Does the use of Nintendo Wii Sports™ improve arm function and is it acceptable to patients after stroke? Publication of the Protocol of the Trial of Wii™ in Stroke – TWIST

Introduction: Many stroke patients experience loss of arm function requiring rehabilitation, which is expensive, repetitive, and does not always translate into “real life.” Nintendo Wii Sports™ (Wii™) may offer task-specific training that is repetitive and motivating. The Trial of Wii™ in Stroke (TWIST) is designed to investigate feasibility, efficacy, and acceptability using Wii™ to improve affected arm function for patients after stroke.

Method: This is a randomized controlled trial (RCT), incorporating a qualitative study and health economics analysis that compares playing Wii™ versus arm exercises in patients receiving standard rehabilitation in a home setting within 6 months of stroke with a motor deficit of less than 5 on the MRC (Medical Research Council) scale (arm). In this study, we expect to randomize 240 participants.

Outcome measures: Primary outcome is change in affected arm function at 6 weeks follow-up in intervention and control group using the Action Research Arm Test. Secondary outcomes include occupational performance using the Canadian Occupational Performance Measure, quality of life using the Stroke Impact Scale, cost effectiveness analysis, and a qualitative study investigating factors that influence use of Wii™ for patients and carers.

Conclusion: TWIST is the first UK RCT assessing the feasibility, cost effectiveness, and acceptability of Wii™ in stroke rehabilitation. The trial has been registered with ISRCTN 06807619 and UK CRN 11030. Results of the study will be published after completion of study in August 2014.

Keywords: virtual reality, rehabilitation

Introduction

About 70% of stroke patients experience altered arm function, and about 40% are left with a nonfunctional arm.¹ Arm weakness limits the individual’s activities of daily living and impacts negatively on quality of life.² The greatest recovery in upper limb function is achieved in the 6 months following a stroke, and this period offers the best opportunity for rehabilitation interventions. The main predictor of success in physical therapy is the amount of therapy undertaken, and guidelines for patients recommend high intensity repetitive motions.³ Rehabilitative therapy has focused on practicing “normal” movements to encourage return of relevant function and inhibit compensatory habits that may prevent further recovery. More recently, there has been an emphasis on strengthening, practice of functional tasks, and forcing use of the weak limb to complete everyday activities.
using constraint-induced movement therapy. The National Stroke Guidelines endorse 45 minutes of daily physiotherapy in the rehabilitation phase of stroke recovery. Physiotherapy, however, is both labor-intensive and expensive, and service provision varies widely. At present, only 50% of people with stroke receive the rehabilitation to meet their needs during the crucial first 6 months. Furthermore, although therapists prescribe a home exercise regimen, only about 31% of patients complete the recommended exercise.

Rehabilitation after stroke using virtual reality therapy is of increasing interest. A Cochrane review on the effect of virtual reality on arm function found limited evidence that it may be beneficial in improving arm function and activities of daily living when compared with the same dose of conventional therapy. The authors’ conclusion was that present studies were too small and too few to draw conclusions and more randomized controlled trials (RCTs) were needed.

Nintendo Wii Sports™ (Wii™) is commercially available and offers task specific training that is repetitive and motivating and may be a useful adjunct to rehabilitation. Wii™ games include tennis, golf, boxing, baseball, and bowling activities, which are played using a remote control held in the same way that real world objects such as the handle of a racket are held and manipulated. An accelerometer measures the person’s movements and maps them to the screen. Visual, auditory, and haptic feedbacks contribute to maintaining users’ attention. The motivational and entertainment value of the Wii™ is reflected in its commercial success. The research into its efficacy is limited, although it is being used by stroke therapists. Pilot studies have suggested faster task performance following use of Wii™, with no Wii™-related side effects or injuries.

Methods
The Trial of Wii™ in Stroke (TWIST) is a multicenter, pragmatic, parallel group, RCT with blinded outcome assessment, incorporating a qualitative study and cost-effectiveness analysis (Table 1). Inclusion and exclusion criteria for study participants are listed in the table.

Outcome measures
The primary outcome in the RCT is arm function as measured by the Action Research Arm Test (ARAT) at 6 weeks. The ARAT assesses ability to handle objects and tests grasp, grip, pinch, and gross movement of elbow and shoulder of the affected arm.

Secondary outcome measures include occupational performance, stroke impact, and severity. The Canadian Occupational Performance Measure (COPM) is used to detect change in self-perception of occupational performance over time. The Stroke Impact Scale (SIS) assesses change in impairments, disabilities, and handicaps following a stroke. The Modified Rankin Scale (mRankin) measures disability following stroke. These outcome measures will be applied at baseline, 6 weeks, and 6 months. Arm function will be assessed at 6 months using the ARAT and Motor Activity Log-14 (MAL14). The MAL14 ascertains how well the participant has performed day to day tasks using their affected arm. Participants will be asked to complete a diary to capture a daily record of duration of arm exercises and adverse events. The diary is brief and enables the participant or carer to record daily exercise time, adverse events, and visits from the National Health Service (NHS), private carers, and social services staff.

Baseline data collection will include demographic data, type of stroke using the Oxfordshire Community Stroke Project Classification, affected arm strength using the Medical Research Council Scale of Muscle Strength, and cognitive function using the Montreal Cognitive Assessment. Outcome measures will be purchased (ARAT, COPM) or permission to use in study will be obtained from authors (MAL14, EQ-5D™ 3L, mRankin, and SIS).

The qualitative study will explore participants’ and carers’ experiences of using the Wii™ and barriers to its implementation. The health economic analysis will estimate the incremental cost per quality-adjusted life year (QALY) gained from the cost perspective of health care and personal social services.

Table 1 Exclusion and inclusion criteria

| Inclusion criteria | Exclusion criteria |
|--------------------|--------------------|
| Clinical diagnosis of stroke within previous 6 months | Pacemaker or ICD device (possible interference from the Wii™) |
| Aged 18 years or older | |
| Living in a suitable environment to safely comply with the protocol and therapy program | |
| Weakness in the affected arm (MRC strength <5 in any joint plane of movement) due to stroke | |
| Comorbidity which impairs ability to participate (eg, severe arthritis, severe cognitive impairment, and severe cardio-respiratory disease) | |
| Symptomatic shoulder subluxation | |
| Consideration of other interventional studies in line with Stroke Research Network guidance | |
| Pacemaker or ICD device (possible interference from the Wii™) | |

Abbreviations: ICD, implantable cardioverter-defibrillator; MRC, Medical Research Council scale.
Recruitment and flow through study
A total of 240 participants will be recruited to the RCT across ten sites in the UK by the local research practitioners.

Once participants have given written informed consent, outcome measures will be assessed at baseline, 6 weeks, and 6 months. The research practitioner conducting the outcome measures will be blinded to study group allocation.

A research therapist will either install the Wii™ in the participant’s home and instruct them on the use of the Wii™, or will advise the participant on tailored arm exercises to be performed during the 6-week intervention phase. All participants will be instructed to perform warm-up exercises prior to tailored arm exercises or Wii™ exercises to minimize the risk of injury. Written instructions for both groups will be left with the participants. The research therapist will visit the patient prior to the 6-week assessment to collect participant’s diary and Wii™ if applicable. The research therapist will remind participants not to disclose their treatment allocation during the subsequent assessment visits by the research practitioner.

Participants will be telephoned by a non-blinded member of the local research team on a weekly basis to encourage them to complete their diary and enable them to express any concerns they may have had about the study.

All research staff will be trained at site initiation in all outcome measures use of the trial website, case report form (CRF) completion and safety considerations. Training DVDs and telephone conferencing will be made available. Please see Figure 1 for study flow diagram.

Trial intervention
Eligible participants with arm weakness following stroke will be randomized to one of two groups.

The intervention group will be instructed to undertake up to 45 minutes of exercise, in a seated position, using the Wii™ game daily for 6 weeks at home. The Wii™ console and game will be provided on loan to trial participants as part of the study for the duration of the intervention period.

The control group will be instructed to undertake up to 45 minutes of tailored arm exercises, in a seated position, daily for 6 weeks at home.

Both groups will continue to receive usual care and rehabilitation as provided by their services in the area.

Randomization
Allocation to intervention will be determined by use of a Web-based randomization service, accessed by the research therapist prior to the setup visit. Participants will be randomized using computer-generated randomization codes. Random permuted blocks of varying size will be used to generate the allocation sequence. Allocation will be stratified by center, baseline ARAT score (scores 0–49 and 50–57), and previous use of a Wii™.

Equipment check
The research team will visually inspect the Wii™ and clean with antiseptic wipes prior to allocation to the next participant in the intervention group.

Adverse-event recording
Serious adverse events will be reported by the site’s principal investigator (PI) to the clinical trials unit (CTU) and reported on a monthly basis to the trial steering committee (TSC), chief investigator (CI), and sponsor. Minor adverse events thought not to be related to the trial will not be reported.

Sample size
For the primary outcome of ARAT score at 6 weeks, the literature suggests a standard deviation of about 15 and that a clinically important effect is six points. For a two-tailed $t$-test at the 5% level and with 80% power, completed data are required on 99 patients per group. To allow for attrition, we plan to recruit about 120 patients per group.

Statistical analysis
A statistical analysis plan will be prepared by the study statistician, in advance of any statistical analysis of the study data. Analysis of study data will be on an intention-to-treat basis. Participants choosing to withdraw from either intervention arm will be followed up where possible, and reasons for withdrawal, if elicited, will be reported according to the CONSORT (Consolidated Standards of Reporting Trials) guidelines. Baseline characteristics will be summarized using suitable descriptive statistics. The primary outcome will be the ARAT score at 6 weeks. The principal analysis will be analysis of covariance with terms for treatment group and stratification variables. A further analysis will replace baseline ARAT score group (as stratified) by the actual ARAT scores in order to explore the robustness of conclusions. In each case, least-squares mean treatment differences and their 95% confidence intervals will be reported. Residual plots will be produced to check compliance with assumptions. Both analyses will be repeated for the secondary outcome measure of ARAT at 6 months, and other continuous outcome measures. The interactions between treatment group and the stratification
variables will be examined and allowed for in the analyses as appropriate.

Analysis of nested qualitative study

All audio recordings will be transcribed verbatim, and the transcribed interviews will be analyzed using thematic analysis.\(^{31}\) The field notes and observation data obtained during the interviews will be included in the analysis process. Themes will be drawn from the data using constant comparison methods; participants’ accounts will be compared and contrasted to enhance interpretation. Deviant cases will be reviewed and accounted for. If data are unclear, findings will be presented to participants to allow further comment in order to aid interpretation. The qualitative researcher will use a
computer-aided program to manage the data. For trustworthi-
ness, the lead qualitative researcher will analyze a subset of five
transcripts. Any unresolved disagreements will be resolved by
discussion with the CI, ensuring that data will be presented in
such a way as to maintain blinding of treatment group.

Cost-effectiveness evaluation
The economic evaluation will estimate the incremental cost
per QALY gained from the perspective of health and social
care utilization. The costs of the Wii™ equipment will be the
price paid annuitized over a useful life of 3 years assuming
the equipment could be used by eight clients per year. The
setup costs of the Wii™ service will be reported separately.
The main source of information on resource use will be the
participant diaries which will include prompts derived from the
Service Receipt Inventory (SRI).32 The SRI will also be used
retrospectively at 6 months. When an assessment of need is
completed during the trial, details of agreed care package will
be recorded. Unit costs of health and social care services will
be taken from standard published sources.33,34 Health-related
quality of life will be assessed by EQ-5D 3L35 and valued
using the York Tariff.36 The economic evaluation will provide
within-trial estimates of the incremental cost-effectiveness
ratio. If appropriate, modelling beyond the term of the trial
will be undertaken. Sampling variation will be analyzed using
probabilistic sensitivity analysis, reported as a scatterplot on
the cost-effectiveness plane. Sensitivity analysis to estimate the
effects of parameter uncertainty will include an exploration of
the sensitivity of results to differences in the costs and effects
of different provisions of rehabilitation services.

Data collection
Data will be recorded on study-specific data-collection forms
(CRFs). Persons authorized to collect and record trial data at
each site will be listed on the study site delegation log and
authorized by the PI.

Completed CRFs will be checked and signed at the
research site by the research practitioner or research therapist
(as applicable) before being sent to the CTU for double-data
entry onto a password-protected database accessed via the
Internet. Forms will be tracked using a Web-based trial-
management system. Double-entered data will be compared
for discrepancies using a stored procedure. Discrepant data
will be verified using the original paper data sheets.

Study oversight
The CI will be responsible for the overall running of the
study and will be in regular contact with the principle
investigators at the other trial centers. Each trial center will
have a PI, a research administrator, a research practitioner,
and a research therapist to conduct this study. The CTU will
coordinate trial activities and assist with overall trial manage-
ment and monitoring. A data-monitoring committee will not
be convened due to the nature of the intervention and short
duration of the trial. The trial-management group (TMG) will
include the CI, CTU trial coordinator, trial statistician, and
other members of the team and will meet regularly to moni-
tor progress. The TSC will oversee the conduct and safety
of the trial. The TSC will include a representative from the
funder and a lay person.

Protocol amendments
Early on in the recruitment phase, the TMG reported two
emerging issues of concern to the TSC. These were 1) that a
proportion of patients were assessed as having the highest pos-
sible ARAT score at baseline and 2) the slow recruitment rate.
Further to this, the research therapists asked that patients with
severe shoulder subluxation be excluded, as pain precluded
participants from playing the Wii™ or doing arm exercises.

In response to these concerns, the TSC recommended
baseline ARAT stratification for randomization was changed
from 30 to 50 points and the MAL14 be added as a secondary
outcome measure at 6 months follow-up as a second outcome
measure for arm function. The TSC also recommended some
to the eligibility criteria which were implemented by
the TMG: to exclude patients with symptomatic shoulder sub-
luxation, to broaden the inclusion criteria to include patients
with non-dominant weakness, and to remove the requirement
for participants to have supervision during their exercises.

Finally, the number of participating centers was increased
from seven to ten, and the TMG applied to the funder for an
extension to the recruitment period in order to maximize the
chances that the trial could recruit the full sample size. All
changes to the protocol were approved by the Sponsor, the
Research Ethics Committee, and the funder.

Conclusion
TWIST is the first UK RCT assessing the feasibility,
cost effectiveness, and acceptability of Wii™ in stroke
rehabilitation. The trial has been registered with ISRCTN
06807619 and UK CRN 11030. Results of the study will be
published after it is completed in August 2014.

Acknowledgments
We would like to thank our participants and caregivers
and participating centers. We would also like to thank the
Research Design Service South West. We thank Jane Vickery, Senior Clinical Trials Manager (Peninsula Clinical Trials Unit) for her comments on drafts of this paper.

Funding
This paper represents independent research funded under the Research for Patient Benefit Programme (PB-PG-0110-20332). The views expressed in this publication are those of the authors and not necessarily those of the NHS, NIHR (National Institute for Health Research), or Department of Health. The trial has been registered with ISRCTN 06807619 and UK CRN 11030.

Disclosure
The authors report no conflicts of interest in this work.

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