

# BMJ Open Rehabilitation via HOME Based gaming exercise for the Upper-limb post Stroke (RHOMBUS): protocol of an intervention feasibility trial

Cherry Kilbride,<sup>1</sup> Daniel J M Scott,<sup>1</sup> Tom Butcher,<sup>1</sup> Meriel Norris,<sup>1</sup> Jennifer M Ryan,<sup>1,2</sup> Nana Anokye,<sup>1</sup> Alyson Warland,<sup>1</sup> Karen Baker,<sup>1</sup> Dimitrios A Athanasiou,<sup>3</sup> Guillem Singla-Buxarrais,<sup>3</sup> Alexander Nowicky<sup>4</sup>

**To cite:** Kilbride C, Scott DJM, Butcher T, *et al*. Rehabilitation via HOME Based gaming exercise for the Upper-limb post Stroke (RHOMBUS): protocol of an intervention feasibility trial. *BMJ Open* 2018;**8**:e026620. doi:10.1136/bmjopen-2018-026620

► Prepublication history and additional material for this paper are available online. To view please visit the journal (<http://dx.doi.org/10.1136/bmjopen-2018-026620>).

Received 11 September 2018  
Revised 1 October 2018  
Accepted 3 October 2018



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<sup>1</sup>Ageing Studies Theme, Institute of Environment, Health and Societies, Brunel University, London, UK

<sup>2</sup>Department of Epidemiology and Public Health Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland

<sup>3</sup>Neurofenix, London, UK

<sup>4</sup>Centre for Cognitive Neuroscience, College of Health and Life Sciences, Brunel University, London, UK

## Correspondence to

Dr Cherry Kilbride;  
[Cherry.Kilbride@brunel.ac.uk](mailto:Cherry.Kilbride@brunel.ac.uk)

## ABSTRACT

**Introduction** Effective interventions to promote upper-limb recovery poststroke are characterised by intensive and repetitive movements. However, the repetitive nature of practice may adversely impact on adherence. Therefore, the development of rehabilitation devices that can be used safely and easily at home, and are motivating, enjoyable and affordable is essential to the health and well-being of stroke survivors. The Neurofenix platform is a non-immersive virtual reality device for poststroke upper-limb rehabilitation. The platform uses a hand controller (a NeuroBall) or arm bands (NeuroBands) that facilitate upper-limb exercise via games displayed on a tablet. The Rehabilitation via HOME Based gaming exercise for the Upper-limb post Stroke trial aims to determine the safety, feasibility and acceptability of the Neurofenix platform for home-based rehabilitation of the upper-limb poststroke.

**Methods and analysis** Thirty people poststroke will be provided with a Neurofenix platform, consisting of a NeuroBall or NeuroBands (dependent on impairment level), seven specially designed games, a tablet and handbook to independently exercise their upper limb for 7 weeks. Training commences with a home visit from a research therapist to teach the participant how to safely use the device. Outcomes assessed at baseline and 8 weeks and 12 weeks are gross level of disability, pain, objectively measured arm function and impairment, self-reported arm function, passive range of movement, spasticity, fatigue, participation, quality of life (QOL) and health service use. A parallel process evaluation will assess feasibility, acceptability and safety of the intervention through assessment of fidelity to the intervention measured objectively through the Neurofenix platform, a postintervention questionnaire and semistructured interviews exploring participants' experiences of the intervention. The feasibility of conducting an economic evaluation will be determined by collecting data on QOL and resource use.

**Ethics and dissemination** Ethics approval granted from Brunel University London (10249-MHR-Mar/2018-12322-2). Trial results will be submitted for publication in journals, presented at national and international conferences and distributed to people with stroke.

**Trial registration number** ISRCTN60291412; Pre-results.

## Strengths and limitations of this study

- The Rehabilitation via HOME Based gaming exercise for the Upper-limb post Stroke trial will investigate the feasibility, acceptability and safety of a novel gaming platform (the Neurofenix platform) at home for upper-limb exercise after stroke.
- Upper-limb activity data will be objectively measured by the device. Assessment outcome measures include objective (assessed blind to timepoint) and self-reported measures.
- To be maximally inclusive, stroke survivors with moderate to severe arm impairment will be included in the study.
- The feasibility of conducting an economic evaluation will be determined by collected data on quality of life and resource use.
- This is a home-based intervention study; thus, participants and researchers collecting the data will not be blinded.

## INTRODUCTION

Stroke is the leading cause of severe disability worldwide with approximately 17 million new strokes each year.<sup>1 2</sup> The UK has 1.2 million stroke survivors with 110 000 first-time strokes occurring each year resulting in an estimated societal cost of £26 billion per year.<sup>1 2</sup> Following stroke, 85% of people initially experience upper-limb weakness, and of those with minimal movement on hospital admission, only 11%–14% regain full function of their arm.<sup>2–4</sup> This loss in upper-limb function results in increased dependence and decreased quality of life (QOL).<sup>5</sup> Reduced upper-limb function has been identified as a strong predictor of lowered psychological well-being poststroke.<sup>5 6</sup> Innovation and investigation of effective treatments for arm recovery has been identified as a priority for stroke research.<sup>7</sup>

Evidence indicates the most effective interventions to improve upper-limb function are characterised by high intensity and repetitive practice.<sup>8</sup> A higher intensity and frequency of upper-limb stroke rehabilitation is associated with improved QOL,<sup>9</sup> motor function and ability to perform activities of daily life<sup>10</sup> and is cost-effective.<sup>11</sup> The UK quality standard for stroke advises 45 min of each relevant therapy for a minimum of 5 days a week.<sup>11</sup> However, a 2015 UK national stroke audit showed on average most hospitals are unable to meet this quality standard.<sup>12</sup> Specifically, time spent retraining the upper limb is very low, with an average of 32 repetitions per rehabilitation session.<sup>13 14</sup> As such, there is a growing emphasis on the stroke survivor exercising independently without the presence of a therapist. However, adherence to home exercise is known to be poor.<sup>15 16</sup> A perceived lack of support and feedback along with boredom with exercises are the most frequently cited factors associated with poor compliance.<sup>17 18</sup>

Virtual reality (VR)-based activities have been suggested as an intervention to improve upper-limb recovery by providing motivating environments or gameplay to facilitate rehabilitation.<sup>19</sup> This digital health solution helps address boredom and compliance problems, can facilitate increased time in therapy and may not be reliant on therapist contact time.<sup>19 20</sup> In addition, the ability of VR activities to provide feedback may enhance motor learning.<sup>21 22</sup> Visual feedback via an on-screen character (avatar) can activate mirror neurones, which may aid recovery from stroke.<sup>23 24</sup>

VR can be considered in terms of the level of immersion provided, that is, the degree the user feels present in the virtual world due to the technical aspects of the VR environment. Immersive systems can generate life-scaled, three-dimensional images, with surround sound auditory and sensory feedback such as vibration, and pressure,<sup>25</sup> whereas non-immersive systems involve two-dimensional images typically viewed on a screen with interaction being via controller-based systems (such as computer keyboards, joysticks, balance boards and handheld devices) or via camera-based tracking systems.<sup>26</sup> Non-immersive systems are more commonly used for rehabilitation as they have smaller space requirements, cost less and have fewer side effects (eg, motion sickness).<sup>27</sup>

The Neurofenix platform is a non-immersive device designed to enable and encourage stroke survivors to independently exercise their upper limb with minimal therapist input. The platform was developed by Neurofenix, a bioengineering enterprise ([www.neurofenix.com](http://www.neurofenix.com)), along with stroke survivors and neurological physiotherapists. The platform consists of a hand controller or armbands, seven specially designed games, a tablet and an instruction handbook.

### Study aims and objectives

This study aims to determine the safety, feasibility and acceptability of the Neurofenix platform for home-based rehabilitation of the upper-limb poststroke. A secondary

aim is to test procedures to inform a definitive randomised controlled trial to assess the clinical and cost-effectiveness of the Neurofenix platform with stroke survivors. The study objectives are:

1. To assess the safety, feasibility and acceptability of using the Neurofenix platform intervention at home for the rehabilitation of the upper limb after stroke.
2. To assess the feasibility of conducting a definitive trial of the clinical and cost-effectiveness of the Neurofenix platform intervention.
3. To understand the factors relating to people with stroke and the intervention that may impact on fidelity to the intervention.

## METHODS AND ANALYSIS

### Trial design

The Rehabilitation via HOME Based gaming exercise for the Upper-limb post Stroke study is a non-randomised intervention trial ([figure 1](#)). A total of 30 participants will be recruited to use the Neurofenix platform at home for 7 weeks (1 week training, 6 weeks exercise). Assessments will be performed at baseline and 8 and 12 weeks. A parallel process evaluation will assess the safety, feasibility and acceptability of the intervention and the feasibility of conducting a definitive trial. Semistructured interviews will be used to explore the perspectives of participants receiving this complex intervention.

### Study setting

The Department of Clinical Sciences, Brunel University London will coordinate the study. Assessments will be conducted, and the intervention delivered in participants' homes.

### Trial status

At the time of submission of this study protocol, data collection is ongoing.

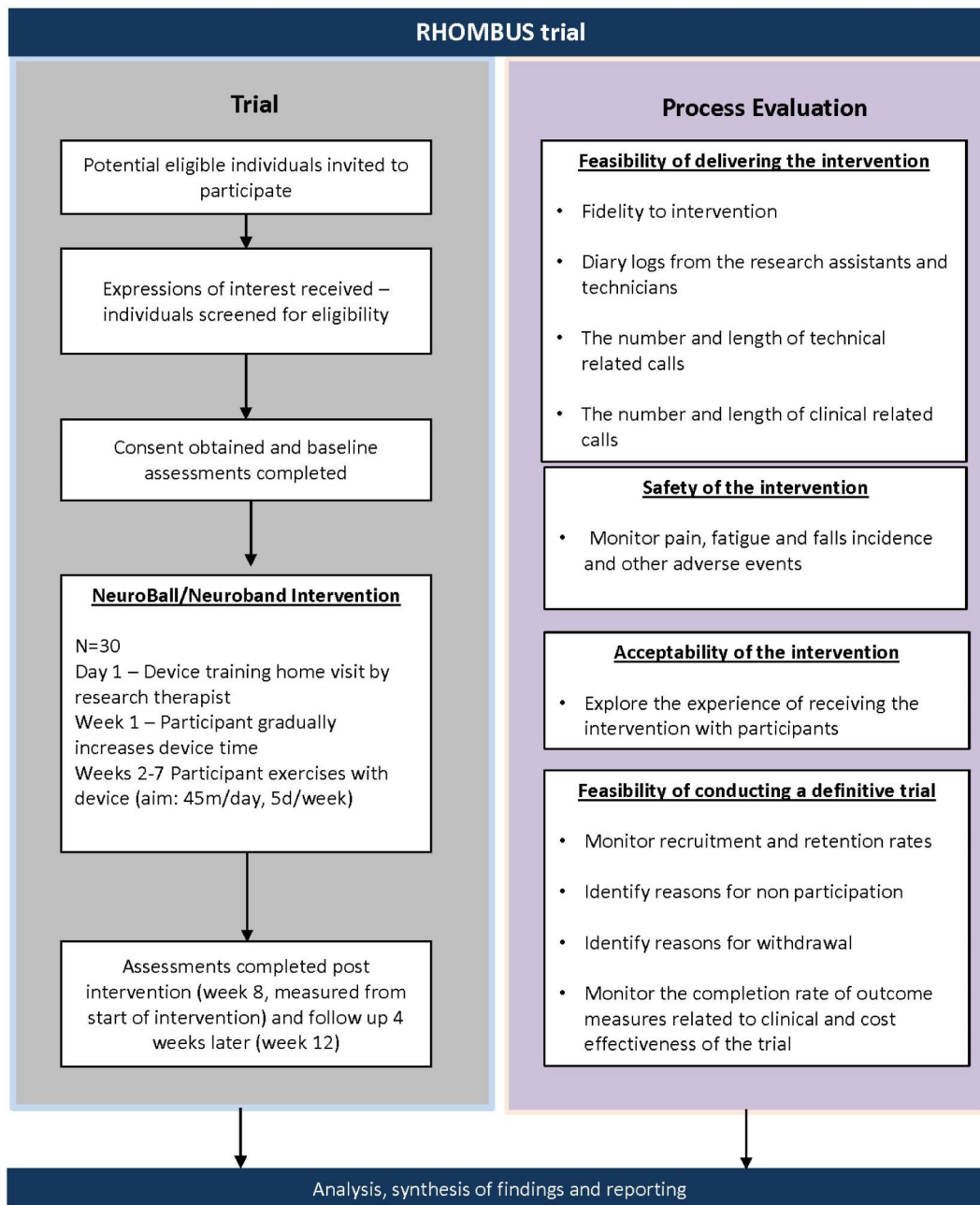
### Participants

#### Inclusion criteria

- ▶ Aged 18 or over
- ▶ Capacity to consent
- ▶ Self-reported diagnosis of stroke (unilateral haemorrhagic or ischaemic)
- ▶ 12 weeks minimum poststroke and finished formal rehabilitation for their arm, that is, National Health Service (NHS) or private provider
- ▶ Mild to severe reduction in arm function poststroke, estimated by a Motricity Index<sup>28</sup> score between 9 and 25 for elbow and shoulder movement
- ▶ Able to sit or stand independently (using an aid if necessary) for a minimum of 5 min
- ▶ Can communicate in English, that is, sufficient for completion of trial intervention and assessment

#### Exclusion criteria

- ▶ Unstable medical conditions
- ▶ Uncontrolled photosensitive epilepsy



**Figure 1** Rehabilitation via HOME Based gaming exercise for the Upper-limb post Stroke (RHOMBUS) trial design.

- ▶ Acquired brain injury from other causes, bilateral or cerebellar lesions
- ▶ Uncompensated visual neglect, hemianopia or uncorrected visual field deficits (assessed by the National Institutes of Health Stroke Scale)<sup>29</sup>
- ▶ Pre-existing, unremitting arm pain at rest

### Sample size

This is a feasibility study and no power calculation for the primary outcome(s) is required. The primary analytic aim is to evaluate the safety, feasibility and acceptability via the process evaluation data.

### Recruitment

Participants will be recruited from Brunel's established database of people with stroke who have consented to contact about future stroke research studies and the ISRCTN Registry website. Participants will also be recruited through Different Strokes and the Action for Rehabilitation in Neurological Injury Institute. These participants will be accessed via gatekeepers and informed written consent will be taken by research therapists (see online supplementary appendices A, B and C for examples of the informed consent materials used).

Recruitment will run from April 2018 to August 2018. Thirty participants will be recruited over 5 months, equating to approximately 1.5 participants per week.

### Reasons for non-participation

A non-participation questionnaire will be distributed to those who do not wish to participate in the study. This will help identify reasons for refusal and any differences in baseline characteristics between participants and non-participants.

### Intervention

The Neurofenix platform is a portable non-immersive VR device for gamification of upper-limb stroke rehabilitation. The platform uses either a hand controller, the NeuroBall or armbands, NeuroBands, to promote specific practice of movements in the shoulder, elbow, wrist and/or hand through uniquely designed games displayed on a tablet. To ensure adequate reporting of the intervention a Template for Intervention Description and Replication checklist was completed (table 1).

This study will examine the Neurofenix platform intervention over a 7-week period, commencing with a home visit from a research therapist. The participant will be given the Neurofenix platform (see table 1 for content details) and trained how to use their device independently or with the help of a carer (if requested). The participant will then be advised to use the platform with an aim of 45 min a day, 5 days a week or more if they are able, self-limiting use based on fatigue and pain, and slowly increasing their use of the device over the first week. Participants will be advised to contact the research therapists as necessary for clinical and technical support throughout the intervention. A more detailed description of the intervention process can be found in table 1.

### Assessments

Assessments will be completed in the participant's home at baseline and 8 and 12 weeks postintervention commencement. All participants will be requested to complete follow-up assessments, including those who withdraw or were withdrawn from the intervention. Those participants will also be asked to complete a questionnaire to identify reasons for withdrawal. The assessment lasts approximately 2 hours and regular breaks will be given to mitigate fatigue and burden. In addition to the stated outcomes, further information will be collected on at baseline on socioeconomic status, stroke and relevant medical history and lifestyle factors.

### Outcomes

All outcome measures follow a standardised operating procedure.

#### Objectively measured arm function

Arm function will be objectively assessed using the Action Research Arm Test (ARAT). The ARAT assesses upper-limb function using observational methods and is divided into four subtests of grasp, grip, pinch and gross

arm movement. Performance on each item is rated on a four-point ordinal scale from 0 to 3 with a maximum score of 57, a higher score indicating a better level of function. The ARAT has excellent inter-rater reliability in chronic stroke populations<sup>30–32</sup> and excellent test–retest reliability, moderate construct validity and responsiveness.<sup>30</sup> The ARAT has a minimally clinically important difference (MCID) in people with chronic stroke of 5.7 points, equivalent to roughly 10% of the measure's total range.<sup>31</sup> The ARAT has been shown to have floor and ceiling effects and a moderate burden.<sup>30</sup> Completion of the ARAT at each timepoint will be videoed for blinded assessor scoring at a later date.

#### Objectively measured arm impairment

The Fugl-Meyer Assessment-upper limb (FMA-UL) will assess arm impairment. Performance is rated on a three-point ordinal scale from 0 to 2, with a maximum score of 66, a higher score indicates minimal or no impairment. The FMA-UL has excellent inter-rater reliability when used in the chronic stroke population.<sup>33</sup> MCID ranges from 4.25 to 7.25 depending on different facets of upper-limb movement.<sup>34</sup>

#### Passive range of movement

Passive range of movement of the upper limb will be assessed for the shoulder, elbow, wrist, thumb and index finger using goniometry to increase the inter-rater reliability of these measurements.<sup>35</sup>

#### Spasticity

The Modified Modified Ashworth Scale (MMAS) will assess for spasticity. The MMAS tests resistance to passive movement of a joint with varying degrees of velocity. Performance is rated on a six-point ordinal scale from 0 to 5 with a higher score indicating higher spasticity.<sup>36</sup> The MMAS has good to very good intra-rater and inter-rater reliability for the elbow and wrist flexors.<sup>37 38</sup>

#### Self-reported arm function

Self-reported arm use will be assessed using the 28-item Motor Activity Log (MAL). The MAL is a semistructured interview where individuals are asked to rate the amount of movement during 28 daily functional tasks. The MAL has excellent test–retest reliability in chronic stroke patients.<sup>39</sup> The MCID is 1.0–1.1.<sup>40</sup> A higher score on the amount of use scale indicates the respondent's ability to use the stroke-affected arm is closer to their prestroke ability.

#### Fatigue

Fatigue will be assessed using the seven-item Fatigue Severity Scale (FSS-7). This questionnaire explores how fatigue interferes with stated activities, the participant rates the severity on a seven-point Likert scale for each item. The FSS-7 is recommended as it has better validity and reliability and is likely more sensitive for measuring change in fatigue in people with stroke.<sup>41</sup> Minimum score

**Table 1** The Rehabilitation via HOMe Based gaming exercise for the Upper-limb post Stroke (RHOMBUS) Template for Intervention Description and Replication (TIDieR)

TIDieR item	RHOMBUS intervention
<p>1. Brief name: 'provide the name or phrase that describes the intervention'</p>	<p>Non-immersive virtual reality gaming exercise for upper-limb training poststroke</p>
<p>2. Why?: 'describe any rationale, theory, or goal of the elements essential to the intervention'</p>	<p>Rehabilitation for the arm poststroke is at best scant, with demand outstripping available resources; especially in the community setting where there is greater emphasis on the stroke survivor exercising independently. Virtual reality (VR)-based activities have been suggested as an intervention to improve upper-limb recovery through providing a motivating treatment that helps to address problems with both boredom and compliance but is not reliant on increased time with a therapist.<sup>19 20</sup></p> <p>The average number of upper-limb repetitions completed in outpatient rehabilitation sessions conducted by both occupational therapists and physiotherapists has been shown to be as low as 45 repetitions.<sup>13</sup> Repetition is known to be a key principle in driving neural plasticity in the learning and relearning of a task after brain damage.<sup>58</sup> The use of video gaming to elicit purposeful upper-limb movements in stroke rehabilitation has also been shown to facilitate up to five times the number of purposeful movement repetitions per session as traditional therapy.<sup>59</sup> VR training has been shown to facilitate longer active training time compared with conventional training.<sup>60</sup> In this manner, the Neurofenix platform aims to promote high repetition active upper-limb movements through non-immersive VR video gaming.</p>
<p>3. What materials?: 'describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed'</p>	<p>The Neurofenix platform is used (<a href="http://www.neurofenix.com">www.neurofenix.com</a>). The platform consists of non-immersive VR software and Bluetooth-connected hand and arm controllers for gamification of upper-limb stroke rehabilitation. The platform is a portable system that uses either a hand controller, the NeuroBall or elasticated arm bands, the NeuroBands. These allow all-in-one arm training through specifically designed rehabilitation games displayed on a tablet or laptop.</p> <p>The NeuroBall: an innovative gaming controller which is spherical in shape allowing it to move freely on a base in all planes of movement, or to be held comfortably in both hands. The NeuroBall is secured to the impaired upper-limb hand through a system of straps and elastic finger holds. Motion sensors within the NeuroBall detect movements produced by the upper limb and translates these to control games on a tablet computer.</p> <p>The NeuroBands: for those who do not have sufficient strength and range of movement in the hand and wrist to control the NeuroBall the NeuroBands are used as an alternative. The NeuroBands are two small motion sensors, the first straps around the upper arm and the second around either the forearm or the hand. If the second NeuroBand is placed on the forearm, then elbow flexion and extension can be trained, and if placed around the hand wrist flexion and extension can be used to control the games.</p> <p>Bespoke rehabilitation games include Scuba Diver, Space Shooter, Pongoal, Holidays Jogging and adapted games such as Coin Frenzy, Pac Man and Solitaire. The games are controlled by the NeuroBall via movements of wrist flexion and extension (eg, in Scuba Diver, Pongoal), forearm pronation and supination (eg, SpaceShooter, Scuba Diver) and power grip (eg, Holidays Jogging). The same games can also be controlled by the NeuroBands through movements of elbow flexion and extension, shoulder flexion, extension (to neutral) internal and external rotation and wrist flexion and extension.</p> <p>A handbook and 'Quickstart' page was produced to facilitate participants' independent use of the Neurofenix platform. This contained key instructions of how to fit and use the NeuroBall and NeuroBands, how to navigate the menu and game screens, safe and comfortable use, individual game instructions and troubleshooting/help.</p> <p>Study-specific documentation is used by the research therapists to record home visit sessions and a training checklist ensures all the content is covered. The software automatically measures activity data including game played, duration of play and number of repetitions performed.</p> <p>The research therapists providing the Neurofenix platform training visit and following clinical and technical support received two half-days of specific training from Neurofenix. Neurofenix engineers are available for additional technical support if required.</p>

Continued

Table 1 Continued

**TIDieR item**
**RHOMBUS intervention**

4. What (procedures)?: 'describe each of the procedures, activities and/or processes used in the intervention, including any enabling support activities'

This study will examine the Neurofenix platform as an upper-limb exercise intervention over a 7-week intervention period. This commences with a training home visit followed by a 1-week training phase and a subsequent 6-week training phase. The training home visit commences with a brief questionnaire about the participant's prior experience with technology and video games and confidence in using new technology. This allows the research therapist to tailor the pace and depth of teaching based on the participant's experience and confidence level. The participant will then be given the Neurofenix platform consisting of a NeuroBall or two NeuroBands, a tablet, a tablet stand, chargers and a handbook. A research therapist will then train the participant how to use the platform independently or with the help of a carer if requested.

Specifically, the participant will be trained in the following key activities: (1) how to turn the NeuroBall or NeuroBands and Tablet on and off, (2) safety precautions, (3) how to don the device, (4) calibrate the device, (5) how to use the device to play each of the games on the tablet, (6) how to navigate the menus, (7) how to track their progress, (8) how to use the handbook and (8) how to charge the devices.

The research therapist will monitor for discomfort, fatigue, eye strain, headache and increases in spasticity throughout the session. Participants will be advised to contact the research therapists using the contact details in the handbook for clinical and technical support throughout the intervention. At the end of the training home visit, the participant is encouraged to use the NeuroBall or NeuroBands for 5 days a week, gradually and safely increasing the amount of use with an aim to achieve 45 min a day by the end of the training week.

The participant will receive two scheduled phone calls from the research therapists 1 week and 3 weeks after the training home visit to ensure no clinical problems or technical faults have occurred. After this second follow-up telephone call, the participant will have no input from the research team unless the participant contacts the team for clinical or technical support. The participant will be called at the end of week 7 and asked to stop using the device on the final day of the 7-week intervention.

5. Who provided?: 'for each category of intervention provider (for example, psychologist, nursing assistant) describe their expertise, background and any specific training given'

The initial screening, physical screening, assessments and training home visits are all performed by the two research therapists who are registered physiotherapists.

The research therapists involved in the study received study-specific training on the assessments and intervention delivery.

6. How?: 'describe the modes of delivery (such as face to face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group'

1:1 face-to-face delivery: Training home visit, unscheduled follow-up clinical and technical home visits (as required)  
Telephone: Scheduled follow-up calls, unscheduled clinical and technical phone calls (as required)  
Self-administered: NeuroBall or NeuroBand exercise throughout the 7-week intervention.

7. Where?: 'describe the type of location(s) where the intervention occurred'

Participants' homes

Continued

**Table 1** Continued

**TIDieR item**

**RHOMBUS intervention**

<p>8. When and how much?: 'describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, duration, intensity or dose'</p>	<p>The training home visit is provided at the participants' preferred time usually requiring 1.5–2 hours. The participant will be encouraged to use the Neurofenix platform independently with an aim of 45 min a day, 5 days a week or more if they are able, self-limiting use based on fatigue and pain. The Neurofenix platform records data on the game(s) played, the duration of the session and number of repetitions of upper-limb movements performed. The data are uploaded at the end of each session. The participants will receive two scheduled follow-up phone calls to ensure they have not experienced clinical or technical difficulties. This will happen at the end of the training phase and 2 weeks into the exercise phase.</p>
<p>9. Tailoring: 'if intervention was planned to be personalised or adapted, then describe what, why, when and how'</p>	<p>If participants are assessed by the research therapists to have sufficient range of movement in the wrist and fingers to use the NeuroBall, they will be issued with this device. If they are unable to achieve a hand position compatible with using the NeuroBall, they will use the NeuroBands. Once issued with their NeuroBall/NeuroBands, participants will independently decide the duration and frequency with which they use the device, as well as which games they choose to play. To help guide participants on the duration and frequency of use, the research therapists will assess for signs of pain and fatigue during the training visit and give advice accordingly. During the intervention, the participant is responsible for how often or little they use the device and will not be prompted by the research therapists. The only exception will be if they are significantly overusing the device (&gt;2 hours a day).</p>
<p>10. Modifications: 'if intervention was modified during the course of the study, describe the changes what, why, when and how'</p>	<p>There have been no modifications of the interventions to date.</p>
<p>11. How well (planned)?: 'if intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them'</p>	<p>Research therapists complete a training visit checklist to document content of instructions given to participants and to verify completion of home visits. The Neurofenix platform records data on the game(s) played, the duration of the session and number of repetitions of upper-limb movements performed. The data are uploaded at the end of each session. Usage data are updated and made available to the research therapists once a week to allow monitoring of participant adherence, but feedback based on this is only given to the participants if they are overusing the device.</p>
<p>12. How well (actual)?: 'if intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned'</p>	<p>To be explored post hoc.</p>

is 7 and maximum 49, a higher score indicates a greater impact of fatigue on a person's activities.

#### Quality of life

QOL will be assessed using the EuroQol 5 Dimensions 5 Levels (EQ-5D-5L). The EQ-5D-5L describes and values health in five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.<sup>42</sup> Each dimension has five response categories ranging from no problems to extreme problems. Participants also rate their overall health on the day of the interview on a visual analogue scale from 0 to 100 (EuroQol-Visual Analogue Scale).<sup>42</sup> In people with stroke, the EQ-5D-5L has been shown to have reasonable concurrent validity ( $\rho=0.255-0.703$ ,  $p<0.05$ ), acceptable responsiveness and a MCID of 0.10.<sup>43</sup>

#### Participation

Participation will be assessed using the 10-item Subjective Index of Physical and Social Outcome (SIPSO).<sup>44</sup> The SIPSO measures factors relating to physical functioning/mobility and social/emotional functioning. The SIPSO is a valid and reliable measure of social and physical integration in people with stroke,<sup>44</sup> with a higher internal construct validity when the subscales are used, instead of the total scale.<sup>45</sup> Each question is scored from 0 to 4; minimum score of 0 and maximum of 40, a higher score indicates an increased ability to reintegrate to a 'normal' lifestyle.

#### Pain

Pain will be assessed using a visual analogue scale (VAS) from 0, no pain, to 10, excruciating pain, over the last 7 days. A VAS is a valid measure of pain intensity and is responsive to change.<sup>46 47</sup> To help those with language or mild cognitive problems, the scale is illustrated with emotive faces.

#### Gross level of disability

The simplified modified Rankin Scale questionnaire (smRSq) will be used to measure the participant's level of disability. The smRSq requires yes or no answers from a patient or caregiver. The smRSq has excellent reliability by telephone ( $\kappa=0.76$  (0.63 to 0.90)) and in person ( $\kappa=0.71$  (95% CI 0.57 to 0.86)) and correlates with QOL and initial stroke severity.<sup>48 49</sup>

#### Health service use

A modified version of the Client Service Receipt Inventory (CSRI) will assess health service use. The CSRI collects retrospective information on service utilisation, service-related issues and income.<sup>50</sup> The CSRI has been successfully used to estimate service use among adults with stroke.<sup>51</sup>

#### Fidelity to use of the Neurofenix platform

Fidelity to use of the Neurofenix platform will be assessed objectively using data collected via the sensors in the NeuroBall and NeuroBands and the software on the

tablet. These automatically collect data on the time spent actively exercising in each game and the number of movement repetitions.

#### Clinical and technical support provided

The amount of clinical and technical support will be recorded by the research therapists: the number, length and content of all calls and visits with participants.

#### Economic evaluation

This study will assess the feasibility of conducting an economic evaluation alongside a definitive clinical effectiveness of the Neurofenix platform. The aim of this feasibility study is to examine the practicality of collecting resource use and QOL data, the quality of the data and the amount of missing data observed. Resource use will include the following: therapist training; training home visits; clinical and technical support; participants' out-of-pocket expenses related to any additional exercise being undertaken; and health and personal social service use. These will be collected through diaries, management records, questionnaires and interviews.

In the definitive trial, the economic evaluation will take NHS, personal social services and participants' perspective.<sup>52</sup> The main outcome of the economic analysis will be an incremental cost per quality-adjusted life-year (QALY), based on EQ-5D-5L. Unit costs will be taken from the NHS reference costs (eg, DH 2016), standard unit costs (eg, PSSRU 2015) and published literature.

#### Process evaluation

A parallel process evaluation will be conducted alongside the trial to determine the feasibility, acceptability and safety of the intervention. The feasibility of delivering the intervention will be assessed through multiple mechanisms following the guidelines for fidelity in complex rehabilitation interventions.<sup>53</sup> Specifically, feasibility and perceived adequacy of training the research therapists will be assessed by analysis of their field notes. Feasibility of delivering the training session, clinical or technical calls and visits, and carrying out assessments will be determined by number, length and content of training sessions, the clinical and technical call and visit logs and therapists' field notes on assessment and intervention participant burden.

The feasibility and acceptability of the intervention for people with stroke will be assessed by evaluating the distribution of fidelity to the intervention, as measured by the Neurofenix platform, in terms of duration of active game play. Associations between participant-related factors, such as level of impairment, and fidelity will be explored. In addition, participant-reported experience will be investigated using the pretraining and post-training questionnaires, postintervention questionnaire, and by conducting semistructured interviews, as described next.

#### Pretraining and post-training questionnaire

Each participant will complete a pretraining questionnaire prior to the training session to explore previous



experience with technology and gaming and to measure confidence levels with new technology. A post-training questionnaire will be completed after the training session to assess their confidence level with using the Neurofenix platform and to explore how the participant might use the device in the following weeks.

#### Postintervention questionnaire

A postintervention questionnaire will be conducted after completion of the intervention period to assess the participant's perception of the Neurofenix platform and its components.

#### Interviews

Semistructured interviews will be conducted with a purposive sample of 18 participants to explore the perspectives of those receiving the intervention. Sampling will involve key criteria such as gender, age, device used (NeuroBall or the NeuroBands), amount of use (use of the device 4 or more days a week pragmatically classified as high use, 3 or less as low use), level of upper-limb impairment and function (ARAT scores 0–9 as severe, 10–21 as moderately severe, 22–43 as moderate, 43–53 as mild and 55–57 as full).<sup>54</sup>

Interviews will be conducted at the participant's house by a researcher trained in qualitative research methods. Topic guides developed from relevant literature and the specific aims of the process evaluation will be used. Where possible, the participant will be interviewed by a research therapist not involved in the intervention training to reduce the risk of socially desirable responses.

#### Safety

Pain and fatigue will be assessed at baseline, 8 weeks and 12 weeks. Self-reported pain will be assessed using a pain VAS and asking the average pain over the last week, the section relating to pain in the EQ-5D-5L. Fatigue will be assessed using the FSS-7. The number of episodes of pain, falls, fatigue, eye strain and other reported adverse events will be collated to assess the safety of the intervention. Research therapists will proactively enquire about changes in the participant's health or any compromises of safety since the last contact. A record of the incidence of adverse events from baseline measures until the end of the trial for each participant will be maintained. Falls incidence will be determined by asking participants at each contact point if they have fallen or tripped since the last contact. Although this method of assessing falls relies on the recall ability of the participant, it accurately detects injurious falls in community-dwelling older adults.<sup>55</sup> An adverse event is considered serious if it results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation and results in persistent or significant disability or incapacity. Participants who experience a serious adverse event will be withdrawn from the study.

A summary of all data collected and when these are collected is provided in [table 2](#).

#### Data management

Personal data collected during the trial will be handled and stored in accordance with the 1998 Data Protection Act and the General Data Protection Regulation 2018. Consent forms will be kept separate from other data in site trial master files at Brunel University London in a locked, secure environment. To preserve participant anonymity, only their allocated trial number and initials will be recorded on trial documentation (except the consent form). Confidentiality of all participant data will be maintained and information by which a participant could be identified will not be disclosed to a third party. Only non-identifiable clinical data will be shared with Neurofenix. Neurofenix will automatically collect data from the Neurofenix platform including user name, active game play and number of movement repetitions. Data generated by the Neurofenix platform will adhere to a Data Privacy Protocol, informed by Information Commissioner's Office guidelines and is compliant with the General Data Protection Regulation.

Use of study data will be controlled by the principal investigator. All data and documentation related to the trial will be stored in accordance with applicable regulatory requirements and access to data will be restricted to authorised trial personnel.

Qualitative interviews will be audio recorded and will be stored electronically and identified by trial number only. Transcripts will be anonymised or assigned a pseudonym; files will be stored using password-protected files. The ARAT video recordings will be stored electronically on encrypted and password-protected devices and identified by trial number only. Pseudonymised quantitative data will be made available in a public repository following publication of findings.

#### Patient and public involvement

People with stroke have been involved in the ongoing development of the intervention, including 18 stroke survivors who participated in an earlier study examining the usability of the Neurofenix platform. Two additional stroke survivors have provided input to the protocol, reviewed trial documentation, including participant information sheets, participant invite letters and questionnaires. The stroke survivors will continue to advise the research team throughout the trial, including dissemination of the results.

#### Data analysis

##### Qualitative data

To determine the feasibility, acceptability and safety of the intervention with people poststroke, interviews will be analysed using framework analysis.<sup>56</sup> This method provides a strong audit trail of the analytical process, which enhances transparency.<sup>57</sup> The technique involves five iterative stages: familiarisation, identifying thematic framework, labelling, charting and mapping and interpretation, following which significant themes can be presented.<sup>57</sup> As a further step to enhance rigour in this

**Table 2** Schedule of assessments and outcome measures

Clinical assessments	Preintervention	Intervention	Eight weeks	Postintervention	Twelve weeks
Informed consent	X				
Sociodemographic measurement	X				
ARAT	X		X		X
FMA-UL	X		X		X
PROM-UL	X		X		X
MAL	X		X		X
FSS-7	X		X		X
SIPSO	X		X		X
smRSq	X		X		X
Pain VAS	X		X		X
EQ-5D-5L	X		X		X
CSRI	X		X		X
Training and training questionnaire		X			
Neurofenix platform use		X			
Clinical and technical support		X			
Postintervention questionnaire		X		X	
Semistructured interview		X		X	
Falls		X	X	X	X
Upper-limb pain		X	X	X	X
AE and SAE		X	X	X	X

AE, adverse event; ARAT, Action Research Arm Test; CSRI, Client Service Receipt Inventory; FMA-UL, Fugl-Meyer Assessment-upper limb; FSS-7, seven-item Fatigue Severity Scale; MAL, Motor Activity Log; PROM-UL, passive range of movement-upper limb; SAE, serious adverse event; SIPSO, Subjective Index of Physical and Social Outcome; smRSq, simplified modified Rankin Scale questionnaire; VAS, visual analogue scale; EQ-5D-5L, EuroQol 5 Dimensions 5 Levels.

process, three researchers will independently code the same three transcripts and then meet to discuss and agree on codes assigned to each passage and their definitions.

#### Quantitative data

Distribution of the data will be examined using histograms, Q-Q plots and cross-tabulations. Descriptive statistics will be used to report pain and fatigue at baseline and follow-up, the number of participants experiencing adverse events during follow-up and the number of adverse events per participant. Generalised estimating equations will be used to examine change in pain and fatigue across timepoints.

Descriptive statistics will be used to report all data relating to fidelity, feasibility and acceptability of the intervention including the number and duration of clinical and technical calls, average session length and time spent in each game, enjoyment of games and number of episodes of pain experienced during intervention. Recruitment, retention and outcome measure completion will be described using frequencies and percentages.

Descriptive statistics will be used to report key participant characteristics across levels of fidelity to the intervention in terms of frequency and duration of active game play. Participant characteristics will include level

of disability, pretraining confidence in using new technology, post-training confidence in using the NeuroBall/Bands, level of support provided to use the NeuroBall/Bands and age.

The practicality, quality of data, quantity of missing data and reasons for missing data associated with the data collection tools will be recorded as part of determining the feasibility of conducting a phase three trial.

#### Timeline

The trial is funded for a period of 14 months and commenced in January 2018. Recruitment commenced in April 2018 and will be completed in August 2018. The final follow-up assessment is projected to be completed in October 2018 with data analysis and report writing being conducted from October onwards.

#### Ethics

The study is sponsored by Brunel University London and will be conducted in accordance with the approved protocol. Any protocol modifications will be notified to the Brunel University London Ethics Committee and consent will be reobtained from participants if required. The principles of the Declaration of Helsinki and Good Clinical Practice guidelines will be adhered to, along with

UK legislation and Brunel University Research integrity guidance.

### Monitoring

As the intervention is low risk and the potential harm is not anticipated, there will be no Data Monitoring Committee, interim analyses or stopping rules.

### Administrative structures

The trial will be run by the principal investigator, coinvestigators and two research therapists. The Chair of the College Research Ethics Committee will provide additional trial oversight, along with quarterly monitoring meetings with the funder and Neurofenix. Financial accounts will be externally audited.

### Dissemination

The dissemination plan will be developed in the early phases of the trial and will involve social media, broadcast media, the internet and electronic mail as well as more traditional routes, that is, peer-reviewed journal and national and international conferences. Publications will follow the Enhancing the Quality and Transparency of Health Research guidelines for reporting non-randomised studies. Authorship will follow international guidelines (International Committee of Medical Journal Editors criteria). The results will be disseminated to all participants and to those who wanted to participate but did not meet the inclusion criteria and who agreed to be contacted for research purposes.

**Acknowledgements** The authors would like to thank the two stroke survivors who assisted the development of the intervention and study materials. Further thanks to the group facilitators of Different Strokes and the Action for Rehabilitation from Neurological Injury. Thanks to Professor Christina Victor for her continuing support.

**Contributors** All authors listed meet the International Committee of Medical Journal Editors criteria for authorship. CK and GSB conceived the study, DJMS, TB, AN, JMR, NA, AW and MN designed the study. GSB, DAA, DJMS, TB and CK designed the intervention. CK will lead the running of the trial. DJMS and TB will lead the collection, management and analysis of the data. KB will lead blinded ARAT assessment. MN will lead the process evaluation. JMR will lead the statistical analysis. NA will lead the evaluation of the feasibility of the economic evaluation. All authors have read and approved the final manuscript.

**Funding** This work was supported by Innovate UK grant number 104188[3463]. The study sponsor is Brunel University London. Contact: Professor Peter Hobson, University Research Ethics Committee Chair (peter.hobson@brunel.ac.uk), Brunel University London, London.

**Disclaimer** Neurofenix has no influence on the design of the study, data collection, analysis and interpretation of the data and in writing the manuscript.

**Competing interests** GSB and DAA are employed by Neurofenix (UK), a company that manufactures and markets home-based training solutions. Neurofenix will provide the Neurofenix platforms and technical support to the research therapists.

**Patient consent** Obtained.

**Ethics approval** Ethical approval has been granted by the College of Health and Life Sciences Research Ethics Committee (REC) in Brunel University London (10249-MHR-Mar/2018-12322-2).

**Provenance and peer review** Not commissioned; peer reviewed for ethical and funding approval prior to submission.

**Data sharing statement** Pseudonymised data will be made available in a public repository once the data have obtained validation through publication.

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### REFERENCES

1. Ward NS. Restoring brain function after stroke - bridging the gap between animals and humans. *Nat Rev Neurol* 2017;13:244–55.
2. Stroke Association. State of the nation stroke statistics. 2018. <https://www.stroke.org.uk/resources/state-nation-stroke-statistics>
3. Kwakkel G, Kollen BJ. Predicting activities after stroke: what is clinically relevant? *Int J Stroke* 2013;8:25–32.
4. Nakayama H, Jørgensen HS, Raaschou HO, et al. Recovery of upper extremity function in stroke patients: the Copenhagen Stroke Study. *Arch Phys Med Rehabil* 1994;75:394–8.
5. Nichols-Larsen DS, Clark PC, Zeringue A, et al. Factors influencing stroke survivors' quality of life during subacute recovery. *Stroke* 2005;36:1480–4.
6. Wyller TB, Sødning KM, Sveen U, et al. Are there gender differences in functional outcome after stroke? *Clin Rehabil* 1997;11:171–9.
7. Pollock A, St George B, Fenton M, et al. Top 10 research priorities relating to life after stroke—consensus from stroke survivors, caregivers, and health professionals. *Int J Stroke* 2014;9:313–20.
8. Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: a systematic review. *Lancet Neurol* 2009;8:741–54.
9. Veerbeek JM, van Wegen E, van Peppen R, et al. What is the evidence for physical therapy poststroke? A systematic review and meta-analysis. *PLoS One* 2014;9:e87987.
10. Sehatzadeh S. Effect of increased intensity of physiotherapy on patient outcomes after stroke: an evidence-based analysis. *Ont Health Technol Assess Ser* 2015;15:1.
11. Dworzynski K, Ritchie G, Fenu E, et al. Rehabilitation after stroke: summary of NICE guidance. *BMJ* 2013;346:f3615.
12. Royal College of Physicians. *Clinical effectiveness and evaluation unit on behalf of the intercollegiate stroke working party. Sentinel Stroke National Audit Programme (SSNAP) Clinical audit August–November 2016 public report*, 2016.
13. Lang CE, MacDonald JR, Gnip C. Counting repetitions: an observational study of outpatient therapy for people with hemiparesis post-stroke. *J Neurol Phys Ther* 2007;31:3–10.
14. Hayward KS, Brauer SG. Dose of arm activity training during acute and subacute rehabilitation post stroke: a systematic review of the literature. *Clin Rehabil* 2015;29:1234–43.
15. Donoso Brown EV, Dudgeon BJ, Gutman K, et al. Understanding upper extremity home programs and the use of gaming technology for persons after stroke. *Disabil Health J* 2015;8:507–13.
16. Jurkiewicz MT, Marzolini S, Oh P. Adherence to a home-based exercise program for individuals after stroke. *Top Stroke Rehabil* 2011;18:277–84.
17. Hendrie W. *The dog ate my trainers*: Synapse, 2011.
18. Tijou I, Yardley L, Sedikides C, et al. Understanding adherence to physiotherapy: findings from an experimental simulation and an observational clinical study. *Psychol Health* 2010;25:231–47.
19. Laver KE, Lange B, George S, et al. Virtual reality for stroke rehabilitation. *Cochrane Database Syst Rev* 2017;31.
20. Turolla A, Dam M, Ventura L, et al. Virtual reality for the rehabilitation of the upper limb motor function after stroke: a prospective controlled trial. *J Neuroeng Rehabil* 2013;10:85.
21. Subramanian SK, Lourenço CB, Chilingaryan G, et al. Arm motor recovery using a virtual reality intervention in chronic stroke: randomized control trial. *Neurorehabil Neural Repair* 2013;27:13–23.
22. Kiper P, Piron L, Turolla A, et al. The effectiveness of reinforced feedback in virtual environment in the first 12 months after stroke. *Neurol Neurochir Pol* 2011;45:436–44.
23. Celnik P, Stefan K, Hummel F, et al. Encoding a motor memory in the older adult by action observation. *Neuroimage* 2006;29:677–84.
24. Franceschini M, Ceravolo MG, Agosti M, et al. Clinical relevance of action observation in upper-limb stroke rehabilitation: a possible role in recovery of functional dexterity. A randomized clinical trial. *Neurorehabil Neural Repair* 2012;26:456–62.
25. Man D. Common issues of virtual reality in neuro-rehabilitation. *Virtual reality*: InTech, 2010.
26. Anderson F, Annett M, Bischof WF. Lean on Wii: physical rehabilitation with virtual reality Wii peripherals. *Stud Health Technol Inform* 2010;154:229–34.
27. Prashun P, Hadley G, Gatzidis C, et al. Investigating the trend of virtual reality-based stroke rehabilitation systems. *Information Visualisation (IV), 2010 14th International Conference; IEEE* 2010.

28. W Bohannon R. Motricity index scores are valid indicators of paretic upper extremity strength following stroke. *Journal of Physical Therapy Science* 1999;11:59–61.
29. Goldstein LB, Samsa GP. Reliability of the National Institutes of Health Stroke Scale: extension to non-neurologists in the context of a clinical trial. *Stroke* 1997;28:307–10.
30. Sivan M, O'Connor RJ, Makower S, et al. Systematic review of outcome measures used in the evaluation of robot-assisted upper limb exercise in stroke. *J Rehabil Med* 2011;43:181–9.
31. Van der Lee JH, De Groot V, Beckerman H, et al. The intra- and interrater reliability of the action research arm test: a practical test of upper extremity function in patients with stroke. *Arch Phys Med Rehabil* 2001;82:14–19.
32. Yozbatiran N, Der-Yeghiaian L, Cramer SC. A standardized approach to performing the action research arm test. *Neurorehabil Neural Repair* 2008;22:78–90.
33. Duncan PW, Propst M, Nelson SG. Reliability of the Fugl-Meyer assessment of sensorimotor recovery following cerebrovascular accident. *Phys Ther* 1983;63:1606–10.
34. Page SJ, Fulk GD, Boyne P. Clinically important differences for the upper-extremity Fugl-Meyer Scale in people with minimal to moderate impairment due to chronic stroke. *Phys Ther* 2012;92:791–8.
35. van de Pol RJ, van Trijffel E, Lucas C. Inter-rater reliability for measurement of passive physiological range of motion of upper extremity joints is better if instruments are used: a systematic review. *J Physiother* 2010;56:7–17.
36. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther* 1987;67:206–7.
37. Gregson JM, Leathley MJ, Moore AP, et al. Reliability of measurements of muscle tone and muscle power in stroke patients. *Age Ageing* 2000;29:223–8.
38. Gregson JM, Leathley M, Moore AP, et al. Reliability of the Tone Assessment Scale and the modified Ashworth scale as clinical tools for assessing poststroke spasticity. *Arch Phys Med Rehabil* 1999;80:1013–6.
39. van der Lee JH, Beckerman H, Knol DL, et al. Clinimetric properties of the motor activity log for the assessment of arm use in hemiparetic patients. *Stroke* 2004;35:1410–4.
40. Simpson LA, Eng JJ. Functional recovery following stroke: capturing changes in upper-extremity function. *Neurorehabil Neural Repair* 2013;27:240–50.
41. Lerdal A, Kottorp A. Psychometric properties of the Fatigue Severity Scale-Rasch analyses of individual responses in a Norwegian stroke cohort. *Int J Nurs Stud* 2011;48:1258–65.
42. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;20:1727–36.
43. Chen P, Lin KC, Liang RJ, et al. Validity, responsiveness, and minimal clinically important difference of EQ-5D-5L in stroke patients undergoing rehabilitation. *Qual Life Res* 2016;25:1585–96.
44. Trigg R, Wood VA. The Subjective Index of Physical and Social Outcome (SIPSO): a new measure for use with stroke patients. *Clin Rehabil* 2000;14:288–99.
45. Kersten P, Ashburn A, George S, et al. The subjective index for physical and social outcome (SIPSO) in stroke: investigation of its subscale structure. *BMC Neurol* 2010;10:26.
46. Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. *Pain* 1986;27:117–26.
47. Ferreira-Valente MA, Ribeiro JL, Jensen MP, et al. Coping with chronic musculoskeletal pain in Portugal and in the United States: a cross-cultural study. *Pain Med* 2011;12:1470–80.
48. Bruno A, Akinwuntan AE, Lin C, et al. Simplified modified rankin scale questionnaire: reproducibility over the telephone and validation with quality of life. *Stroke* 2011;42:2276–9.
49. Bruno A, Shah N, Akinwuntan AE, et al. Stroke size correlates with functional outcome on the simplified modified Rankin Scale questionnaire. *J Stroke Cerebrovasc Dis* 2013;22:781–3.
50. Beecham J, Knapp M. Costing psychiatric interventions. *Measuring mental health needs* 2001;2:200–24.
51. Rodgers H, Shaw L, Cant R, et al. Evaluating an extended rehabilitation service for stroke patients (EXTRAS): study protocol for a randomised controlled trial. *Trials* 2015;16:205.
52. NICE. Developing NICE guidelines: the manual. 2014. <https://www.nice.org.uk/process/pmg20/chapter/introduction-and-overview>
53. Poltawski L, Norris M, Dean S. Intervention fidelity: developing an experience-based model for rehabilitation research. *J Rehabil Med* 2014;46:609–15.
54. Hoonhorst MH, Nijland RH, van den Berg JS, et al. How do Fugl-Meyer arm motor scores relate to dexterity according to the action research arm test at 6 months poststroke? *Arch Phys Med Rehabil* 2015;96:1845–9.
55. Ganz DA, Higashi T, Rubenstein LZ. Monitoring falls in cohort studies of community-dwelling older people: effect of the recall interval. *J Am Geriatr Soc* 2005;53:2190–4.
56. Ritchie J, Lewis J, Nicholls CM, et al. *Qualitative research practice: a guide for social science students and researchers*: Sage, 2013.
57. Holloway I, Galvin K. *Qualitative research in nursing and healthcare*: John Wiley & Sons, 2016.
58. Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. *J Speech Lang Hear Res* 2008;51:S225.
59. Rand D, Givon N, Weingarden H, et al. Eliciting upper extremity purposeful movements using video games: a comparison with traditional therapy for stroke rehabilitation. *Neurorehabil Neural Repair* 2014;28:733–9.
60. Brunner I, Skouen JS, Hofstad H, et al. Is upper limb virtual reality training more intensive than conventional training for patients in the subacute phase after stroke? An analysis of treatment intensity and content. *BMC Neurol* 2016;16:219.