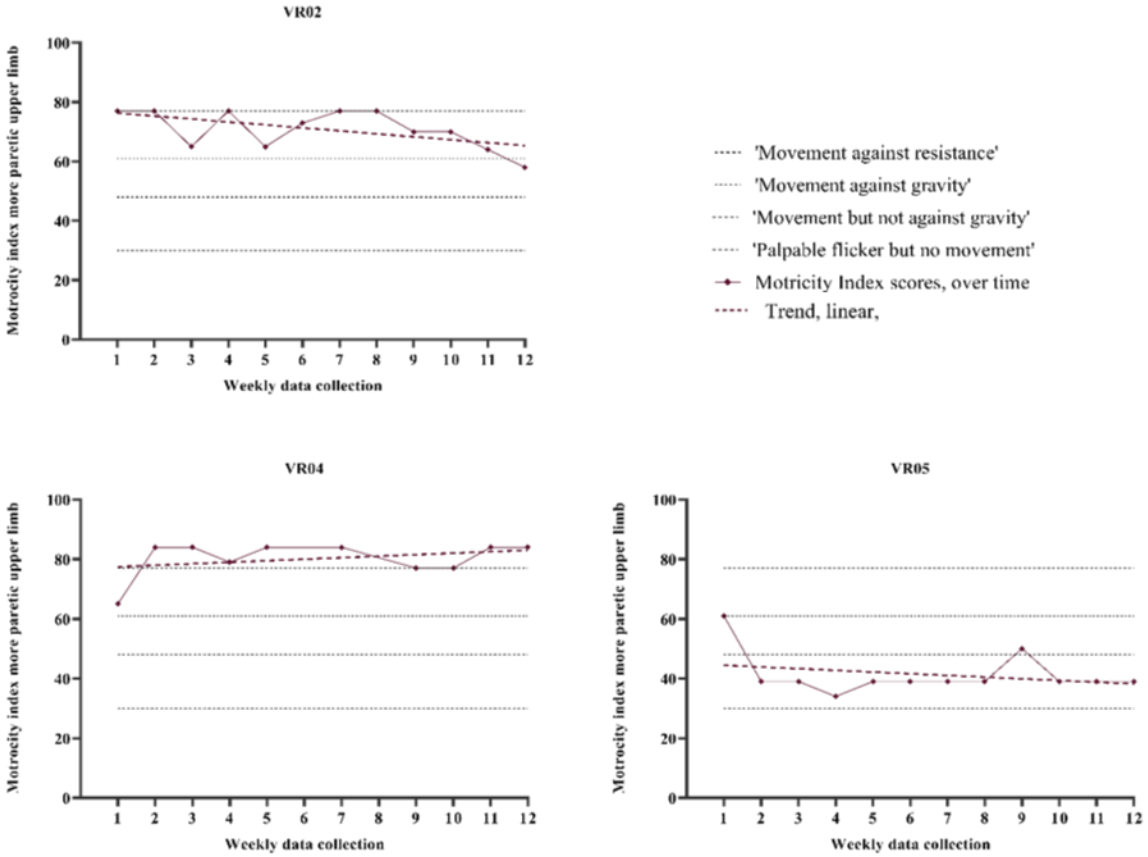


Figure 43: Weekly progress, motor impairment, more paretic, VR06, VR07 and VR09

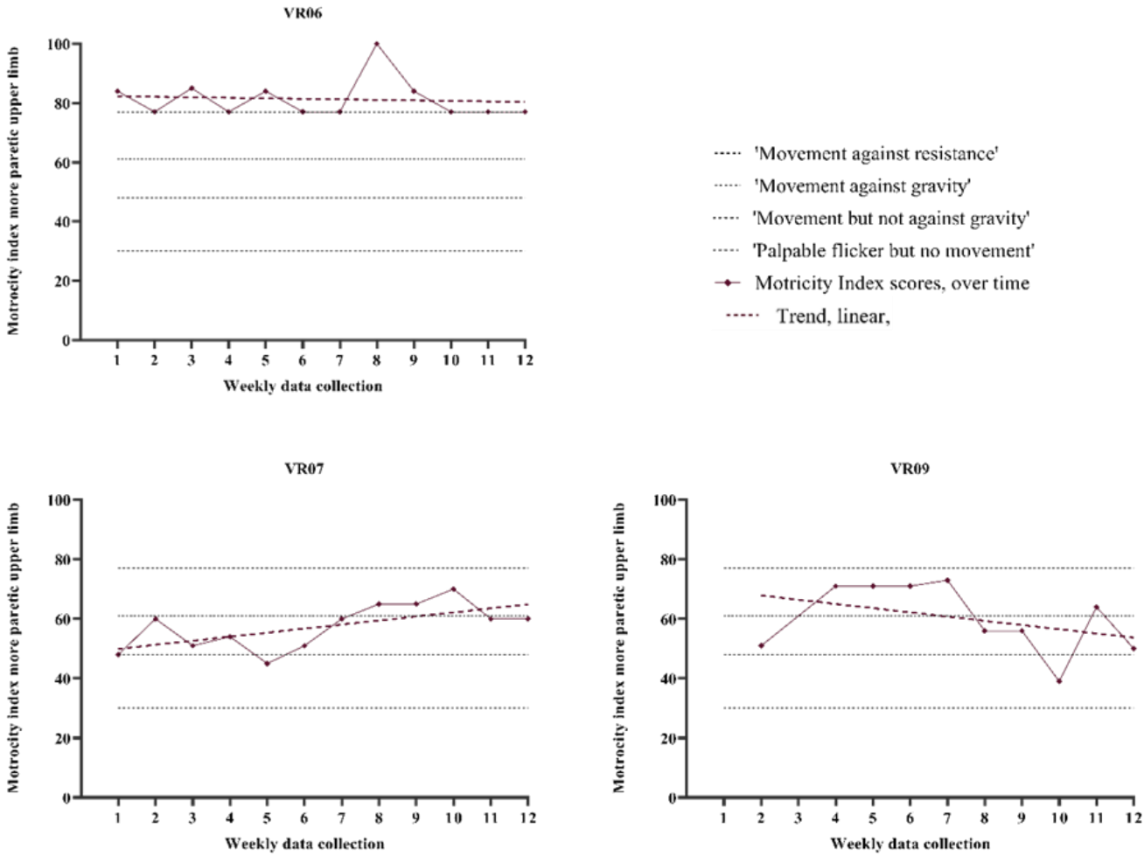
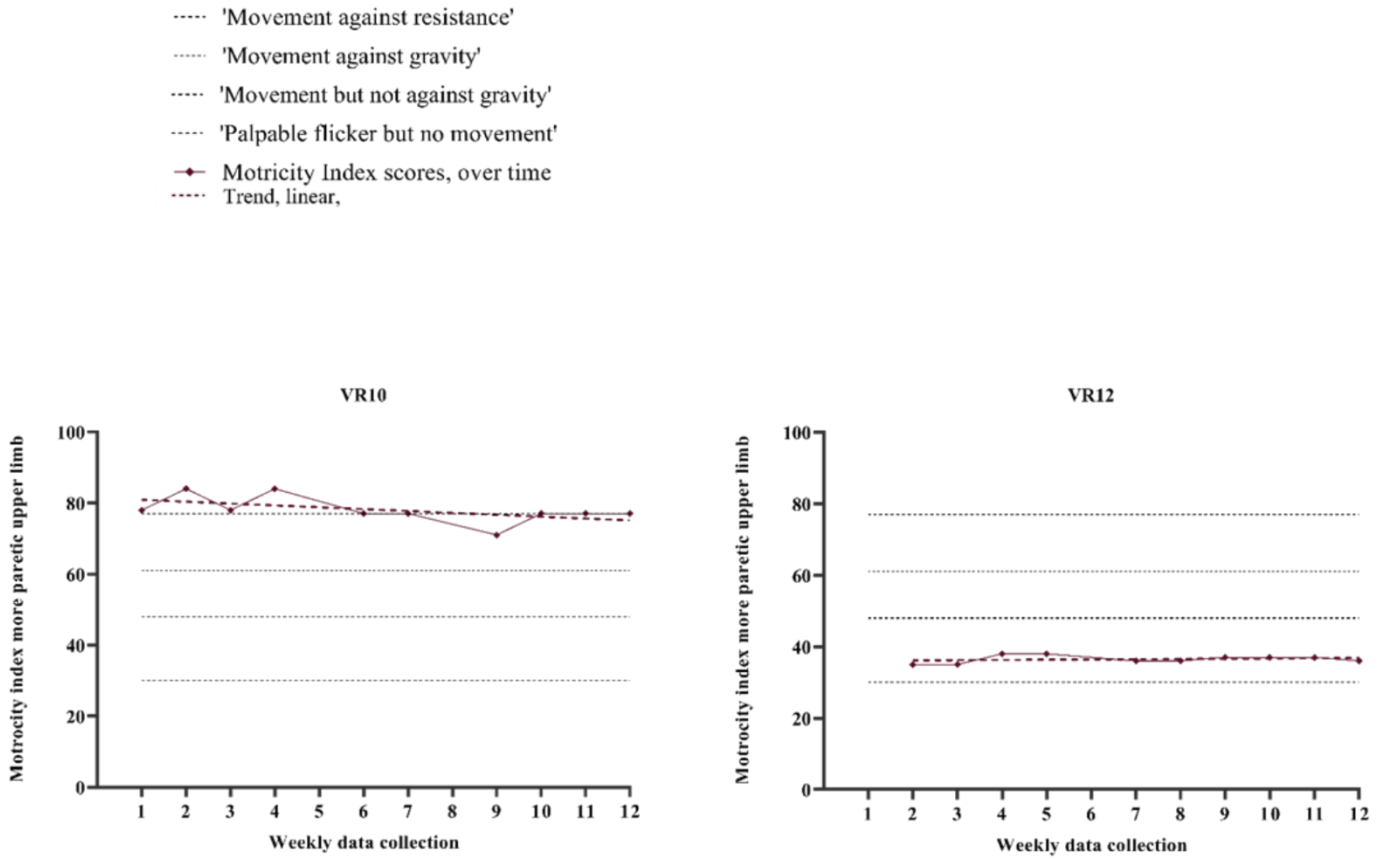


Figure 44: Weekly progress, motor impairment, more paretic, VR10 and VR12



7.4.8.3 Neural measures (i.e. time to onset of muscle activity)

The time to onset of muscle activity during the cup task for each stroke and healthy participant and their overall group means can be found in Appendix 8D to 17D[1]. The stroke participants varied during the intervention period, with increases and decreases in their time to onset for muscles in each weekly measure, and in comparison, with the normative values collected. In regard to the feasibility design of this study, the lack of validated MCID or prior literature on this measure, the small number of participants, missing data (particularly pre/post-intervention) meant further empirical investigation was not possible. The stroke participants' time to onset data is visualised in Figures 42 to 49 to demonstrate the variation in muscle activity over time and in comparison, with the normative values.

[1] **NB.** Participants VR01, VR03, VR08 and VR11 withdrew before intervention phase. No data was collected for VR08 as they withdrew before the first data collection measures (baseline 1). VR01, VR03 and VR11 had no valid trials.

Figure 45: Time to onset of muscle activity during reach to cup, VR02

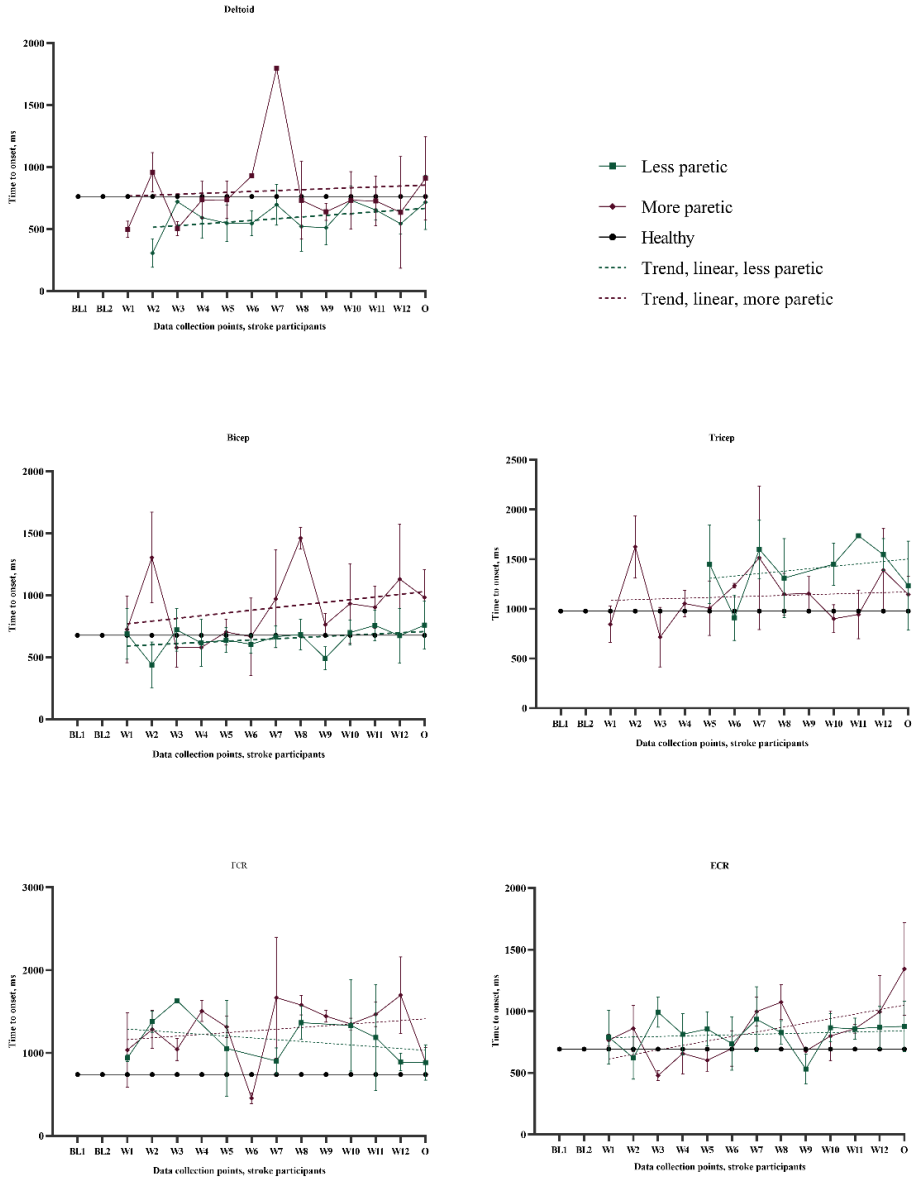


Figure 46: Time to onset of muscle activity during reaching, VR04

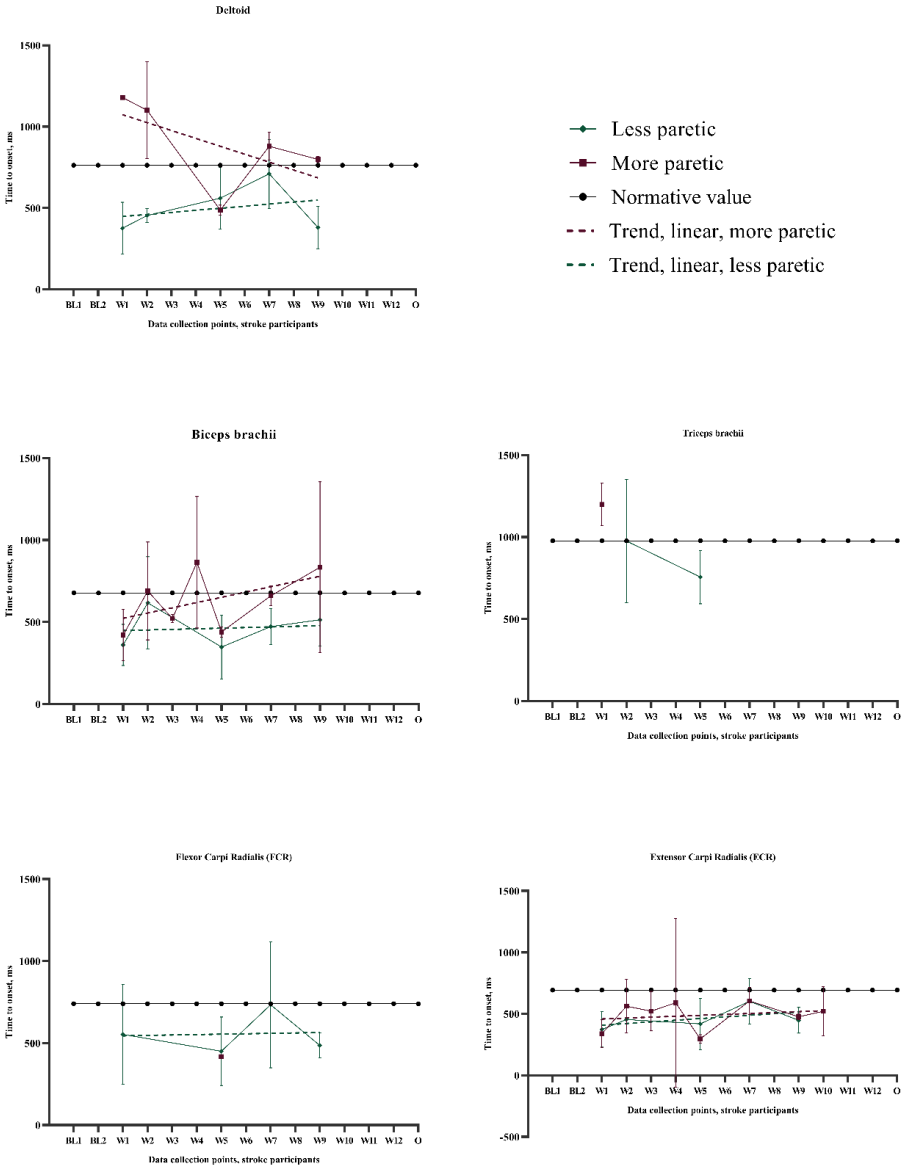


Figure 47: Time to onset of muscle activity during reaching, VR05

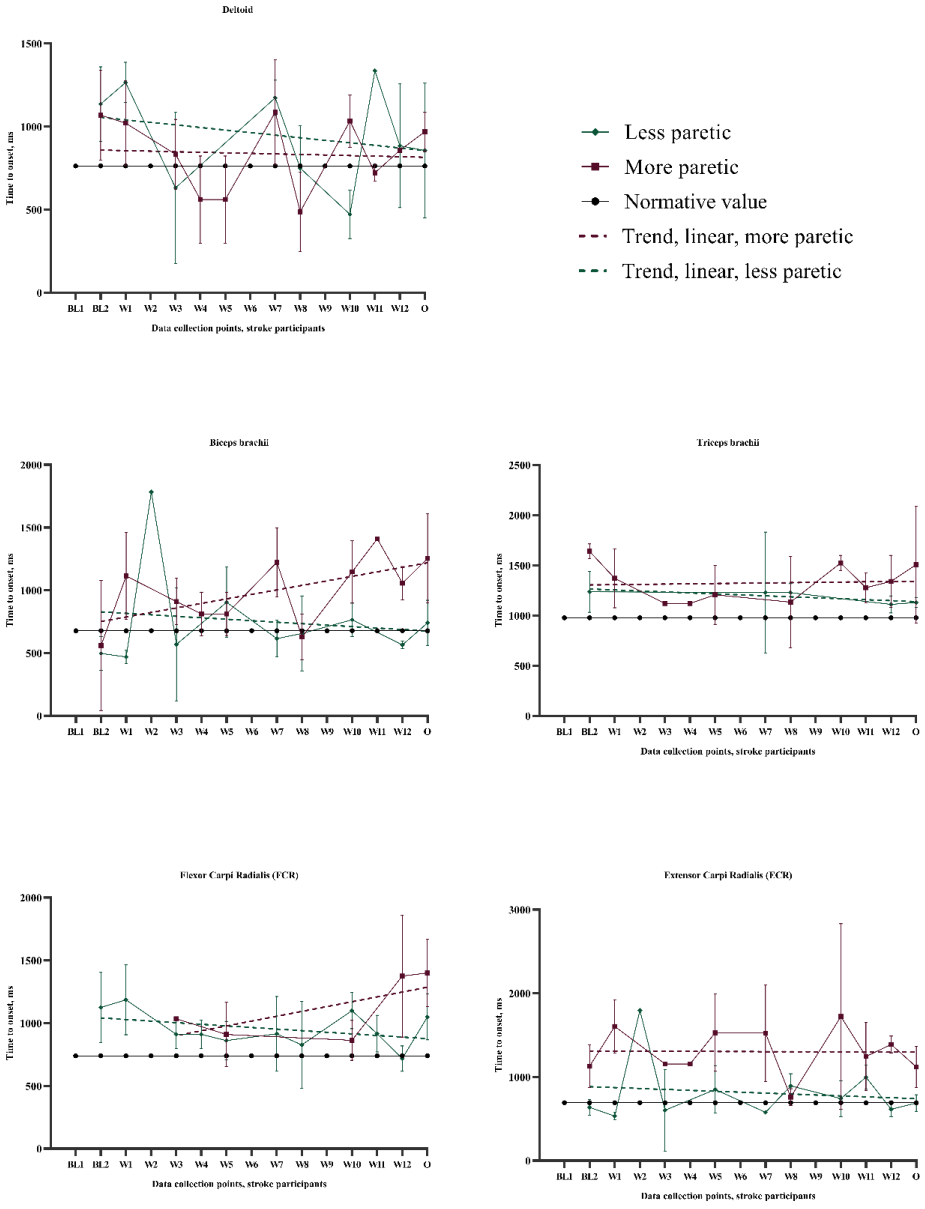


Figure 48: Time to onset of muscle activity during reaching, VR06

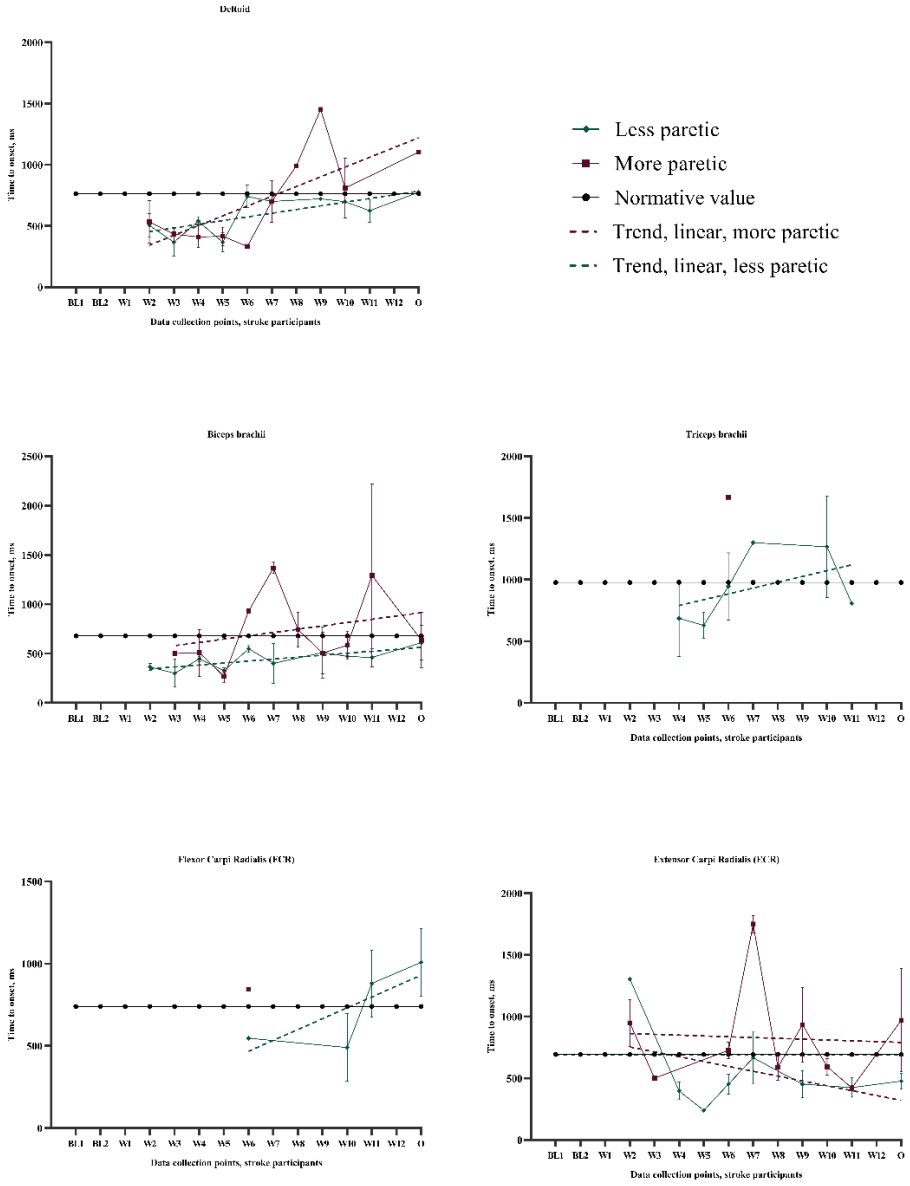


Figure 49: Time to onset of muscle activity during reaching, VR07

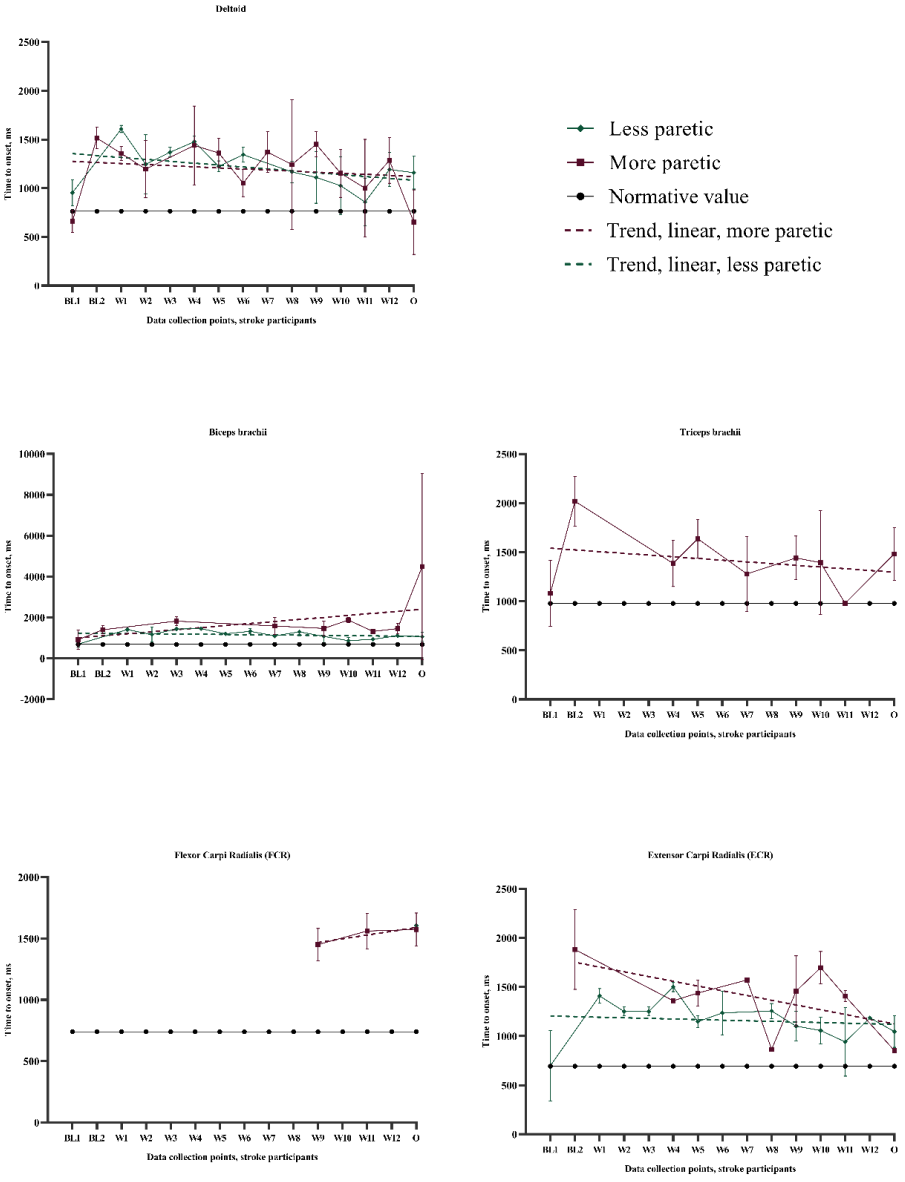


Figure 50: Time to onset of muscle activity during reaching, VR09

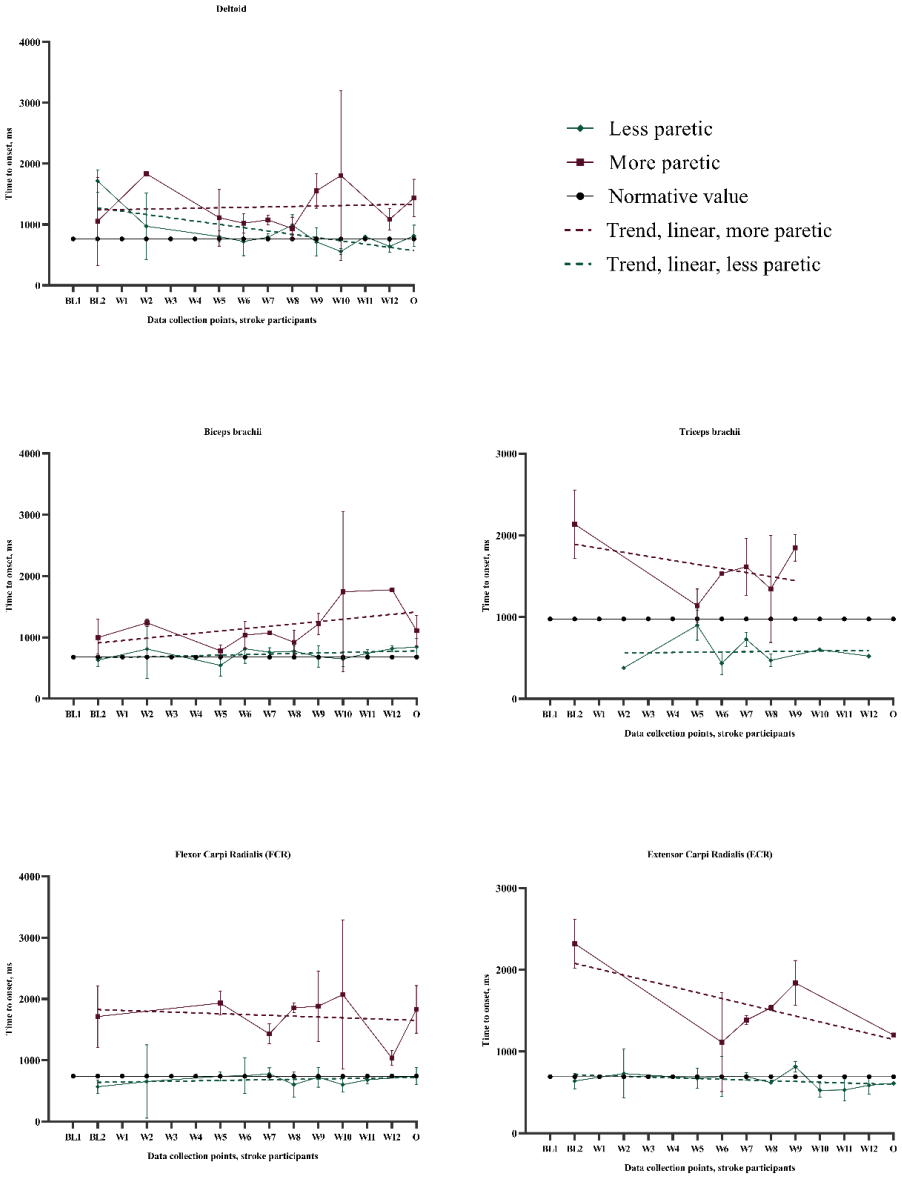


Figure 51: Time to onset of muscle activity during reaching, VR10

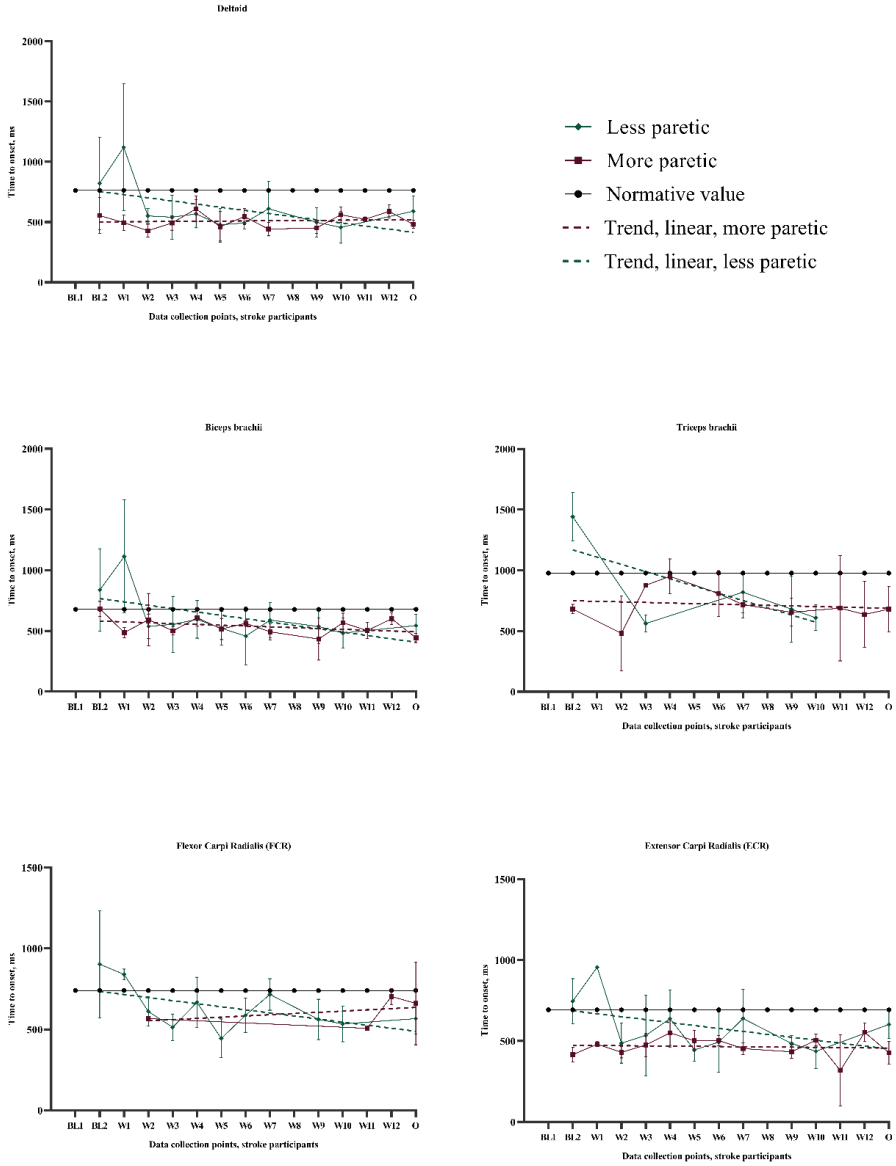
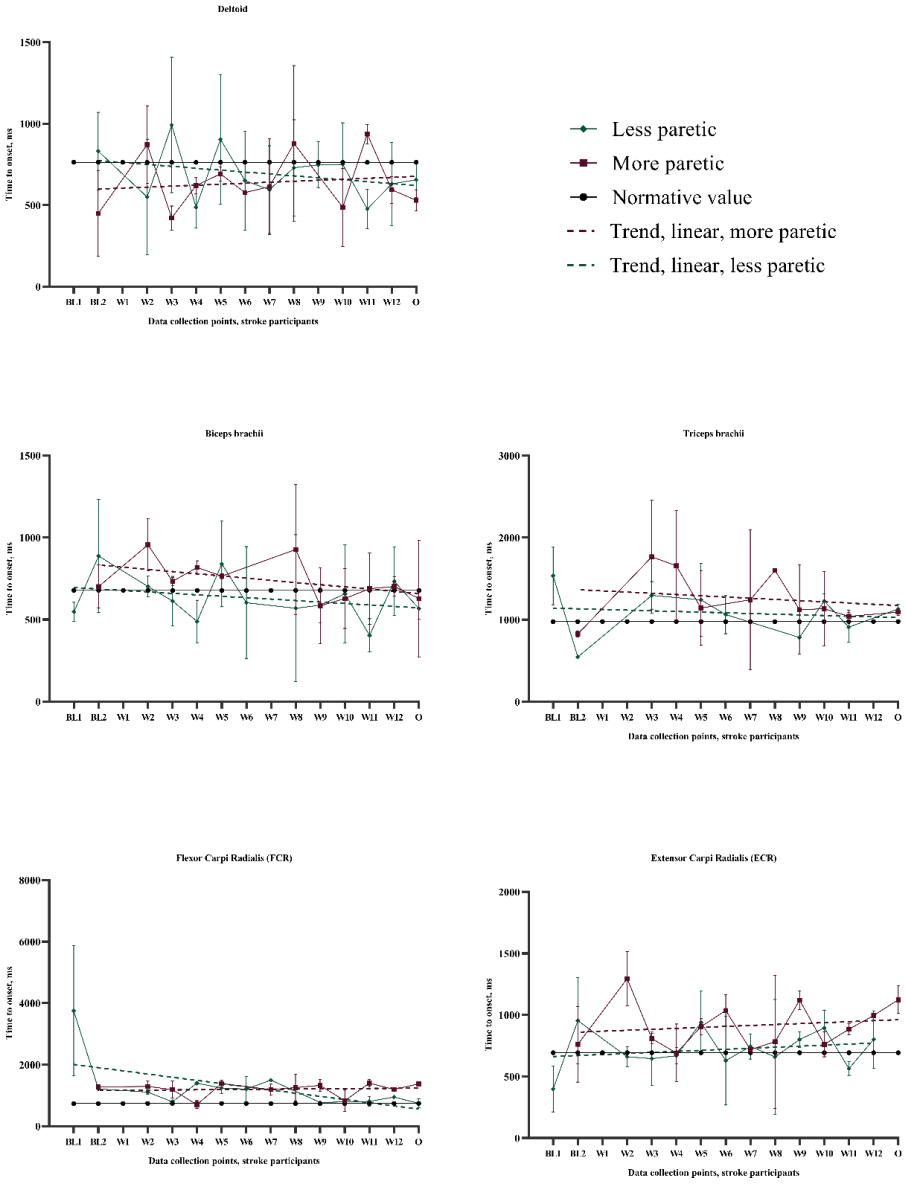


Figure 52: Time to onset of muscle activity during reaching, VR12



7.5 DISCUSSION

Phase III has demonstrated the feasibility of delivering upper limb stroke rehabilitation via virtual reality within the home (aim 3a). This is in line with prior research that reported the initial feasibility of VR therapy within the home (i.e. (Standen *et al.*, 2013; Tsekleves *et al.*, 2016; Warland *et al.*, 2019) and specifically for Kinect V2 (Microsoft, Washington, United States), similar to the Virtualrehab platform (Proffitt and Lange, 2015; Türkbey, Kutlay and Gök, 2017).

The use of GP practices as recruitment sites revealed limitations that need considering for future studies (objective 1). Each GP practice had differing resources available to undergo the recruitment procedure (i.e. time, personal, facilities) and the number of stroke survivors in their service area varied. Notable was the number of repetitions of prescribed exercise that were performed by participants (objective 2). The results also demonstrate the viability of adjusting prescribed training over time (objective 3). The adherence is higher than have been reported for routine therapy (Pomeroy *et al.*, 2016; Hunter *et al.*, 2018). The adherence data collected also meets the need for greater accuracy in dose reporting (Bernhardt, Hayward, *et al.*, 2019) and overall this data supports earlier findings that VR has the potential to increase the intensity of therapy (Brunner *et al.*, 2016).

The technical reliability of the Virtualrehab platform varied; key considerations were identified that future work needs to incorporate for future trials (objective 4). Further, it was viable to collect neuromechanical and behavioural data in the home (objective 5), although caution is needed for the neuromechanical data collection as a large percentage was invalid. Future work needs to allow for such lost trials. For the subsequent study to find the optimum therapeutic dose, randomisation of participants to different baseline durations is not indicated by the findings reported here. However, repeated measures of functional ability and motor impairment, including sEMG-derived muscle activity onset time are viable (objective 6). Finally, several participants noted initial changes in paretic upper limb motor function (five of seven participants) and functional impairment (two of six) (objective 7).

These findings strengthen the potential for the robust evaluation of delivering stroke rehabilitation via non-immersive virtual reality (Coscia *et al.*, 2019), and more specifically by the Virtualrehab platform, especially within the homes of stroke survivors (Hung *et al.*, 2016). Improved documentation and increased sharing of findings concerning research into home-based VR and gaming interventions, is important, including the approaches that have worked well as well as the practical difficulties encountered.

The strengths and limitations of the study need to be acknowledged. The sample size was smaller than anticipated, with data lost due to illness and scheduling difficulties. In addition, the amount of invalid data within the lab

was due to challenges encountered in refining the ‘Go’ signal procedure, rather than in relation to the feasibility. Finally, Microsoft withdrew support for the Kinect V2 in 2017/18. However, the sensor technology used in the camera is common to the majority of non-immersive systems, and the industrial collaborator developed the software.

The key strength is the robust, transparent reporting used within this feasibility trial. In addition, 12weeks was a longer than usual period for the intervention, allowing a more in-depth understanding of the usability and acceptability of such a device and study. This study also highlights the Virtualrehab platform’s potential for delivering stroke rehabilitation within the home setting, where the majority of stroke rehabilitation takes place.

7.6 CONCLUSIONS

The next research steps are: to recruit an adequately powered sample of healthy adults to establish the normative values for time to onset of muscle activity during the standardised reach-to-grasp task used in this study. These normative values will enable the robust assessment of whether stroke survivors move closer to normative values over time, in response to exercised-based therapy via the Virtualrehab platform. Then it will be possible to identify the optimum therapeutic dose of exercise-based therapy delivered using the Virtualrehab platform, followed by a clinical trial to investigate clinical efficacy.

8 PHASE III: PARTICIPANTS EXPERIENCES

8.1 INTRODUCTION

Phase III addressed the third research question (chapter 2, section 2.3):

How feasible is virtual reality-aided exercise-based training as a mode to deliver upper limb stroke rehabilitation within the home?

The research question was investigated with a feasibility study consisting of replicated single-case studies. This work aligns with the 'development', 'feasibility' and 'piloting' stages of the Medical Research Council's (MRC) Framework for Complex Interventions (Craig *et al.*, 2008).

The following chapter presents the study's qualitative methods, results and discussion; two semi-structured interviews carried out with stroke participants (specific research objectives 8 and 9).

8.2 RESEARCH AIMS

To answer the third research question, phase III aimed to:

Aim 3a: Determine the feasibility of delivering exercise-based upper limb stroke rehabilitation within the home via the Virtualrehab platform.

The specific research objectives reported in this chapter are:

8. To ascertain the acceptability of home-based task-orientated upper limb training via non-immersive virtual reality to stroke survivors in their own homes.

9. To establish the acceptability of participation in the study.

8.3 METHODS

The study's design, ethics, participant, recruitment and procedural details are provided in chapter seven. The following details procedures and analysis related to the qualitative components. A qualitative descriptive design was followed for the interviews (detailed in chapter six, section 6.3.1)

8.3.1 Procedures

8.3.1.1 Participant characteristics: Experience and confidence with technology

This data provided useful background information about participants' experience and confidence with technology against which responses related to the main study aims should be evaluated. Prior experience and confidence with using technology, similar to the Virtualrehab platform were obtained via a proforma using the same questions devised for phase I of this thesis (for full details refer to chapter six, section 6.3.4.3). In addition, a specific question

was included in baseline two to ascertain participants' understanding of the term 'virtual reality'. The term is widely used in society and often misconstrued in technology rehabilitation (as explained in chapter one, section 1.6).

8.3.2 Interviews

After the control and intervention phases, 1:1 semi-structured interview were carried out (topic guides are detailed in Table 48 and Table 49). Interviews were audio-recorded, with paper available in the event that a participant may wish to write their answer or help them construct a response, for example; those with aphasia. In addition, visual aids such as pictures identifying different hardware and software components of the Virtualrehab platform, were available to aid participant's recollection of the intervention. An hour was allocated for each interview, with time scheduled for breaks where necessary.

Table 48: Semi-structured topic guides for baseline two interviews

Interview 1: Semi-structured questions
Using virtual reality for stroke rehabilitation within the home
What do you think when you hear the term 'virtual reality'?
What do you think of using technology for stroke rehabilitation?
How do you feel about using such a device in your home?
Feasibility of the study procedures
How did you find the recruitment process?
How did you find the control period of the study?
How did you find coming back to the lab
How did you find the measures we completed today?
Is there anything that could have improved your experience in this study so far?

NB. Where required the semi-structured interviews were followed by appropriate prompts to generate discussion.

Table 49: Semi-structured topic guides for outcome interviews

Interview 2: Semi-structured questions
Delivering an exercise-based intervention through the Virtualrehab platform
What did you think of the physical device? (i.e. Microsoft Xbox Kinect and laptop)
What did you think about the graphics of the device? (i.e. background, instructions, feedback)
How did you find using the device? (i.e. set-up, ease of use)
How did you find the rehabilitation programme? (i.e. tailoring, perceived difficulty, motivation)
Using the Virtualrehab platform for stroke rehabilitation
What benefits and challenges could this potentially have for stroke survivors?
How do you feel about carrying out such a programme within the home environment?
Do you feel this can be implemented into stroke rehabilitation?
Feasibility of study procedures
How did you find the weekly visits to your home?
How did you find coming back to the lab?
How did you find the training to use the device?
How did you find the measures we completed today? (i.e. neural, motor function)
How do you feel about the overall length of this study?
Is there anything that could have improved your experience in this study?

NB. Where required the semi-structured interviews were followed by appropriate prompts to generate discussion.

8.3.3 Data analysis

8.3.3.1 Contextual information: Experience and confidence with technology

Descriptive statistics were used to describe the participants' characteristics responses.

8.3.3.2 Interviews

The same data processing and analysis that was used in phase I was carried out for the qualitative data (chapter six, section 6.3.5.3), a summary is given below of these steps.

Transcription

The interviews (interview 1, post control phase A; and interview 2, post-intervention phase B) were transcribed following an 'intelligent verbatim style'. In summary, the steps followed were:

Step 1. Listen to the recorded audio and consult any notes taken during the discussions;

Step 2. Transcribe using an intelligent verbatim method (chapter six, section 6.3.5.3);

Step 3. Compare the transcription to the audio recording, making alterations or changes as and when needed — repeated as often as required.

Step 4. A supervisor quality checked a random selection of transcription to increase accuracy.

The anonymised transcripts were imported into NVIVO 12 (QSR International technology and software solutions, Australia) for thematic analysis.

Thematic analysis

Then Braun and Clarke (2006) six-stage thematic analysis was applied to each interview (phase A and B were analysed separately), with themes being created underneath the research objective 8 and 9, respectively (a full explanation of this technique in chapter six, section 6.3.5.5). In summary, the steps followed were:

1. Familiarisation of the data;
2. Generating initial codes;
3. Searching for themes;
4. Reviewing the themes;
5. Defining and naming the themes;
6. Producing the report.

Research objective 9 was analysed with pre-determined overarching themes. The objective focused on the feasibility of participation in the study; thus, the data were coded underneath each of the following topics to generate subthemes.

1. The outcome measurement battery.
2. The frequency of measurement.
3. Travelling to the university research centre to undertake outcome measures at key time points in the study.
4. The period of participation during which no intervention was provided.
5. Whether there were aspects of participation that could be improved.

Quality check

To ensure the trustworthiness of the results a second coder is standard practice for quality checking qualitative data analysis (Nowell *et al.*, 2017). One of the thesis supervisors quality checked a random selection of transcripts (two from each interview phase) and applied thematic analysis to check the themes that had emerged from the Researcher's analysis. Any disagreements were discussed within the research team.

Research rigour

The same steps used in Phase 1 (chapter six, section 6.3.5.3) were followed to demonstrate rigour. Table 16 details the steps undertaken in chapter six, followed for this study.

8.4 RESULTS

Seven participants took part in both interviews; five of which completed both phases (Table 50).

Table 50: Stroke participant IDs from the baseline one and outcome measure interviews

Participant ID	Interview 1 (baseline two)	Interview 2 (outcome)
VR01	y	wd
VR02	y	y
VR03	wd	wd
VR04	y	wd
VR05	y	y
VR06	y	y
VR07	ill	y
VR08	wd	wd
VR09	y	y
VR10	ill	y
VR11	Fatigued	wd
VR12	y	y
Total	**7**	**7**

NB. wd, withdrew

8.4.1 Research rigour

The rigour and subsequent trustworthiness of the qualitative data collected are evidenced in Table 51. In addition, the research team met regularly at all stages of the study to improve the credibility of findings and challenge assumptions. Although these steps increase rigour, it is also important to consider the bias of the researcher background when considering qualitative data. As mentioned in chapter six, the Researcher's psychology and cognitive neuroscience background with prior experience volunteering in stroke support groups may have influenced the analysis and interpretation of the data. Further, the Researcher carried out the interviews and had built a prior rapport with the participants in the recruiting stage, which may have influenced their responses in interview 1. Finally, the Researcher visited the participants every week for the 12-week intervention, further building a rapport with them and thus would have potentially biased their responses in interview 2. As the Researcher carried out the intervention and the interviews, the open-ended questions were prompted for both positives and challenges of their experience, and they were encouraged to feedback for future trials and the next iteration of the Virtualrehab platform.

Table 51: Operationalisation of rigour within the study, Phase III

Means to support a demonstration of rigour	Operationalised within the study	Rigour demonstrated
1. Establish a rapport prior to commencing interviews;	The Researcher met with the participants before the data collection sessions to establish a rapport and develop a trusting relationship. Further weekly visits for the 12-week intervention facilitated the relationship built.	Credibility
2. Express compassion and empathy during interviews; 3. Prolonged engagement with participants throughout the study;	Active listening skills (of which the Researcher is trained in) were employed during the data collection sessions to express compassion and prolong engagement.	Credibility Credibility
4. Participants to verify the accuracy of the transcripts (member checking);	The participants were unable to verify the accuracy of the transcripts due to the potential added participant burden; a summary was given at the end of the data collection sessions to ensure their views were accounted and understood.	Credibility/confirmability*
5. Maintaining a reflexive journal;	The Researcher kept a reflexive journal which detailed the rationale for and methodological or procedural changes, and personal reflections were recorded.	Confirmability/Transferability
6. Establishment of an audit trail describing the study's procedures and processes;	In addition, an audit trail was kept for all data collection and analysis processes.	Confirmability/Dependability
7. Description of participants characteristics;	The participants' characteristics were described (chapter seven, section 7.4.1).	Confirmability

Means to support a demonstration of rigour	Operationalised within the study	Rigour demonstrated
8. Findings represent the data gathered and are not biased by the research, evidenced by the inclusion of direct quotations from participants;	Although the Researcher carried out the intervention and the interviews direct quotations used from participants, to ensure representativeness of data (section 8.4.2 and 8.4.3).	Confirmability
9. Purposeful sampling is used;	A non-probability purposeful sampling technique was used (chapter seven, section 7.3.3).	Transferability
10. Providing sufficient study details so recreation can occur;	Sufficient study details have been provided to allow for recreation (chapter seven and eight).	Transferability
11. Rich description is shown in the findings;	In-depth information (i.e. rich description) was gained from the discussions, shown via the thematic analysis, which addressed the research aims (section 8.4.2 and 8.4.3).	Transferability
12. Account for any changes that occur in the study.	An audit trail was kept to account for any changes within the study.	Dependability

NB. *Despite not checking the transcripts participants found the summaries accounted for their discussions, and thus it can be argued that credibility/confirmability was demonstrated

8.4.1.1 Confidence with technology

The majority of stroke participants felt confident in using a TV, a key aspect of setting up and using the Virtualrehab platform (81%) (Table 52). Almost half of the participants felt confident with commonly used technology that requires similar features of the platform (i.e. using Wi-Fi). However, there was a reported lack of confidence in stroke participants with using the computer (27%), another key aspect of the Virtualrehab platform.

Table 52: Stroke participants reported confidence with technology

Technology	Confident	Unsure	Unconfident	Never used
TV	9 (81.82%)	0	1 (9.09%)	1 (9.09%)
Mobile	6 (54.55%)	1 (9.09%)	2 (18.18%)	2 (18.18%)
Tablet or iPad	5 (45.45%)	0	3 (27.27%)	3 (27.27%)
Wi-Fi	5 (45.45%)	1 (9.09%)	2 (18.18%)	3 (27.27%)
Email	5 (45.45%)	1 (9.09%)	2 (18.18%)	3 (27.27%)
Internet	4 (36.36%)	1 (9.09%)	3 (27.27%)	3 (27.27%)
Computer	3 (27.27%)	1 (9.09%)	4 (36.36%)	3 (27.27%)

NB. number of respondents (percentage of the group)

8.4.1.2 Experience with technology

The stroke participants had no prior experience with the Kinect V2 sensor (Microsoft, Washington, United States), the main component of the Virtualrehab platform (Table 53). This was also true for other technology similar to the platform's hardware; only 27% of participants had experience with mobile games.

Table 53: Prior experience with technology similar to the Virtualrehab platform

Technology	Experienced	Unsure	Not experienced
Xbox	0	0	11 (100%)
Wii	1 (9.09%)	0	10 (90.91%)
Computer game	1 (9.09%)	0	10 (90.91%)
PlayStation	1 (9.09%)	0	10 (90.91%)
Mobile games	3 (27.27%)	0	8 (72.73%)

8.4.1.3 Prior knowledge of the term 'virtual reality'

Interview 1, baseline 2, included a question "what does the term virtual reality mean to you" to explore the participants' sample prior experience, expectations or assumptions about virtual reality. The prior bias that participants bring to the interviews will influence the themes arising; thus, it is important to understand this characteristic.

Of the seven who responded, three had no prior knowledge and felt the term was '*meaningless*' to them. Another three participants felt virtual reality was an environment that enables someone to '*attempt something that is not real*'. Finally, one participant identified virtual reality with computers, technology and online monitoring and updating.

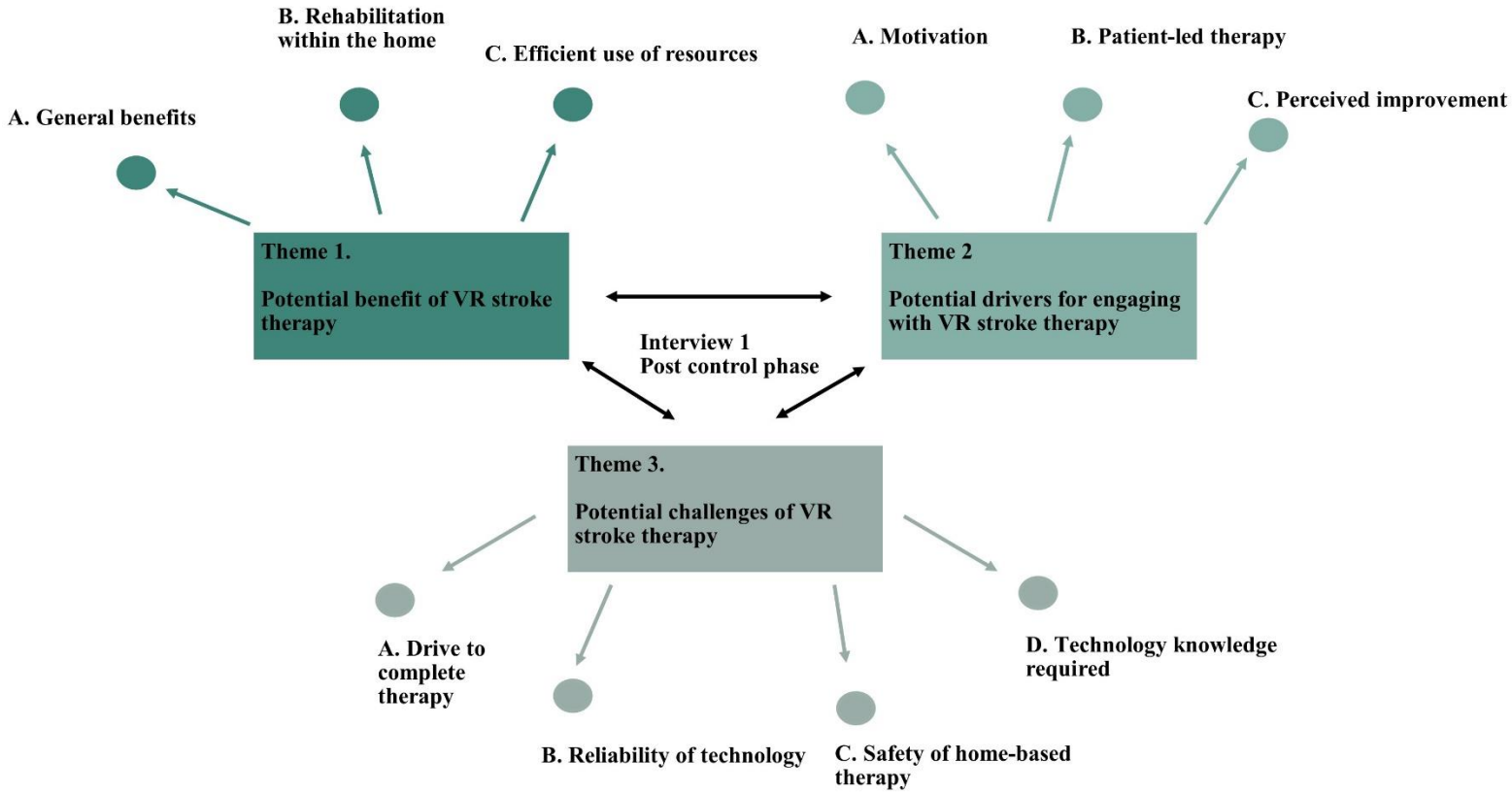
8.4.2 Objective 8. To ascertain the acceptability of home-based task-orientated upper limb training via non-immersive virtual reality (VR) to stroke survivors in their own homes.

The following section will describe the results of a thematic analysis of interview 1 (phase A, post control period, baseline two) and interview 2 (phase B, post-intervention period, outcome).

8.4.2.1 Interview 1: Phase A, post-control phase, themes

When participants were asked about the potential acceptability of delivering upper limb exercise-based stroke therapy within the home via virtual technology, three overarching themes arose (Figure 53). Participants identified the potential benefits of using virtual reality in stroke therapy (theme 1). They also suggested potential drivers of engagement for patients when delivering therapy in the home via technology (theme 2). Finally, participants cautioned several potential challenges that may prevent stroke survivors from engaging with such therapy (theme 3). The following details each theme with its appropriate subthemes.

Figure 53: Thematic map, interview 1, objective 8



8.4.2.1.1 Theme 1. Potential benefit of VR stroke therapy

Stroke participants identified potential benefits for utilising VR within stroke therapy. Three subthemes were identified as detailed in Table 54. The participants identified general potential benefits of using technology within stroke rehabilitation; overall participants felt positive about using such devices to aid their therapy. The participants also focused on the benefit of delivering rehabilitation within the home, specifically the potential of lowering the travel burden on participants. Participants felt that carrying out therapy within their home at a time of their choosing would allow additional control and autonomy over their rehabilitation. Finally, discussions identified the potential of technology as efficient use of therapy resources. Participants felt that having remote monitoring and updating features would lower the burden on clinicians while maintaining a daily therapy prescription.

Table 54: Objective 8. Interview 1 (Baseline two). Theme 2. Potential benefit of VR stroke therapy

Subtheme	**Illustrative quotes**
A. General benefits	*I think technology is improving every day and it's something that may help stroke survivors a lot in other kinds of rehabilitation as well in the future.*
B. Rehabilitation within the home	*I think it's probably better to do it at home than you know to travel to somewhere or do it somewhere else.*
C. Efficient use of resources	*It's obviously a much more efficient way of doing. If you come every day, it's too time consuming.*

8.4.2.1.2 Theme 2. Potential drivers for engaging with VR stroke therapy

Stroke participants identified potential drivers that would facilitate a patient's engagement with VR stroke therapy. Three subthemes were identified as detailed in Table 55. Carrying out repetitive therapy plans in a gamified, visually engaging manner was thought to be more motivating than traditional exercises carried out from therapy sheets. It was suggested that this method of delivery could promote improvement, a key driver for stroke survivors when choosing a therapy. Finally, the chance to input into their therapy prescription was seen as a crucial aid to facilitate adherence.

Table 55: Interview 1. Objective 8. Theme 1. Potential drivers for engaging with VR stroke therapy

Subtheme	Illustrative quotes
A. Motivation	*I think it enthuses you, to do things.*
B. Patient-led therapy	*I can do it at the moment in the day when I feel like I could cope with it, I like that. It's freedom for me and less pressure on the physio.*
C. Perceived improvement	*I think it's great to try something different from physiotherapy and something that I think may stimulate my brain to do more and to find new pathways and new challenges.*

8.4.2.1.3 Theme 3. Potential challenges of VR stroke therapy

Stroke participants identified potential challenges for delivering stroke therapy via VR. Four subthemes were identified as detailed in Table 56. Participants voiced concern over the technical knowledge and expertise required to use a virtual reality system within the home. The ability of participants to set-up, use and troubleshoot the technology was discussed. In particular, participants were cautious about potentially increasing the burden on friends and family if they needed help using the devices. Participants also cautioned over the safety and reliability of technology within the home, particularly concerning the reliability, maintenance and uptake of such technology. There was particular mention to the training and support required not only from clinicians, to ensure safe movement, but also for the technical requirements of the platform.

Table 56: Objective 8. Interview 1 (Baseline two). Theme 3. Potential challenges of VR stroke therapy

Subtheme	**Illustrative quotes**
A. Drive to complete therapy	*I think the challenges are what you feel in your mind. Challenges of getting things improved and getting things better that is the only challenge I can see anyway.*
B. Reliability of technology	*As long as it works, I don't see a problem*
C. Safety of home-based therapy	*It's only if it goes wrong really, I think that's the biggest I don't sometimes perhaps be over ambitious, I think part on the participants part is trying to do it for too long. So, it's a case of pacing yourself and taking your time, and not trying to do it all at once. Those are the things, but they are easy remedied.*
D. Technology knowledge required	*Being able to set-it up correctly*

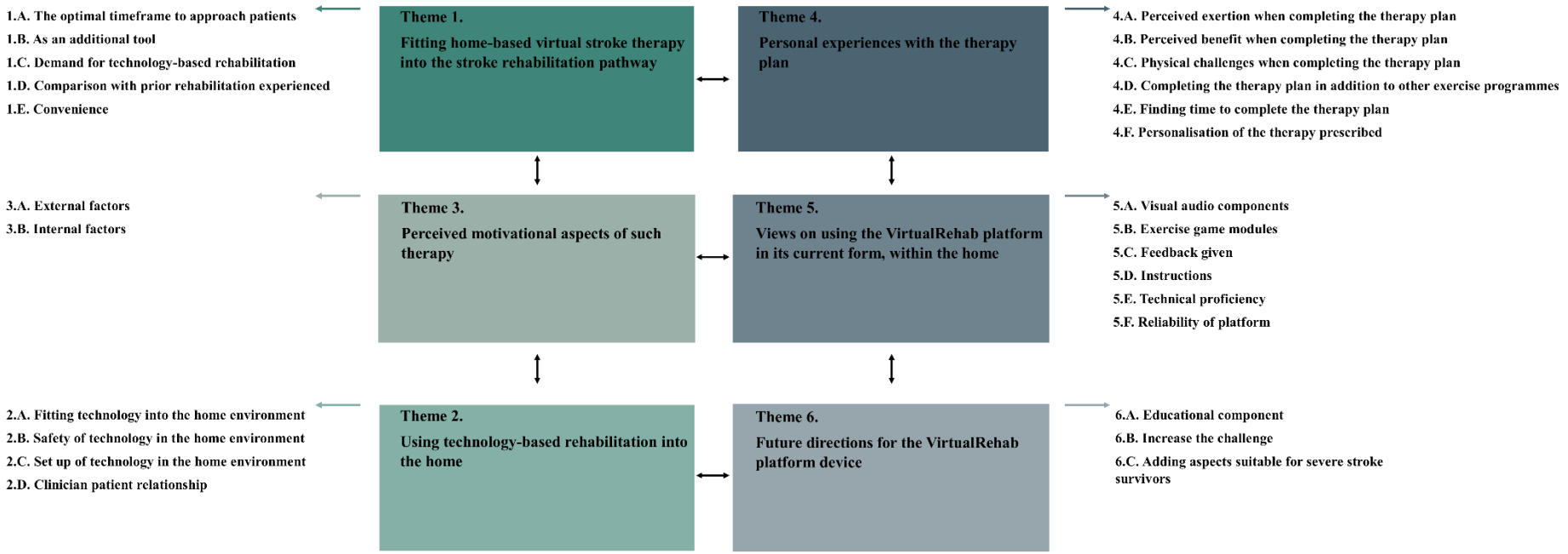
8.4.2.2 Interview 2: Phase B, post-Intervention phase (Outcome)

When participants were asked about the potential acceptability of delivering upper limb exercise-based stroke therapy within the home via virtual technology, six overarching themes arose visualised in Figure 54.

- Theme 1. Fitting home-based virtual stroke therapy into the stroke rehabilitation pathway
- Theme 2. Using technology-based rehabilitation into the home
- Theme 3. Perceived motivational aspects of such therapy
- Theme 4. Personal experiences with the therapy plan
- Theme 5. Views on using the Virtualrehab platform in its current form, within the home
- Theme 6. Future directions for the Virtualrehab platform device

The following described each theme, its subthemes alongside illustrative quotes.

Figure 54: Research Objective 8. Interview 2



8.4.2.2.1 Theme 1. Fitting home-based virtual stroke therapy into the stroke rehabilitation pathway

Stroke participants discussed fitting virtual stroke therapy into the rehabilitation pathway. Five subthemes were identified as detailed in Table 57. The main message from stroke survivors was the need for clinical input into home-based virtual reality therapy. Participants felt the Virtualrehab platform had the potential to facilitate the delivery of therapy but required clinical oversight. Overall, they agreed that demand for technology-based rehabilitation does exist but requires an individualised approach in offering such equipment to patients, as everyone's 'journey is different'. Finally, in comparison with prior rehabilitation, they had experienced they felt the Virtualrehab platform was engaging, motivating and provided a convenient mode of carrying out therapy, within their own time at home.

Table 57: Objective 8. Interview 2 (Outcome). Theme 1. Fitting home-based virtual stroke therapy into the stroke rehabilitation pathway

Subtheme	**Illustrative quote**
A. The optimal timeframe to approach patients	*I think once they've gone home and perhaps after they have had the own physio package it should be offered.*
B. As an additional tool	*I think a device like this can be part of a recovery programme helping stroke patients recover will help them quite a lot; but of course, you will need other things to go along with it.*
C. Demand for technology-based rehabilitation	*It's certainly helped me so I imagine it must help other people, if they have got the right attitude. They have to want to do it, it would make little difference to me if I didn't want to do it. I mean you know it's just the way I am. I don't like doing anything if there is no point to it and there certainly was a point to this, obviously cos you can see the difference it has made to my shoulder.*
D. Comparison with prior rehabilitation experienced	*Doing these exercises [referring to the Virtualrehab platform plan] helped me in that way, I now want to do that, I probably would not have thought of them otherwise. I mean it is pointless now not doing any exercise with my shoulder because I might not get any better, I suppose.*
A. Convenience	*Yea it's good. If I had something like that, one of those boxes in the home all the time I would do it as and when I wanted to do it.*

8.4.2.2.2 Theme 2. Using technology-based rehabilitation into the home

Stroke participants discussed the use of technology rehabilitation within the home. Four subthemes were identified as detailed in Table 58. Stroke survivors felt that using technology within the home showed promise. They felt their environments adapted well to the Virtualrehab platform, and they could use it with ease. Several participants raised concern over the safety of not only carrying out exercise without clinical supervision but of the equipment within their home in the presence of small children and animals. They proposed a lighter, more portable version with strict clinical oversight would alleviate some concern. Further, the potential lack of human contact was discussed as a challenge for survivors completing the therapy plans and carrying out correct movement, as opposed to doing so in the presence of a clinician. Participants reiterated that such devices would aid stroke therapists and could not replace those interactions or relationships.

Table 58: Objective 8. Interview 2 (Outcome). Theme 2. Using technology-based rehabilitation into the home

Subthemes	Illustrative quotes
A. Fitting technology into the home environment	*Yea it was fine it didn't bother me, it was a bit unwieldy with the cables but it didn't get in my way at all.*
B. Safety of technology in the home environment*	*Not really as long as you are being safe, as long as you when you first have a stroke it depends on how bad you are. I mean if you are really bad you would have to do the exercises lying on the bed, and lift your legs up, or arms up. As long as you have someone there and you don't try and get out of bed or something.*
C. Set-up of technology in the home environment	*The first couple of times it took a little time to adjust the sensors and get the right position, but after using it a couple of times it was fine. The only problem we had was with a little toddler we could not keep the equipment there we had to put it away because they could have damaged that. But we got used to it quite quickly.*
D. Less human contact	*Maybe not so personalised and when you have a physiotherapist with you, they can see exactly how you are behaving at the moment and the only disadvantages that I can see is that I can probably, this is more like for the public in general, and it's like either you use it or you don't. Well if you can adjust it like we did you do then its good*

8.4.2.2.3 Theme 3. Perceived motivational aspects of such therapy

Stroke participants discussed potential motivational aspects of using virtual rehabilitation. Two subthemes were identified as detailed in Table 59. Overall stroke survivors found their therapy plans and using the Virtualrehab platform to be motivating, challenging and engaging; which importantly did not decrease over time. In particular, participants praised the support they received from their family and friends and the enjoyment they gained carrying out therapy within their company. Finally, participants suggested internal motivational factors had helped to keep them engaged during the 12-week intervention period; particularly the idea of competing with themselves and working towards personal improvement goals.

Table 59: Objective 8. Interview 2 (Outcome). Theme 3. Perceived motivational aspects of such therapy

Subtheme	Illustrative quotes
A. External factors (i.e. family, the platform itself)	*My wife she is my carer and personal assistant let's say or physiotherapist. She thought it was really good and kept motivating me to do it, and she helped me set-it up, especially in the beginning, after a couple of times I could do it myself.*
B. Internal factors (i.e. trying to improve impairment; trying to compete with themselves)	*Trying to better what you had done before, it made you do different movements that perhaps you wouldn't have done. Like the rowing, and the reaching to stop the water getting in. So you have to learn to reach.*

8.4.2.2.4 Theme 4. Personal experiences with the therapy plan

Stroke participants discussed their personal experiences with the 12-week therapy plan delivered with the Virtualrehab platform. Six subthemes were identified as detailed in Table 60. Participants felt positive about the exertion the therapy plan require during the 12-weeks, the personalised approach with their input allowed them to set their challenge and update it when required over the intervention period. In addition, all stroke survivors felt they had improved during the intervention period; this perception was an important motivator for them to complete the sessions as often as they could. They were aspects of the therapy plans that participants felt were challenging, and they did not enjoy, this was mitigated when they proposed changes each week and once more shows the importance of their voice in prescribing therapy. Several participants were carrying out additional exercise programmes during the intervention period (i.e. personal trainer). Participants mentioned that they separated the two exercise programmes on different days. However, this meant they did not complete all of the prescribed Virtualrehab platform therapy days, they often increased the number of repetitions to compensate or completed the plans multiple times a day.

Table 60: Objective 8. Interview 2 (Outcome). Theme 4. Personal experiences with the therapy plan

Subthemes	Illustrative quotes
A. Perceived exertion when completing the therapy plan	*It was as difficult as I wanted to make it and I prefer to challenge me a bit, which I think it did.*
B. Perceived benefit when completing the therapy plan	*I think it go easier, better I could do it better as my arm was improving or my brain in this case for the exercises that I was doing. Even though that one I couldn't raise my arm as much as I wanted but my arm got use to the position, 90^{o} I got used to.*
C. Physical challenges when completing the therapy plan	*Yea that was one I got a bit fed up with, the one lifting your arm above your head, I mean it starting hurting your back because I was trying so hard it was giving me back pain so we took that one off in the end.*
D. Completing the therapy plan in addition to other exercise programmes	*I tried to separate them, so I would do the trainer exercises in the morning where yours I did do in the afternoon, and if I couldn't do yours, I tended to do exercises on my legs then.*
E. Finding time to complete the therapy plan	*I don't it every day, if I could do it every day. I only missed a couple of days. I really enjoyed doing the game as it made me do something otherwise if I didn't do it, I wouldn't have done nothing.*
F. Personalisation of the therapy prescribed	*I think that's perfect when we discussed what we could do different, it helped me more. I think it did help a lot from one week to the other it was perfect yea.*

8.4.2.2.5 Theme 5. Views on using the Virtualrehab platform in its current form, within the home

Stroke participants discussed their views on the current version of the Virtualrehab platform. Five subthemes were identified as detailed in Table 61. Overall, they praised the graphics of the virtual environment and the instructions/feedback provided. The exercise and games offered were generally viewed positively, even for participants who had no particular interest in games felt the perceived potential to help their impairment would encourage them to take part. Stroke survivors also felt they received adequate instructions on using the platform and were confident during the intervention period in its set-up and use. In addition, survivors felt the feedback the platform provided was encouraging and allowed them to compete with their prior scores; although they noted that more explanation was needed in terms of the exact meaning of the scores. Finally, participants raised concerns with the reliability of the equipment and how certain challenges led to lost intervention days; they noted that this, in particular, would be a key barrier in the uptake of such devices for stroke survivors.

Table 61: Objective 8. Interview 2 (Outcome). Theme 5. Views on using the Virtualrehab platform in its current form, within the home

Subtheme	**Illustrative quotes**
A. Visual, audio components	*Graphics I think were quite good, I like the especially the one with the kitchen objects and balloons. I think on this kind of things colours help a lot, bright colours help stimulate you more and make you want you to do more and make it easier for you to do the exercises. I think the balloon one and the kitchen they had nice colours.*
B. Feedback given	*Yea it was always good to feel rewarded when you say you did a good job or something. Yea I think it was important yea.*
C. Instructions	*To be honest I think for that one where you raise your arms [referring to the exercise module] I think it took too long, I think it should be a bit shorter the time you wait for the, at least for myself. It should be more time on the exercises and less time on the waiting bit.*
D. Technical proficiency	*How much do you need really, I mean you came in with instructions and they were so easy to follow, I probably looked at them the first two times and never looked at them again, I knew what I was doing.*
E. Reliability of platform	*I think the software could be refined, as you know I had one or two problems with it. Especially the last one, we had to hold down the [researcher mentioned sinking boat game] ah yes that's the one. That never went to well, most of the problem was on my [less paretic] hand rather than my [more paretic hand].*

8.4.2.2.6 Theme 6. Future directions for the Virtualrehab platform device

Stroke participants discussed future directions for the next iteration of the Virtualrehab platform. Three main subthemes were identified as detailed in Table 62. Participants suggested adding an educational component could aid stroke survivors and their families in the autonomy of rehabilitation. In addition, they felt more options were required in terms of different difficulty or challenge levels with the platform for changes to the therapy plan over a long period; with the recommendation that options are included for those with more severe impairments to be able to use the device and potentially benefit.

Table 62: Objective 8. Interview 2 (Outcome). Theme 6. Future directions for the Virtualrehab platform device

Subtheme	Illustrative quote
Educational component	*Yea what's happened to them, that would be a good thing, I think that would be good. I mean when I first had my stroke, I thought right two weeks later I will be running about again, but that didn't happen I didn't know. Now six years down the line I still can't do it, it would be nice to know to be more educated on it*
Increase the challenge	*The games that you set for me, were enjoyable but they need to get harder.*
Adding aspects suitable for severe stroke survivors	*Even if you had something like this on your TV when you have first had your stroke you are lying in your bed. But if you had something like this come up on TV in the bedroom you could lie on the bed and move your legs and arms, so a programme like that would be good. You can't obviously jump about too much when you have first had a stroke but if you are lying in your bed and starting to move your legs and arms that would be a good thing. I mean when I first had the stroke I could not, wouldn't have been able to do this. I was lying in my front room on the bed for seven months. But if they had been something like that on the TV to exercise your legs and arms then I would've done it instead of lying there watching TV.*

8.4.3 Objective 9. To establish the acceptability of participation in the study, specifically investigating the views of stroke survivors.

The semi-structured interview asked questions relating to the following feasibility of participating in the study. The data were analysed according to the initial topics (overarching themes) which were discussed, for each of them subthemes were generated. Any other themes any arising during the intervention relating to this objective but not the specific feasibility aspects were coded under ‘other’ as the sixth overarching theme.

1. The outcome measurement battery.
2. The frequency of measurement.
3. Travelling to the university research centre to undertake outcome measures at key time points in the study.
4. The period of participation during which no intervention was provided.
5. Whether there were aspects of participation that could be improved.
6. Other.

The following details each topic with their subthemes and an overview of stroke survivors views from both intervention 1 (baseline 2, pre-intervention) and interview 2 (outcome, post-intervention),.

8.4.3.1.1 Theme 1. The outcome measurement battery

This overarching theme related to participants' views of the outcome measurement battery carried out throughout the study. Two subthemes arose relating to this topic, detailed in Table 63. Overall, the measurement battery was acceptable to participants in both interviews. The participants were interested in learning about the tasks, tasks, equipment and purpose of the data being collected. The only concern raised was the reliability of the data collection equipment; in interview 1 several participants had witnessed challenges with the measures (i.e. laptops crashing, sEMG error). It should be noted that this concern was not raised in interview 2, as there were less incidences.

Table 63: Objective 9. Theme 1. The outcome measurement battery

Subtheme	Interview	Illustrative quote
A. General positives of the measurement battery	1	*I was fascinated by them that's all and when we had problems with them last time and you were taking them and looking at the numbers and saying oh yea that one goes over there, I was kind of joining in a bit and I liked that, I thought it was fascinating*
	2	*I thought they were quite interesting actually, again I did try, and the following week try and beat the time, or have a better result every week as it went on. I think that did happen the way I see it.*
B. The equipment was unreliable	1	*It was ok, i mean it was a bit long, because some of those things you had to repeat, for reasons that they did not work out exactly how it should.*
	2	*n/a*

NB. **Interview 1,** following control phase A, baseline two.

Interview 2, following intervention phase B, outcome.

n/a. Not applicable.

8.4.3.1.2 Theme 2. The frequency of measurement

This overarching theme related to participants views of the frequency of the measurements carried out during the study (i.e. three lab-based measurements and 12 weekly home-based). Three subthemes arose relating to this topic, detailed in Table 64. In the first interview, participants discussed the time it took to complete both baseline measurement batteries, although they felt it took a long time they did not have a problem with carrying them out or fitting the baselines into their schedules, whereas in interview 2 participants were positive about the time it took to complete the measurements (i.e. weekly visits to their home). In general, participants felt the weekly visits were useful to allow them input into their therapy prescription.

Table 64: Objective 9. Theme 2. The frequency of measurement

Subtheme	Interview	Illustrative quote
General positives	1	*n/a*
	2	*They were good, I looked forward to them.*
Time positives	1	*The time is no problem; I have got plenty of time.*
	2	*I don't mind, obviously I'm not working now so I don't have a problem with it, I've got more time now than I have ever had. I have appointments and that's about it. I'm not working 24/7 anymore so that's about it. You are coming out to see me is a not a problem.*
Time negatives	1	*I enjoyed the experience. It was just a wee bit too long. I think if you can reduce some of it, somehow reduce it to an hour and a half. It just went over the edge for me. A bit too long. I was knackered that night.*
	2	*n/a*

NB. **Interview 1,** following control phase A, baseline two.

Interview 2, following intervention phase B, outcome.

n/a. Not applicable.

8.4.3.1.3 Theme 3. Travelling to the university research centre to undertake outcome measures at key time points in the study

This overarching theme related to participants' views of travelling to the university research centre (UEA MovExLab). Two subthemes arose relating to this topic, detailed in Table 65. Interview 1 participants felt travelling to the UEA MovExLab was generally a positive experience but challenging the first time, but this was mitigated by detailed parking instructions given, and the Researcher meeting them at the car park to show them to the lab. It should be noted that several participants felt the travel requirements put an additional burden on their carer as they could not drive themselves. The participants in interview 2 did not highlight any challenges in travelling to the UEA MovExLab.

Table 65: Objective 9. Theme 3. Travelling to the university research centre to undertake outcome measures at key time points in the study

Subtheme	Intervention	Illustrative quotes
Positives	1	*It was also quite easy we didn't know exactly where it was but you were there to guide us exactly to the right place and in the end we ended up getting to know how to get there and for later meetings we had so it was quite easy with your help.*
	2	*Yea I came in 12 times for [reference to prior research study] and came in three times for this. I enjoy coming up here. My brother-in-law [who drives participant] likes it as well.*
Challenges	1	*Well I enjoyed coming but of course I was very concerned that [Identifying information removed] was responsible for getting me and took his time, I can't do anything about that. I said I could go in by bus and he said you would never get from the bus stop to the lab, it's too far for you to walk. Of course, he's right it's too far I would not have got there. That was the only reservation I had that it would impinge on him.*
	2	*n/a*

NB. **Interview 1,** following control phase A, baseline two.

Interview 2, following intervention phase B, outcome.

n/a. Not applicable.

8.4.3.1.4 Theme 4. The period of participation during which no intervention was provided

This overarching theme related to the period of no intervention (control) between baseline one and two. Three subthemes arose relating to this topic, detailed in Table 66. Interview 1 participants discussed general positives, although they noted the time in-between could have been shorter, they wanted to start the intervention period as soon as possible. In addition, one participant noted that communication was needed throughout the control period to keep in touch with the Researcher to ensure the participant is confident in their participation.

Table 66: Objective 9. Theme 4. The period of participation during which no intervention was provided

Subtheme	Interview	Illustrative quote
A. Contact experience	1	*I suppose, and this is me, this is no reflection on you. I thought maybe I was not good enough for the study, maybe I didn't meet the criteria initially, but that was my uncertainty. Because I don't work anymore you lack confidence in yourself, so that was a nice. My husband will tell you, he said don't be silly and I know but you know what I'm like. So, I was really pleased to hear from you again, you said to me oh contact me if needed, but I couldn't do that I'd look daft. That's all.*
	2	*n/a*
B. General positives	1	*I think it was quite perfect yea, it was exactly what was needed.*
	2	*n/a*
C. Time challenges	1	*I thought it might be shorter, but it came, I thought it could've been the next week put it that way.*
	2	*n/a*

NB. **Interview 1,** following control phase A, baseline two.

Interview 2, following intervention phase B, outcome.

n/a. Not applicable.

8.4.3.1.5 Theme 5. Whether there were aspects of participation that could be improved.

When participants were asked for suggestions to potentially improve their and future participants experience in the study. Respondents in interview 1 (post-control period) felt it was ‘too early’ to speculate and they would attempt suggestions after the intervention stage (interview 2); at which point none of the participants had any suggestions and were only positive about their experience.

> *We always want to get better but there are no magical formulae, but for what we had in mind everything went perfect*
>
> (Stroke survivor, interview 2)

8.4.3.1.6 Theme 6. Other themes arising from discussions

This overarching theme related to other topics raised in the discussions. Three subthemes arose relating to this topic, detailed in Table 67. Interview 1 participants discussed the overall length of the study positively, several participants worried it would feel '*too long*' but felt the longer they had the device for the more perceived improvement; interview 2 participants were once more positive and praised their perceived improvements. Interview 1 participants also praised the contact with the research team and the invitation pack given when recruited through their GPs. While in interview 2 participants focused on the training, and remote updating of the therapy plan with positive feedback.

Table 67: Objective 9. Theme 6. Other themes arising from discussions

Subtheme	Interview	Illustrative quote
A. Overall length of study participation	1	*I think the longer I have the better.*
	2	*Well at first when you said 12 weeks that was a long while, but the time has been flying by.*
B. Remotely updating the Virtualrehab platform	1	*n/a*
	2	*When we discussed it then you went away and did it, that wasn't a problem, it didn't always go right, to be fair.*
C. Training given to use the Virtualrehab platform	1	*n/a*
	2	*The instructions were good*
D. Contact with research team	1	*That was easy.*
	2	*n/a*
E. Hope for improvement	1	*Hopefully after twelve weeks I will see some sort of improvement.*
	2	*n/a*
F. Recruitment through GP	1	*It was so simple, yea it was really simple, because the instructions on it was really good, I knew what I was aiming for and every time I was not a bit sure, initially after the first session I had with you I knew you said you would contact me, sometimes my memory isn't as good as others. I thought did she say she was going to contact me, did I have to do any exercises, but I only had to look on the paperwork that came through and it answered all my questions.*
	2	*n/a*

NB. **Interview 1,** following control phase A, baseline two.
Interview 2, following intervention phase B, outcome.
n/a. Not applicable.

8.5 DISCUSSION

The qualitative components found that delivering task-orientated upper limb training via non-immersive virtual reality to stroke survivors in their own homes was acceptable (objective 8). For example, interview 1 participants felt the Virtualrehab platform showed potential for efficient use of resources and delivering therapy within the home could promote autonomy for stroke survivors. Following 12-weeks with the device this autonomy was also noted in interview 2 as they particular praised the tailored therapy plans that they inputted into updating each week. Further, interview 1 participants identified potential drivers for engaging with such devices, for example, the gamified exercise could promote motivation and the patient involvement in therapy was of particular interest. In interview 2 participants also praised the motivation they felt using the device over 12-weeks, in particular inputting into the therapy changes was praised highly. In addition, they reiterated the importance of clinical oversight and ensuring contact and relationships with stroke therapists are maintained. Overall participants identified aspects of the platform that needs adjusting for future work, for example maintaining the technical reliability would require access to support in the long term. Stroke survivors also suggested adding particular components for severe impairments, increasing the challenge offered and an educational component.

The stroke survivors also ascertained the acceptability of participation in the study (objective 9). In particular, they praised the outcome measurement battery and frequency of these measures, they felt positive about travel to the

UEA MovExLab as long as they had appropriate directions and contact with the Researcher. They felt the study design was acceptable, particularly the length of the intervention period, they enjoyed having access to the equipment and the therapy plan for 12 weeks. However, they noted that equipment failures and measurement errors were frustrating and would need to be considered for future participants.

These findings support the potential for investigating the delivery of upper limb therapy via virtual reality within the home (Laver *et al.*, 2017; Subramanian, Cross and Hirschhauser, 2020). The findings in this study concur with prior research that reported engaging motivating responses from stroke survivors after an experience with such devices (Donoso Brown *et al.*, 2015; Proffitt and Lange, 2015; Pallesen *et al.*, 2018; Herne *et al.*, 2019; Warland *et al.*, 2019). As in previous research, and agreement with the findings of phase II, this study found that the instructions for using the platform, and a design, that facilitates independent undertaking of therapy were important (van Ommeren *et al.*, 2018).

Participant's characteristics and prior experiences with technology are important to highlight a possible bias in the results. The majority of participants reported confidence when using a TV (a key aspect of setting up and using the platform). The stroke survivors had limited prior knowledge of 'Virtual Reality' and no experience with the Kinect V2 sensor (Microsoft, Washington, United States) and other technology similar to the platform; this

may have influenced the discussions with interview 1 on the prospect of using the technology.

It should be noted that Microsoft withdrew support for the Kinect V2 in 2017/18. However, the developer (Evolve) has adapted the Virtualrehab platform software to work with the new Microsoft Azure Kinect. The Azure Kinect is: half the size of the old Kinect; can be plugged straight into a desktop or laptop computer; and uses state-of-the-art computer vision, speech models and advanced artificial intelligence (AI) sensors. Thus, the updated Virtualrehab platform has incorporated participants' request from phase II and III for a lighter, more portable, design.

Strengths and limitations of the study

The key strength of this study is it demonstrated the acceptability of delivering therapy via virtual reality in the home for stroke survivors over a 12-week intervention period, longer than typical of other qualitative investigations (Proffitt *et al.*, 2019; Warland *et al.*, 2019). This study also highlights the Virtualrehab platform's potential for delivering stroke rehabilitation within the home. The next step is to incorporate the findings of phase III into the development of future investigations.

The limitations of this study are acknowledged, interview 1 participants were asked about the Virtualrehab platform after only a brief demonstration. However, following interview 2 they had 12 weeks of experience with the device and there was no disagreement between shared views in the results.

Further, it was not possible to use an interviewer that was unknown to participants which may have inflated the positive responses from participants due to the relationship built with the Researcher throughout the study. However, this relationship also promoted credibility from the rapport built.

8.6 CONCLUSIONS

The findings from this study demonstrated the acceptability of delivering exercise-based upper limb functional training via virtual reality within the home. It also identified the acceptability of participation within this feasibility trial, a key finding for future trial design.

9 DISCUSSION

The three original studies reported within this thesis investigated Virtual Reality (VR) as an innovative model of delivery for evidence-based stroke rehabilitation. This knowledge can be used to develop future research aims and direct a dose optimisation study, followed by a clinical efficacy trial within the home environment.

In this chapter, a summary of each research question is given, followed by a discussion of key findings within the context of published literature. Finally, the contributions and recommendations for future research arising from this thesis are explored, with reference to its strengths and limitations.

9.1 SUMMARY OF RESULTS

The overarching thesis aim was addressed with three research questions, using a multi-phased mixed-methods framework. This design was influenced by the progressive staging of pilot studies to improve phase three trials for motor interventions (Dobkin, 2009) and followed the Medical Research Council's (MRC) Framework for Complex Interventions (Craig *et al.*, 2008).

The first two research questions focussed on the 'development' stage of the MRC's framework and were addressed by conducting the systematic review (phase I, reported in chapter five) and a user-refinement study (phase II, detailed in chapter six).

The first research question was:

Is there evidence that neurophysiological changes are correlated with, or accompany, reduction in motor impairment, in response to virtual reality-aided exercise-based training?

The first research question was addressed by conducting a systematic review of the literature (chapter five). The results demonstrated that there was insufficient robust data to identify neurophysiological changes that are correlated with a reduction in motor impairment (aim 1a). The four included studies demonstrated a reduction in some of the motor impairment measures, accompanied by a neurophysiological change in response to the virtual reality intervention; however, the majority of measures showed no change between pre to post-intervention time points (aim 1a.2). Finally, the results showed that there were methodological weaknesses, with a high risk of potential bias (i.e. lack of reporting, heterogeneous outcomes and protocols). Thus, phase I identified an apparent lack of adequately powered studies investigating the relationship between reduction in motor impairment and neurophysiological change. Consequently, there remains a need for research to address (1) the underlying mechanisms by which VR potentially drives motor recovery and (2) more robust initial investigations that can provide the foundation for future clinical trials.

The second research question was:

What are the views of end-users on using and refining virtual reality-aided exercise-based training for stroke rehabilitation?

The second research question was addressed by conducting a qualitative descriptive user-refinement study (chapter six), involving demonstrations of the Virtualrehab platform (chapter three) and a small two-week home-trial with data collected through focus groups, interviews and questionnaires. The three end-user groups found the Virtualrehab platform was usable and acceptable; in particular, the personalisation and interactive nature of the platform were praised (aim 2a). Unfortunately, this did not include and LEAP hand motion sensor (Ultraleap, San Francisco, United States). The sensor was not working during this thesis and thus could not be proved acceptable or usable. Additional development work before further usability investigations with the LEAP hand motion sensor (Ultraleap, San Francisco, United States) would need to account for the limited motion stroke survivors with hand paresis typically experience. Further, suggestions were sent to the industrial collaborator to incorporate into the next iteration of the Virtualrehab platform. These centred on increasing the portability of the platform for accessibility, to help promote independence for stroke survivors and to ensure the platform was reliable; they also highlighted the need for strong, robust evidence of efficacy and effectiveness to promote uptake for clinical practice (aim 2b). Thus, phase II concluded that there is a need for a low-cost non-immersive VR gaming technology for upper limb impairments, with the ability to conduct personalised therapy in the home; it also identified development

aspects that are key to facilitate acceptability, usability and uptake of such technology.

Phase III addressed the third research question and aligned with the 'feasibility/piloting' stage of the MRC's Framework (Craig *et al.*, 2008) (chapter seven and eight).

The third research question was:

How feasible is virtual reality-aided exercise-based training as a mode to deliver upper limb stroke rehabilitation within the home?

The third research question was addressed by conducting a convergent parallel mixed-methods feasibility study, using replicated single-case studies with a 12-week intervention period. The feasibility study identified key procedural aspects that can be carried out in a future clinical trial (aim 3a). The results demonstrated that this mode of delivery in the home environment was feasible and acceptable to stroke survivors. The rate of adherence to the tailored, personalised therapy plans demonstrated the potential for delivering high-dose repetitive functional exercises via the Virtualrehab platform. The investigation also identified practical challenges for delivering therapy and collecting appropriate outcome measures in the home. Thus, phase III provided results to inform a future dose-optimisation study, followed by an adequately powered clinical efficacy trial.

9.2 ALL FINDINGS IN THE CONTEXT OF THE LITERATURE

This section details the key findings from the three reported studies, within the context of the literature.

9.2.1 The evidence of neurophysiological changes correlated with, or accompanying reduction in motor impairment, in response to virtual reality-aided exercise-based training (Aims 1a and 1a.2)

The systematic review found insufficient data to identify the neurophysiological correlates of change in motor impairment in response to VR training for the upper limb after stroke (aim 1a). Thus, demonstrating that there is insufficient data to provide an understanding of the neurophysiological underpinnings of potential benefit. A contrast to statements made in prior reviews that evidence of neuroplastic changes is "guiding the development of virtual reality" (Laver *et al.*, 2017), that "many clinical trials have investigated the efficacy and mechanisms of VR [..] and reported that recovery of the upper limb proceeded in parallel with brain plasticity and functional reorganization" (Mekbib *et al.*, 2020).

The statements from Laver and colleagues were from the introduction of the updated Cochrane review and referenced several studies, one of which was included in the thesis's systematic review (Jang *et al.*, 2005). The Cochrane review claimed Jang and colleagues showed functional improvements that were associated with positive neural changes (Laver *et al.*, 2017). However, this systematic review found that they reported no significant changes pre/-post VR-intervention within their motor impairment measures, only when

compared with the control group scores; furthermore, there was only a reported change in neurophysiological outcomes pre to-post intervention. The additional studies referenced in support of the statements made in the Cochrane review were not included in the Researcher's (author of the thesis) systematic review due to a lack of a motor impairment outcome (You *et al.*, 2005; Bagce *et al.*, 2012; Tunik, Saleh and Adamovich, 2013; Saleh, Adamovich and Tunik, 2014). Further, Mekbib and colleagues supported their claims with two references, one mentioned above (You *et al.*, 2005) and the other combined the VR intervention with conventional therapy (Wang *et al.*, 2017). Thus, the interpretation of the systematic review's results reported here argues that the development of VR cannot be 'guided' by neuroimaging studies; such statements should be interpreted cautiously until further robust trials have examined the underlying mechanisms of effect. In order to understand the applicability of VR in stroke rehabilitation, it must be clear if such therapy can drive neural recovery (Pomeroy and Tallis, 2000; Bernhardt *et al.*, 2017).

The use of such studies as references for claims of underlying neural mechanisms is concerning. There is thought to be a wealth of published research investigating VR for stroke rehabilitation, and this is used as an evidence base to claim efficacy (Domínguez-Téllez *et al.*, 2020; Levin, 2020). By contrast, the systematic review conducted for this thesis has shown that there is a significant gap in the evidence base and how these small studies are being interpreted is problematic. Of the 91 full texts screened for inclusion in

this review, only four met the criteria. The reasons for exclusion ranged from a lack of neurophysiology outcome (75%) to a lack of a clinical measure of motor impairment (37%). Without the inclusion of both measures, studies can conclude either: a reduction of motor impairment in response to therapy but cannot comment on the type of recovery; or, a change in neural mechanisms, but it is unknown if this is reflected in motor impairment and/or behavioural change.

The systematic review revealed that there is a lack of studies including both neurophysiology and motor impairment measures; concurring with a recent report of commonly used outcomes in investigations of VR for upper limb impairments (Subramanian, Cross and Hirschhauser, 2020). Out of 125 included studies, only a few were using outcomes that differentiated between both substitute compensation and either behavioural recovery (n = 8) or adaptive compensation (n = 2) or all (n = 1). It is clear that despite the wealth of studies investigating VR, there needs to be further consideration of the appropriate outcomes that can elucidate the underlying mechanisms, in order to 'guide the development of VR'. This recommendation is in line with the Stroke Recovery and Rehabilitation Roundtable taskforce who noted that researchers need to "consistently measure neural injury and function and apply outcome measures that can distinguish behavioural restitution from compensation" (Bernhardt *et al.*, 2017). It is important to build therapies with a strong understanding of the mechanisms in order to offer treatment that is individualised to the patient's responsiveness (i.e. recovery phenotypes).

The systematic review did reveal initial changes in motor impairment and neurophysiology in response to VR, but only for two of the four included studies and a small number of measures (aim 1a.2). Further, this evidence was of poor methodological quality (e.g. inconsistent reporting, heterogeneous protocols, procedures and participants). These findings concur with claims from prior reviews of VR's potential to reduce motor impairment and the need for further robust studies in order to develop evidence-based guidelines for clinical practice (Henderson, Korner-Bitensky and Levin, 2007; Mumford and Wilson, 2009; Laver *et al.*, 2012, 2017; Chen *et al.*, 2015; Aramaki *et al.*, 2019; Maier *et al.*, 2019; Rohrbach, Chicklis and Levac, 2019; Subramanian *et al.*, 2019; Valkenborghs *et al.*, 2019). Unfortunately, this recommendation for larger robust trials in response to the low quality of evidence has not changed in the past decade. There is a clear need to address these consistent recommendations to drive the evidence base forward.

The poor methodological quality highlighted in this systematic review concurs with similar prior reports (Henderson, Korner-Bitensky and Levin, 2007; Mumford and Wilson, 2009; Laver *et al.*, 2012, 2017; Chen *et al.*, 2015; Aramaki *et al.*, 2019; Maier *et al.*, 2019; Rohrbach, Chicklis and Levac, 2019; Subramanian *et al.*, 2019; Valkenborghs *et al.*, 2019). Patients' engagement in technology-based rehabilitation is a key feature of uptake in clinical practice (Proffitt *et al.*, 2019). Therefore, the lack of reporting recruitment and retention information, found in this systematic review reported in this thesis, is problematic and increases the risk of selection bias. Future clinical

trials rely on such information to understand potential sample sizes, challenges with recruitment and the likelihood of reaching targets with similar interventions and protocols. These findings are similar to reports in a recent review of efficient recruitment to stroke rehabilitation RCTs (McGill *et al.*, 2020). In addition, although studies report a reduction in motor impairment, there can be discrepancies between the published manuscript and what was intended to be investigated, thus confounding interpretation of results with potential reporting bias. For example, one study in the systematic review reported in this thesis changed its primary outcome measure from a published protocol to the final manuscript. The other three studies did not prospectively register their trials; unfortunately, this was reported as a challenge for stroke research over a decade ago, where researchers were urged to register trials (Liebeskind *et al.,* 2006). This is particularly concerning as all results are required to judge the evidence base appropriately and can help understand the mechanisms of the intervention and the extent to which they work. Finally, the variety of VR devices and protocols have been a consistent challenge in carrying out meta-analyses of the evidence-base; this systematic review reported a variety of intervention duration, immersion and exercise-based tasks. This has been noted in prior reviews and discussed in a recent review of commonly used types of VR platforms (Subramanian, Cross and Hirschhauser, 2020). The number of studies excluded in this review as they included VR with additional interventions, or excluded a comparator therapy is also concerning (44%). Prior reviews have claimed large effect sizes and high methodological quality using trials that included additional interventions (Domínguez-Téllez *et al.,* 2020; Mekbib *et al.,* 2020); interpretation of the

effect sizes is limited when VR therapy is combined with an additional intervention (i.e. robotics).

In summary, it is clear that despite the wealth of VR research, consistent, standardised outcomes, procedures and a categorisation system for VR devices is required to analyse the evidence robustly. Although this is not new information, this systematic review once more highlights the unchanged need that recently published studies have not met, from a search current to August 2020. Further, the systematic review highlighted a gap in the evidence that has not previously been reported: the need to robustly investigate the neurophysiology changes in response to VR that accompany a reduction of motor impairment.

9.2.2 The views of end-users on using and refining virtual reality-aided exercise-based training for stroke rehabilitation (Aim 2a, Aim 3a)

Phase II and III demonstrated the usability and acceptability of delivering exercised-based upper limb training via virtual reality within the home (aims 2a, and 3a – objective 8). Stroke survivors, informal carers and clinicians all felt that this mode of delivery could promote beneficial psychosocial effects, in particular, increasing motivation with engaging features such as gamified-exercises, feedback and competitive scoring. Overall, participants felt that this could alleviate boredom, facilitate adherence and thus, acceptance of rehabilitation. This concurs with prior research where the engaging nature of VR therapies provided a 'distraction' for stroke survivors, from their intensive repetitive rehabilitation prescription (Lewis *et al.*, 2011; Donoso Brown *et al.*, 2015; Proffitt and Lange, 2015; Pallesen *et al.*, 2018; Demers, Chan Chun Kong and Levin, 2019; Warland *et al.*, 2019).

The reported feelings of engagement and motivation did not decrease in survivors following 12-weeks with the Virtualrehab platform; participants noted that these were key features of the device that had the potential to keep them interested in long-term therapy. This contrasts with prior research that suggests engaging and motivating features are a 'novelty' that will wear off over time (Linder *et al.*, 2013; Brokaw, Eckel and Brewer, 2015; Warland *et al.*, 2019). Nevertheless, the views of participants in phase III were collected after 12 weeks with the device in their home. This was a longer period than the contrasting research, which used only a single demonstration (Brokaw, Eckel and Brewer, 2015); or three weeks (Warland *et al.*, 2019); or eight

weeks, but with a case study (Linder *et al.*, 2013). Unfortunately, studies that include longer intervention periods have not reported the views of survivors (i.e. six (Proffitt and Lange, 2015; Adie *et al.*, 2017), eight (Standen *et al.*, 2013) and 12 weeks (Wolf *et al.*, 2015)). Perhaps concerns that the 'novelty' would wear off is a perception held by end-users and not necessarily the views of survivors' post-experience with such devices, as seen in phase III. However, it is known that perceived enjoyment is a key factor in the acceptance of technology-based interventions (Langan *et al.*, 2018). Thus, such findings could indicate that pre-conceived perceptions are a potential barrier to acceptance and uptake.

Nevertheless, the 12-weeks in the study may not have been long enough for the 'novelty' to wear off, and only seven survivors were interviewed post-intervention. Overall, the studies reported in phases II and III show the importance of gathering the views of end-users, following both a demonstration and experience of the device in their home. This allows further understanding of pre-conceived perceptions end-users have when choosing a technology-based device and how comparable these are with actual experiences. This information is required to understand the acceptability of technology-based rehabilitation.

The study reported in phase III found that the 'variation', 'challenge', and 'personal involvement' in the therapy were key factors that maintained engagement and motivation. Survivors in prior studies have also highlighted

these factors after four weeks with a device; but these numerous factors required attention and increased fatigue, despite being engaging and motivating (Pallesen *et al.*, 2018). This was a concern of clinicians and informal carers in phase II and cautioned by a survivor pre-intervention in phase III. Participants worried that patients may not be fully capable of judging their limits. Post-intervention in phase III stroke survivors did not report this issue, but this was a small sample whose therapy prescription did not aim to push them past what they were comfortable undertaking. Despite this, the findings clearly showed that an individualised approach with patient input was an additional key factor in the usability and acceptability of the Virtualrehab platform. This concurs with prior research that reported inclusion of patients in therapy prescription has shown to mitigate potential fatigue, as they can carry out therapy within the home to their capabilities and interests (Glegg *et al.*, 2013; Schmid, Glässel and Schuster-Amft, 2016; Threapleton, Drummond and Standen, 2016; Palmcrantz *et al.*, 2017).

The studies reported in phase II and III of this thesis also highlighted potential barriers to usability and uptake in clinical practice (i.e. set-up, ease of use, space required), technical difficulty (i.e. navigation through software, troubleshooting) and the training/support given. The results showed that the personalisation of the device, in terms of therapy plan, set-up, training and support given was essential in promoting independent, confident use of the Virtualrehab platform. Prior research has previously noted that level of engagement, and therefore adherence is dependent on both the perceived

benefit and the level of support offered (Mountain *et al.*, 2010; Balsam *et al.*, 2013; Hamilton, McCluskey, *et al.*, 2018).

Phase III also noted several technical challenges (i.e. equipment failing) which caused frustration with stroke survivors. This concurs with prior research where participants praised the support and guidance given in using the equipment but were still frustrated with the device's reliability; they reported emotional effects when the game froze and did not save results (Pallesen *et al.*, 2018). The findings of phases II and III clearly showed that the Virtualrehab platform's usability and acceptability were dependent on ensuring patients' involvement in their individualised therapy and the equipment's reliability in the long term. From these findings, it is clear that future research needs to determine if engagement and motivation can be maintained over time and identify the potential limits of such features.

Phase II reported that informal carers carried a perception that stroke survivors lacked the technical ability to use virtual reality; this was also a concern for stroke clinicians and a barrier in their uptake of such technology. However, stroke survivors disagreed: they acknowledged a lack of experience with the technical aspects of the Virtualrehab platform (i.e. the computer), but they were confident that appropriate training would facilitate the usability. This was further supported following the 12-week trial in phase III, where stroke survivors reported that even without prior experience with the Virtualrehab platform technical features, they could use it with ease. Overall

results from stroke survivors in phases II and III showed a positive perception of the technical knowledge required to use the equipment of the Virtualrehab platform. This positive view of technology use has been noted in prior work, with the ultimate value of telerehabilitation devices determined by prior perceptions, experience and usability (Mitzner *et al.*, 2010; Mountain *et al.*, 2010; Balsam *et al.*, 2013; Threapleton, Drummond and Standen, 2016).

This belief that stroke survivors may lack technical ability can be linked with the societal perception that age is a barrier to engaging with technology (Mitzner *et al.*, 2017). This conflict between societal views and older adults' opinions on technology is not a new challenge in technology-based rehabilitation research. Often the 'digital divide' whereby, those who do not engage in technology are at risk of being left behind, is cited as the main challenge for the uptake of older adults with technology (Mitzner *et al.*, 2010). The findings of phases II and III demonstrated this difference in perception and showed that the ability of stroke survivors depends on the usability of the device itself and not on their age. This concurs with prior reports from stroke survivors (Nasr *et al.*, 2016; Warland *et al.*, 2019), and reviews on the use of barriers in the uptake of technology-based interventions (Edgar, Monsees, Rhebergen, Waring, Van Der Star, *et al.*, 2017; Glegg and Levac, 2018; Kerr *et al.*, 2018; Langan *et al.*, 2018; Chen *et al.*, 2019; Proffitt *et al.*, 2019). One study, in particular, found that age was not correlated with the frequency of use of home-based VR gaming interventions (Standen *et al.*, 2015); indeed, several studies reported that older adults found gamification

of their rehabilitation enjoyable (Casserly and Baer, 2014; Wingham *et al.*, 2015; Threapleton *et al.*, 2017). Despite the agreement with prior research, the age of participants included in phase III could have biased the results. The age ranged from 53 to 93 years (mean = 67.5 and standard deviation = 12.6); the average age for stroke survivors in the UK is 72 (men) and 78 women) (Bowen, James and Young, 2016), with the rate of stroke in those aged 45 and above expected to rise 59% in the next 20 years (King *et al.*, 2020). Although there were participants in this thesis whose age is lower than the average, the range included the UK stroke onset ages, and therefore, their views of technology are relevant. This study indicated that age is not a barrier to stroke survivors using the devices, but is a perception held by informal carers and clinicians, which could impact their uptake in practice. It is clear that the devices need to be developed in collaboration with the end-users and appropriate training and support offered.

One of the main concerns of stroke survivors, informal carers and clinicians in phase II, further confirmed by participants in phase III, was the potential that technology could 'replace' visits to clinicians. It is critical that virtual reality is a tool to aid clinicians and does not interfere with the patient-clinician relationship that is key in rehabilitation. This view concurs with prior research which found that clinicians were a key feature of engagement and uptake of technology by stroke survivors (Edgar, Monsees, Rhebergen, Waring, Van Der Star, *et al.*, 2017; Pallesen *et al.*, 2018; Lehmann, Baer and Schuster-Amft, 2020). Other studies have also identified this concern from

stroke clinicians; the danger of technology resulting in fewer interactions with clinicians, the quality of care would be less than in-person and they would lack the social interaction (Edgar, Monsees, Rhebergen, Waring, Van der Star, *et al.*, 2017). The integral role of the therapist in the prescription, use and monitoring of technology was highlighted by therapists to ensure that technology is used to achieve rehabilitation goals (Hamilton, Lovarini, *et al.*, 2018). Participants in both phase II and III were concerned that choosing therapy via VR in their home could result in fewer interactions with clinicians, they felt this would impact their motivation to carry out therapy and potentially their improvement. The rapport they have built-in their rehabilitation journeys with clinicians was strongly highlighted as positive for therapy. These findings strongly support prior research, in that the inclusion of the therapy editor (monitoring, updating and crucial involvement of therapists) in the Virtualrehab platform was praised by clinicians, stroke survivors and informal carers in terms of the device's acceptability for stroke rehabilitation.

In summary, phases II and III of this thesis found that to increase older adults' uptake of such devices there needs to be: (1) appropriate input from end-users in the development; (2) adequate education and training in the use of the technology and potential benefit; (3) care that reliable equipment and support is available for troubleshooting. These findings strengthen the published literature in the area by underlining the need to provide technical reliability, practical information and include the views of users in trials. Essentially, the

Virtualrehab platform can provide an engaging and motivating method of delivering therapy, that can be maintained over time in consultation with patients and careful monitoring, to ensure limited fatigue and variation is maintained.

9.2.3 The feasibility of virtual reality-aided exercise-based training as a mode to deliver upper limb stroke rehabilitation within the home (Aim 3a)

There is an acknowledged challenge in translating research findings into meaningful clinical changes in practice; this is in part due to a lack of appropriate reporting in home-based research, such as practicalities of equipment set-up, standardisation of outcomes in the home (Glegg and Levac, 2017; Threapleton *et al.*, 2017; Lynch, Chesworth and Connell, 2018). Phase III demonstrated the feasibility of delivering upper limb stroke rehabilitation via virtual reality within the home (aim 3a). This is in line with prior research reporting initial feasibility of VR therapy within the home (i.e. (Standen *et al.*, 2013; Tsekleves *et al.*, 2016; Warland *et al.*, 2019) and specifically for Kinect V2 (Microsoft, Washington, United States), similar to its use in phase III (Proffitt and Lange, 2015; Türkbey, Kutlay and Gök, 2017). The findings from phase III provide information beyond common feasibility reports, with details on the pragmatics of carrying out a 12-week intervention, with weekly behavioural and neuromechanical outcomes in the home environment. This is crucial information for the development and success of future clinical trials.

Phase III demonstrated the potential of recruitment and retention from a rural community, specifically noting the small numbers and a need for adaptability to equipment availability and participants' schedules (i.e. sickness, family commitments, holidays). This concurs with prior research that reported missing data from a VR intervention due to a holiday (Slijper *et al.*, 2014), a participant in phase III lost two weeks of intervention due to holidays. Another study mitigated this risk with a portable system that was taken on holiday by the participants (Wingham *et al.*, 2015). Increasing the portability of such devices was proposed by stroke survivors in phase III, which could increase associability to therapy and improve the adaptability of research in such environments.

To ensure that prototypes are sufficiently robust for repeated use outside the laboratory, appropriate pre-testing should also be carried out in the environment for which the intervention was devised. Usability testing should be taken before feasibility and efficacy studies. Phase II used a small-home trial where the practicalities of the platform were tested in the home; however, this did not account for all the challenges experienced in phase III. Participants in phase III expressed some frustration with intervention days lost, although they felt that this was mitigated by quick responsive support. This frustration with equipment failures has been noted in prior research, where equipment failures also threatened data recording and influenced participants' views (Kiselev *et al.*, 2015; Levac *et al.*, 2015).

The viability of collecting neuromechanical and behavioural data within the home was demonstrated over the 12-week intervention. To this Researcher's knowledge, prior feasibility trials have not reported on collecting such measures within the home. However, these results concur with a report that proposed that there would be potential barriers to completing assessments within the home as opposed to a clinical setting (Threapleton, Drummond and Standen, 2016). They proposed that measures designed and standardised for controlled clinical settings would not be feasible in the home. The results from the feasibility study found the main challenges of collecting standardised behavioural measurements were space requirements, standardised equipment and other members of the household (i.e. children, pets). However, the portability of the behavioural measures allowed for half of the participants to achieve 100% data collection rate and the other half, were only missing two weeks each due to their schedules. The Researcher argues that future trials need to consider the most appropriate behavioural measures that can be carried out within the home and be adapted to the pragmatic challenges such as participants' schedules and home environments. The results of this study regarding the neuromechanical data show the need to develop protocols and normative data to provide rigorous evidence of collecting neural and behavioural outcomes within the home environment. The study did show it was possible to collect valid trials from sEMG within the home, which has not been previously demonstrated in research. However, the percentage of invalid trials shows that the consistency of collecting such measures in the home requires further work. The lack of research investigating these measures in the home shows a clear lack of reporting the

viability of collecting behavioural data within the home environment and identify the barriers.

Further, participants felt the frequency of measurement (weekly) and the procedures in their home acceptable. There is a clear lack of reporting the viability of collecting behavioural data within the home environment; arguably this is often seen in reviews as a potential bias, wherein the reasons for lost data are not accounted for (Threapleton, Drummond and Standen, 2016; Lynch, Chesworth and Connell, 2018). Pre/-post measurements are typically used in feasibility studies (Subramanian, Cross and Hirschhauser, 2020). In order to find the optimal dosage, weekly home-based measurements are needed. This study has demonstrated an important first step in assessing measures within the home.

Finally, the feasibility study revealed a high adherence rate, 87.5% with a performance of between 1,710 and 9,377 repetitions. This supports earlier findings that VR has the potential to increase the intensity of therapy (Brunner *et al.*, 2016); for example, a pilot study found participants completed a median of 4713 movements during five weeks, although this was in a clinical setting with a therapist monitoring and guiding (Perez-Marcos *et al.*, 2017). However, contrasting studies are reporting a poor completion rate of technology-based therapy programmes in the home (Standen *et al.*, 2015). The difference in study findings could be explained by participants' schedules and enablers for adherence. In phase III, participants reported that scheduling

conflicts limited the completion of therapy in some weeks, also found by Standen and colleagues. In phase III, participants felt a key enabler to completing their therapy plans was support from their family and friends, concurring with prior studies (Scorrano, Ntsiea and Maleka, 2018; Grau-Pellicer *et al.*, 2020). The findings of phase III suggest that VR has the potential to facilitate high-intensive therapy prescription, but success depends on the patient-input and adaptability to other aspects of their lives. The number of repetitions performed by participants was higher than have been reported for routine therapy (Pomeroy *et al.*, 2016; Hunter *et al.*, 2018), meeting the need for greater accuracy in dose reporting (Bernhardt, Hayward, *et al.*, 2019). Whether this range of repetitions is the optimal therapeutic dose requires further study, especially as it cannot be assumed that higher doses always produce better outcomes (Lang *et al.*, 2016) although the intensity is needed to drive neuroplastic change (Nudo, 2013). Subsequent studies need to be conducted to identify the optimum therapeutic dose using methodologies already developed for use in stroke rehabilitation research (Lang *et al.*, 2016; Colucci *et al.*, 2017).

In summary, phase III provided an initial investigation of a virtual reality intervention and feasibility of delivering to chronic stroke survivors in the home. Improved documenting and increased sharing of findings concerning research into home-based VR and gaming interventions is important, including the approaches that have worked well, as well as the practical difficulties encountered. This feedback is vital to the development of

interventions for home-based therapy that participants will find acceptable and develop robust implementable evidence from future clinical trials.

9.3 THESIS LIMITATIONS AND STRENGTHS

It is important to consider the findings in light of the thesis limitations and strengths.

9.3.1 Limitations

The systematic review carried out in phase I was limited to studies published in the English Language. Although multiple databases were searched, with reference lists of relevant papers being hand searched, it is possible relevant manuscripts were missed, potentially leading to a reporting bias in the results. The search included a broad definition of virtual reality, which could account for the heterogeneity in the included studies. An appropriate, concise stratification of devices and protocols falling under the umbrella of 'Virtual Reality' is therefore required.

The user-refinement study from phase II did not reach the desired recruitment numbers, creating a small sample size, potentially impacting the generalisability of the results. For example, the stroke clinicians were recruited from one hospital in Norfolk. Their views are influenced by the policies and procedures they experience in that setting, and it is known that wide variations in working conditions and policies exist across NHS sites. However, the views of the stroke clinicians included both physiotherapists and occupational therapists with varying experiences and agreed with prior

research (Nguyen *et al.*, 2018; Demers, Chan Chun Kong and Levin, 2019). In addition, all participants, bar the two dyads (stage 2), in the study, discussed the platform prospectively, following only one brief demonstration, potentially limiting the views gathered. However, to mitigate this, phase III gathered views of stroke survivors following 12 weeks of experience with the device.

Phase III required an internet connection to set-up the Virtualrehab platform within the home determined through the initial screening criteria, potentially excluding participants, although the screening revealed all potentially interested participants met this criterion. The participant sample was heterogeneous in terms of their impairments and home environments. However, this revealed important feasibility information and practicalities of researching in the stroke population and home environment.

Unfortunately, the perceptions of potential participants could not be fully controlled by the Researcher and this may have introduced a bias into who volunteered for the studies; however, both phases II and III did include participants with a wide range of prior experience and confidence with technology. Both phases II and III included qualitative methodologies which have inherent biases due to the Researcher (author of the thesis) conducting the data collection. Using an interviewer unknown to the participants was not possible within the confines of time and funding-limited study. The rapport built between the Researcher and participants throughout recruitment and

data collection may have precipitated more positive responses from study participants. To help address this, the open-ended questions were framed to incorporate both beneficiary and critical feedback from answers, with prompts to help the inclusion of both types of responses.

Finally, as the virtual reality system participants experienced was the VirtualRehab platform, there needs to be caution when generalising the findings to other systems. Indeed, a limitation inherent in all studies using gaming technology is the risk of redundancy with devices rapidly being superseded; for example, the hardware used for the platform used in this study (i.e. Kinect V2) is no longer manufactured. However, there are aspects of the platform that are similar to the majority of virtual reality devices, such as the use of exercises, exergames, feedback, real-time movement replicated onscreen and use of the TV and a laptop within the home environment. Finally, the Kinect V2 uses sensors to replicate users' movements, similar to most non-immersive hardware systems used in virtual rehabilitation technology.

9.3.2 Strengths

The systematic review (phase I) included multiple databases and did not restrict the date of searches. While the user-refinement study (phase II) involved stroke survivors, informal carers and clinicians; it is crucial to include end-users in the refinement of technology-based devices. Further, the views of users in both phase II and III have been reported to the industrial collaborator in regards to developmental suggestions for the next iteration. This was a key strength that enabled the Virtualrehab platform to be refined with views from its three key stakeholders and following a long home-trial of 12 weeks in phase III. Finally, the 12-week intervention period used in the feasibility study (phase III) was a key strength; as mentioned previously, other research in the area has not tested virtual reality over such a period of time and rarely gathers the views of stroke survivors.

Overall, this thesis benefited from a multi-disciplinary research team with a variety of expertise. This allowed an in-depth holistic approach to be adopted in each study phase that benefitted from physiotherapeutic, psychological, biomechanical and software engineering input.

9.4 CONCLUDING REMARKS AND FUTURE DIRECTIONS

This thesis investigated the use of virtual reality as a mode to deliver upper limb stroke rehabilitation within the home. Three original empirical studies were reported to address gaps in the evidence base.

Firstly, a systematic review demonstrated there was insufficient robust data to identify neurophysiological changes that are correlated with a reduction in motor impairment. The four included studies demonstrated a reduction in some of the motor impairment measures accompanied by a neurophysiological change. Finally, the results showed methodological weaknesses with a high risk of potential bias. Thus, revealing the need for future research to address (1) the underlying mechanisms by which VR potentially drives motor recovery and (2) the need for more robust initial investigations that can provide the foundation for larger clinical trials.

Secondly, three end-user groups (ten stroke survivors, seven informal carers and nine clinicians) found a virtual reality device (the Virtualrehab platform) was usable and acceptable; in particular, the personalisation and interactive nature of the platform were praised. Further, suggestions were sent to the industrial collaborator to incorporate into the next iteration of the device (i.e. increasing portability and promoting independence). Thus, concluding the need for a low-cost non-immersive VR gaming technology for upper limb impairments, with the ability to conduct personalised therapy in the home; also identifying development aspects that are key to facilitate acceptability, usability and uptake of such technology.

Finally, a 12-week intervention was carried out with the Virtualrehab platform within the home of eleven stroke survivors. The results demonstrated that this mode of delivery in the home environment was feasible and acceptable to stroke survivors. The rate of adherence (87.5%) to the tailored, personalised therapy plans demonstrated the potential for delivering repetitive functional exercises via the Virtualrehab platform. The investigation identified practical challenges for delivering therapy and collecting appropriate outcome measures in the home. Future research needs to identify normative neuromechanical measures following the procedures reported here and develop a dose-optimisation and clinical efficacy trial.

The work reported in this thesis demonstrated the feasibility of delivering upper limb motor rehabilitation via virtual reality within the home. Incorporated the views of end-users in the Virtualrehab platform and identified key future research aims. The findings also reported challenges faced in researching technology for motor recovery within the home. Further reiterating the need for careful consideration of trial design for the home environments, including transparent reporting, to develop robust clinical trials to inform practice.

The need for an evidence-based model of delivering motor rehabilitation within the home, with remote monitoring capabilities, is particularly apparent in the ongoing pandemic and the effect this has had on stroke survivors accessing appropriate treatments, as detailed in a recent report (The Stroke Association, 2020).

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11 APPENDIX

11.1 APPENDIX A. PERMISSION FOR THE USE OF THE VIRTUALREHAB PLATFORM IMAGES

Fiona Ellis (HSC - Postgraduate Researcher)

From: David Fried <dfried@evolvrehab.com>
Sent: 14 September 2020 13:04
To: Fiona Ellis (HSC - Postgraduate Researcher)
Cc: Ruben Gonzalez; Valerie Pomeroy (HSC - Staff); Nicola Hancock (HSC - Staff)
Subject: RE: Permission to use pictures of the VirtualRehab platform within the thesis
Attachments: vlcsnap-2017-07-06-14h17m03s299.png; Pajarito.png; P1090336(new).jpg

Hi Fiona,
Here's the link to the photos. https://we.tl/t-L9xJpPwEQR

In terms of patients, there are five photos in the folder. Unfortunately, none are of stroke patients. Two from Hobbs Rehabilitation in Winchester are of an MS patient, one from a patient called Pablo Garcia here in Spain, and the rest are from us. All rights have been given to use the images in any way we want, so that's not a problem. If you do use Hobbs, can you please simple say courtesy of Hobbs Rehabilitation and similar with Pablo Garcia.

I've also added some screenshots of body exergames and from the Manager. I forgot to add some of Hands, so I've attached them here.

Best,

David Fried
CEO
UK Mobile: +44 (0) 7900 043 184
Spain Mobile: +34 633 18 18 43
Spain Office: +34 946 52 63 47

De: Fiona Ellis (HSC - Postgraduate Researcher) <Fiona.Ellis@uea.ac.uk>
Enviado el: 14 September 2020 10:58
Para: David Fried <dfried@evolvrehab.com>
CC: Ruben Gonzalez <rgonzalez@virtualwareco.com>; Valerie Pomeroy (HSC - Staff) <V.Pomeroy@uea.ac.uk>; Nicola Hancock (HSC - Staff) <N.Hancock@uea.ac.uk>
Asunto: RE: Permission to use pictures of the VirtualRehab platform within the thesis

Dear David,

1

Thank you for the confirmation – I look forward to receiving these images.

I hope you all have a good day.

Best wishes,

Fiona

From: David Fried <dfried@evolvrehab.com>
Sent: 10 September 2020 09:02
To: Fiona Ellis (HSC - Postgraduate Researcher) <Fiona.Ellis@uea.ac.uk>
Cc: Ruben Gonzalez <rgonzalez@virtualwareco.com>; Valerie Pomeroy (HSC - Staff) <V.Pomeroy@uea.ac.uk>; Nicola Hancock (HSC - Staff) <N.Hancock@uea.ac.uk>
Subject: RE: Permission to use pictures of the VirtualRehab platform within the thesis

Warning: This email is from outside the UEA system. Do not click on links or attachments unless you expect them from the sender and know the content is safe.

Hi Fiona,

I'll send you a package of usable images via WeTransfer a bit later.

Best,

David Fried
CEO
UK Mobile: +44 (0) 7900 043 184
Spain Mobile: +34 633 18 18 43
Spain Office: +34 946 52 63 47

De: Fiona Ellis (HSC - Postgraduate Researcher) <Fiona.Ellis@uea.ac.uk>
Enviado el: 09 September 2020 14:39
Para: David Fried <dfried@evolvrehab.com>
CC: Ruben Gonzalez <rgonzalez@virtualwareco.com>; Valerie Pomeroy (HSC - Staff) <V.Pomeroy@uea.ac.uk>;

2

NB. Email from CEO of Evolv and Researcher (author of the thesis) giving permission and images to use within the thesis.

11.2 APPENDIX B: PHASE I

11.2.1 Appendix 1B. Systematic Review database search strategy

The tables below detail the search strategies for each database utilised in phase I of this thesis.

The MEDLINE database search strategy

Participant *(title and abstract only)*	Stroke survivors OR stroke patients OR cerebrovascular accident OR stroke OR CVA OR stroke rehabilitation
Intervention *(title and abstract only)*	Virtual reality rehabilitation OR VR OR telerehabilitation OR telehealth OR computer rehabilitation OR technology rehabilitation OR user-computer interface
Outcome *(full text)*	Electromyography OR EMG OR Electroencephalography OR EEG OR M-waves OR H-reflex OR Functional electrical stimulation OR FES OR peripheral stimulation OR electrical stimulation OR Biomechanic* OR TMS OR Trans Magnetic Stimulation OR Evoked potential OR non-invasive brain stimulation (NBS) OR Functional Magnetic Resonance Imaging OR FMRI OR SMRI OR MR imag* OR MR scan OR magnetic resonance scan OR structural adj2 MR* OR volum adj2 OR MR OR vMRI OR MRI OR Diffusion tensor imaging OR DTI OR BOLD OR Tomography OR X-ray computed OR computer adj3 tomograph OR Positron Emission Tomography OR Magneto-encephalography OR MEG OR Neural correlate OR neurophysiological measure OR cortical reorgani* OR MEP OR PET OR CAT OR CT

Limits: English Language, human, full text.

NB. Each search row was combined using the command 'AND'

The EMBASE via Ovid database search strategy

Participant *(title and abstract only)*	Stroke survivors OR stroke patients OR cerebrovascular accident OR stroke OR CVA OR stroke rehabilitation
Intervention *(title and abstract only)*	Virtual reality rehabilitation OR VR OR telerehabilitation OR telehealth OR computer rehabilitation OR technology rehabilitation OR user-computer interface
Outcome *(full text)*	Electromyography OR EMG OR Electroencephalography OR EEG OR M-waves OR H-reflex OR Functional electrical stimulation OR FES OR peripheral stimulation OR electrical stimulation OR Biomechanic* OR TMS OR Trans Magnetic Stimulation OR Evoked potential OR non-invasive brain stimulation (NBS) OR Functional Magnetic Resonance Imaging OR FMRI OR SMRI OR MR imag* OR MR scan OR magnetic resonance scan OR structural adj2 MR* OR volum adj2 OR MR OR vMRI OR MRI OR Diffusion tensor imaging OR DTI OR BOLD OR Tomography OR X-ray computed OR computer adj3 tomograph OR Positron Emission Tomography OR Magneto-encephalography OR MEG OR Neural correlate OR neurophysiological measure OR cortical reorgani* OR MEP OR PET OR CAT OR CT OR EP

Limits: English Language, human, full text.

NB. Each search row was combined using the command ‘AND’

The PubMed Central database search strategy

Participant *(title and abstract only)*	Stroke survivors OR stroke patients OR cerebrovascular accident OR stroke OR CVA OR stroke rehabilitation
Intervention *(title and abstract only)*	Virtual reality rehabilitation OR VR OR telerehabilitation OR telehealth OR computer rehabilitation OR technology rehabilitation OR user-computer interface
Outcome *(full text)*	Electromyography OR EMG OR Electroencephalography OR EEG OR M-waves OR H-reflex OR Functional electrical stimulation OR FES OR peripheral stimulation OR electrical stimulation OR Biomechanic* OR TMS OR Trans Magnetic Stimulation OR Evoked potential OR EP OR MEP OR non-invasive brain stimulation (NBS) OR Functional Magnetic Resonance Imaging OR FMRI OR SMRI OR MR imag* OR MR scan OR magnetic resonance scan OR structural adj2 MR* OR volum adj2 OR MR OR vMRI OR MRI OR Diffusion tensor imaging OR DTI OR BOLD OR Tomography OR X-ray computed OR CT OR CAT OR computer adj3 tomograph OR Positron Emission Tomography OR PET OR Magneto-encephalography OR MEG OR Neural correlate OR neurophysiological measure OR cortical reorgani

Limits: English Language, human, full text..

NB. Each search row was combined using the command ‘AND’

Other: The following terms were not found in PMC: computer rehabilitation[Abstract], technology rehabilitation[Abstract], user-computer interface[Abstract]

The Cochrane trials database search strategy

Participant *(title and abstract only)*	Stroke survivors OR stroke patients OR cerebrovascular accident OR stroke OR CVA OR stroke rehabilitation
Intervention *(title and abstract only)*	Virtual reality rehabilitation OR VR OR telerehabilitation OR telehealth OR computer rehabilitation OR technology rehabilitation OR user-computer interface
Outcome *(full text)*	Electromyography OR EMG OR Electroencephalography OR EEG OR M-waves OR H-reflex OR Functional electrical stimulation OR FES OR peripheral stimulation OR electrical stimulation OR Biomechanic* OR TMS OR Trans Magnetic Stimulation OR Evoked potential OR MEP OR non-invasive brain stimulation (NBS) OR Functional Magnetic Resonance Imaging OR FMRI OR SMRI OR MR imag* OR MR scan OR magnetic resonance scan OR structural adj2 MR* OR volum adj2 OR MR OR vMRI OR MRI OR Diffusion tensor imaging OR DTI OR BOLD OR Tomography OR X-ray computed OR CT OR CAT OR computer adj3 tomograph OR Positron Emission Tomography OR PET OR Magneto-encephalography OR MEG OR Neural correlate OR neurophysiological measure OR cortical reorgani*

Limits: English Language, human, full text..

NB. Each search row was combined using the command 'AND'

The CINHAL via EMBESCO database search strategy

Participant *(title and abstract only)*	Stroke survivors OR stroke patients OR cerebrovascular accident OR stroke OR CVA OR stroke rehabilitation
Intervention *(title and abstract only)*	Virtual reality rehabilitation OR VR OR telerehabilitation OR telehealth OR computer rehabilitation OR technology rehabilitation OR user-computer interface
Outcome *(full text)*	Electromyography OR EMG OR Electroencephalography OR EEG OR M-waves OR H-reflex OR Functional electrical stimulation OR FES OR peripheral stimulation OR electrical stimulation OR Biomechanic* OR TMS OR Trans Magnetic Stimulation OR Evoked potential OR non-invasive brain stimulation (NBS) OR Functional Magnetic Resonance Imaging OR FMRI OR SMRI OR MR imag* OR MR scan OR magnetic resonance scan OR structural adj2 MR* OR volum adj2 OR MR OR vMRI OR MRI OR Diffusion tensor imaging OR DTI OR BOLD OR Tomography OR X-ray computed OR computer adj3 tomograph OR Positron Emission Tomography OR Magneto-encephalography OR MEG OR Neural correlate OR neurophysiological measure OR cortical reorgani* OR MEP OR PET OR CAT OR CT

Limits: English Language, human, full text..

NB. Each search row was combined using the command ‘AND’

The ProQuest (both A + I and UK + Ireland) database search strategy

Participant *(title and abstract only)*	Stroke survivors OR stroke patients OR cerebrovascular accident OR stroke OR cva OR stroke rehabilitation
Intervention *(title and abstract only)*	Virtual reality rehabilitation OR VR OR telerehabilitation OR telehealth OR computer rehabilitation OR technology rehabilitation OR user-computer interface
Outcome *(full text)*	Electromyography OR EMG OR Electroencephalography OR EEG OR M-waves OR H-reflex OR Functional electrical stimulation OR FES OR peripheral stimulation OR electrical stimulation OR Biomechanic* OR TMS OR Trans Magnetic Stimulation OR Evoked potential OR non-invasive brain stimulation (NBS) OR Functional Magnetic Resonance Imaging OR FMRI OR SMRI OR MR imag* OR MR scan OR magnetic resonance scan OR structural adj2 MR* OR volum adj2 OR MR OR vMRI OR MRI OR Diffusion tensor imaging OR DTI OR BOLD OR Tomography OR X-ray computed OR computer adj3 tomograph OR Positron Emission Tomography OR Magneto-encephalography OR MEG OR Neural correlate OR neurophysiological measure OR cortical reorgani* OR MEP OR PET OR CAT OR CT OR EP

Limits: English Language, human, full text..

NB. Each search row was combined using the command ‘AND’

Other: Full txt, English, top row was abstract (for A + I) top two rows were abstract only for UK and Ireland.

The OpenGrey database search strategy

Participant *(title and abstract only)*	Stroke survivors OR stroke patients OR cerebrovascular accident OR stroke OR cva OR stroke rehabilitation
Intervention *(title and abstract only)*	Virtual reality rehabilitation OR VR OR telerehabilitation OR telehealth OR computer rehabilitation OR technology rehabilitation OR user-computer interface
Outcome *(full text)*	Electromyography OR EMG OR Electroencephalography OR EEG OR M-waves OR H-reflex OR Functional electrical stimulation OR FES OR peripheral stimulation OR electrical stimulation OR Biomechanic* OR TMS OR Trans Magnetic Stimulation OR Evoked potential OR non-invasive brain stimulation (NBS) OR Functional Magnetic Resonance Imaging OR FMRI OR SMRI OR MR imag* OR MR scan OR magnetic resonance scan OR structural adj2 MR* OR volum adj2 OR MR OR vMRI OR MRI OR Diffusion tensor imaging OR DTI OR BOLD OR Tomography OR X-ray computed OR computer adj3 tomograph OR Positron Emission Tomography OR Magneto-encephalography OR MEG OR Neural correlate OR neurophysiological measure OR cortical reorgani* OR MEP OR PET OR CAT OR CT OR EP

Limits: English Language, human, full text..

NB. Each search row was combined using the command ‘AND’

11.3 APPENDIX C: PHASE II

11.3.1 Appendix 1C. User-led refinement of the Virtualrehab platform: Ethical approval

Faculty of Medicine and Health Sciences Research Ethics Committee

University of East Anglia

Research & Enterprise Services
West Office (Science Building)
University of East Anglia
Norwich Research Park
Norwich, NR4 7TJ

Telephone: +44 (0) 1603 591490
Email: fmh.ethics@uea.ac.uk

Web: www.uea.ac.uk/researchandenterprise

Fiona Ellis
HSC

17th February 2017

Dear Fiona,

Title: Investigating the usability and feasibility of technology to enhance stroke rehabilitation
Reference: 2016/17 27

There are still some spacing issues, including placement of photos, which if placed side by side would reduce the length of the document. However this is a usability issue rather than an ethical one. Therefore the amendments to your above proposal have been considered by the Faculty Research Ethics Committee and we can confirm that your proposal has been approved.

Please could you ensure that any further amendments to either the protocol or documents submitted are notified to us in advance and also that any adverse events which occur during your project are reported to the Committee. Please could you also arrange to send us a report once your project is completed.

Yours sincerely,

Mark Wilkinson
Chair FMH Research Ethics Committee

cc Niamh Kennedy

Faculty of Medicine and Health Sciences Research Ethics Committee

Fiona Ellis
HSC

Research & Enterprise Services
West Office (Science Building)
University of East Anglia
Norwich Research Park
Norwich, NR4 7TJ

Telephone: +44 (0) 1603 591490

Email: fmh.ethics@uea.ac.uk

Web: www.uea.ac.uk/researchandenterprise

16th March 2017

Dear Fiona,

Title: Investigating the usability and feasibility of technology to enhance stroke rehabilitation
Reference: 2016/17 27

Thank you for your e-mail dated 09.03.17 notifying us of the amendments you would like to make to your above proposal. These have been considered and we can now confirm that your amendments have been approved.

Please can you ensure that any further amendments to either the protocol or documents submitted are notified to us in advance, and also that any adverse events which occur during your project are reported to the Committee.

Please can you also arrange to send us a report once your project is completed.

Yours sincerely,

Mark Wilkinson
Chair FMH Research Ethics Committee

cc Niamh Kennedy

11.3.2 Appendix 2C. Stroke survivors and informal carers consent form, stage 1

Date of visit |__|__|-|__|__|-|__|__|__|__| (DD-MM-YYYY)

Participant Identification Number: | _____|

University of East Anglia

Consent Form: Version 3 (15.02.17)

Project Title: Investigating the usability and feasibility of technology to enhance stroke rehabilitation.

Name of Researcher: _____

Name of Participant: _____

NB. If the potential participant is unable to write, please find an independent witness who may complete this form as verbal consent is given by the potential participant. The independent witness should read each of the items to the potential participant and if the participant agrees, the independent witness should initial each of the boxes.

The purpose of the independent witness is to physically complete this consent form on the instruction of a participant in the instance that the participant cannot do so for him or herself due to a physical inability to hold and or use a pen, or in the instance in which attempting to do so would or appears to cause distress to the participant. The independent witness cannot provide consent on behalf of a participant.

An independent witness must:

- Not be part of the research team
- Not be managed by a member of the research team

One original copy of this form should be completed. The original should be stored in the investigator site file. A photocopies should be made of the original and given to the participant.

Participant Identification Number: | _____|

I confirm that I have read and understood version 3 of the Information sheet for the above study.

I have had the opportunity to consider the information, ask questions and have had these questions answered to my satisfaction.

I have read and understood the information sheet

Please initial the box below (with the thumbs up and thumbs down)

Yes	No

I understand that taking part in this project is voluntary and that I am free to withdraw at any time, without giving any reason.

I have understand that I can stop at any time

Please initial the box below (with the thumbs up and thumbs down)

Yes	No

I understand that I will be attending the MoveEx Lab at the University of East Anglia and will be asked to view a demonstration of the rehabilitation system and be given the opportunity to try it out. I understand that I will then be asked to give my views on the rehabilitation system.

I agree to attend the MoveEx Lab at the University of East Anglia to try the rehabilitation system out and give views regarding it.

Please initial the box below (with the thumbs up and thumbs down)

Yes	No

I understand that I will be asked to complete a survey asking for: demographic Information (e.g. age, gender…), impact of stroke, experiences with technology and further views on the rehabilitation system.

I am happy to complete the survey

Please initial the box below (with the thumbs up and thumbs down)

Yes	No

I understand that the researchers may wish to use anonymised quotes and transcription extracts in publications arising from this study.

I agree to anonymised quotes and movement data being used in publications and presentations.

Please initial the box below (with the thumbs up and thumbs down)

Yes	No

I understand that the discussion will be audio recorded. Only the researchers will have access to the recordings. The resultant recording will be anonymised when analysed.

I agree to being audio recorded during the discussion

Please initial / tick the box below (with the thumbs up and thumbs down)

Yes	No

I understand that if I try the rehabilitation system it will involve physical activity. I will be in a safe environment with appropriate health and safety precautions taken and in the presence of trained healthcare professionals.

Please initial the box below (with the thumbs up and thumbs down)

Yes	No

There may be other stroke related research projects being carried out by the University of East Anglia that may be of interest to yourself. We would like to add your details to a database in case a project may interest you. Your details would be protected by the data protection act (1998). You can withdraw your details from this database at any point.

I agree to be contacted regarding other Stroke related research for the University of East Anglia.

Please initial / tick the box below (with the thumbs up and thumbs down)

Yes	No

I agree to take part in this project.

Please initial the box below (with the thumbs up and thumbs down)

Yes

No

.....	.....	.....
Name of participant	Date	Signature
_____	_____	_____
Name of witness (In cases of oral consent)	Date	Signature
_____	_____	_____
Researcher (Person taking consent)	Date (In full, i.e. 01 January 2017)	Signature

11.3.3 Appendix 3C. Stroke clinicians consent form, stage 1

Date of visit |__|__|-|__|__|-|__|__|__|__| (DD-MM-YYYY)

Participant Identification Number: | _____|

University of East Anglia

Consent Form: Version 3 (15.02.17)

Project Title: Investigating the usability and feasibility of technology to enhance stroke rehabilitation.

Name of Researcher: _____

Name of Participant (Stroke clinicians):

_____

	Please initial
I have read and understood the participant information sheet (version 3).	
I understand I can ask any additional questions if I need to.	
I understand that I have been asked to try out the Virtualware stroke rehabilitation tool, after which I will be asked for my opinion on it in a focus group.	
I agree to also complete a survey asking for: my demographic information (e.g. age, gender…), profession, technological proficiency and further opinions on the Virtualware stroke rehabilitation tool.	
I understand that I will be audio recorded during the focus group.	
I understand that while information gained during the study may be published, I will not be identified and my personal results will remain confidential.	
I agree to anonymised quotes being used in publications and presentations.	
I understand that if I try the rehabilitation system it will involve physical activity. The appropriate health and safety precaution will be taken and by the trained healthcare professionals.	
I understand my right to withdraw, without giving a reason.	
I agree to take part in the study.	
I agree to be contacted regarding other Stroke related research for the University of East Anglia.	

Name of Participant	Signature	Date
.....	.....	.....
Name of Researcher	Signature	Date
.....	.....	.....

11.3.4 Appendix 4C: Example of Transcription of a Stroke participants focus group (anonymised)

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
1	**R$^{(3A)}$:** To begin with, I want to think about the actual physical device. So the Xbox and the tiny LEAP, with the bracket. What did you think of it?
2	**F1$^{(3A)}$:** Not too intrusive, I mean that could be quite big and you know hits you in the eye when you go into the room. That's quite neat and tidy. Well you can't make that any neat and tidier than it is, I mean it's quite big *[referring to the LEAP]* if it works, that is the main thing. Even though it's a bit, I mean it's not unwieldy, but if you are in your lounge and you're not using it and it's stuck on your coffee table. People come in and go what's that sort of thing, I mean if it works ok.
3	**R$^{(3A)}$:** Just to clarify for the recorders, you are talking about arm bracket as being unwieldy but the Kinect itself is
4	**F1$^{(3A)}$:** I think that's quite reasonably neat, it could be a lot bigger but you can hide that quite easily. That shape, but that *[pointing to bracket]* is not easy to hard.
5	**M1$^{(3A)}$:** I find anything to do with computers, very difficult to understand. I was a teacher for many years, but when they started to put computers in I thought it's time to call it a day. I have quite a lot of difficulty with the one at home. I mean I am quite worried about working on this with you now
6	**R$^{(3A)}$:** In terms of making this slightly easier to use, is there anything you can suggest at any level

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
7	**M1$^{(3A)}$:** Only that your guiding us and telling us what to do and hopefully we can understand your guidance and what to do
8	**R$^{(3A)}$:** Thank you
9	**M2$^{(3A)}$:** I feel the same, I am not very good with computers, I belong to the heritage and they are teaching me what to do and how to use one. But it's getting to grips with them
10	**M3$^{(3A)}$:** I don't think I would, I don't even have a computer, or mess about on it. But anything that helps stroke patients is a good thing
11	**M1$^{(3A)}$:** it's like the men are not so good on the computers as the ladies
12	*[laughing]*
13	**F1$^{(3A)}$:** I haven't got one
14	**M2$^{(3A)}$:** What worries me, is the physio people teaches you all to do this and get you better. Is it going to take them over and that's going to be it, rather than a physio teaching you what to do, that worries me

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
15	**R$^{(3A)}$:** that's a very valid worry and will not be used without a physio input.
16	**M3$^{(3A)}$:** Who pays for it?
17	**R$^{(3A)}$:** In terms of who would like to see pay for it, or how to pay for it what do you think?
18	**M1$^{(3A)}$:** The government
19	**R$^{(3A)}$:** In an ideal world
20	**M1$^{(3A)}$:** you wouldn't expect any patients to pay for it would you
21	**R$^{(3A)}$:** At the moment we are discussing all of our options, any charities or the NHS
22	**M2$^{(3A)}$:** That's what is going to help you the charities
23	**F1$^{(3A)}$:** Would it be loaned to patients, not given to them.
24	**R$^{(3A)}$:** At the moment it is all open to what will happen, one potential possibilities is loaning it and see if people like it and then the individuals can see if they want to rent it, or again through groups such as this. There is the possibility of a loan, if that was

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
	an option how would you feel? To have it loaned to you for a little while and then discuss the payments.
25	**F1$^{(3A)}$:** It's still a computer
26	**M1$^{(3A)}$:** Could it be loaded onto your own computer at home then?
27	**R$^{(3A)}$:** If you had a computer that was compatible then yes, but at the moment this isn't the final product. So we are hoping to put it into that briefcase. That would be an open, you touch a button and go. So do you think that would be slightly easier to handle technology wise?
28	**F1$^{(3A)}$:** Yes, I mean I've used a computer, it's alright when you start. I mean I did a lot of google on it and I put in the question I want, and if it came up £14 or whatever, but if it started coming up with 'have you looked at this page and this page' and then I think no. Unless it gave me an answer straight away then I am not that bothered. If I have to ask, then I have two daughters who are computer literate and I just say can you put this in for me and they do so that's it. It's a lot easier having two daughters.
29	**M1$^{(3A)}$:** I'm the same, I have three daughters and when they come home they help me on the computer, but when they are away no way.
30	**F1$^{(3A)}$:** We haven't got one at all, so it's a case of on the phone and getting a phone call back. So I don't know really. I think I prefer in a way, to having the exercises and somebody to show me *[agreement from 3 others]*. I mean I had the community

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
	nurse came around and she showed me some exercises. That was fine, because I could sit there in the arm chair and my husband was like come on do your legs and that was great. But if I have to, just no, I prefer a body as oppose to
31	**R(3A):** Human touch? *[agreement from 2 ppts]*
32	**R(3A):** If this had a way of working alongside somebody else such as a family member, would that help with the human element?
33	**M1(3A):** I think so yes, *[general agreement],* because then my wife would be able to help.
34	**F1(3A):** Because *[identifying information removed]* used to, when I had to do it he would sit on the seatee and do his legs at the same time, not because he needed to but more to encourage me to mine. But I much prefer the human touch.
35	**M2(3A):** Me too really, my wife could not do anything of this. She is not computer minded at all, she would be out in the cold, you couldn't ask. I could ask my granddaughter.
36	**M1(3A):** The older you get the harder it is to understand.
37	**M3(3A):** We would be shown what to do.
38	**F2(3A):** It also depends on what you are being shown what to do. One of my sons said it's ever so easy you just do this. And I

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
	haven’t got a clue what he’s showing me or telling me.
39	**M1$^{(3A)}$:** And the person who is telling you, often gets frustrated because you don't pick it up.
40	**R$^{(3A)}$:** Ok to summarise all of that, if there was a way of making it straight forward and easy. Where you open it up and press a button, which is all you do. Then it will run through the exercises that would be preferable as an output. That way it would be very clear and explained.
41	**M1$^{(3A)}$:** Unless you are computer literate, then you would probably not have the problems.
42	**R$^{(3A)}$:** Ok, thinking about the games themselves, the avatar on the screen there, what did you think of layout?
43	**M1$^{(3A)}$:** It looks good. We did something similar a little while ago, with some man who came in and talked to us. It wasn't all computerised.
44	**R$^{(3A)}$:** In terms of the feedback, where it tells you how you did at the end and gives you the congratulations. What did you think of that?
45	**F1$^{(3A)}$:** It's nice to know you have been doing it right. So you have not got someone there saying 'well done, see you next week' but you have at least got something that comes up and says the same thing 'well done', or whatever you computer language.

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
46	**M1$^{(3A)}$:** Does it give you a negative report if you don't do well?
47	**R$^{(3A)}$:** At the moment there are no negative reports included.
48	**F1$^{(3A)}$:** Ah
49	**M1$^{(3A)}$:** That would be preferable.
50	**R$^{(3A)}$:** In terms of feedback what sort of feedback would you like to see?
51	**M1$^{(3A)}$:** I mean would you be able to, if you did it for the first time, would that then be assessed on that first attempt. Then would you be able to try again, I mean if your first result wasn't that good.
52	**R$^{(3A)}$:** You can do it as many times as you like, it does record every attempt. At the moment it wouldn't tell you 'you didn’t do as well on the previous attempt. Would that be useful?
53	**M1$^{(3A)}$:** Yea, I mean if it’s something that tells you you aren’t doing very well. I think that would put you off it a bit.
54	**R$^{(3A)}$:** Ok, so no negative feedback.

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
55	**M1$^{(3A)}$:** Everyone likes praise *[f1- agrees]*
56	**R$^{(3A)}$:** So stick to the positive?
57	**F1$^{(3A)}$:** If you have got an instructor or whatever they are, and they are doing this sort of thing and they think you are not doing it right, they can tell you, show you, come and hold your arm to show you where you should be. Whereas a computer can't hold my hand.
58	**R$^{(3A)}$:** A computer can't hold your hand. But what it can do is tell you when you are making a wrong movement. So for instance the exercises it looks at where your spine is positioned. Where your arm joints are. Which is what we feedback from clinicians what they look at. But if your postures out, or if you are doing it in the wrong movement. It will tell you.
59	**F1$^{(3A)}$:** Does it show you then what the correct movement is?
60	**R$^{(3A)}$:** The avatar next to the outline, you are controlling, would show you the correct movement.
61	**M1$^{(3A)}$:** I do tai chi and the man that leads the tai chi is always saying posture *[identifying information removed]* posture, and *[identifying information removed]* is also saying that.

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
62	**R$^{(3A)}$:** Posture is important
63	**M1$^{(3A)}$:** Be telling me off for sitting with my legs crossed *[group laugh]*.
64	**M2$^{(3A)}$:** Instead of slouching you sit up straight when she is there.
65	**M3$^{(3A)}$:** Don't really cog with me, because if you cross your legs then your good leg helps your bad leg. I mean if you have got your bad leg on top, your good leg is underneath helping your good one.
66	**F2$^{(3A)}$:** Bad for your circulation.
67	**M3$^{(3A)}$:** I don't know, that's what they say.
68	**R$^{(3A)}$:** Thank you, in terms of the written instructions you get on this and the music in the background. What did you think of that? Is there any other way you can think of to get instructions that you prefer?
69	**F3$^{(3A)}$:** I think the music in the background is wrong, for people who have hearing problems it can confuse them.
70	**M1$^{(3A)}$:** Is there a time limit when you are doing it?

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
71	**R$^{(3A)}$:** There is and it is completely individualised, so it can longer and shorter.
72	**M1$^{(3A)}$:** And you can ask for a longer time?
73	**R$^{(3A)}$:** Yes when you create the plan you can. Going back to the music aspect, would it be preferable to not have the music in the background? Or to have a different type of music
74	**M1$^{(3A)}$:** I can't remember how loud the music was when you demonstrated it *[**R$^{(3A)}$:** You can turn it up]* or down? *[**R$^{(3A)}$:** Yes, or down]*
75	**F1$^{(3A)}$:** I don't mind the music if its soft or how can I explain this, but when you go into shops and you have got music blaring out.
76	**F2$^{(3A)}$:** It confuses the customers.
77	**F1$^{(3A)}$:** Yea, if you are looking for a dress or pair of shoes, it tends to put you off. But if it's very quiet and sort of thing, yea it's ok. But if you were doing exercises in the class you would have music on and you can always tell the women to turn it down if it's too loud. I don't like music in the background, a lot of things, but that if it was quite and a gentle tune, then I could cope with that. But if it was something loud and yea you know.

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
78	**R$^{(3A)}$:** So a gentler or quieter music *[general agreement]* or the option of the option for no music ***[M1$^{(3A)}$:** Background music]* *[general agreement]*.
79	**R$^{(3A)}$:** In terms of the difficulty, in something like this, where you get your own rehab plan how would you like to see the difficult levels go?
80	**M1$^{(3A)}$:** So would you do it in your own home?
81	**R$^{(3A)}$:** Yea
82	**M1$^{(3A)}$:** And you could have help from someone to assist you?***[R$^{(3A)}$:** Yes]* and someone in the family
83	**R$^{(3A)}$:** Yes, or on your own depending on your circumstances.
84	**F2$^{(3A)}$:** The only problem with doing it on your own at home, is do you? I mean I know when I had some very simple exercises for my legs sometimes I just think 'why should I be bothered' but if there is somebody there instructing is not quite the right word, showing me, encouraging me. That sort of thing.
85	**F3$^{(3A)}$:** I would prefer someone there.

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
86	**F2$^{(3A)}$:** Telling you not if you are doing it right or wrong, but just to ensure you keep going. Because you might start and do three of this and think oh blow that.
87	**F3$^{(3A)}$:** Or somebody else.
88	**F2$^{(3A)}$:** I would much rather go do the ironing.
89	**M2$^{(3A)}$:** Would you wait a few days after stroke before you had this?
90	**R$^{(3A)}$:** It would come in whenever you talk about your care plan for your home. So when you get discharged from home. Going along those lines, in terms of motivating someone to do their exercises is there anything else that you can think of?
91	**F2$^{(3A)}$:** I mean if people give up, it's because they have not gone onto the more difficult exercise.
92	**F1$^{(3A)}$:** Yea.
93	**F2$^{(3A)}$:** I don't know how to express it, if it's just doing this *[demonstrated arm movement]* all the time, you can see how people get fed up with it. But if they say a slightly different exercise which is more complicated. They are more likely to go ahead.
94	**F1$^{(3A)}$:** Yes, I agree with that. It can get boring if you do as you said just raising your leg up and down twenty times or whatever.

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
	But if you then go on to something more, depending what your stroke is of course, onto more exciting. You are more likely to want to do it,
95	**R$^{(3A)}$:** making sure that next level is always there.
96	**M2$^{(3A)}$:** I had a physio coming in once a week to see me, but as *[identifying information removed]* said I know you are not doing any exercises straight away. My friends and family are always pushing me. I was doing it over and over, and in the end I was walking better.
97	**R$^{(3A)}$:** So having someone tell you when you have not done it. To remind you, to keep on.
98	**M2$^{(3A)}$:** The physio women knew straight away, knew right away, knew you weren't doing it.
99	**M1$^{(3A)}$:** How soon after you had a stroke would you be expected to have ago on it.
100	**R$^{(3A)}$:** It would be completely up to you and the physio but this is to be used in the home. When you have been discharged after hospital, so anytime from when you are back in the home.
101	**M1$^{(3A)}$:** Is it better to do it as soon as possible when you have been discharged from hospital, or is it better to leave it for a while and see how you do.

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
102	**R$^{(3A)}$:** As with all rehabilitation *[**M1$^{(3A)}$:** the progress you make]* and what your problems are, with all rehabilitation the sooner you can do something the more you get into the routine and go up those levels. But this can be used any time after your stroke, up to any point.
103	**F2$^{(3A)}$:** Do you not think peoples frame of mind come into it. I am sure we have all known people who have had quite nasty strokes and are determined not to make an effort and then you get other people who have had smaller one. They have the determination to keep going and so they can keep living the way they have always lived. I am convinced there is something psychological about it as well.
104	**R$^{(3A)}$:** Well then I am going to turn that question back to the group, along those lines when do you think this should be offered to people after their stroke.
105	**F2$^{(3A)}$:** Right at the beginning
106	**R$^{(3A)}$:** And do you think as you mentioned there frame of mind would come into that?
107	**F2$^{(3A)}$:** Yes *[general agreement]*
108	**R$^{(3A)}$:** Is there anything we can do with this arrangement to help them

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
109	**M1$^{(3A)}$:** would the physiotherapist come to your home and help you be aware of this equipment.
110	**R$^{(3A)}$:** Yes they would be giving this to you
111	**F2$^{(3A)}$:** Just things I remember when I was first ill, I could not even feed myself and I thought if I order mince beef and mash potatoe for my meal I may as well spoon it in. It was little things like that, that got me going again.
112	**F1$^{(3A)}$:** I couldn't even a couple of days after mine, I was having trouble with a cross-word puzzle. I went and put an answer in and don't remember what I wrote but it wasn't the answer I expected to come out. I couldn't cope with that bit. But within a day or so, I kept on doing these cross-words and it all clicked into place. I couldn't at one time cut my dinner up, I forgotten what I had but meat of some description which you would have no problem cutting up. I had to get a nurse to come and cut it up into several pieces. But several days later I was fine.
113	**F2$^{(3A)}$:** That's determination again, isn't it. You wanted to do it. *[general agreement]*
114	**F1$^{(3A)}$:** Because I knew when I got home, I would have to do it. I mean *[identifying information removed]* has been very good and he has encouraged me to do things, to get going.
115	**M3$^{(3A)}$:** See I had my stroke a long time ago, 17 years and I was in the hospital 5 weeks, apparently that's usual 7.

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
116	**F1$^{(3A)}$:** *[Identifying information removed]* I was there 4 and a half months.
117	**M3$^{(3A)}$:** I wasn't in any fit state to use anything when I first came home. I couldn't do anything.
118	**M1$^{(3A)}$:** How soon after you came out of the hospital would you start using this equipment?
119	**R$^{(3A)}$:** It would be completely up to yourself and the physiotherapist, but in terms of your experience when do you think would be the best time to approach someone who has had a stroke about this option?
120	**F1$^{(3A)}$:** Right at the beginning.
121	**M1$^{(3A)}$:** As soon as possible. If it's going to improve their situation.
122	**R$^{(3A)}$:** Thinking to your experiences as you went through care after you have had a stroke. Do you think there is a place for this? In the current care system?
123	**M1$^{(3A)}$:** It might be beneficial if the carers could be trained to use something like this as well, then they could assist you, rather than you being left on your own to try and use it. *[general agreement]*

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
124	**M2$^{(3A)}$:** But there will be more and more people used to computers in years to come.
125	**R$^{(3A)}$:** Is there any benefits or negatives to having something like this in your home for your rehab that you can think of? Such as an emotional, or social, or any negatives?
126	**M1$^{(3A)}$:** I think it would be very good if there was someone in the house at the same time as you. I mean I am often in the house on my own, and I very computer illiterate and when I get stuck on something that's it. I will fold up the machine for the day and forget about it. If there was someone there that could help you, I think I would preserve and use it a bit more.
127	**F2$^{(3A)}$:** When our generation has died out and all the youngsters who are being educated now will be computer literate.
128	**M1$^{(3A)}$:** That's what I mean.
129	**R$^{(3A)}$:** Thank you all for this discussion, do you have anything further or any final remarks? Anything you would want to see from this?
130	**M1$^{(3A)}$:** How long has this been in operation. Is it fairly new?
131	**R$^{(3A)}$:** In the last year it has been operational, so fairly new. The prototype for the next phase is currently in development. Which is what this information will be used for.

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
132	**M1$^{(3A)}$:** Do you think hospitals will be given one of these?
133	**R$^{(3A)}$:** We shall see, hopefully. Is there any further remarks for this?
134	**M1$^{(3A)}$:** It's going to be costly I suppose?
135	**R$^{(3A)}$:** These are about £50 *[pointing to the Kinect]* which is not as expensive as the older equipment.
136	**M1$^{(3A)}$:** Would hospitals be given this equipment.
137	**R$^{(3A)}$:** They would be given a package where all the software and equipment would be incorporated.
138	**M1$^{(3A)}$:** So you could do it while you were in hospitals?
139	**R$^{(3A)}$:** potentially, at the moment we are aiming for the home. Do you think that would be a benefit?
140	**M1$^{(3A)}$:** If you are there for a long time, but you are fairly ok.
141	**F2$^{(3A)}$:** Can I make a suggestion, if the patient is able to use that could they not make a donation towards the use of it rather than

Row	**Content: R,** research; **F1,** Female participant speaker; **M1**, Male participant speaker; 3A – reference number for the focus group
	charging them the full price. Because that depends on their financial situation.
142	**M1$^{(3A)}$:** I mean you could have a programme they purchase and then send back. It won't stay in the home for a long time.

11.4 APPENDIX D: PHASE III

11.4.1 Appendix 1D. Ethical approval letters, Favourable ethical opinion from the London – Surrey Research Ethics Committee, for the Health Research Authority

NHS
Health Research Authority

London - Surrey Research Ethics Committee
Whitefriars
Level 3, Block B
Lewins Mead
Bristol
BS1 2NT

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

04 May 2018

Miss Fiona Ellis
PhD student
University of East Anglia
Queen's Building
School of Health Sciences
University of East Anglia
NR4 7TJ

Dear Miss Ellis

Study title:	**Task-orientated training via the VirtualRehab platform for the upper limb after stroke: Feasible dose and predictive markers of response**
REC reference:	**18/LO/0562**
IRAS project ID:	**233548**

Thank you for your letter of 26 April 2018, responding to the Committee's request for further information on the above research and submitting revised documentation.

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

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact hra.studyregistration@nhs.net outlining the reasons for your request.

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Health Research Authority

Confirmation of ethical opinion

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

Conditions of the favourable opinion

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

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

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System, at www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

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

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

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

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

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

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

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

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

Ethical review of research sites

NHS sites

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

Non-NHS sites

The Committee has not yet completed any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as an SSA application(s) has been reviewed. In the meantime no study procedures should be initiated at non-NHS sites.

Approved documents

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

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Poster for Neurologically Intact Recruitment:Would you like to help us investigate using technology for Stroke Rehabilitation?]	1	10 November 2017
Covering letter on headed paper [Covering letter for ethics]	1	09 March 2018
Covering letter on headed paper [Response to PO letter]		23 April 2018
GP/consultant information sheets or letters [General Practice Enquiry Email]	1	10 November 2017
Interview schedules or topic guides for participants [Interview guide following the control period]	1	10 November 2017
Interview schedules or topic guides for participants [Interview guide following trial with virtual reality device]	1	10 November 2017
IRAS Application Form [IRAS_Form_13032018]		13 March 2018
IRAS Checklist XML [Checklist_27032018]		27 March 2018
Letter from funder [Contract for Industry Funding]	1	27 October 2016
Letter from statistician [Statistical feedback email]	1	09 March 2018
Letter from statistician [Letter from statistician]	1	10 November 2017
Letters of invitation to participant [Upper limb stroke rehabilitation via the VirtualRehab platform: research study invitation (v.1: 10th	1	10 November 2017

November, 2017)]		
Letters of invitation to participant [Upper limb stroke rehabilitation via the VirtualRehab platform: research study invitation (v.1: 10th November, 2017)]	1	10 November 2017
Letters of invitation to participant [Letter/email of acceptance for neurologically intact people and Letter/email of rejection for neurologically intact people]	1	10 November 2017
Other [Demographic questions for people with stroke]	1	09 March 2018
Other [Screening for skin preparation]	1	10 November 2017
Other [GP initial screening form]	1	10 November 2017
Other [Neurologically Intact Demographic Questions]	1	10 November 2017
Other [People with stroke demographic questions]	1	10 November 2017
Other [Wolf Motor Function Test (WMFT) Data Collection Form]	1	10 November 2017
Other [Action Research Arm Test (ARAT) Data Collection Form]	1	10 November 2017
Other [The Motricity Index Data Collection Form]	1	10 November 2017
Other [Word Association Task]	1	10 November 2017
Other [People with stroke demographic questions]	2	23 April 2018
Participant consent form [Investigating the feasibility of delivering upper limb physiotherapy training via the VirtualRehab platform Participant Consent Form]	1	14 September 2017
Participant consent form [Investigating the feasibility of delivering upper limb physiotherapy training via the VirtualRehab platform: Consent Form]	1	10 November 2017
Participant consent form [Consent form for neurologically intact people.]	2	23 April 2018
Participant consent form [Consent form for people with stroke]	2	23 April 2018
Participant information sheet (PIS) [Investigating the feasibility of delivering upper limb physiotherapy training via the VirtualRehab platform Participant Information Sheet]	1	10 November 2017
Participant information sheet (PIS) [Investigating the feasibility of delivering upper limb physiotherapy training via the VirtualRehab platform Participant Information Sheet]	1	10 November 2017
Participant information sheet (PIS) [Participant information sheet for neurologically intact people]	2	23 April 2018
Participant information sheet (PIS) [Participant information sheet for people with stroke]	2	23 April 2018
Research protocol or project proposal [Task-orientated training via the VirtualRehab platform for the upper limb after stroke: Feasible dose and predictive markers of response]	1	08 March 2018
Summary CV for Chief Investigator (CI) [Fiona Ellis CV]	1	08 February 2018
Summary CV for student [Fiona Ellis CV]	1	08 February 2018
Summary CV for supervisor (student research) [Nicola Hancock CV]	1	04 December 2017
Summary CV for supervisor (student research) [Valerie Pomeroy CV]	1	17 November 2017
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Study flowchart]	1	10 November 2017
Validated questionnaire [People with stroke equipment usability	1	10 November 2017

NHS
Health Research Authority

survey]		

Statement of compliance

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

After ethical review

Reporting requirements

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

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

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

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

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

18/LO/0562	**Please quote this number on all correspondence**

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

Yours sincerely

Rebecca Moulton

Pp

Mrs Chrissie Lawson
Chair

Email:nrescommittee.secoast-surrey@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: *Tracy Moulton*

11.4.2 Appendix 2D. Ethical approval letters, Favourable ethical opinion for site-specific assessments. from the London – Surrey Research Ethics Committee, for the Health Research Authority

NHS
Health Research Authority

London - Surrey Research Ethics Committee
Whitefriars
Level 3, Block B
Lewins Mead
Bristol
BS1 2NT

Telephone: 0207 1048058

13 June 2018

Miss Fiona Ellis
Queen's Building
School of Health Sciences
University of East Anglia
NR4 7TJ

Dear Miss Ellis

Study title:	**Task-orientated training via the VirtualRehab platform for the upper limb after stroke: Feasible dose and predictive markers of response**
REC reference number:	**18/LO/0562**
SSA reference number:	**18/LO/1076**
IRAS project ID:	**233548**

The REC gave a favourable ethical opinion to this study on 03 May 2018.

Following site-specific assessment by the Committee, I am pleased to confirm the extension of the favourable opinion to the new site(s) and investigator(s) listed below:

Research site	*Principal Investigator / Local Collaborator*
University of East Anglia Movement and Exercise Physiology Laboratory	Miss Fiona Ellis

The favourable opinion is subject to management permission or approval being obtained from the host organisation prior to the start of the study at the site concerned.

Statement of compliance

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

18/LO/0562 ***Please quote this number on all correspondence***

Yours sincerely

Rebecca Howling

Rebecca Howling
Rec Assistant

Email: nrescommittee.secoast-surrey@nhs.net

11.4.3 Appendix 3D. Ethical approval letters, Confirmation of Health Research Authority approval

Fiona Ellis (HSC - Postgraduate Researcher)

From: KESHVARA, Rekha (HEALTH RESEARCH AUTHORITY) <rekha.keshvara@nhs.net>
Sent: 08 May 2018 08:55
To: Fiona Ellis (HSC - Student)
Subject: RE: IRAS 233548 – Request for information
Attachments: HRA Schedule of Events.xls; HRA Statement of Activities.docx

Thanks Fiona,

I have now approved the study. Please see attached validated SoA/SoE and use these for the sites. Thanks.

Best wishes,
Rekha

Rekha Keshvara
Senior Assessor
Health Research Authority
T. 0207 1048191
E. Rekha.Keshvara@nhs.net
W. www.hra.nhs.uk

11.4.4 Appendix 4D. Go signal acquisition details

Previous research within the UEA MovExLab used an integrated trigger delivering a randomised audible 'Go' signal, which automatically marked the movement and neurophysiology data. The trigger was run through Vicon motion capture camera's (Oxford Metrics, Oxford, UK) with integrated sEMG data capturing capabilities. This allowed for movement and neurophysiology data to be time-matched and marked with the 'Go' signal, enabling time to onset to be calculated. Unfortunately, this set-up was tailor-built for the UEA MovExLab and could not be used within the home environment, as required for this study; Thus, another trigger method was devised.

The Researcher wrote a series of scripts, using the open-source programming language, Python (Rossum and Jr, 1995) to: provide a randomised (between 10 to 15 seconds) audible 'Go' signal, record the sEMG recording onset and to mark the data accurate to 10 milliseconds (full details in Appendix 4C). A randomised trigger was used to potentially prevent anticipatory movements and allowing for a resting baseline to be collected.

The trigger script (created with PyCharm) (JetBrains, Prague, Czechia) was designed to run in parallel with the sEMG software. Once opened, the python script asks the Researcher to name a folder. This folder is then used to store all data from the participant, output from the python script and the sEMG. Once the participant is ready, the Researcher starts the 'trigger' option for that

task, and a randomised beep is then given as the Go signal. After the first go signal is given the ‘trigger script’ waits for 10 seconds to allow the participant to complete the trial. A random timer then begins before giving the second go signal and the ‘trigger script waits for 10 seconds again before the random timer begins again and the third go signal is given. As the muscle and trigger data were collected using two different methods, there was an inherent delay between when each would start recording. Therefore, the final challenge in creating a manual trigger was ensuring the data could be marked accurately; this required additional software.

To capture raw data from the sEMG a free and open-source network protocol analyser ‘Wireshark’ was used. Wireshark allows users to capture, in real-time, and analyse what is happening on network interfaces, both wired and wireless. An extension module to Wireshark also allows users to capture raw data on USB interfaces. The captures produced contain nanosecond timestamps of when data was sent or received and can be exported to various formats for later use. Packets are units of data which are sent between a source and destination over a network. A wireless network exists between the sEMG sensors and the base station. The base station then sends the data to the laptop via the USB interface. When performing a capture, before recording any data from the sensors thousands of packets are exchanged to and/or from the sensors. These packets are small in size and contain environment information such as battery level, temperature, humidity etc. When starting a recording the packets containing sensor data for the sEMG and can easily be identified

as they are much larger in size and contains sensor positioning information. The timestamps of these packets are accurate to nanoseconds. Hence, the data could then be fed back into another Python script and accurate go signals marked.

11.4.5 Appendix 5D. Time to onset of muscle activity-specific calculations

	Formulae
Baseline mean (BLM)	$\bar{x} = {(sum\ of\ 500ms\ prior\ to\ Go\ signal)}\Big/{(N\ of\ records\ 500ms\ prior\ to\ Go\ signal)}$
Baseline standard deviation (BLSD)	$SD = \sqrt{\frac{\sum_{i=1}^{N}(x_i - \bar{x})^2}{N-1}}$
Baseline threshold, muscle 'on'	$BLM + (3 * BLSD)$

NB: $\bar{x}$ *is the mean value and* N *is the sample number*

11.4.6 Appendix 6D. Stroke participants motricity index raw data (KG)

Participant ID	Arm	Baseline one measures			Baseline two measures			Outcome measures		
		Trial 1	Trial 2	Trial 3	Trial 1	Trial 2	Trial 3	Trial 1	Trial 2	Trial 3
VR02	Less paretic	12.05	19.05	22	19	18	16	20	20	20
	More paretic	0.01	0.01	0.01	0	0	0	0.01	0.01	0.01
VR05	Less paretic	18	22	20	22	22.2	22	22	21	22
	More paretic	1.5	1.5	1.5	2	2	2.5	0.25	0.25	0.75
VR06	Less paretic	29	30	28	36	34.5	28.5	27	24	30
	More paretic	26	26	23	33	36	25	26	28	26
VR07	Less paretic	22	28	27	18	19	22	31	30	33
	More paretic	4	2	2	4	4	1	9	4	2
VR09	Less paretic	28	26	22	22	22	22	25	22	16
	More paretic	0	0.5	1	1	1	1	2	2	2
VR10	Less paretic	16	18	18	18	12	16	18	21	10
	More paretic	2	4	3	4	2.75	4	4	5	6
VR12	Less paretic	25	23	22	24	24	22	31	21	22
	More paretic	2	3	4	5	5	6	8	8	6

NB. VR01, VR08 and VR11 withdrew before data collection

11.4.7 Appendix 7D. Action Reaction Arm Test raw scores

Participant ID	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12
VR01	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd
VR02	77	77	65	77	65	73	77	77	70	70	64	58
VR03	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd
VR04	65	84	84	79	84	n/c	84	n/c	77	77	84	84
VR05	61	39	39	34	39	39	39	39	50	39	39	39
VR06	84	77	85	77	84	77	77	100	84	77	77	77
VR07	48	60	51	54	45	51	60	65	65	70	60	60
VR08	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd
VR09	n/c	51	n/c	71	71	71	73	56	56	39	64	50
VR10	78	84	78	84	n/c	77	77	n/c	71	77	77	77
VR11	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd	wd
VR12	n/c	72	84	70	70	m/c	77	77	76	71	77	77

NB. wd-withdrawn, **W**-weekly measurement, **n/c** – not collected

11.4.8 Appendix 8D. Time to onset of muscle activation (miliseconds) during reach task (cup) for the healthy participant group

Participant ID		Deltoid		Bicep		Tricep		FCR		ECR	
		Right arm	Left arm	Right arm	Left arm	Right arm	Left arm	Right arm	Left arm	Right arm	Left arm
H01	m	475	299.00	340.33	432.33	568.33	739.00	261	336.50	273	486.67
	sd	90.27	46.51	36.95	143.18	445.78	538.82	936.47	37.48	39.28	121.55
H02	m	823.5	833.00	1015.67	675.00	1345.33	743.33	x	714.33	993	611.00
	sd	78.49	98.00	430.93	48.08	423.18	175.24	x	32.72	392.63	47.84
H03	m	643.33	467.33	597.00	425.00	946	736.00	x	754.00	625	518.33
	sd	218.53	90.39	168.14	82.87	247.79	241.83	x	87.68	220.62	56.77
H04	m	492.33	626.33	577.67	504.00	1101.67	n/a	556.50	926.67	500.33	541.00
	sd	103.93	83.61	80.75	26.21	210.33	x	50.20	401.08	83.93	1.00
H05	m	531.33	655.33	482	613.67	723.33	662.00	667.33	678.00	491	645.00
	sd	93.35	78.36	55.05	39.15	379.52	0.00	146.37	60.75	24.27	57.98
H06	m	493.67	560.33	462.33	453.67	843.50	805.67	517.67	426.67	450.50	385.00
	sd	127.03	170.41	109.99	62.18	72.83	117.54	106.09	46.76	43.13	107.13
H07	m	1444.5	773.33	1263.33	995.33	1992.67	850.00	1858.50	x	1212	1184.00
	sd	70	177.09	106.51	268.26	251.91	137.18	19.09	x	60.81	0.00
H08	m	770	741.50	710.33	689.00	1155	849.50	802.33	x	780.33	871.67
	sd	9.00	91.22	48.58	19.80	70.71	762.97	13.61	x	7.51	140.54
H09	m	1271.67	1219.67	1243.33	823.00	1099	1273.67	1094.67	742.67	960	832.33

Participant ID		Deltoid		Bicep		Tricep		FCR		ECR	
		Right arm	**Left arm**	**Right arm**	**Left arm**	**Right arm**	**Left arm**	**Right arm**	**Left arm**	**Right arm**	**Left arm**
	sd	8.02	209.66	29.02	302.25	201.91	189.64	274.80	395.04	333.51	336.70
H10	m	1171.67	972.33	713	538.00	1302.67	962.00	709.33	799.50	761	747.67
	sd	349.87	170.58	294	200.82	663.10	383.06	227.31	40.31	457.16	200.24
Group m		**811.70**	**714.82**	**740.50**	**614.90**	**1107.75**	**846.80**	**808.42**	**672.29**	**704.62**	**682.27**
Group sd		**360.08**	**260.06**	**325.75**	**185.81**	**396.46**	**182.33**	**487.27**	**195.45**	**290.46**	**234.36**

Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)

NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; therefore, no standard deviation;

11.4.9 Appendix 9D. Time to onset of muscle activation (milliseconds) during reach task (cup) for the stroke participant group

Less paretic arm

Stroke participant group		BL1	BL2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	O
Deltoid	mean	954.33	1126	1092.66	631.94	778.37	744.42	659.15	749.22	771.58	831.86	663.94	667.47	724.18	788	796.75
	SD	133.63	442.81	527.36	378.08	434.38	409	296.36	321.77	248.17	295.21	280.37	249.35	238.82	317.41	252.92
	number participants (number of valid trials)	1 (3)	4 (12)	4 (12)	7 (19)	6 (16)	5 (14)	7 (19)	6 (18)	7 (17)	5 (15)	7 (19)	7 (19)	6 (16)	5 (14)	7 (20)
Bicep	mean	620.33	712.91	815.21	708.1	722.82	726.92	670.43	724.22	655.85	812.57	627.71	674.26	630.92	798.76	741.44
	SD	122.27	273.73	466.51	412.23	412.03	408.31	324.95	341.39	244.05	327.07	256.8	186.98	268.91	223.51	222.58
	number participants (number of valid trials)	2 (6)	4 (12)	5 (14)	8 (20)	6 (17)	5 (14)	8 (23)	6 (18)	7 (20)	5 (14)	7 (21)	7 (19)	5 (13)	5 (13)	7 (18)
Tricep	mean	1536	1225.28	x	826.25	1002.4	686.66	1020.92	871.8	1123.64	1002.55	706.25	1031.76	1055.2	1213	1169.12

Stroke participant group		BL1	BL2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	O
	SD	352.85	357.35	x	429.7	167.5	311.5	420.01	305.22	437.64	451.58	229.25	404.48	404.52	389.01	247.82
	number participants (number of valid trials)	1 (3)	3 (7)	x	2 (4)	2 (5)	1 (3)	5 (13)	4 (10)	5 (14)	3 (9)	2 (4)	5 (13)	3 (5)	3 (7)	3 (8)
FCR	mean	3750.5	802.71	745	949.2	828.71	911	802.31	841.88	842.75	909.2	623.9	764.4	911.3	1061.66	924.5
	SD	2119.19	317.94	255.63	413.5	409.86	436.7	383.06	382.36	287.26	453.8	154.57	401.7	376.78	333.51	353.35
	number participants (number of valid trials)	1 (2)	3 (7)	3 (7)	4 (10)	4 (7)	2 (3)	6 (16)	4 (9)	5 (12)	2 (5)	4 (11)	5 (15)	4 (10)	3 (6)	7 (18)
ECR	SD	548.16	743.83	790.25	785.05	694.25	826.69	708.27	720.35	698.75	864.78	649.42	753.66	711.11	812.42	739
	mean	304.13	217.33	426.62	404.42	316.94	422.84	335.38	331.99	189.32	280.43	234.29	250.43	274.46	255.74	223.09
	number participants (number of valid trials)	2 (6)	4 (12)	5 (12)	7 (17)	4 (12)	5 (13)	8 (22)	6 (17)	7 (20)	5 (14)	7 (19)	6 (18)	6 (17)	5 (14)	6 (16)

Stroke participant group	BL1	BL2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	O
Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)															
NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; therefore no standard deviation; **BL**, baseline measures; **W**, weekly measures; Outcome measures															

More paretic arm

Stroke participant group		BL1	BL2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	O
Deltoid	mean	661	873.31	858.73	900.53	540.29	763.07	730.39	825.5	922.77	863.36	1050.21	963	800.43	855.44	820.65
	SD	115.50	465.62	384.42	393.96	187.85	404.48	376.86	269.57	390.8	379.97	491.83	640.6	271.34	346.17	358.11
number participants (number of valid trials)		1 (3)	5 (13)	5 (11)	7 (19)	5 (14)	5 (15)	8 (23)	6 (14)	8 (22)	6 (14)	6 (14)	7 (20)	5 (14)	6 (16)	7 (17)
Bicep	mean	913.33	888.21	936.57	936.57	824.79	682.71	602.25	772.7	1029.53	908.92	788	1067.6	947.13	1067.47	1212.37
	SD	472.21	373.58	329.14	364.09	479.272	236.8	208.28	278.30	398.16	352.46	415.41	681.83	438.5	411.95	1617.32
number participants (number of valid trials)		1 (3)	5 (14)	4 (10)	5 (14)	7 (19)	5 (14)	7 (20)	4 (10)	7 (19)	5 (12)	7 (16)	7 (16)	6 (15)	6 (15)	7 (19)
Tricep	mean	1080.67	1495.30	1137.89	1053.33	1180.38	1261.42	1201.39	1156.57	1228	1565.5	1235.46	1242.4	1004.92	1122.11	1157.93

Stroke participant group		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**O**
	SD	334.15	675.32	296.98	686.58	643.72	429.69	332.79	376.06	517.61	678.28	501.445	407.264	258.135	461.373	380.425
number participants (number of valid trials)		1 (3)	5 (13)	3 (9)	2 (6)	4 (8)	4 (12)	5 (13)	4 (7)	5 (12)	5 (12)	(13)	(10)	(13)	3 (9)	(14)
FCR	mean	x	1330.88	1096	1168.67	1066.125	1185.4	1300.54	585	1336.18	1364	1564.5	1386.3	1234.72	1080.17	1207.88
	SD	x	347.44	355.75	338.45	204.3725	455.91	479.95	229.82	451.83	462.22	419.74	775.19	372.55	459.625	476.286
number participants (number of valid trials)		x	3 (8)	2 (5)	3 (6)	3 (8)	2 95)	5 (13)	2 (3)	4 (11)	4 (9)	3 (8)	4 (10)	5 (11)	5 (12)	6 (16)
ECR	mean	x	1178.77	797.25	839.39	654.64	678.42	913.88	822.14	1088.68	914.23	924.78	903.55	852.43	983.33	1000.59
	SD	x	733.33	533.45	354.85	255.82	381.61	517.49	348.02	513.92	387.37	505.22	562.317	446.706	336.554	378.357
number participants		x	5 (13)	4 (12)	5 (13)	6 (14)	5 (12)	6 (16)	5 (14)	8 (19)	6 (13)	(18)	(20)	(14)	(12)	(17)

Stroke participant group	**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**O**
(number of valid trials)															

Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)

NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; therefore, no standard deviation; **BL**, baseline measures; **W,** weekly measures; Outcome measures

11.4.10 Appendix 10D. Time to onset of muscle activation (milliseconds) during reach task (cup) for stroke participant group, VR02

Less paretic, right		BL1	BL2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	Outcome
Deltoid	m	x	x	x	307.33	722	592.66	548	547	697	521	512.66	733.33	654.66	543.66	716.66
	sd	*x*	*x*	*x*	*115.21*	^	*167.25*	*144.44*	*100.64*	*164.58*	*201.5*	139.23	115.47	*78.92*	*84.24*	*218.62*
Bicep	m	x	x	690	439.66	722	615.66	639	605.66	666.5	684.33	492.33	700	757.66	674.33	760
	sd	*x*	*x*	*206.47*	*185.04*	*171.49*	*190.11*	*99.2*	*72.39*	*85.55*	*125.16*	92.93	100	*125*	*220.66*	*193.52*
Tricep	m	x	x	x	x	x	x	1449	911.5	1599	1310	x	1450	1737	1545.66	1235
	sd	*x*	*x*	*x*	*x*	*x*	*x*	*394.82*	*229.8*	*292.8*	*397.83*	x	212.13	^	*162.17*	*447.75*
FCR	m	x	x	938.5	1379	1634	x	1055.33	x	904	1366	x	1333.33	1188.33	890	886
	sd	*x*	*x*	*38.89*	*129.94*	^	*x*	*580.27*	*x*	*159.36*	*203.64*	x	550.75	*638.87*	*105.08*	*214.65*
ECR	m	x	x	790.5	621.66	993.33	814	856	738	935	827.66	531.33	866.66	859.5	870	879
	sd	*x*	*x*	*217.08*	*172.54*	*122.65*	*167.59*	*137.27*	*216.63*	*264.05*	*97.68*	120.08	115.47	*85.55*	*169.92*	*204.62*
More paretic, left		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	x	x	499.33	959.66	504.33	736.33	738	930.66	1798	733.66	641	733.33	728.00	635.66	910
	sd	*x*	*x*	*66.34*	*157.81*	*55.89*	*148.85*	*151.33*	^	^	*313.83*	*69.29*	*230.94*	*199.24*	*450.49*	*335.41*
Bicep	m	x	x	725.33	1306.33	579.33	580	704.33	665.66	972	1461.50	763	933.33	903.33	1131.66	982.33
	sd	*x*	*x*	*269.35*	*365.69*	*158.05*	*1.41*	*104.80*	*312.02*	*394.56*	*88.38*	*89.09*	*321.45*	*170.21*	*443.47*	*227.45*
Tricep	m	x	x	844.33	1626.33	715.66	1053.33	1007.66	1234.50	1513.5	1147.50	1153	900	945.00	1389.66	1145.66
	sd	*x*	*x*	*182.65*	*311.96*	*299.75*	*131.46*	*274.88*	*23.33*	*721.95*	*210.01*	*172.53*	*141.42*	*245.12*	*420.50*	*182.98*
FCR	m	x	x	1036.33	1285.33	1044.66	1508	1314.33	455	1668.66	1579	1444.5	1350	1467.33	1698.33	891.66
	sd	*x*	*x*	*448.50*	*229.34*	*134.90*	*129.20*	*130.53*	*65.05*	*729.46*	*118.79*	*72.83*	*70.71*	*146.65*	*462.36*	*178.30*
ECR	m	x	x	765.66	861.66	478.33	658.33	602.66	697.66	997.66	1073.50	678.5	800	859.50	995.66	1345

sd	*x*	*x*	*49.01*	*186.12*	*39.80*	*165.56*	*88.18*	*143.50*	*119.13*	*142.12*	*7.77*	*200*	*36.06*	*293.99*	*376.55*

Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)

NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; **^,** only 1 valid trial therefore no standard deviation; **BL**, baseline measures; **W**, weekly measures; **Outcome,** outcome measures

NB. More paretic hand could not grasp cup – touched to complete movement

11.4.11 Appendix 11D. Time to onset of muscle activation (milliseconds) during reach task (cup) for stroke participant group, VR04

Less paretic, Right		BL1	BL2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	Outcome
Deltoid	m	x	x	376.66	454.00	x	x	561.00	x	710.50	x	380.33	x	x	x	x
	sd	x	x	158.68	43.00	x	x	190.76	x	211.42	x	129.53	x	x	x	x
Bicep	m	x	x	360.66	617.00	x	x	348.00	x	472.33	x	513.66	x	x	x	x
	sd	x	x	125.83	280.80	x	x	195.42	x	109.24	x	159.06	x	x	x	x
Tricep	m	x	x	x	976.00	x	x	756.00	x	x	x	x	x	x	x	x
	sd	x	x	x	377.38	x	x	162.63	x	x	x	x	x	x	x	x
FCR	m	x	x	553.00	x	x	x	450.33	x	733.33	x	486.00	x	x	x	x
	sd	x	x	305.06	x	x	x	209.06	x	384.77	x	76.21	x	x	x	x
ECR	m	x	x	373.00	453.50	x	x	418.66	x	602.00	x	447.33	x	x	x	x
	sd	x	x	144.18	12.02	x	x	209.10	x	185.26	x	104.27	x	x	x	x
More paretic, Left		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	x	x	1179.00	1101.33	x	x	487.66	x	879.66	x	799.00	x	x	x	x
	sd	x	x	0.00	298.32	x	x	30.13	x	86.74	x	18.38	x	x	x	x
Bicep	m	x	x	420.66	689.66	521.00	864.66	439.66	x	660.33	x	834.50	x	x	x	x

	sd	x	x	157.57	298.32	25.45	400.91	30.13	x	59.37	x	521.13	x	x	x	x
Tricep	m	x	x	1198.33	x	x	x	x	x	x	x	x	x	x	x	x
	sd	x	x	129.45	x	x	x	x	x	x	x	x	x	x	x	x
FCR	m	x	x	x	x	x	x	417.00	x	x	x	x	x	x	x	x
	sd	x	x	x	x	x	x	0.00	x	x	x	x	x	x	x	x
ECR	m	x	x	337.66	562.33	522.00	590.33	296.50	x	605.33	x	476.00	520.66	x	x	x
	sd	x	x	113.02	217.49	161.22	685.85	34.64	x	112.75	x	24.33	199.61	x	x	x

Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)

NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; **^,** only 1 valid trial therefore no standard deviation; BL, baseline measures; W, weekly measures; Outcome, outcome measures

11.4.12 Appendix 12D. Time to onset of muscle activation (milliseconds) during reach task (cup) for stroke participant group, VR05

Less paretic, left		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	x	1136.33	1265.67	x	631.67	x	x	x	1174	750.67	x	471.67	1337	884.67	856.33
	sd	*x*	*224.18*	*121.23*	*x*	*457.47*	*x*	*x*	*x*	*105.96*	*256.21*	*x*	*145.07*	*x*	*372.22*	*407.32*
Bicep	m	x	497	469	1783	569.33	x	904.67	x	615.33	656.67	x	765.33	x	565	740.67
	sd	*x*	*133.37*	*53.84*	^	*450.25*	*x*	*279.69*	*x*	*146.4*	*299.51*	*x*	*132.15*	*x*	*31.11*	*180.48*
Tricep	m	x	1235.67	x	x	x	x	x	x	1230	1227.67	x	x	x	1110.67	1129
	sd	*x*	*203.49*	*x*	*x*	*x*	*x*	*x*	*x*	*602.51*	*89.52*	*x*	*x*	*x*	*85.11*	*48.28*
FCR	m	x	x	x	x	1035	x	909.67	x	x	x	x	862.67	x	1375.5	1400.33
	sd	*x*	*x*	*x*	*x*	^	*x*	*256.32*	*x*	*x*	*x*	*x*	*159.53*	*x*	*485.78*	*269.34*
ECR	m	x	636	533	1797	603.67	x	850.33	x	577.67	894	x	742	997	615	690
	sd	*x*	*92.48*	*45.18*	^	*490.09*	*x*	*285.44*	*x*	^	*145.68*	*x*	*214.27*	*145.08*	*87.11*	*99.69*
More paretic, right		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	x	1069.33	1021.33	x	833.66	561.33	561.33	x	1086.66	486.5	x	1034	722	857.5	969
	sd	*x*	*270.11*	*254.57*	*x*	*209.87*	*262.07*	*262.07*	*x*	*315.68*	*239.7*	*x*	*157.77*	*49.12*	*13.43*	*119.02*
Bicep	m	x	560	1114.5	x	910	812	812	x	1223.33	628	x	1147.33	1411	1057	1254.33
	sd	*x*	*517.6*	*347.18*	*x*	*185.03*	*173.94*	*173.94*	*x*	*275.72*	*182.34*	*x*	*246.79*	^	*131.73*	*355.18*
Tricep	m	x	1639	1371	x	1120	1120	1206.33	x	x	1133	x	1523.5	1277.66	1340.33	1506.5

	sd	*x*	*73.53*	*293.95*	*x*	^	^	*294.19*	*x*	*x*	*453.59*	*x*	*75.66*	*148.71*	*260.16*	*581.94*
FCR	m	x	1124.66	1185.5	x	911.5	911.5	861.33	x	915.5	826.5	x	1099.66	916.33	717.33	1049.33
	sd	*x*	*281.71*	*277.89*	*x*	*113.84*	*113.84*	*153.46*	*x*	*297.69*	*347.18*	*x*	*143.49*	*146.4*	*100.82*	*183.41*
ECR	m	**x**	1129.33	1605.33	x	1155.5	1155.5	1530	x	1525.33	759.33	x	1723.5	1245	1388.33	1121
	sd	*x*	*257.82*	*317.68*	*x*	*12.02*	*12.02*	*461.85*	*x*	*578.94*	*100.97*	*x*	*1109.45*	*407.07*	*99.92*	*249.86*

Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)
NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; **^,** only 1 valid trial therefore no standard deviation; BL, baseline measures; W, weekly measures; Outcome measures
NB. More paretic hand could not grasp cup – touched to complete movement

11.4.13Appendix 13D. Time to onset of muscle activation (milliseconds) during reach task (cup) for stroke participant group, VR06

Less paretic - Left		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	x	x	x	505	366.66	539.33	367.33	740.66	700	x	722	698	625	x	776
	sd	*x*	*x*	*x*	*93.33*	*115.47*	*36.63*	*80.32*	*91.94*	^	*x*	^	^	*92.86*	*x*	*4.24*
Bicep	m	x	x	x	362.66	300	445	326.33	547.66	400	x	508.66	470	460	x	610.5
	sd	*x*	*x*	*x*	*36.17*	*141.42*	*28.51*	*28.04*	*32.02*	*200*	*x*	*262.71*	^	*92.06*	*x*	*178.89*
Tricep	m	x	x	x	x	x	686.66	629	945	1300	x	x	1267	808	x	x
	sd	*x*	*x*	*x*	*x*	*x*	*311.5*	*104.32*	*271.66*	*0*	*x*	*x*	*413.36*	^	*x*	*x*
FCR	m	x	x	x	x	x	x	x	547	x	x	x	490.33	880	x	1008.5
	sd	*x*	*x*	*x*	*x*	*x*	*x*	*x*	*0*	*x*	*x*	*x*	*206.35*	*203.64*	*x*	*204.35*
ECR	m	x	x	x	1305	x	396.66	238.66	453	666.66	x	452.5	x	424.66	x	477
	sd	*x*	*x*	*x*	^	*x*	*70.93*	*17.92*	*81.72*	*208.16*	*x*	*109.6*	*x*	*77.55*	*x*	*60.81*
More paretic - Right		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	x	x	x	533.66	433.33	411	416.33	333	700	990	1452	808.66	x	x	1104
	sd	*x*	*x*	*x*	*172.77*	*57.73*	*89.23*	*75.14*	^	*173.2*	^	^	*246.24*	*x*	*x*	^
Bicep	m	x	x	x	x	500	508.33	268.33	932	1366.66	741.5	504	584	1290.5	x	637.33
	sd	*x*	*x*	*x*	*x*	^	*236.87*	*58.52*	^	*57.73*	*178.9*	*209.3*	*137.5*	*929.84*	*x*	*278.39*
Tricep	m	x	x	x	x	x	x	x	1668	x	x	x	x	x	x	x
	sd	*x*	*x*	*x*	*x*	*x*	*x*	*x*	^	*x*	*x*	*x*	*x*	*x*	*x*	*x*
FCR	m	x	x	x	x	x	x	x	845	x	x	x	x	x	x	x
	sd	*x*	*x*	*x*	*x*	*x*	*x*	*x*	^	*x*	*x*	*x*	*x*	*x*	*x*	*x*
ECR	m	x	x	x	948	500	x	x	726.5	1750	588.5	934.5	593.33	421	x	969.66
	sd	*x*	*x*	*x*	*192.33*	^	*x*	*x*	*68.58*	*70.71*	*108.19*	*301.93*	*67.41*	*21.51*	*x*	*418.08*

Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)

NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; **^,** only 1 valid trial therefore no standard deviation; BL, baseline measures; W, weekly measures; Outcome measures

11.4.14 Appendix 14D. Time to onset of muscle activation (milliseconds) during reach task (cup) for stroke participant group, VR07

Less paretic, left		BL1	BL2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	Outcome
Deltoid	m	954.33	x	1607	1245.5	1369.33	1476.33	1224.5	1344	x	1166.66	1111.33	1025.66	858	1192.66	1159.33
	sd	133.63	x	38.03	301.93	50.24	59.71	55.86	77.14	x	109.51	265.92	295.23	246.14	174.99	168.88
Bicep	m	693.66	x	1401.33	1161.66	1437	1446.66	1198.66	1318	1093	1297	1072	861.66	929	1104.33	1055.33
	sd	133.61	x	53.87	362.05	29.82	17.95	56.61	128.54	50.08	80.88	332.68	153.32	74.95	64.45	221.71
Tricep	m	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	sd	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
FCR	m	x	x	x	x	x	x	x	x	x	x	x	x	x	x	1605
	sd	x	x	x	x	x	x	x	x	x	x	x	x	x	x	^
ECR	m	698.33	x	1409.33	1251	1251	1500.66	1146.33	1235.66	x	1255.66	1101	1056.33	941	1185.66	1045
	sd	359.54	x	74.86	45.25	45.25	48.58	59.37	223.09	x	76	149.9	137.82	349.08	13.31	160.25
More paretic, right		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	661	1514	1357	1196.33	x	1438	1361.33	1052	1370	1242.5	1450	1154	1000	1284.66	652
	sd	115.5	110.3	73.53	295.55	x	405.71	148.75	139.26	209.25	663.97	130.89	248.49	501.46	235.49	332.34
Bicep	m	913.33	1393	x	x	1820.67	x	x	x	1582.5	x	1458.5	1869.33	1310	1454	4492
	sd	472.21	195.32	x	x	220.82	x	x	x	412.24	x	358.5	112.78	107.78	259.57	4556.59

Tricep	m	1080.66	2019.33	x	x	x	1384.66	1636.5	x	1278.33	x	1441.5	1392.66	979.66	x	1482.33
	sd	334.14	253.05	x	x	x	236.72	194.45	x	382.46	x	222.74	528.84	24.5	x	267.94
FCR	m	x	x	x	x	x	x	x	x	x	x	1450	x	1561	x	1572.5
	sd	x	x	x	x	x	x	x	x	x	x	130.89	x	145.66	x	135.05
ECR	m	x	1881.5	x	x	x	1360	1438.66	x	1571	864	1458.5	1696.33	1406	x	851
	sd	x	406.58	x	x	x	^	130.9	x	^	^	358.5	166	57.98	x	^

Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)

NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; **^,** only 1 valid trial therefore no standard deviation; BL, baseline measures; W, weekly measures; Outcome measures

NB. More paretic hand could not grasp cup – touched to complete movement (aside from W11, W12 where he picked up the cup off the table but not to mouth)

11.4.15 Appendix 15D. Time to onset of muscle activation (milliseconds) during reach task (cup) for stroke participant group, VR09

Less paretic, right		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	x	1714.66	x	973	x	x	801.66	720.33	791.66	991.33	713.66	557.33	802.33	639	815.33
	sd	x	184.71	x	546.93	x	x	91.62	232.63	58	167.5	229.91	48.26	12.66	93.33	175.04
Bicep	m	x	628.66	x	809.5	x	x	543.5	814	757.66	774.66	684	648	740	817.33	845
	sd	x	103.01	x	482.95	x	x	173.24	237.69	74.03	91.35	175.01	122.47	60.81	45.08	144.24
Tricep	m	x	x	x	377	x	x	899.5	435.5	728	470	x	602	x	522	x
	sd	x	x	x	^	x	x	184.55	140.71	86.6	78.88	x	7.07	x	^	x
FCR	m	x	566.66	x	653	x	x	740	746	777.5	604.66	723.33	601.66	681.5	x	741.66
	sd	x	108.28	x	598.21	x	x	73.62	292.57	99.7	208.26	161.77	118.15	62.93	x	142.79
ECR	m	x	639.33	x	730.33	x	x	674	697.33	694.33	619	814.33	526.33	530	587.33	610.5
	sd	x	95.13	x	301.58	x	x	123.03	244.55	47.26	15.62	67.92	86	135.53	112.83	0.7
More paretic, left		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	x	1054	x	1835	x	x	1113	1020.33	1076.66	933.66	1554.66	1805.33	x	1085.33	1436
	sd	x	724.07	x	^	x	x	465.84	158.81	78.5	187.68	285.76	1397.66	x	176.27	306.88

Bicep	m	x	997	x	1238.5	x	x	781	1036	1074.66	918.5	1218.5	1744.33	x	1778	1108
	sd	x	298.64	x	60.1	x	x	92.14	225.59	19.42	198.69	171.82	1307.41	x	^	251.73
Tricep	m	x	2136.33	x	x	x	x	1140.5	1532	1616.5	1344.33	1846.66	x	x	x	x
	sd	x	418.69	x	x	x	x	204.35	^	350.01	655.24	162.05	x	x	x	x
FCR	m	x	1714	x	x	x	x	1933.33	x	1430	1853.5	1881	2070.33	x	1037	1831.33
	sd	x	502.04	x	x	x	x	195.16	x	162.68	81.31	574.25	1216.96	x	120.38	387.27
ECR	m	x	2321	x	x	x	x	x	1115	1384	1536	1838.66	x	x	x	1202
	sd	x	298.39	x	x	x	x	x	604.17	54.14	28.28	276.01	x	x	x	^

Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)

NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; **^,** only 1 valid trial therefore no standard deviation; BL, baseline measures; W, weekly measures; Outcome measures

NB. More paretic hand could not grasp cup – touched to complete movement

11.4.16 Appendix 16D. Time to onset of muscle activation (milliseconds) during reach task (cup) for stroke participant group, VR10

Less paretic, right		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	x	821	1121.33	551.33	540.66	568	478	493	611.00	x	498.33	456	x	x	590.33
	sd	x	384.97	525.72	59.53	184.33	115.96	135.72	52	226.27	x	124.46	132.28	x	x	126.82
Bicep	m	x	839.00	1113.33	537.66	554.33	594.50	521.66	457.66	589.66	x	536	482	x	x	544
	sd	x	338.69	466.53	102.86	229.69	154.85	140.60	238.40	144.07	x	140.27	122.74	x	x	91.98
Tricep	m	x	1441.66	x	x	562	x	x	x	820	x	680.33	608.33	x	x	x
	sd	x	199.77	x	x	69.29	x	x	x	169.05	x	273.50	105.46	x	x	x
FCR	m	x	902.66	839.50	610.33	513.33	667.00	444.50	587.50	716.33	x	562	534	x	x	566.33
	sd	x	331.11	33.23	91.24	82.03	155.56	119.50	105.35	98.08	x	124.92	110.39	x	x	97.29
ECR	m	x	746.66	956.00	486.66	535.00	638.50	445.00	493.00	639.66	x	484.33	436.66	x	x	602.33
	sd	x	139.41	0.00	123.06	249.83	176.06	70.71	185.26	180.35	x	48.33	108.00	x	x	85.61
More paretic, left		**BL1**	**BL2**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W12**	**Outcome**
Deltoid	m	x	554	495.50	429	492.50	609.66	460.66	546	441	x	452.33	560.33	523.50	588.66	481.33
	sd	x	149.10	64.34	53.07	60.10	107.93	127.11	65.79	55.24	x	44.83	63.06	19.09	53.40	34.53

Bicep	m	x	680.66	486.50	593	500.33	608.66	515.66	563.33	492.33	x	433	567	503.33	600	443
	sd	x	62.01	43.13	216.06	32.71	67.67	87.54	25.73	66.28	x	173.45	79.07	66.42	48.08	39.28
Tricep	m	x	681	x	480.33	877	951.00	x	809	717.66	x	654.66	x	688.50	636.33	679.66
	sd	x	38.69	x	310.09	^	144.41	x	188.28	110.57	x	114.82	x	434.87	272.31	187.23
FCR	m	x	x	x	567	x	x	x	x	x	x	x	x	507	703.50	660.66
	sd	x	x	x	^	x	x	x	x	x	x	x	x	^	50.20	255.96
ECR	m	x	416	480.33	430.50	475.50	551	502	503.66	453	x	433.33	505	318.00	554	427
	sd	x	44.54	15.37	34.64	72.83	78.73	63.49	31.89	36.37	x	41.40	36.71	219.20	56.50	70.88

Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)

NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; **^,** only 1 valid trial therefore no standard deviation; BL, baseline measures; W, weekly measures; Outcome measures

11.4.17 Appendix 17D. Time to onset of muscle activation (milliseconds) during reach task (cup) for stroke participant group, VR12

Less paretic (L)		BL1	BL2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	Outcome
Deltoid	m	x	832.00	**x**	549.66	992.33	487.00	903.50	650.33	595.33	729.66	748	750.66	476.66	630.33	656.33
	sd	x	238.19	x	355.42	415.69	126.69	396.68	303.70	269.38	294.90	141.16	256.20	120.40	256.07	110.29
Bicep	m	547	887	x	702	613.33	488.66	839.33	602.33	x	569	587.33	656.66	403.66	733	567.50
	sd	58.23	345.13	x	63.63	150.39	129.89	261.80	341.90	x	448.30	106.82	299.50	101.64	207.88	65.76
Tricep	m	1536.00	545	x	x	1296	x	1242.33	1063	x	x	784	1227.66	910.33	x	1130.50
	sd	352.85	^	x	x	168.43	x	444.64	233.05	x	x	^	89.52	181.17	x	58.68
FCR	m	3750.50	1211	x	1109	796.00	1399.00	1241	1205.66	1497	x	774.50	x	808.33	949	745.33
	sd	2119.19	^	x	73.53	53.74	^	181.01	416.14	^	x	13.43	x	152.13	^	144.18
ECR	m	398.00	953.33	x	659.50	645	668	938	629.33	743.66	659	800	894	564	800	x
	sd	185.27	350.82	x	82.73	216.04	66.46	256.92	361.22	102.86	466.69	63.31	145.68	55.46	233.34	x

More paretic (R)		BL1	BL2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	Outcome
Deltoid	m	x	449	x	871.66	421.66	620.33	692	577	613.66	879	x	486.5	936.33	594.5	530
	sd	x	263.96	x	238.85	74	51.86	43.84	^	293.02	478.3	x	239.7	59.67	82.73	64.37
Bicep	m	x	701	x	956	732.66	817.66	764.66	x	x	926.66	584	628	688.33	702	628
	sd	x	130.9	x	158.5	24.58	41	15.3	x	x	397.54	231.62	182.34	216.5	59.75	355.75
Tricep	m	x	825.5	x	x	1766.33	1656.66	1140.66	x	1244	1600	1122.66	1133	1040	x	1091.66
	sd	x	34.64	x	x	688.24	674.31	455.72	x	855.59	^	542.98	453.59	79.19	x	41.5
FCR	m	x	1281.66	x	1294.5	1190.66	701.5	1387.66	x	1190.33	1252.66	1328	826.5	1401	1197	1377
	sd	x	53.92	x	181.72	271.37	132.22	106.93	x	173.1	436.6	188.85	347.18	127.27	^	^
ECR	m	x	761	x	1294.33	808	691	904.5	1036	718	782.33	1119.66	759.33	884.5	995.33	1123
	sd	x	307.12	x	221.63	41.56	236.17	64.34	128.36	^	540.71	75	100.97	44.54	19.13	112.05

Muscles of interest: Deltoid; Biceps brachii; Flexor Carpi Radialis (FCR); Extensor Carpi Radialis (ECR)

NB. **m,** mean; **sd,** standard deviation, **x,** no valid trials or data wasn't collected; **^,** only 1 valid trial therefore no standard deviation; BL, baseline measures; W, weekly measures; Outcome measures

11.4.18 Appendix 18D. Pre/-post VR intervention period functional ability (Wolf Motor Function Test, per item)

Participant ID		BL1		BL2		Outcome		Change between BL1 and BL2		Change between BL2 and Outcome	
		time	FAS	time	FAS	time	FAS	time	FAS	time	FAS
VR01	m	10.77	2.33	w/d	w/d	w/d	w/d	n/a	n/a	n/a	n/a
	sd	13.92	1.11	w/d	w/d	w/d	w/d				
VR02	m	59.03	2.07	58.19	2.07	51.17	2.20	0.8	0	7 *	0.1
	sd	59.15	0.80	59.88	1.10	58.32	0.86				
VR03	m	46.10	2.27	w/d	w/d	w/d	w/d	n/a	n/a	n/a	n/a
	sd	54.31	1.28	w/d	w/d	w/d	w/d				
VR04	m	21.63	2.87	13	3.13	w/d	w/d	8.6 *	0.3*	n/a	n/a
	sd	40.45	0.64	30.01	0.35	w/d	w/d				
VR05	m	90.52	1.40	90.12	1.27	63.67	1.13	0.41	-0.1	26.5*	-0.1
	sd	51.01	0.91	51.57	1.03	55.65	1.13				
VR06	m	13.53	3.33	6.26	3.33	8.04	3.4	7.3 *	0	-1.8 *	0.1
	sd	30.14	0.62	7.79	0.49	9.83	0.83				

Participant ID		BL1		BL2		Outcome		Change between BL1 and BL2		Change between BL2 and Outcome	
		time	FAS	time	FAS	time	FAS	time	FAS	time	FAS
VR07	m	42.45	2.33	52.69	2	40.61	2.4	-10.2 *	-0.3*	12.1 *	0.4*
	sd	56.95	0.98	57.69	1.13	51.56	1.3				
VR09	m	73.92	1.47	69.23	1.67	69.16	1.67	4.69 *	0.2*	0.7	0
	sd	54.12	0.83	56.67	0.98	57.35	0.98				
VR10	m	7.70	3.87	7.47	3.33	3.8	4.4	0.23	-0.5*	3.7 *	1.1*
	sd	6.76	0.92	8.88	0.72	3.78	0.63				
VR11	m	81.77	1.13	82.33	1.20	w/d	w/d	-0.6	0.1	n/a	n/a
	sd	56.06	0.99	55.44	0.68	w/d	w/d				
VR12	m	5.20	3.20	5.65	3.20	5.54	3.27	-0.5	0	0.1	0.1
	sd	5.95	0.86	6.24	0.68	6.6	0.46				

NB. + change, implies improvement; - change, implies completion of tasks was slower or given a lower functional activity score

*, Minimally clinically important difference reached

w/d, withdrew; n/a, not applicable

11.4.19 Appendix 19D: Weekly progress measures, functional ability, (Action Reaction Arm Test data)

Participant	Weekly measures											
ID	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
VR02	14	11	16	16	17	14	18	25*	25*	31	31	26
VR04	24	31*	31*	34	30	n/c	32	n/c	35	34	37	33
VR05	4	4	3	4	4	4	5	4	4	4	4	4
VR06	26	26	31	31	34*	35*	33	36	36	28	30	33
VR07	13	8	6	8	7	6	7	7	9	6	6	6
VR09	n/c	9	n/c	10	8	7	7	9	11	13	8	12
VR10	34	37	37	45*	n/c	33	32	n/c	31	35	36	35
VR12	n/c	35	35	38	38	n/c	36	36	37	37	37	36

NB. *Minimally clinically important difference reached 6 points.

n/c, not collected

11.4.20 Appendix 20D. Stroke participant therapy prescription and fidelity (more paretic upper limb repetitions)

Week	VR02		VR04		VR05		VR06		VR07		VR09		VR10		VR12	
	C	P	C	P	C	P	C	P	C	P	C	P	C	P	C	P
1	40	30	189	160	105	90	577	645	225	270	0	120	228	174	78	156
2	195	146	195	225	105	90	714	1428	365	410	60	120	289	209	243	208
3	294	294	234	234	270	270	476	1463	312	468	0	120	251	156	245	210
4	316	278	195	234	270	270	906	1629	425	510	260	200	164	126	378	324
5	266	228	195	234	320	320	618	1854	255	510	280	240	123	126	336	336
6	228	228	195	234	350	350	927	1854	352	528	172	258	82	126	401	342
7	223	223	234	234	360	360	927	1854	448	463	258	258	164	126	413	355
8	152	228	169	202	370	445	618	1854	272	408	129	258	164	126	436	365
9	170	198	99	198	480	480	927	1854	287	423	129	215	184	286	515	441
10	196	168	165	198	425	510	927	1854	415	488	86	258	244	186	530	454
11	140	168	175	210	425	510	618	1889	498	498	192	283	244	186	474	469
12	258	258	105	210	425	510	1142	2339	550	630	144	288	305	186	567	486
Total	2478	2447	2150	2573	3905	4205	9377	20517	4404	5606	1710	2618	2442	2013	4616	4146

NB. C, completed; **P**, prescribed

11.5 APPENDIX E. DISSEMINATION

11.5.1 Appendix 1E: The 2nd International Congress on NeuroRehabilitation and Neural Repair (2017)

Title: Investigating the usability and feasibility of a virtual reality stroke rehabilitation tool

Authors: F. ELLIS, N. KENNEDY, N. HANCOCK, V. POMEROY
The University of East Anglia, Norwich, UK

Abstract: Traditional stroke rehabilitation is costly and resource-intensive. Due to this, it is increasingly difficult for clinicians to administer the recommended amount of therapy; often leaving patients with residual impairments. Virtual Reality could provide a novel augmented solution that enables repetitive functional training at a much higher dose. As part of a physical rehabilitation system, using Xbox Kinect and LEAP motion technology, iterative development user involvement is vital to understand the tool's usability and feasibility.

This embedded mixed-methods study investigated factors which could initially draw users to the tool and those which facilitate longer-term use. Data was collected from a series of focus groups with: stroke survivors, their primary informal carers and clinicians. Eight to ten participants, in each group, were given an hour to test the tool. They then, in a focus group, discussed its: usability, applicability, acceptability and barriers to use. Cohort specific questionnaires were also used to further explore demographics, technological proficiency, the stroke's impact and the tool's usability. Two participants from each group then tested it at home for two weeks before discussing the aforementioned themes in a semi-structured interview.

The results of a thematic analysis carried out on the focus groups and interviews will be discussed. With additional focus on how the questionnaire results influenced the interpretation of the themes. The results revealed the user's perception of the tool's usability and feasibility along with potential barriers of use and what recommendations there is to ensure the targeted audience is reached. The results will inform further evolution of stroke rehabilitation.

Word Count: 255/250

Conflicts of interest: A part funded PhD studentship by Virtualware ®

11.5.2 Appendix 2E: The Association of Chartered Physiotherapists in Neurology (ACPIN) International Conference (2018)

Title: Neural correlates of motor impairment response to virtual reality-aided exercise-based training after stroke: a systematic review

Authors: Fiona ELLIS[1], Niamh C. KENNEDY[2], Nicola J. HANCOCK[1], VM. POMEROY[1]
[1]School of Health Sciences, University of East Anglia, Norwich, UK.
[2]School of Psychology, Ulster University, Belfast, Northern Ireland.
Corresponding author: fiona.ellis@uea.ac.uk

Word Count: 290

Background

Using virtual reality to deliver upper limb motor training, as an adjunct to usual care, has shown preliminary clinical benefit post-stroke. Further clarity is required to understand the neurological mechanisms of this effect. Identifying such neural correlates could facilitate tailoring the rehabilitation programme for patients and clinicians.

Objectives

Primary objective: to identify neural correlates of upper limb motor impairment response to virtual reality aided exercise-based training following a stroke.

Secondary objectives: to determine any difference in neural correlates of upper limb motor impairment response to virtual reality (VR) training between (a) VR and comparator therapies and (b) VR and no therapy.

Search Methods

We searched the Cochrane Trials Register, EMBASE, MEDLINE and five additional databases up to October 2017.

Selection Criteria

We included all experimental study designs using a virtual reality exercise-based upper limb intervention for adults post-stroke. To isolate the potential effect of virtual reality on stroke recovery additional neurological conditions and technology (e.g. robotics) was excluded. Outcomes of interest included measured the neural correlates, for example, EMG-derived measures or Functional Magnetic Resonance Imaging (fMRI).

Data collection and analysis

Two review authors have independently screened and selected records from the pre-determined inclusion criteria. The Down's and Black (1998) tool has been used to assess the risk of bias. The reviewers will extract the data and if there is sufficient commonality a meta-analysis will be undertaken. Results will be displayed within a

PRISM flowchart and characteristics of the included records summarised, with a critical narrative synthesis exploring the outcomes of interest.

Conclusion

This systematic review will be completed by the end of January 2018. The resultant discussion will explore the neural correlates of change in motor impairment in response to virtual reality-aided exercise-based training for upper limb after stroke.

11.5.3 Appendix 3E: Lanyard used for public dissemination for the Norwich science festival