Qualitative Protocol Development Tool

The research protocol forms an essential part of a research project. It is a full description of the research study and will act as a 'manual' for members of the research team to ensure adherence to the methods outlined. As the study gets underway, it can then be used to monitor the study's progress and evaluate its outcomes.

The protocol should go into as much detail about the research project as possible, to enable the review bodies to fully understand your study.

The use of this collated consensus guidance and template is not mandatory. The guidance and template are published as standards to encourage and enable responsible research.

The document will:

- Support researchers developing protocols where the sponsor does not already use a template
- Support sponsors wishing to develop template protocols in line with national guidance
- Support sponsors to review their existing protocol template to ensure that it is in line with national guidance.

A protocol which contains all the elements that review bodies consider is less likely to be delayed during the review process because there will be less likelihood that the review body will require clarification from the applicant.

We would appreciate self-declaration of how you've used this template so we are able to measure its uptake.

Please indicate the compatibility of this template with any existing templates you already use by stating one of the following on the front of each submitted protocol:

- **This protocol has regard for the HRA guidance and order of content; OR**
- **This protocol has regard for the HRA guidance; OR**
- **This protocol does not have regard to the HRA guidance and order of content**

FULL/LONG TITLE OF THE STUDY
ReHabGame: A Markerless, Game-Based Rehabilitation program

SHORT STUDY TITLE / ACRONYM

ReHabGame

PROTOCOL VERSION NUMBER AND DATE

V5.2

31.10.2025

RESEARCH REFERENCE NUMBERS

IRAS Number:	1012073
SPONSORS Number:	ETH2425-3331/ReHabGame
FUNDERS Number:	Generated by the funder. Enter if applicable

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature:

Date:
...25./04./2025.
.

.....
.....

Name (please print):

..... Dr Dannielle Green.....

Position: Chair of Faculty Research Ethics Panel of the Faculty of Science and Engineering.....
.....

Chief Investigator:

Date:
19/03/2025

Signature: .....
.....

Name: (please print):

..... Shabnam Sadeghi Esfahlani.....

LIST of CONTENTS

KEY STUDY CONTACTS

Insert full details of the key study contacts including the following

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Sponsor	Anglia Ruskin University (Dannielle Green) Anglia Ruskin University; Dannielle Green; Telephone +441223698234; E-mail dannielle.green@aru.ac.uk
Joint-sponsor(s)/co-sponsor(s)	N/A
Funder(s)	Anglia Ruskin University
Key Protocol Contributors	Dr Shabnam Sadeghi Esfahlani
Committees	N/A

STUDY SUMMARY

It may be useful to include a brief synopsis of the study for quick reference. Complete information and, if required, add additional rows.

Study Title	ReHabGame: A Markerless, Game-Based Rehabilitation program
Internal ref. no. (or short title)	ReHabGame

Study Design	Parallel, two-cohort (Neurological, MSK), two-arm RCT **Arms (within each cohort):** 1. **Usual Care only** 2. **Combined ReHabGame + Usual Care**
Study Participants	• Age 18+ years • Ability to follow simple instructions and give consent • No severe cognitive impairment (MoCA ≥ 22) • Stable medical condition (no recent cardiovascular event)
Planned Size of Sample (if applicable)	Planned Sample Size per cohort (Neurological or MSK): 23 participants per arm: 2 arms = 46 participants Total across both cohorts: 46 (Neurological) + 46 (MSK) = 92 participants Allowing for ~20% attrition,
Follow up duration (if applicable)	4-week post-intervention follow-up (Week 12)
Planned Study Period	Participants to be **randomised** to: 1. **ReHabGame**: 30–45 min sessions, 2×/week for 6–8 weeks 2. **Usual care**: standard physio sessions, 2×/week for 6–8 weeks
Research Question/Aim(s)	**Primary Objectives:** feasibility endpoints (Combined = ReHabGame + usual care; Control = usual care only) • **Neurological cohort:**

	○ Compare change in FMA-UE score from baseline to week 8 between arms • **MSK cohort:** ○ Compare change in SPADI score from baseline to week 8 between arms **Secondary Objectives:** clinical outcomes • Within each cohort, compare between-arm differences in: ○ **Adherence & Engagement:** session attendance, System Usability Scale (SUS) ○ **Functional Independence:** Barthel Index (neurological), DASH (MSK) ○ **Pain & ROM (MSK only):** VAS pain, goniometric ROM ○ **Motion-tracking metrics:** accuracy, smoothness, range captured by Kinect **Exploratory Objectives** • Cost and resource use (therapist time, equipment) across arms • Participant satisfaction and motivation (mixed-methods interviews) • Barriers/facilitators to implementing gamified rehab

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
Anglia Ruskin University	Financial and non-financial support

ROLE OF STUDY SPONSOR AND FUNDER

Anglia Ruskin University serves as the study sponsor, providing overall responsibility for initiating, managing, and overseeing the trial. The sponsor's role includes ensuring adherence to the protocol, monitoring progress, and maintaining compliance with ethical and regulatory requirements. The internal institutional grant provides financial support but does not influence the study design, conduct, data analysis, interpretation, or dissemination of results. Final decisions regarding publication and reporting rest with the principal investigators, ensuring the integrity and independence of the research.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Study Steering Groups

Study Management Committees/Groups
These committees and groups oversee the planning, implementation, and execution of the research project. Their responsibilities include:

- Ensuring adherence to ethical and regulatory standards.
- Providing guidance and oversight to research teams.
- Reviewing study protocols and procedures.
- Monitoring progress and addressing any issues or challenges that arise.
- Facilitating communication and collaboration among research team members.
- Reviewing and approving study-related documents, such as informed consent forms and data management plans.

Individuals

- Principal Investigator (PI):
    - Leads the research project and is responsible for its overall direction and management.
    - Develops the research protocol and obtains necessary approvals.
    - Supervises research team members and coordinates their activities.
    - Ensures compliance with regulatory requirements and ethical guidelines.
    - Analyses and interprets study data.
    - Reports study findings to relevant stakeholders.
- Research Team Members:
    - Co-investigators: Collaborate with the PI on specific aspects of the research project.
    - Research Assistants: Assist in data collection, analysis, publication, reporting, and other research activities.
    - Data Managers: Organize and manage study data.
    - Study Coordinators: Coordinate various aspects of the research project, such as liasing with the gatekeepers for participant recruitment and scheduling.
- Study Participants:
    - Contribute valuable data and insights by completing questionnaires, or providing other forms of information.

- Their involvement is essential for achieving the study objectives and generating meaningful findings.

Independence: The PPI Group operates as an advisory body, offering perspectives distinct from those of the research team. They do not control final decisions but strongly influence study conduct to ensure alignment with patient needs and priorities.

PROTOCOL CONTRIBUTORS

Principal Investigator

- Led the development of the research protocol, ensuring alignment with the study objectives and ethical guidelines.
- Developed the data analysis plan, including sample size calculations and statistical methods.
- Reviewed the protocol for methodological rigor and feasibility.
- Coordinated input from co-investigators and other team members.

Co-Investigators

- Provided subject matter expertise, contributed to study design, and advised on methodological considerations.
- Assisted in drafting specific sections of the protocol (e.g., data collection procedures, outcome measures).

Sponsor Representative

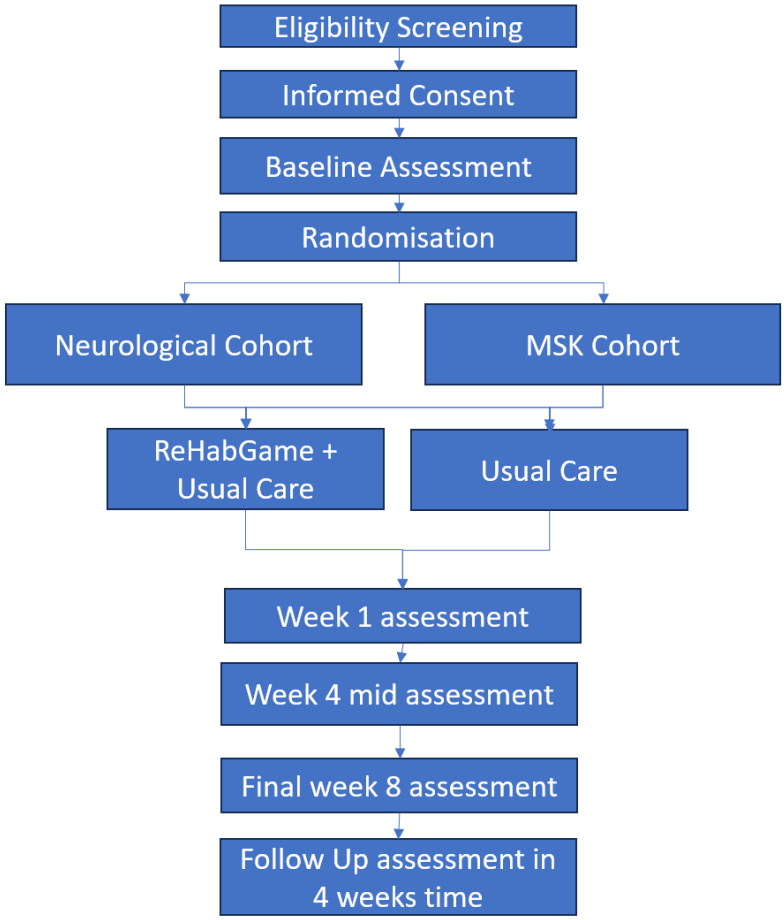
- Ensured compliance with institutional policies, funding requirements, and regulatory standards.
- Offered final approval for protocol submission.
- Patient/Public Involvement (PPI) Representatives
- Reviewed participant-facing documents to enhance clarity and relevance.
- Offered insights on study procedures to improve participant experience and engagement.

KEY WORDS:

- Game-Based Rehabilitation
- Markerless Motion Capture
- Virtual Rehabilitation

STUDY FLOW CHART

- Screen → Consent → Baseline (cohort-specific tests)
- 1:1 Randomisation into Game+ Usual-care, & Usual-care
- 6–8 week intervention (2 sessions/week)
- Assessments at Week 4 (interim), Week 8 (end), Week 12 (follow-up)
- Data analysis & dissemination



Study Timeline and Procedures

The therapist collects feedback and shares their recommendations in a written format with the research team. This may include a brief interview or written feedback on usability, motivation, and any perceived barriers.

1. Screening & Consent (Week 0)

- Therapist confirms diagnosis and eligibility.
- Patient to review and sign the consent form **(via the above Link).**
- Assign study ID or name via the ReHabGame platform and keep the same name/ID though out the trial.
- Baseline functional test administered by an assessor.
- Randomisation occurs immediately afterward.

3. Intervention Sessions (Weeks 1–8): Questionnaire at week 2, 4, 8 (via the above Link)

  - Combined arm only; 2×/week, Weeks 1–8

Usual care only:

o 30–45 min therapist-led physiotherapy per session
o 2 sessions/week for 6–8 weeks (standardised protocol)

- **Combined care- Usual-care + ReHabGame:**
    - 30–45 min Kinect-guided exercises per session.
    - Real-time difficulty adaptation; metrics auto-logged.
    - Both modalities, each 2×/week (on separate days or back-to-back).
    - Each session is logged in the PDF format.

4. **Mid-Point Assessment (week 4)**

Quick re-test of the cohort's primary functional score (FMA-UE subset or SPADI). Assessments occur at Week 1 (if applicable), Week 4 (interim), Week 8 (end), and Week 12 (follow-up).

Kinect captures a snapshot of your movement metrics.

5. **End-Of-Intervention Assessment (Week 8)**
    - Full repeat of baseline tests supervised by a clinician the above link can be *used "ReHabGame: Assessments at Week 4 (interim), Week 8 (end), Week 12 (follow-up)*".
    - Patients receive session report PDF summarising all movement metrics over the course of the study.
6. **Follow-Up (Week 12)**
    - Final SUS and engagement surveys to gauge lasting impressions.
    - Update on any late-emerging adverse events.
    - Optional brief functional check to see if gains were maintained.
    - We remind you how to request the lay summary of overall study findings.

Outcome Measures
Primary Objective

Evaluate feasibility of ReHabGame in improving motor recovery and functional independence in:

1. Neurological cohort
2. MSK cohort

Secondary Objectives

- Assess usability of the system in clinical environments
- Determine impact of personalized difficulty adjustment on engagement and adherence
- Analyse accuracy and reliability of motion-tracking data
- Explore participant perceptions of motivation and user experience
- Identify barriers and facilitators to adopting gamified rehab technologies

Planned Statistical Analyses

All analyses will be conducted **separately within each cohort** (Neurological and MSK), by original randomised allocation (intention-to-treat). Two-sided tests with $\alpha = 0.05$ will be used throughout.

1. Descriptive / Feasibility Metrics

- **Recruitment rate:**
  - Number screened, number eligible, number randomised (%)
- **Retention & adherence:**
  - Proportion completing Week 8 assessment in each arm (%)
  - Mean (±SD) number of sessions attended per arm
- **Data completeness:**
  - Proportion of missing outcome data at each timepoint

These will be reported as counts, percentages, and 95% confidence intervals.

2. Primary Outcomes

- **Neurological cohort:** Change in FMA-UE score (baseline → Week 8)
- **MSK cohort:** Change in SPADI score (baseline → Week 8)

Analysis:

- Analysis of covariance (ANCOVA) with Week 8 score as dependent variable, adjusting for:
  1. Baseline score
  2. Age
  3. Sex
  4. Randomisation stratum (high vs low severity)

- Report adjusted mean difference at Week 8 with 95% CI and p-value

3. Secondary Outcomes

1. **Functional independence:**
   - Neurological: Barthel Index change
   - MSK: DASH change
2. **Pain & ROM (MSK only):**
   - VAS pain change
   - Goniometric ROM change
3. **Usability & Engagement:**
   - SUS total score
   - Engagement survey score
4. **Motion-tracking metrics:**
   - Mean ROM achieved, movement smoothness, completion time, accuracy

Analysis:

- Continuous outcomes → ANCOVA as above.
- Repeated measures (baseline, Week 4, Week 8): mixed-effects linear models with fixed effects for time, arm, and time×arm interaction; random intercepts for participant.
- Categorical safety outcomes (adverse events): counts and χ^2 or Fisher's exact tests.

4. Exploratory & Cost Analyses

- **Cost/resource use:** Therapist time and equipment cost per participant—summarised descriptively and compared by arm (t-tests or nonparametric equivalents).
- **Qualitative feedback:** Thematic analysis of interview transcripts to identify barriers and facilitators; illustrative quotes reported.

5. Handling Missing Data

- If < 5% missing on any outcome, complete-case analysis.
- If ≥ 5%, multiple imputation by chained equations (20 imputations), including all baseline covariates and outcomes in the imputation model.
- Sensitivity analyses: per-protocol (participants attending ≥ 75% of sessions).

6. Safety Analyses

- **Adverse events:** Number and proportion of participants experiencing any AE and serious AE in each arm.
- Comparison by arm via χ^2 tests; descriptively summarised by severity and relatedness.

7. Interim Analyses

- No formal interim efficacy analyses planned (feasibility pilot).
- Safety data reviewed by independent Data Monitoring Committee at mid-point (after 50% of participants complete Week 8).

All analyses will be implemented in R (version ≥ 4.0), with scripts and output archived for reproducibility.

Qualitative Analysis

- **Thematic analysis** of open-text questionnaire feedback, following Braun & Clarke's framework.
- Coded and analysed using **NVivo or MAXQDA**.

1 BACKGROUND

Stroke, traumatic brain injury, multiple sclerosis, and musculoskeletal (MSK) shoulder disorders (e.g., rotator cuff repair, adhesive capsulitis, arthroplasty) all lead to significant upper-limb impairment, reduced independence, and diminished quality of life (World Health Organization [WHO], 2021). Traditional rehabilitation for these conditions relies on therapist-guided exercises, often repetitive, time-consuming, and subject to variability in delivery and patient adherence. As a result, many patients fail to achieve their full recovery potential, and therapists are constrained by limited time and resources (Laver et al., 2017).

In recent years, game-based rehabilitation systems have gained attention for their potential to boost patient engagement and foster more frequent, high-quality practice (Maier et al., 2019). These systems use interactive, often motion-capture technology to guide and track movements in real-time, turning therapy into a more enjoyable and rewarding experience. Research suggests that virtual or augmented environments can encourage patients to perform more repetitions and challenge themselves in ways that traditional exercises may not (Cameirão et al., 2010).

Over the last decade, various technologies have emerged as promising tools for delivering objective, repeatable, and engaging exercise programs without the need for wearable sensors or complex setup (Maier et al., 2019). Gamified rehabilitation platforms leverage these technologies to transform therapeutic exercises into interactive games, It has the potential to provide real-time feedback, adaptive difficulty, and motivational elements (scores, levels, and visual rewards) that can enhance patient engagement and long-term adherence.

ReHabGame is a markerless, game-based rehabilitation system that integrates Kinect-derived motion tracking with a bespoke adaptive algorithm to tailor exercise difficulty in real time. In this study we designed a two-cohort, two-arm RCT comparing **Combined ReHabGame + usual care** versus **usual care alone**, in both neurological and MSK cohorts. By stratifying participants and blinding outcome assessors, this study will determine the added value of ReHabGame when combined with usual care, characterize feasibility metrics (recruitment, retention, adherence), and generate robust data on functional gains, pain modulation, and motion-tracking validity.

2 RATIONALE

Upper-limb impairments from neurological injuries (e.g., stroke, traumatic brain injury, multiple sclerosis) and musculoskeletal (MSK) shoulder disorders (e.g., rotator cuff repair, adhesive capsulitis, shoulder arthroplasty) both lead to profound limitations in daily function, independence, and quality of life. However, traditional rehabilitation—whether neuro-focused or MSK-focused—relies heavily on therapist-led, repetitive exercises that can be monotonous, resource-intensive, and subject to variable patient adherence.

Markerless motion-capture and gamification offer a compelling solution:

- Objective feedback: Systems like Microsoft Kinect accurately track joint movement and repetition counts without wearable sensors, reducing setup burden and allowing precise, real-time performance metrics.
- Adaptive challenge: A game-based interface can dynamically tailor exercise difficulty to a patient's current ability, minimizing boredom or frustration and promoting "just-right" challenge.
- Motivation & engagement: Visual rewards, scoring, and level progression have been shown to increase session attendance, enjoyment, and long-term adherence, key factors in driving neural plasticity and tissue remodelling.

Evidence gaps remain, however:

- Lack of rigorous RCTs directly comparing game-based therapy to standard physiotherapy, particularly in MSK populations.
- Unknown additive effects of combining gamified and conventional therapies, clinics often offer "usual care" alongside any novel intervention, but the independent contribution of each is rarely isolated.
- Population differences: Neurological and MSK conditions exhibit distinct pathophysiology (e.g., motor control deficits versus pain-limited range of motion and tendon loading), yet few studies have contrasted gamified rehab across these cohorts within the same trial.

By conducting a two-cohort, two-arm randomized controlled trial, we will:

- Determine whether **Combined ReHabGame + usual care** produces greater gains than **usual care alone** in both cohorts.
- Assess whether a combined approach affords additive benefits
- valuate feasibility, recruitment, retention, adherence, and usability metrics within each cohort.
- Generate cohort-specific data on functional recovery (e.g., FMA-UE, SPADI), pain modulation, and motion-tracking validity, addressing both motor control and musculoskeletal loading concerns.

This design ensures robust, clinically relevant evidence to guide the optimal deployment of gamified rehabilitation, whether as an adjunct to clinic sessions, or an integrated component of standard care, across diverse patient populations.

3 THEORETICAL FRAMEWORK

Our study draws on motor learning principles and motivational theories to explain how a game-based rehabilitation approach can enhance arm function in individuals with motor impairments:

Motor Learning Theory

- Emphasizes repetition, feedback, and task-specific practice as key elements for improving movement control.

- ReHabGame provides repetitive, goal-directed exercises in a virtual environment, allowing participants to practice functional movements repeatedly with real-time feedback.

Self-Determination Theory (SDT)

- Highlights autonomy, competence, and relatedness as core motivational drivers.
- By offering engaging tasks and immediate success indicators (e.g., scores or visual cues), ReHabGame can foster a sense of achievement (competence) and empower users to choose when and how they practice (autonomy).

Gamification and Engagement

- Incorporates game design elements—such as points, levels, and challenges—to boost motivation and adherence.
- The interactive nature of ReHabGame can make repetitive exercises more enjoyable, reducing the boredom often associated with traditional rehab.

Markerless Technology for Accessibility

- Traditional motion-capture systems often rely on markers or complex hardware, limiting widespread use.
- A markerless approach aligns with research suggesting that accessible, easy-to-use technology can expand rehabilitation opportunities to more diverse settings and populations.

By integrating these concepts—motor learning, self-determination, gamification, and accessible technology—ReHabGame addresses gaps identified in the Background (e.g., low engagement, limited practicality) and provides a robust framework for studying how a virtual, game-based system can facilitate upper-limb recovery.

4 RESEARCH QUESTION/AIM(S)

To determine the added benefit of Combined ReHabGame + usual care versus usual care alone on upper-limb function, pain, and usability in two cohorts (Neurological and MSK).

4.1 Objectives

Primary Research Questions

1. **Neurological cohort:**
   - Does Combined ReHabGame + usual care produce greater improvement in upper-limb motor control (FMA-UE, baseline→Week 8) compared to usual-care alone?
2. **MSK cohort:**
   - Does Combined ReHabGame + usual care produce greater improvement in shoulder pain and function (SPADI, baseline→Week 8) compared to usual-care alone?

Secondary Research Questions
Within each cohort, how do the two arms compare on:

- **Functional independence:** Barthel Index (Neurological) or DASH (MSK)
- **Engagement & usability:** System Usability Scale (SUS) scores and engagement survey ratings at Weeks 4, 8, 12
- **Session adherence:** Number and proportion of prescribed sessions completed
- **Motion-tracking performance:** Changes in Kinect-derived metrics (range of motion, smoothness, accuracy)
- **Pain & ROM (MSK only):** Pain VAS and goniometric ROM

Exploratory Aims

1. Compare **cost and resource utilization** (therapist time, equipment) across arms.
2. Identify **barriers and facilitators** to adoption of gamified rehabilitation via participant interviews.
3. Assess **safety outcomes** (adverse events, overuse symptoms) and determine whether combined therapy introduces any incremental risk.

Feasibility Objectives

- Estimate **recruitment rate, retention rate,** and **data completeness** for each arm and cohort.
- Evaluate the acceptability of randomisation into **Combined ReHabGame + usual care** versus **usual care alone**.
- Generate preliminary estimates of **variance** in primary outcomes to inform sample-size calculations for a definitive trial.

4.2 Outcome

Broad Outcome: A clearer understanding of how a markerless, game-based rehabilitation system affects upper-limb motor recovery, motivation, and overall functional independence.

Practical Impact: Evidence to support (or refute) the use of ReHabGame as a routine therapeutic tool, potentially informing clinical guidelines and future technology-driven rehabilitation strategies.

After each gamified rehabilitation session, participants will receive personalised, visual performance feedback generated by the ReHabGame platform. This includes:

- A PDF-based summary showing:
    - Percentage of movement types (e.g. abduction, adduction of the upper arm)
    - Distribution of virtual objects around the participant in the game environment
    - Visual markers of target reach, joint usage, and task completion
- Feedback is presented immediately post-session in a simple, colour-coded format that participants can understand without technical expertise.

A member of the research team will review this feedback in person with the participant to:

- Celebrate progress and encourage engagement
- Clarify what the data means in lay terms
- Address any confusion or concern
- Adjust future gameplay settings if needed to support optimal challenge and safety

The ReHabGame system uses an **automated, performance-based algorithm** to dynamically adjust the difficulty level of gameplay in real time. This ensures that exercises remain **appropriately challenging, engaging, and within the user's capabilities**, thereby reducing frustration and promoting sustained participation.

Difficulty Adjustment Logic

- At each session, the system spawns **three interactive virtual objects** within the participant's reach zone.
- The participant's ability to successfully **interact with or complete tasks involving these objects** determines the next session's difficulty level.
    - If the participant is **unable to interact with all three objects**, the difficulty is **automatically reduced to Level 0**, providing a simplified task setup with wider target zones and reduced motion requirements.
    - If the participant completes the interactions successfully, the difficulty level is **increased incrementally up to Level 5**, which includes:
        - Increased object speed
        - Reduced object size
        - More complex trajectories
        - More demanding spatial configurations

This **fuzzy logic-based scaling** allows for a responsive system that adjusts to moment-to-moment motor performance, thereby personalising therapy without requiring therapist intervention.

No remote questionnaires or feedback sessions will be conducted unless the participant explicitly prefers to complete their follow-up session online.

5 STUDY DESIGN and METHODS of DATA COLLECTION AND DATA ANALYIS

Type: Parallel, two-cohort (Neurological vs MSK), two-arm randomized controlled trial

- Arms (within each cohort):

    1. Usual-care physiotherapy only
    2. Combined ReHabGame + usual-care

Allocation: 1:1 randomisation, stratified by baseline severity (high vs low) within each cohort

- Blinding:
    - Outcome assessors blinded to group assignment

    - Participants & therapists unblinded (interventions are overt)
- Duration: 6–8 weeks of intervention (2 sessions/week) + 4-week follow-up
- Sample size: 23 per arm per cohort (46 per cohort; 92 total), allowing ≈20% attrition.

Domain	Instrument & Timing
Demographics & History	Structured questionnaire at Week 0 (age, sex, diagnosis, time since onset/surgery, comorbidities)
Primary Outcomes	- Neurological: Fugl–Meyer Assessment (upper extremity) at Weeks 0, 8- MSK: SPADI at Weeks 0, 8
Secondary Outcomes	- Neurological: Barthel Index at Weeks 0, 8- MSK: DASH, pain VAS, goniometric ROM at Weeks 0, 8
Interim Metrics	At Week 4 for all: SUS, engagement survey, adverse-event checklist, quick FMA-UE subset (neuro) or SPADI re-test (MSK), Kinect snapshot metrics
Follow-up Metrics	At Week 12: SUS, engagement survey, adverse-event update, optional brief functional check
Motion-Tracking Data	Automatically logged each session via Kinect: range of motion, smoothness (jerk), repetition count, completion time, accuracy
Session Adherence	PDF session log (date, duration, pain VAS, issues) maintained by participant; automatically generated session report PDFs summarising movement metrics
Qualitative Feedback	Semi-structured interview or written feedback at end of Week 8 (usability, barriers, facilitators, motivation)
Safety Monitoring	Adverse events recorded at every session and via AE checklist at Weeks 4, 8, 12; severity and relatedness noted

All analyses conducted separately within each cohort on an intention-to-treat basis, $\alpha = 0.05$ two-sided.

1. **Feasibility & Descriptive Statistics**
    - Recruitment, retention, and adherence rates: counts (%) with 95% CIs
    - Session completion: mean ± SD sessions attended per arm
    - Data completeness: proportion of non-missing data per outcome
2. **Primary Analyses**

    - ANCOVA with Week-8 score as the dependent variable (adjusting for baseline value, age, sex, and severity stratum); report the adjusted mean difference (95% CI) between arms.

3. **Secondary & Repeated-Measures Analyses**
    - **Continuous outcomes** (Barthel, DASH, Pain VAS, ROM, SUS, engagement scores):
        - ANCOVA at Week 8 as above
        - **Mixed-effects linear models** for repeated measures (Weeks 0, 4, 8) with fixed effects for time, arm, and time×arm; random intercepts for participants
    - **Categorical safety outcomes:** AE counts compared via χ^2 or Fisher's exact tests

4. **Motion-Tracking Metrics**
    - Compare mean ROM, smoothness, completion time, and accuracy at Weeks 4 and 8 using ANCOVA, adjusting for baseline Kinect metrics
5. **Exploratory Analyses**
    - **Cost/resource use:** descriptive comparison of therapist time and equipment costs per participant (t-tests or nonparametric equivalents)
    - **Qualitative data:** thematic analysis of interviews to identify barriers/facilitators; representative quotes to illustrate key themes
6. **Missing Data**
    - **< 5% missing:** complete-case analysis
    - **≥ 5% missing:** multiple imputation by chained equations (20 datasets) including baseline covariates and outcomes
    - **Sensitivity:** per-protocol analysis (≥ 75% sessions attended)
7. **Safety Review**
    - AE rates summarised by arm; reviewed by an independent Data Monitoring Committee at midpoint (after ~50% complete)

All statistical programming and reporting will be done in R (≥ 4.0), with scripts version-controlled for reproducibility.

Data Handling Procedures

- De-Identification**: Personal identifiers will be removed or replaced with participant IDs in all datasets.**
- Storage and Transfer:
    - Electronic files (e.g., transcripts, quantitative spreadsheets) will be stored on secure, password-protected servers.
    - Paper records (e.g., signed consent forms) will be kept in locked filing cabinets in a restricted-access area.
- **Access**: Only authorized research staff who have signed confidentiality agreements will have access to identifiable information.
- **Archiving**: At the end of the study, de-identified data will be archived according to institutional and regulatory guidelines, typically for up to three years or as required by policy.

By combining quantitative assessments with in-depth qualitative insights, this study design and data analysis plan will provide a well-rounded understanding of how ReHabGame affects upper-limb rehabilitation outcomes and user experiences.

6 STUDY SETTING

Access to Expertise

- On-site neurologists, physiotherapists, occupational therapists, and rehabilitation nurses can provide immediate clinical support if participants have any medical concerns or adverse events.
- The clinical teams' involvement ensures high-quality, clinically relevant data collection and safe implementation of the study protocol.

This is a multi-centre study involving:

1. Mid and South Essex NHS Foundation Trust Site A
   Southend University Hospital, Prittlewell Chase, Westcliff-on-Sea, Essex SS0 0RY
2. Physio4You – NeuroPhysio Team - Site B

Both sites will follow the same overall protocol, but each location will manage its own recruitment, screening, and data collection processes.

Site A: Southend General Hospital (NHS)

Cohort: MSK only.

Recruitment: Patients with eligible musculoskeletal shoulder conditions will be identified from outpatient orthopaedic and physiotherapy clinics.

All interventions will be delivered on-site by NHS physiotherapists trained in the study protocol.

Site B: Physio4You (Private Neuro-Physiotherapy Centre)

Cohort: Neurological only (stroke, traumatic brain injury, multiple sclerosis).

Location:
Physio4You
16 Watermark Way, John Tate Road, Hertford, Hertfordshire, SG13 7TZ.

Clinical Oversight:
The study at this site will be managed under the supervision of Mr James Creak, Director and NeuroPhysio Clinical Lead Physiotherapist at Physio4You.

Usual Care Referral Pathway:
Neurological patients attending Physio4You are typically referred through one of the following routes:

- NHS consultants or GPs following hospital discharge.
- Community neurological rehabilitation teams.
- Self-referral by patients already diagnosed and managed under the care of an NHS or private neurologist.

Once accepted into Physio4You's care, each patient's overall clinical oversight remains with their referring physician or consultant. Physio4You clinicians provide physiotherapy

input in line with the referring clinician's management plan and within the scope of usual care.

Role in the Study:
Physio4You will provide a controlled clinical environment for:

- Delivery of the ReHabGame intervention to neurological participants.
- Collection of study outcome measures.
- Monitoring participant safety and session adherence.

All intervention sessions will take place within the Physio4You clinic only.
Although Physio4You routinely offers domiciliary services, no home-based or community sessions are included in this study protocol.

Recruitment Pathway & Access to Records:

- Recruitment will be conducted only by clinicians with legitimate access to patient records as part of their usual clinical role (e.g., treating physiotherapists or rehabilitation consultants).
- These clinicians will act as clinical gatekeepers, screening caseloads and medical records for potentially eligible participants and providing study information to suitable patients.
- If patients agree, the study will be conducted at the Physio4You site under Mr Creak's direct supervision.
- Research staff or assistants will not access medical records prior to consent. Their role begins only once a patient has been referred and has provided written consent to participate.

Site Readiness:
Mr Creak has been trained in the use of the ReHabGame software and hardware. A dedicated computer and Kinect sensor have been provided, with all setup requirements completed. The trial of neurological assessments and intervention sessions will therefore be conducted under his direct supervision at the Hertfordshire site.

Refer interested patients to the research team.

Research staff/research assistants will not directly access medical records prior to consent. Their role begins only once a patient has been referred and has provided consent to be contacted.

This ensures that all pre-consent record reviews are compliant with NHS and GDPR requirements, limited to those with a direct clinical care relationship.

Technical Setup

- Motion-Tracking Devices: A designated space with sufficient room (2–3 meters clear space) for Kinect-based tracking.
- Secure Storage: Each site must have secure cabinets or a locked office for paper records (e.g., consent forms).

Ethical and Governance Approvals

- Each hospital may require local governance or R&D approval in addition to overarching ethical approval (e.g., IRAS).
- Formal site agreements must be in place to ensure compliance with data protection (GDPR) and institutional policies.

Staff Training

- Staff at both sites will receive a brief orientation on ReHabGame's operation, the motion-tracking sensors, and participant safety protocols.
- Any site-specific health and safety training required by hospital policy (e.g., manual handling, infection control) must be completed by the research team.

1. Identification & Recruitment
    - At each site, clinical teams (physiotherapists, occupational therapists, rehab consultants) will introduce the study to eligible patients and, if they express interest, refer them to the research team for formal screening.
    - Potential participants will receive an information sheet and have an opportunity to ask questions before providing written informed consent.
2. Baseline Assessments
    - Participants will undergo baseline clinical evaluations (e.g., Fugl-Meyer Assessment), and relevant questionnaires.
    - These may take place in a private clinic room or dedicated rehabilitation space.
3. ReHabGame Intervention
    - Participants will use ReHabGame in designated therapy areas equipped with the Kinect hardware.
    - Session frequency and duration will follow the study protocol (e.g., 1–2 sessions per week over 6–8 weeks).
    - Research staff or designated clinical staff will supervise sessions, ensuring correct usage and participant safety.
4. Data Collection
    - Quantitative: System logs (range of motion, frequency of play), standardized clinical scales (pre-/post-intervention).
    - Qualitative: Questionnaire to gather feedback on user experience and feasibility.
5. Follow-Up Assessments
    - Post-intervention evaluations will be conducted to assess changes in upper-limb function and gather final feedback.
    - Data will be entered into secure, password-protected electronic databases, ensuring confidentiality and compliance with data protection laws.

Resource Optimization

- Leveraging the expertise and facilities at sites ensures sufficient staff support, therapy spaces, and participant pool, thereby strengthening the study's feasibility and overall quality.

7 SAMPLE AND RECRUITMENT

This pilot RCT will recruit 92 participants (46 per cohort), allowing for ~20% attrition to achieve at least 90 completers in total. Recruitment will take place over 12 months across two sites (neurorehabilitation and orthopaedic physio clinics).

- **Recruitment sources:**
  - Referrals from participating physiotherapists and neurologists
  - Clinic screening of outpatient caseloads
  - Posters and leaflets in waiting areas
  - Direct approach **via the treating clinician** during routine appointments; research staff contact patients only **after clinician referral and consent to be contacted**.

  Screening process:

  - Interested patients receive an information sheet and undergo preliminary eligibility check (by phone or in person).
  - Eligible patients invited for a face-to-face screening visit to confirm criteria, obtain written informed consent, and complete baseline assessments.
- **Retention strategies:**
  - Flexible session scheduling (morning/afternoon slots)
  - Interim "progress report" PDFs after each session to maintain engagement

7.1.1 Common Inclusion Criteria

1. Age 18+ years
2. Able to understand study information and provide written informed consent
3. MoCA ≥ 22 (no severe cognitive impairment)
4. Medically stable (no major cardiovascular event or surgery within past 3 months)

7.1.2 Cohort-Specific Inclusion Criteria

- **Neurological cohort:**
  1. Clinically diagnosed stroke, traumatic brain injury, or relapsing-remitting multiple sclerosis
  2. Upper-limb motor impairment: FMA-UE score 20–50 at baseline
  3. ≥ 3 months post-stroke or ≥ 6 weeks post-MS relapse
- **MSK cohort:**
  1. Diagnosed rotator cuff repair (≥ 6 weeks post-op), adhesive capsulitis, or shoulder arthroplasty (< 6 months)
  2. Pain ≤ 6/10 on resting VAS
  3. Active shoulder elevation ≥ 30°
  4. On a stable physiotherapy regimen (≤ 2 sessions/week)

7.1.3 Exclusion Criteria (both cohorts)

1. Uncontrolled hypertension or significant cardiac arrhythmia
2. Severe spasticity (Modified Ashworth ≥ 3) or gross joint instability
3. Severe visual or hearing impairment preventing safe game use

Participants meeting all common and relevant cohort-specific inclusion criteria, and none of the exclusion criteria, will be enrolled and randomized.

7.2 Sampling

To ensure adequate feasibility data and allow for up to 20% attrition, we will recruit 108 participants in total (Kunselman, 2024).

7.2.1 Size of sample

Allocated as follows:

- Per cohort: 46 participants
- Per arm (1:1): 23 participants
- Expected completers per arm: ≥ 18 participants
- Total completers: ≥ 72 participants

This sample size is not powered for definitive hypothesis testing but is sufficient to:

1. Estimate recruitment, retention, and adherence rates with acceptable precision.
2. Generate variance estimates for the primary outcomes (FMA-UE in the Neurological cohort; SPADI in the MSK cohort) to inform sample-size calculations for a future definitive trial.

7.2.2 Sampling technique

Participants will be recruited using a consecutive convenience sampling approach within each cohort at the two collaborating clinical sites:

2. Identification of potential participants:
    - Treating therapists screen their outpatient caseloads and post-surgical lists for patients meeting broad eligibility (age, diagnosis category).
3. Invitation and screening:
    - All eligible patients are approached in person or by telephone, provided with study information, and invited to a formal screening visit.
    - Those who consent and meet detailed inclusion/exclusion criteria at screening are enrolled.
4. Randomisation:

- Enrolled participants are then randomised 1:1 within their cohort (Neurological vs MSK) into the two trial arms using a stratified block randomisation scheme, with stratification by baseline severity (high vs low) to ensure balance across arms.

This approach ensures that we capture a representative sample of the clinic's neurorehabilitation and MSK shoulder populations while maintaining rigorous allocation to the intervention arms.

7.3 Recruitment

Aim: To describe how eligible participants—including those for both intervention and control groups—are identified, approached, and enrolled in the study, ensuring a transparent and ethical process from initial contact to informed consent.

7.3.1 Sample identification

1. **Clinical Gatekeepers**– Identification of Potential Participants
   Treating clinicians—including physiotherapists, occupational therapists, and rehabilitation consultants—at the research centers or/and hospitals will serve as clinical gatekeepers. Their role will include:

   - Identifying potential participants based on the study's inclusion and exclusion criteria.
   - Screening for both the intervention group (Rehabgame users) and control group (usual care recipients).
   - Ensuring that only those patients deemed medically and cognitively suitable to participate are referred.
   - Avoiding any form of coercion by relying on existing therapeutic relationships to introduce the study in an ethical and respectful manner.

2. **Referral to the Research Team Once a suitable participant is identified:**

   - The clinician will briefly introduce the study's purpose, confirming preliminary interest without going into extensive detail.
   - If the individual expresses interest, the clinician will refer them to the research team, either:
     - By sharing the research team information with them or sharing their contact details securely with the research team (in accordance with GDPR/local data protection guidelines); or
     - By facilitating a direct introduction to the research team (e.g., during an outpatient visit or ward round).
   - Referrals will include candidates for both study arms, ensuring equitable identification.

3. **Initial Contact by the Research Team**
   A designated member of the research team—not involved in the patient's direct clinical care—will conduct the next steps:

- Make initial contact via phone, video call, or in person at a convenient time.
- Provide the Participant Information Sheet (PIS) and offer a comprehensive explanation of the study aims, procedures, and randomisation (if applicable).
- Answer any immediate questions and allow participants time to consider their involvement.

7.3.2 Consent

Aim: To outline the procedure for obtaining **informed, voluntary, in-person consent** from participants before any study-related activities commence, in accordance with ethical, legal, and Good Clinical Practice (GCP) standards.
This section also clarifies the **non-consenting role** of **QR code scanning**, which is used solely for session-level attendance confirmation.

Initial Discussion

- Only individuals with legitimate clinical access to medical records and clinic schedule lists will review these prior to obtaining consent. This access is limited to members of the patient's usual care team (e.g., treating physiotherapists, rehabilitation consultants, or clinical supervisors) who are already authorised to view these records as part of their professional duties. The purpose of this review is solely to identify potentially eligible participants in accordance with the inclusion and exclusion criteria.
- Research staff or research assistants will not have access to identifiable patient records or clinic schedules prior to consent. Their involvement will commence only after a patient has been identified by the treating clinician, has been approached about the study by that clinician, and has provided informed consent to be contacted by the research team.
-
- This discussion will cover:
    - The purpose and objectives of the study
    - Study procedures and duration
    - Potential risks and benefits
    - Data handling, confidentiality, and withdrawal rights
- Participants are actively encouraged to ask questions throughout.

Provision of Written Materials
Each participant (or representative) will receive the **Participant Information Sheet (PIS)** and the **Consent Form**, written in plain language and approved by the Research Ethics Committee (REC).
Participants will be given a minimum of **24 hours** to review the documents, consult others if desired, and consider their decision without pressure.

Opportunity to Ask Questions
Before signing the consent form, participants will have the opportunity to clarify any part of the study and confirm understanding with the research team.

Assessment of Capacity

Capacity will be assessed by the **clinical gatekeeper** prior to referral, and again confirmed by the research team before obtaining consent.

Capacity assessment ensures the participant can:

- Understand the research and its implications
- Retain the information long enough to make an informed decision
- Weigh up choices and communicate a voluntary decision

Protecting Vulnerable Participants

- In a rehabilitation setting, some participants may be more vulnerable to perceived coercion.
- To minimize this risk:
  - Consent will be obtained in a private setting, away from direct clinical staff
  - Participants will be reminded that participation is voluntary, and their usual care will not be affected by their decision
  - They may withdraw from the study at any time, without giving a reason

Signing the Consent Form

When all questions have been answered and the participant confirms understanding:

- The participant and the researcher will sign and date the consent form
- A copy is provided to the participant, and the original is stored securely in the study documentation

Use of QR Code – Session-Level Confirmation Only

- This QR code may be scanned at each session to:
  - Confirm attendance
  - Log session data (e.g., time, session type)
- Important: <u>QR code scanning is used solely to confirm attendance and link session-level quantitative data to the participant's study ID; it does not replace informed consent.</u>
- Ongoing verbal confirmation of willingness to proceed with each session will be encouraged.

8 ETHICAL AND REGULATORY CONSIDERATIONS

Aim: To explain how the study's aims and methods comply with ethical principles and relevant regulatory frameworks, highlighting participant risk-benefit balance, data protection measures, and adherence to legal requirements.

Research Question and Study Design:

- The study aims to evaluate the effectiveness of a game-based rehabilitation intervention (ReHabGame) for individuals with upper-limb motor impairments. This directly addresses an important clinical need—enhancing functional recovery—while minimizing participant burden through a relatively low-risk, non-invasive intervention.
- The study design (mixed-methods, quantitative clinical assessments, and qualitative analysis) is in line with the principles of **Respect for Persons**, **Beneficence**, and

Justice, as articulated in international guidelines (e.g., Declaration of Helsinki) and local regulations (e.g., UK Policy Framework for Health and Social Care Research).

Regulatory Framework

- The study will be conducted in compliance with **Good Clinical Practice (GCP)** guidelines, the **Mental Capacity Act (2005)** (if applicable), and the **General Data Protection Regulation (GDPR)** (or equivalent data protection laws).
- Ethical approval will be sought from the appropriate Research Ethics Committee (REC), and site-specific permissions (e.g., NHS R&D approval or private hospital governance) will be obtained before commencement.

8.1 Assessment and management of risk

Potential Benefits

- Participants may experience improved motor function, increased motivation, and enhanced engagement in rehabilitation.
- By contributing to research on innovative rehabilitation methods, participants help advance care for future patients with similar impairments.

Potential Risks

- **Physical Risks:** Mild fatigue or discomfort from repetitive movements. In rare cases, exacerbation of pre-existing conditions.
- **Psychological Risks:** Some participants may feel frustrated if they encounter difficulties with the game tasks or if they perceive limited progress.
- **Data Privacy Risks**: Collection of personal and health data introduces a risk of unauthorized access or disclosure if not properly safeguarded.

Mitigation Strategies

- **Physical Safeguards**: Each session is supervised by trained staff who can modify or pause the activity if the participant experiences discomfort.
- **Psychological Support**: Participants can withdraw at any time, and referral pathways are in place for those who show signs of distress or need additional support.
- **Data Protection Measures:** Secure, encrypted storage for digital data; locked cabinets for paper records; strict access controls and de-identification procedures.

Voluntary Participation and Informed Consent

- The study follows a robust informed consent process (Section 7.3.2), ensuring participants understand the purpose, procedures, and right to withdraw without consequence to their care.

Privacy and Confidentiality

- Data collection (e.g., motion tracking, clinical assessments) is performed in a private or semi-private setting to maintain dignity and comfort.
- Identifiable data are kept separate from research datasets, using pseudonymized identifiers to minimize the risk of re-identification.

Inclusive and Non-Discriminatory Practices

- The study is open to eligible participants regardless of gender, ethnicity, or socioeconomic status, reflecting the principle of Justice.
- Accommodations (e.g., interpreters, adapted interfaces) will be provided to ensure equal access to the intervention.

- **Neurological Impairments**: Participants may have physical or cognitive challenges. Researchers will use accessible language, allow extra time for decision-making, and adapt the game interface as needed to uphold participant dignity.
- **Vulnerable Individuals**: For those with mild cognitive impairment or higher susceptibility to coercion, clear communication and additional checks ensure that consent is freely given and understood.

Compliance with Local and Institutional Requirements

1. Site-Specific Approvals
    - The study will be registered with the relevant hospital governance bodies, adhering to any local R&D approval processes.
    - Documentation of approval (e.g., gatekeeper letters) will be obtained where necessary.
2. Data Protection and Management
    - All personal data handling aligns with GDPR (or local data protection legislation), including secure data transfer, storage, and retention.
    - Participant data will be archived in accordance with institutional policy (e.g., stored for up to three years post-study), and then securely disposed of or anonymized for future research use if consented.
3. Monitoring and Reporting
    - Any adverse events (physical or psychological) will be reported promptly to the REC and other regulatory bodies, following institutional and national guidelines.
    - A Data Protection Impact Assessment (DPIA) or equivalent may be completed to ensure robust data security measures.

8.2 Research Ethics Committee (REC) and other Regulatory review & reports

Aim: To confirm that the study will obtain the necessary ethical approvals and comply with all reporting requirements mandated by relevant regulatory bodies.

Regulatory Review & Compliance

This study has been reviewed by the Essex Research Ethics Committee (REC), which has issued a favourable ethical opinion. The research team will ensure ongoing compliance with all REC requirements and any applicable regulatory frameworks.

Initial Approvals

- Before any participating site can enrol patients, the Chief Investigator (CI) or designated Principal Investigator (PI) will ensure that all required approvals are in place.
- This includes obtaining a favourable opinion from the appropriate Research Ethics Committee (REC) (e.g., NHS REC if the study involves NHS patients/data/facilities, or a university REC for academic research), as well as any local governance or R&D approvals needed at individual sites.
- For NHS sites, the study will follow the Health Research Authority (HRA) processes and any additional local Trust/Health Board approvals as required. For non-NHS sites, the CI/PI will comply with the relevant institutional policies and sponsor guidelines.

Sponsor and Participating Organisations

- The Sponsor (or delegated authority) will ensure that the protocol, informed consent documents, and any participant-facing materials are reviewed and approved by the REC and other regulatory bodies (if applicable) prior to starting the study.
- The CI/PI or designee will confirm that each site has all necessary approvals and support in place (e.g., local R&D confirmation) before enrolling participants.

Ongoing Compliance

- Throughout the study, the CI/PI will maintain communication with the REC and other regulatory bodies, providing annual progress reports and safety updates as required (see Section 8.2 in this protocol for more details on reporting).

Amendments

Aim: to describe the process for dealing with amendments

For studies that are outside of the NHS and do not require NHS REC review or NHS management approval amendments should be handled in line with the sponsors and site management organisations polices.

For studies involving the NHS:

If the sponsor wishes to make a substantial amendment to the REC application or the supporting documents, the sponsor must submit a valid notice of amendment to the REC for consideration. The REC will provide a response regarding the amendment within 35 days of receipt of the notice. It is the sponsor's responsibility to decide whether an amendment is substantial or non-substantial for the purposes of submission to the REC.

If applicable, other specialist review bodies (e.g. Confidentiality Advisory Group (CAG)) need to be notified about substantial amendments in case the amendment affects their opinion of the study.

Amendments also need to be notified to the national coordinating function of the UK country where the lead NHS R&D office is based and communicated to the participating organisations

(R&D office and local research team) departments of participating sites to assess whether the amendment affects the NHS permission for that site. Note that some amendments that may be considered to be non-substantial for the purposes of REC still need to be notified to NHS R&D (e.g. a change to the funding arrangements).

In all instances the protocol should describe:

- *The* process for making amendments.
- Who will be responsible for the decision to amend the protocol and for deciding whether an amendment is substantial or non-substantial?
- How substantive changes will be communicated to relevant stakeholders (e.g., REC, R&D, regulatory agencies).
- How the *amendment history will be tracked to identify the most recent protocol version.*

Guidance on the categorisation of amendments for studies involving the NHS can be found on the HRA website. http://www.hra.nhs.uk/resources/after-you-apply/amendments/

8.3 Peer review

Aim: To describe the peer review process for the study, including how it meets the National Institute for Health Research (NIHR) Clinical Research Network (CRN) standards of independence, expertise, and proportionality.

1. Sponsorship and Review Authority
    - This study is sponsored by the Faculty of Science and Engineering at Anglia Ruskin University (ARU).
    - As part of its sponsorship responsibilities, the Faculty conducted a formal peer review of the study protocol prior to ethics submission.
2. NIHR CRN Standards for High-Quality Peer Review

    a. Independent

    - In accordance with NIHR guidelines, the protocol was reviewed by two individual experts who are external to the investigators' immediate host research group and have no direct involvement in the study.
    - The reviewers are not employed by ARU's research team, ensuring an unbiased assessment of the study's scientific and methodological rigour.

    b. Expert

    - The chosen reviewers possess relevant expertise in neurorehabilitation, clinical trial methodology, and/or advanced digital health technologies.
    - This ensures they can critically evaluate both the clinical/service-based aspects of the protocol (e.g., feasibility, participant safety) and the methodological elements (e.g., study design, data analysis approach).

    c. Proportionate

- Given the study's scope (e.g., a multicentre design, moderate sample size, or the use of specialized technology), the level of peer review was commensurate with its complexity.
- If the study expands or adds international sites, additional peer reviewers or an independent review board with broader expertise may be convened, consistent with NIHR recommendations.

Outcome of the Peer Review

- The reviewers' feedback focused on refining the study's aims, design, and data collection methods.
- Suggested revisions were incorporated to enhance clarity, strengthen the intervention protocol, and ensure robust participant safety measures.
- The Faculty of Science and Engineering at ARU then confirmed that the study met the required standards for scientific and methodological integrity.

Documentation and Transparency

- A summary of the reviewers' comments, along with the research team's responses and subsequent protocol amendments, has been retained in the study master file.
- While the reviewers are not anonymous, their specific identities and affiliations are not disclosed in this protocol without their explicit permission.

8.4 Patient & Public Involvement

Aim: To describe how patients, service users, and/or their carers have been involved—and will continue to be involved—in shaping the research, ensuring that ReHabGame meets the needs of those with motor impairments.

Planning and Design Input

- During the early planning stages, we consulted service users with motor impairments and their carers to gather feedback on potential game features, interface design, and overall feasibility.
- Their insights ensured that the initial concept was acceptable to the target population, helping us refine the tasks and exercises to align with real-life rehabilitation needs.

Game Features and User-Friendliness

- Service users' feedback influenced key design elements, such as the layout of on-screen prompts, levels of difficulty, and pacing of exercises.
- This direct input helped ensure that ReHabGame is both engaging and accessible to individuals with varying degrees of motor impairment.

Project Advisory Panel

- A patient representative will serve on the project advisory panel, regularly reviewing study progress and contributing to decision-making.

- This representative will voice user perspectives at management meetings, ensuring that the research remains user-centered throughout.

- **Participant Feedback Sessions**
    - During the study, participants will take part in **periodic feedback sessions** (via questionnaires) to share their experiences with ReHabGame.
    - Feedback will address **ease of use**, **perceived benefits**, and any challenges or improvements needed.
    - This approach ensures **continuous refinement** of the intervention, allowing the research team to adjust tasks or features in real time based on participant needs.

Analysis of Results

- **Incorporating User Perspectives**
    - Qualitative feedback from service users (e.g., thematic analysis of the questionnaire) will be integrated alongside quantitative measures of motor function.
    - By examining user-reported outcomes and personal experiences, the research team can gain a **holistic understanding** of ReHabGame's effectiveness and usability.

Dissemination of Findings

1. **Lay Summaries and User-Friendly Formats**
    - Study results will be presented in accessible formats (e.g., plain-language summaries, infographics) for service users and their carers.
    - Where possible, we will co-create these summaries with the patient representative or other service users to ensure clarity and relevance.
2. **Public Engagement**
    - Findings may be shared at community events or support groups for individuals with neurological impairments, offering a platform for **knowledge exchange** and feedback.
    - This ensures that those who contributed to the research remain informed about how their input shaped the final outcomes.

Ongoing Commitment to PPI

- We recognize that **patient and public involvement** is an iterative process. As the project evolves, additional opportunities for user feedback and collaboration will be identified.
- In line with **INVOLVE** guidance, we will continue to evaluate and document our PPI activities, aiming to **strengthen user partnerships** in future phases of the ReHabGame initiative.

    - Design of the research
    - Management of the research
    - Undertaking the research

8.5 Protocol compliance

Investigator Responsibilities

- The Chief Investigator (CI) and site Principal Investigators (PIs) are responsible for ensuring that all study personnel understand and adhere to the protocol.
- Routine training and refresher sessions will be provided, focusing on key procedures (e.g., participant consent, data collection methods, safety monitoring).

Study Team Oversight

- The CI or designated team members will conduct periodic checks (e.g., monitoring visits or spot audits) to confirm that the protocol is being followed correctly.
- Findings from these checks will be documented, and any issues identified will be addressed promptly.

Definition

- A protocol deviation or non-compliance is any unplanned departure from the approved protocol or relevant study procedures.
- Examples include:
    - Missing a scheduled assessment.
    - Using a non-approved version of the Participant Information Sheet.
    - Failing to follow the specified data collection methods.

Accidental Deviations

- Accidental or one-off deviations can occur at any time (e.g., a participant misses an appointment due to illness).
- These must be promptly documented using the designated Deviation Form, including details of the nature of the deviation, date, and any corrective actions taken.
- The CI and sponsor (or sponsor delegate) must be notified immediately if the deviation impacts participant safety, data integrity, or the study's overall conduct.

Frequent or Systemic Deviations

- Deviations that recur frequently or indicate a systemic issue are not acceptable.
- If repeated deviations occur, the study team will:
    - Investigate the root cause (e.g., staff training gaps, unclear protocol instructions).
    - Implement corrective and preventive actions (CAPA) to avoid further occurrences.
- Frequent or systemic deviations may be escalated to the sponsor and could be deemed a serious breach if they significantly affect participant safety or data integrity.
- The CI and sponsor will periodically review deviation reports to identify any trends or potential risks to the study's integrity or participant safety.

- Ongoing training, protocol clarifications, or amendments (if needed) will be employed to ensure high compliance standards are maintained throughout the study's duration.

8.6 Data protection and patient confidentiality

Aim: To describe how participant confidentiality will be maintained and how the study complies with the requirements of the Data Protection Act 1998 in relation to the collection, storage, processing, and disclosure of personal information.

All investigators and study site staff involved in this research will adhere to the Data Protection Act 1998, ensuring that personal data are:

1. Processed fairly and lawfully.
2. Obtained only for specified, lawful purposes.
3. Adequate, relevant, and not excessive.
4. Accurate and up to date.
5. Not kept longer than necessary.
6. Processed in accordance with the rights of data subjects.
7. Protected by appropriate technical and organisational measures.
8. Not transferred to a country outside the European Economic Area (EEA) without adequate protection.

Collection and Depersonalisation of Data

1. **Coded, Depersonalised Data**
    - Each participant will be assigned a **unique study ID** that replaces any direct identifiers (e.g., name, date of birth, hospital number).
    - The study ID will be used in all electronic and paper records to ensure personal details are not directly linked to the research data.
2. **Linking Code Storage**
    - The **linking code** (i.e., the key matching participant identity to the study ID) will be stored **separately** from the main dataset.
    - Only the Chief Investigator (CI) or a designated data manager will have access to this code.

Secure Maintenance and Access Control

1. **Digital Data Security**
    - Electronic data (e.g., spreadsheets, transcripts) will be stored in **encrypted digital files** on password-protected computers or servers.
    - Access will be limited to authorized study personnel who require the data for **quality control**, **audit**, or **analysis**.
2. **Physical Records**

- Any paper records (e.g., signed consent forms, paper questionnaires) will be kept in **locked filing cabinets** in areas with restricted access.
- The study ID, rather than personal identifiers, will be used on these forms wherever possible to further protect participant confidentiality.

3. Limiting Access

- The **minimum number of individuals** necessary for study operations will be granted access to identifiable or linked data.
- A log of who has accessed the data, and when, may be maintained for audit purposes.

When sharing data with **sponsors**, **co-investigators**, or external collaborators, only **coded, depersonalised datasets** will be transmitted.

Secure transmission methods will be used (e.g., **encrypted email**, secure file transfer services).

The linking code or any personally identifiable information will **not** be shared outside the immediate research team without explicit participant consent or additional ethical approval.

In accordance with **institutional policy** and the Data Protection Act 1998, research data will be held on **encrypted university servers**, maintained by Anglia Ruskin University's (ARU) IT department as required by the sponsor's data retention policy.

After this period, all personal data will be securely destroyed or anonymised beyond re-identification (e.g., by secure deletion of electronic files and shredding of paper records).

The **Chief Investigator (CI)** will act as the **data custodian**, bearing overall responsibility for ensuring compliance with data protection regulations and safeguarding participant confidentiality.

If a data manager or delegated staff member oversees daily data handling, they will report to the CI and follow the same data protection procedures.

To protect participants from harm, the study includes clear procedures for identifying and managing psychological distress or risk disclosures.

All participants will complete the PHQ-9 and GAD-7 questionnaires during screening. If a PHQ-9 score is ≥15 or indicates suicidal ideation (Item 9), the screening will be paused, and the clinical gatekeeper will be informed. The clinical team will assess whether urgent mental health support is needed and whether study participation is appropriate. Participants will be supported with contact details for mental health services and guidance to access their GP. Data will not be used until informed consent is reconfirmed and clinical stability is ensured.

During intervention or follow-up sessions, participants may disclose worsening mental health, risk of harm, or abuse. In such cases, the researcher will respond supportively, notify the Principal Investigator (PI) and safeguarding lead, and refer the concern to the clinical gatekeeper or relevant health professional. The participant may be paused or withdrawn from the study if necessary.

All safeguarding concerns will be documented confidentially and shared only with appropriate professionals in line with GDPR and NHS safeguarding policy. All research staff are trained in safeguarding, and participants are informed of this policy during consent.

The PHQ-9 and GAD-7 will be administered at **baseline** to all participants by a trained medical student who will be recruited specifically for this project. These questionnaires will help to assess participants' levels of depression and anxiety at study entry, and will also be **repeated at the end of the intervention period** to capture any changes in these symptoms, in line with our secondary outcome measures.
To ensure safeguarding, if a participant's PHQ-9 or GAD-7 score indicates significant risk (e.g., severe depression or suicidal ideation), the medical student will follow a predefined **safeguarding protocol**: (i) immediate escalation to the principle Investigator or a clinically qualified supervisor, (ii) provision of information on appropriate support services, and (iii) if necessary, referral to relevant NHS support services with their consent. This ensures that any risks identified during the study are managed safely and appropriately.

8.7 Indemnity

Aim: Anglia Ruskin University (ARU), as the Sponsor, provides insurance and indemnity coverage under its institutional policies, covering all potential liabilities arising from this study. Details are outlined below, addressing each of the five key areas:

1. **Sponsor's Legal Liability for Harm Arising from the Management of the Research**
    - ARU holds an institutional insurance policy that indemnifies the Sponsor (ARU) against legal liability for harm to participants arising from the overall management of the research. This includes oversight responsibilities, study coordination, and compliance with regulatory requirements.
2. **Sponsor's/Employer's Legal Liability for Harm Arising from the Design of the Research**
    - ARU's insurance policy also covers liabilities associated with the design of the study (e.g., protocol development, methodology). Should any participant incur harm directly attributable to flaws or negligence in the study design, ARU's indemnity policy would respond.
3. **Investigators'/Collaborators' Legal Liability for Harm Arising from Conduct of the Research**
    - For ARU-employed investigators: They are covered by ARU's institutional indemnity when conducting research within the scope of their employment.
    - For NHS-based investigators: NHS staff typically receive indemnity through the NHS scheme (e.g., CNST in England). However, they must ensure local trust approvals and confirm coverage for this specific study.
    - For non-NHS or external collaborators: They are expected to hold their own professional indemnity or ensure that their employer's liability insurance covers research-related activities if they are not covered by NHS indemnity. Each site must confirm that appropriate coverage is in place before enrolling participants.
4. **Compensation in the Event of Harm Where No Legal Liability Arises**

- ARU does not routinely provide a “no-fault” compensation scheme. Participants who believe they have suffered harm due to the study may seek recourse under common law (e.g., a negligence claim).
- If local regulations or REC conditions require additional no-fault compensation provisions, ARU will review on a case-by-case basis in consultation with the relevant ethics committees and insurance providers.

5. **Insurance/Indemnity for Study Equipment**
   - If ARU provides any specialized equipment (e.g., motion-tracking devices) to participating sites, ARU’s institutional policy covers loss or damage of the equipment itself while under ARU’s responsibility.
   - Sites are responsible for ensuring that appropriate public liability or other relevant coverage is in place if their staff or participants use the equipment on-site.
   - Maintenance responsibilities, training, and safe use guidelines will be documented in a study-specific Equipment Use Agreement, ensuring clarity on who covers liabilities if harm to participants or site staff arises from misuse or malfunction.

8.8 Access to the final study dataset

Aim: To describe who will have access to the complete dataset at the end of the study, and under what conditions.

1. **Individuals with Full Access**
   - The Chief Investigator (CI) will have full access to the final dataset.
   - Key members of the research team (e.g., the study statistician, co-investigators directly responsible for data analysis) will also be granted access, as needed, to fulfill their roles in analyzing and interpreting the study’s results.
   - Any sponsor-appointed auditors or monitors may review the dataset to ensure regulatory compliance and data integrity.
2. **Restrictions on Access**
   - Other study investigators (e.g., site-specific PIs in a multicentre trial) may only access de-identified or aggregated data by default, to prevent premature disclosure of overall results.
   - If site investigators wish to access the full dataset for secondary analyses or other research purposes, they must submit a formal request (including a brief proposal outlining their planned analysis) to the study’s Steering Group (or equivalent oversight committee).
   - The Steering Group will review each request to ensure it aligns with the study’s objectives, participant consent agreements, and data protection requirements.
3. **Secondary Analysis**
   - If future secondary analyses are anticipated, participants will have provided informed consent for their data to be used in this way.
   - All patient-facing materials (e.g., Participant Information Sheet, Consent Form) clearly state that anonymized data may be used for further research, provided ethical approvals and data protection measures remain in place.
4. **Data Sharing and Publication**

- Any publication or dissemination of findings will present de-identified, aggregated data to protect participant confidentiality.
- Individual-level data will not be shared publicly unless specifically approved by the Steering Group and in line with participant consent.

5. **Long-Term Data Storage**
   - The final dataset will be securely stored (e.g., on an encrypted server, within a password-protected database) in accordance with the study's Data Management Plan.
   - Access to this archive will remain restricted to authorized personnel who have undergone data protection training and have a legitimate need to access the information.

9 DISSEMINIATION POLICY

At the end of the study, participants in the **intervention group** will **not** retain access to the ReHabGame system, and the control group will **not** receive delayed access unless a separate, follow-up study is conducted.

Any future or ongoing access to ReHabGame outside the research context will be contingent on:

- The **completion of regulatory approval** processes, including **CE marking** and/or **MHRA approval** as a medical device, if applicable.
- Decisions by the clinical site or sponsor regarding future implementation or licensing of the system in clinical settings.

Participants will be informed that the game is currently a **research prototype**, and not yet approved for general clinical use.

Participants will **not receive individual-level performance or outcome data** beyond the in-session summaries already provided during the intervention.
However, once the study is completed and the data analysis is finalised, a **plain-language lay summary of the overall study results** will be made available to all participants upon request. This summary will:

- Present key findings from the study (e.g., group trends, overall usability and effectiveness data)
- Avoid identifying any individual participant
- Be distributed via email or post, or made available on a dedicated web page

9.1 Dissemination policy

Aim: To describe how the data and findings from this study will be communicated, including ownership of data, reporting processes, publication rights, and participant notification of results.

- Anglia Ruskin University (ARU), as the Sponsor, retains ownership of all data generated by this study. Investigators and collaborators may access and use the data in accordance with their roles and responsibilities, subject to any specific agreements with funding bodies or external partners.
- Upon completion of the study, all data will be **analysed and tabulated**. A **Final Study Report** (FSR) will be prepared, summarizing the study objectives, methodology, results, and conclusions.
- The FSR will be stored in the **Trial Master File (TMF)** and made available to relevant stakeholders (e.g., sponsor, ethics committee, and any regulatory bodies as required).

- **Rights to Publish**

  - The Chief Investigator (CI) and the core research team have the right to publish study findings in peer-reviewed journals, conference proceedings, or other scientific forums.
  - Collaborating investigators may publish or present sub-analyses or site-specific data if a formal request is submitted and approved by the study's Steering Group (or equivalent oversight committee).
  - Draft manuscripts, abstracts, or presentations arising from the study will typically be **reviewed** by the Sponsor and any relevant funders prior to submission to ensure accuracy, confidentiality, and protection of intellectual property.
  - This review will not unduly delay publication; any **time limits** for review (e.g., 30 or 60 days) will be stipulated in collaboration or funding agreements.
  - Any **funding or supporting bodies** (e.g., NIHR, ARU internal grants) will be **acknowledged** in all publications, as required by their guidelines.
  - If the funder has specific publication rights (e.g., to review manuscripts before submission), these rights will be respected in accordance with the contractual agreement.
  - The FSR will be accessible to the Sponsor, regulatory authorities, and relevant ethics committees. It may also be made available on request to participating sites and investigators, subject to confidentiality agreements.
  - A summary of the main findings will be **shared with participants** via a lay summary, newsletter, or presentation.
  - Participants can request **individual site-level results** (e.g., their own data or general site outcomes) through their Principal Investigator (PI) once the FSR is finalized and results are published or otherwise publicly disclosed.
  - If participants wish to see their personal results, these will typically be made available **after** the FSR is complete and any primary publications are accepted or published. This timeline ensures data accuracy and proper contextualization of findings.

Participants will receive their individual personal results at the end of each session in a PDF format. Once the trial has been completed and the data analysed, a **lay summary of the overall study findings** will be made available to all participants upon request. This summary will present the results in clear, plain language and will focus on what the study found at a group level, rather than reporting individual outcomes. Participants will be informed of how to access this summary at the end of the study (by emailing the CI at the email address ss48@aru.ac.uk).

- **Study Protocol**

    - The final version of the study protocol (with confidential information redacted, if necessary) may be **published** in an open-access repository or appended to any journal article describing the study design.
    - An anony**mized participant-level dataset** and the statistical analysis code may be made publicly available in a suitable repository (e.g., an institutional repository or recognized open-data platform) after the primary publications are released.
    - Any data-sharing will align with **participant consent** agreements, ensuring no identifiable information is disclosed.
    - Access to these materials may require a formal data-sharing agreement, specifying conditions of use and adherence to ethical guidelines.
    - Typically, data will be shared within **6–12 months** following the primary publication.
    - Researchers requesting access must submit a **data request** outlining their intended use. The Steering Group (or CI) will evaluate such requests to ensure compliance with ethics and data protection standards.

9.2 Authorship eligibility guidelines and any intended use of professional writers

Aim: To outline the criteria for authorship on the final study report and any planned use of professional medical writers. We will follow the International Committee of Medical Journal Editors (ICMJE) Guidelines. Authorship will be determined in accordance with the ICMJE recommendations, which require each author to have:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data.
2. Drafted or critically revised the work for important intellectual content.
3. Approved the final version of the manuscript.
4. Agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
5. Individuals who do not meet the ICMJE criteria but who have made other significant contributions (e.g., data collection, administrative support, patient recruitment) will be **acknowledged** in an “Acknowledgments” section, provided they give permission to be named.
6. Named Authorship: Individuals meeting the above criteria will be listed as named authors on the final study report and any subsequent publications.
7. Group Authorship: In large, multi-centre studies, a group name may be used to acknowledge the collaborative nature of the research, with specific contributors listed separately as authors or in an appendix, in accordance with journal guidelines.

The Chief Investigator (CI) will propose a preliminary authorship list based on each individual’s contributions, in consultation with the study’s Steering Group or senior collaborators.

- Authorship roles may be revised as the study progresses and contributions become clearer, ensuring that those who have meaningfully contributed meet ICMJE standards.

- The final list of authors will be agreed upon before manuscript submission. Any disputes will be resolved by discussion between the CI, the Steering Group, and the individuals involved, referring to ICMJE guidelines as needed.

10 REFERENCES

1. da Silva Cameirão, M., Bermudez i Badia, S., Duarte, E. and Verschure, P.F., 2011. Virtual reality based rehabilitation speeds up functional recovery of the upper extremities after stroke: a randomized controlled pilot study in the acute phase of stroke using the rehabilitation gaming system. *Restorative neurology and neuroscience*, *29*(5), pp.287-298.
2. Laver, K.E., Lange, B., George, S., Deutsch, J.E., Saposnik, G. and Crotty, M., 2017. Virtual reality for stroke rehabilitation. *Cochrane database of systematic reviews*, (11).
3. Maier, M., Rubio Ballester, B., Duff, A., Duarte Oller, E. and Verschure, P.F., 2019. Effect of specific over nonspecific VR-based rehabilitation on poststroke motor recovery: a systematic meta-analysis. *Neurorehabilitation and neural repair*, *33*(2), pp.112-129.
4. **Stroke Association.** (2022). *State of the nation: Stroke statistics*. Stroke Association. https://www.stroke.org.uk/
5. **World Health Organization (WHO).** (2021). *World report on disability*. WHO. *https://www.who.int/publications/i/item/9789241564182*
6. *Kunselman, A.R., 2024. A brief overview of pilot studies and their sample size justification. Fertility and sterility, 121(6), pp.899-901.*

11. APPENDICIES

11.1 Appendix 1- Required documentation

List here all the local documentation you require prior to initiating a participating site (e.g. CVs of the research team, Patient Information Sheet (PIS) on headed paper etc.).

- Web-based Patient Information Sheet (PIS) and Participant Consent Form (PCF)
- Web-based Questionnaire
- ReHabGame's study protocol

11.2 Appendix 2 – Schedule of Procedures

Procedures	**Visits (insert visit numbers as appropriate)**					
	Screening	**Baseline (week 0)**	**Week 2**	**Week 4**	**Week 8**	**12 weeks (follow up)**
Therapist confirms diagnosis and eligibility.	x					
Randomisation occurs immediately afterward.		x				
Assign study ID or name via the ReHabGame platform and keep the same name/ID though out the trial.		x				
Patient to review and sign the consent form via the web-based link below.		x				
Baseline functional test Assessments at Week 4 (interim), Week 8 (end), Week 12 (follow-up)		x		x	x	x
Questionnaire at week 2, 4, 8 (via the Link below)			x	x	x	
30–45 min Kinect-guided exercises per session. 8 weeks twice a week			x	x	x	
Observation of treatment and a questionnaire				x	x	x

Follow up						x
Remind patients to email ss48@aru.ac.uk to request the lay summary of overall study findings.						x
Verbal conversation, recommendation and feedback	x	x	x	x	x	x

ReHabGame: Participant's information and Consent form (base line)	https://app.onlinesurveys.jisc.ac.uk/s/angliaruskin/rehabgame-transforming-neurorehabilitation-through-ai-and-vr	
ReHabGame: A Game-Based Rehabilitation Program - Questionnaire at week 2, 4, 8	https://app.onlinesurveys.jisc.ac.uk/s/angliaruskin/rehabgame-a-game-based-rehabilitation-program-duplicate	
ReHabGame: Assessments at Week 4 (interim), Week 8 (end), Week 12 (follow-up)	https://app.onlinesurveys.jisc.ac.uk/s/angliaruskin/rehabgame-a-game-based-rehabilitation-program-duplicate-duplica	

13.3 Appendix 3 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC.