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Running head: Exercise enhances SCI health-related quality of life

Title: Home-based exercise enhances health-related quality of life in persons with spinal cord injury: A randomized controlled trial

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Abstract

Objective: To assess the influence of a home-based exercise intervention on indices of health-related quality of life (HRQOL) in persons with spinal cord injury (SCI).

Design: This was a randomized controlled trial (HOMEX-SCI; ISRCTN57096451). After baseline laboratory testing and a week of free-living physical activity monitoring, eligible participants were randomly assigned (2:1 allocation ratio) to a home-based moderate-intensity upper-body exercise intervention (INT, n = 13), or a lifestyle maintenance control group (CON, n = 8), for 6 weeks.

Setting: Home-based with short laboratory visits immediately before and after the intervention/control period.

Participants: Twenty-one inactive participants with chronic (> 1 year) SCI (injury level range, T4 – L5).

Intervention: Participants assigned to the exercise intervention group (INT) completed 4 x 45 min moderate-intensity (60-65% peak oxygen uptake [V̇O2 peak]) arm-crank exercise per week for 6 weeks. Participants assigned to the control group (CON) were asked to maintain their habitual physical activity behaviour.

Main Outcome Measures: Secondary outcome measures were assessed, including physical and emotional component scores (PCS and MCS) of health-related quality of life (SF-36), fatigue, global fatigue (FSS) and shoulder pain index (WUSPI). Cardiorespiratory fitness (CRF), objectively measured habitual moderate-to-vigorous physical activity (MVPA) and exercise self-efficacy (ESE) were also assessed at baseline and follow-up.

Results. Changes in the PCS (P = 0.017) of the SF-36, ESE (P = 0.011) and FSS (P = 0.036) were significantly different between the two groups, with moderate to large effect sizes (*d* =

0.75 – 1.37). Various HRQOL outcomes demonstrated ‘likely’ to ‘very likely’ positive inferences in favour of the INT group following the 6-week exercise intervention. Changes in ESE were significantly ($P < 0.01$) associated with changes in PCS ($r = 0.62$) and MCS ($r = 0.71$), FSS ($r = -0.71$) and global fatigue ($r = 0.57$).

Conclusions. A 6-week upper-body exercise intervention improved indices of HRQOL in persons with SCI. Improvements were associated with increases in ESE. While this intervention demonstrated a positive impact on perceived physical functioning, future interventions should aim to support social and mental functioning and exercise maintenance.

Key words: Spinal cord injury; exercise intervention; health and wellbeing; self efficacy; quality of life

Abbreviations:

CON- Lifestyle maintenance control group,

ESE- Exercise Self-Efficacy

ESES- Exercise Self-Efficacy Scale

FSS- fatigue severity scale

HOMEX-SCI- Home-based upper-body exercise randomized controlled trial,

HRQOL- Health-related quality of life

INT- Home-based moderate-intensity upper-body exercise intervention group,

MVPA- moderate-to-vigorous physical activity,

SCI- spinal cord injury,

SF36- short form 36 health survey,

CRF- cardiorespiratory fitness,

$\dot{V}O_{2peak}$ - peak oxygen uptake,

WUSPI- wheelchair user shoulder pain index

INTRODUCTION

Disability can negatively impact physical activity behaviour [1]. The reasons for the adoption of a more sedentary lifestyle are multifactorial, but the perceived psychosocial and environmental barriers to engage in physical activity are numerous for wheelchair users living with a spinal cord injury (SCI) [2, 3]. Consequently, persons with SCI are relatively inactive [4] and new ways to support the initiation of physical activity in this population are needed.

Besides an increased incidence of chronic diseases (e.g. cardiovascular disease, type 2 diabetes) [5], persons with SCI have significantly elevated levels of fatigue, anxiety, depression and poorer exercise self-efficacy (ESE) compared to non-disabled controls [6, 7]. This is important because physical activity can improve quality of life for people with SCI and ESE is considered a modifiable predictor of physical activity behaviour change, specifically in this population [8-12]. Therefore, it is essential to develop strategies capable of improving exercise self-efficacy in order to increase physical activity participation and accrue enhancements in quality of life.

Educational interventions, covering physical activity, nutrition and lifestyle management, have been shown to improve exercise self-efficacy and self-rated health, and result in fewer and less severe secondary conditions in persons with SCI [13, 14]. Following a 9-month, twice-weekly strength and arm-ergometry intervention, participants reported significantly higher levels of satisfaction with physical function, level of perceived health, overall quality of life and less pain than a control group [15]. However, these findings have not been demonstrated with shorter term, higher volume aerobic exercise training *per se*. Moreover, it has previously been suggested that upper-body exercise, primarily arm-crank ergometry as a training modality, might contribute to shoulder overuse injuries and trigger the onset of pain [16].

Therefore, the available evidence is currently inconclusive about whether upper-body arm-crank exercise is an effective treatment modality for improving health-related quality of life (HRQOL) in persons with SCI. Furthermore, a lack of access to gym facilities and exercise equipment, as well as poor information and support, have been identified as key barriers to exercise for adults with SCI [17-19]. Therefore, the provision of exercise equipment and a tailored exercise programme within a home setting could provide a mastery experience and help enhance ESE in people with SCI.

A recent meta-analysis on physical activity and wellbeing among individuals with SCI noted that most of the evidence to date has been from cross-sectional studies, with little consistency in the constructs and measures of HRQOL [20]. Therefore, the aim of this study was to test the hypothesis that a 6-week home-based upper-body exercise intervention would improve HRQOL component scores compared to a lifestyle maintenance control group, in persons with SCI. In keeping with Dijkers [21] conceptualisation of HRQOL and supported by previous research [10, 20, 22], it was hypothesized that physical activity behaviour would positively correlate with objective measures of physical and mental component scores (derived from the short-form 36 health survey). These summary component scores describe what the individual can achieve in both the physical and psychological domains. In addition, and grounded on the propositions of social cognitive theory [23], it was further hypothesized that exercise barrier self-efficacy would positively correlate with quality of life [10, 12].

METHODS

Study design

This randomised controlled trial (HOMEX-SCI; ISRCTN57096451) was approved by the National Research Ethics Service Committee. A detailed trial protocol has previously been

published [24] and is in accordance with current Consolidated Standards of Reporting Trials (CONSORT) guidelines Schulz [25]. It should be noted that the primary outcome measures related to biomarkers of cardiometabolic disease are reported elsewhere [26]. Data reported in this article are based on the secondary outcome measures associated with HRQOL.

Participants were initially recruited by displaying advertisements on national disability charity websites, online forums and social media networking sites. Members of our Patient and Public Involvement (PPI) group, who met the inclusion criteria, were notified directly via email. Written informed consent was obtained from all participants. After baseline laboratory testing and a week of free-living physical activity monitoring, eligible participants were randomly assigned (2:1 allocation ratio) to a home-based moderate-intensity upper-body exercise intervention (INT), or a lifestyle maintenance control group (CON), for 6 weeks. Minimisation was used to ensure balance between the two groups for baseline characteristics of; age, body mass, level of spinal cord lesion and physical activity level. All participants attended the Centre for DisAbility Sport and Health (DASH) laboratory at the University of Bath, on two occasions, for baseline (week 0) and follow-up testing (week 7). The same experimental procedures were performed during both baseline and follow-up testing. It should be noted that we did not plan an intention to treat (ITT) analysis but instead a treatment exposure analysis (TEA), where only participants that complied with the intervention were included in the final analyses.

Sample Size

The sample size was calculated for the primary outcome measure (i.e. fasting serum insulin concentration), as detailed in the previously published trial protocol [24]. It was estimated that nine participants would be required to detect a statistically significant change in insulin

sensitivity in the INT group, based on an estimated effect size (Cohen's *d*) of 1.1. The power was set at 0.8 and the alpha at 0.05. However, a 2:1 allocation ratio was adopted in anticipation of more dropouts in the intervention group (INT) compared to the control group (CON), where there were concerns that by the end of the study the INT group sample might not be sufficiently large to have adequate power for our planned statistical analyses. Consequently, a computer programme was used to calculate sample size adjustments for two groups with unequal size, to account for any consequences of unequal allocation on statistical power. Also, taking into account an expected drop-out rate of approximately 15%, we aimed to recruit at least 24 (INT: 16, CON: 8) participants with chronic paraplegia.

Participants

Participant eligibility criteria were as follows: aged between 18–65 years, inactive (habitual physical activity level; PAL <1.60); chronic (>1 year) spinal cord lesion below the second thoracic level; no immediate plans to alter diet and/or physical activity behaviour; weight stable (±3 kg over the previous 6 months) and; free from active medical issues [i.e. pressure sores, urinary tract infections and cardiovascular contra-indications for testing] or musculoskeletal complaints.

Trial day protocol

Anthropometric characteristics: supine height [a] and body mass [b] were measured at 0830 ± 1 hr. While participants remained in a 10 hr overnight fast, resting metabolic rate was measured in a supine position via indirect calorimetry from gaseous exchange [c], in accordance with best practice guidelines [27]. Participants then completed various HRQOL-related questionnaires: the short form-36 health survey (SF-36); the Wheelchair User's Shoulder Pain index

(WUSPI); the Fatigue Severity Scale (FSS) and the Exercise Self-Efficacy Scale (ESES). These questionnaires were completed, without any time pressures, in a well-lit, private setting by the participants themselves.

Participants performed a discontinuous, incremental sub-maximal arm-crank ergometry test on the same portable desktop ergometer [d] provided to them during the intervention. Following a short rest, peak oxygen uptake ($\dot{V}O_{2\ peak}$) and workload were measured at the point of volitional exhaustion during a continuous, incremental exercise protocol [24], performed on an electrically braked arm-crank ergometer [e]. During both of these exercise protocols, expired gases were continuously analysed using a calibrated computerised metabolic system [f]. Heart rate was also recorded using a heart rate monitor [g].

Objective measurement of physical activity

During the 7-days following baseline laboratory testing, participants wore a chest-mounted Actiheart™ device [h] to estimate free-living habitual physical activity. The Actiheart™ was individual calibrated for each participant using heart rate data collected at rest and across a range of exercise intensities during laboratory testing [24]. This method has been shown to be a valid measure of physical activity energy expenditure (PAEE) in wheelchair users [28]. Time spent performing moderate-to-vigorous physical activity [MVPA; $\geq$ 3.0 metabolic equivalents (METs)], PAL (total energy expenditure/RMR) and absolute PAEE were estimated. A further 7-day habitual physical activity monitoring period was repeated during the final week (week 6) of observation, for the INT and CON groups.

Home-based moderate-intensity aerobic exercise intervention

The intervention group performed moderate-intensity exercise four times per week on a portable desktop arm-crank ergometer set up in their own home. The exercise intensity was increased from ~60% $\dot{V}O_{2\ peak}$ during the first 3 weeks to ~65% $\dot{V}O_{2\ peak}$ for the final 3-weeks. To attain the desired exercise intensity, participants wore a Polar T31 heart rate monitor [g] during each exercise session and were shown how to manually adjust the resistance to achieve the prescribed target heart rate. Compliance with the intervention was monitored via a GENEActiv tri-axial accelerometer [i], worn on the wrist, and an activity diary where participants recorded the difficulty, total revolutions (RPM) and heart-rate during each exercise session.

Processing health-related quality of life measures

HRQOL was measured using the SF-36, with data scored using the RAND 36-item Health survey (Version 1.0) method [29]. Pre-coded numeric values for each item were transformed into a score, ranging from 0 to 100, while also accounting for items that were negatively scored. Items in the same scale were then averaged together to create 8 subscales (four represent physical quality of life (Physical Component Summary; PCS) and four represent emotional quality of life (Mental Component Summary; MCS). Using the original SF-36 [30] in persons with SCI is not without complications. The rehabilitation research community has raised concerns about the inclusion of three and two questions that refer to walking and stair climbing, respectively [31, 32]. Given that these five physical functioning items are insulting and irrelevant for persons with SCI, we replaced the words ‘walk’ and ‘climb’ with ‘go’ and ‘go up’, as previously recommended [33, 34]. Construct validity remains acceptable with this approach [33]. The SF-36 was also used to derive health utility through the calculation of

quality adjusted life years (QALY) [35]. Shoulder pain was measured using the sum of the 15-item WUSPI [36]. The raw WUSPI score was divided by the number of items completed, then multiplied by 15 to give the performance-corrected WUSPI score (PC-WUSPI). This was used to accommodate participants who were unable to undertake certain functions (e.g. item 13: driving?). Fatigue and self-efficacy were also measured using the FSS [37] and ESES [38], respectively.

Outcome measures

A total of seven outcome measures (scale of measurement) were assessed, as follows:

- Physical quality of life (PCS, SF-36)
- Emotional quality of life (MCS, SF-36)
- Quality adjusted life years (QALY)
- Fatigue severity (FSS)
- Global fatigue (FSS Visual Analogue Fatigue Scale)
- Shoulder pain (WUSPI)
- Exercise self-efficacy (ESES).

The main outcome variables of interest were physical quality of life and exercise self-efficacy. Shoulder pain was primarily recorded to assess any changes in shoulder-specific pain in the intervention group and was not intended as a secondary measure of HRQOL.

Statistical analyses

Responses within and between trials were analysed by two-way (group [intervention, control] x time [baseline, follow-up]) mixed-model analysis of variance (ANOVA). ANOVAs were

performed irrespective of any minor deviations from a normal distribution Maxwell [39] but with Greenhouse-Geisser corrections applied to intra-individual contrasts where $\varepsilon < 0.75$ and the Huynh-Feldt corrections applied for less severe asphericity Atkinson [40]. Where significant interaction effects were observed, paired and independent t-tests were applied to determine significant differences within and between groups. Magnitude-based inferences were used to provide an interpretation of the real-world relevance of the outcomes [41]. A value equivalent to a standardised difference in means of 0.20 was set as the smallest worthwhile effect threshold [42]. Effects were classified as unclear if the percentage likelihood that the true effect crossed both positive and negative smallest worthwhile effect thresholds were both greater than 5%. Otherwise, the effect was deemed clear, and was qualified with a probabilistic term using the following scale: <0.5%, most unlikely; 0.5-5%, very unlikely; 5-25%, unlikely; 25-75%, possible; 75-95%, likely; 95-99.5%, very likely; >99.5%, most likely [43]. Standardised effect sizes (Cohens *d*) were also calculated, based on the magnitude of correlation between trials, thresholds of >0.2 (small), >0.5 (moderate) and >0.8 (large) were used [44]. Pearson product moment correlation coefficients (*r*) were conducted on participants who complied with the intervention (n = 21) to assess the associations between change (Δ) scores for various outcomes (i.e. Δ MVPA vs. Δ PCS). The distributions of all Δ scores were analysed for normality of distribution using the Shapiro-Wilk test. Non-parametric Δ scores were log-transformed to allow the use of parametric statistics. Data from an ITT analysis (n = 23) is also presented for comparative purposes (Supplementary Table). Statistical analyses were performed using SPSS version 22 [j], with statistical significance set *a priori* of $\alpha \leq 0.05$.

RESULTS

Twenty-five participants were recruited into the study between September 2014 and May 2016, with follow-up assessments in a further 8 weeks. One participant was deemed too

active at baseline, one participant did not complete the trial due to illness and two participants were excluded from the analysis due to a lack of adherence to the INT (Figure 1). Baseline demographic characteristics for the participants included in the treatment-exposure analysis (n = 21) were; age 47 ± 8 years, time since injury 16 ± 11 years, injury lesion below the T4 level and 71% were male (n = 15). None of these baseline characteristics differed significantly between groups (P > 0.28). Over the 6-week period mean: subjective ratings of difficulty for the intervention group sessions was 7 ± 1 (1: easy, 10: hard); exercise session duration was 44 ± 1 min; power output was 46 ± 18 W and; heart rate was 144 ± 11 $b \cdot min^{-1}$.

[Insert Figure 1 About Here]

Participants were asked to eat *ad-libitum* during the 6-week period and the intervention did not positively influence body mass relative to the control group. Whereas there were significant (P < 0.05) interaction effects for objectively measured physical activity (MVPA and PAEE), cardiorespiratory fitness ($\dot{V}O_2$ peak) and exercise self-efficacy (Table 1). The standardised effect of the intervention on these outcomes ranged from moderate (d = 0.62) to large (d = 1.37) with mechanistic inferences of '*most likely*' and '*very likely*' positive.

[Insert Table 1 About Here]

Intervention effects on health-related quality of life

Changes in PCS were significantly different between the two groups (interaction effect; P = 0.017) with a moderate effect size and a '*very likely*' positive inference, in favour of the INT

group (Table 1 and Figure 2). There were also trends for an interaction effect in MCS (P = 0.055) and QALY (P = 0.056) with moderate (*d* = 0.76) and large (*d* = 0.82) effect sizes, respectively, for the INT relative to the CON group. The change in the arithmetic mean of the FSS was significantly different between groups (interaction effect; P = 0.036), with a significant reduction in the INT group (P = 0.027) (Table 1 and Figure 2). Lower scores on these 9-items indicate reduced fatigue severity. There was also a trend for an interaction effect (P = 0.084) in global fatigue measured using the 11-point visual analogue fatigue scale (VAFS; 0 = worst, 10 = normal). These measures of fatigue demonstrated large effect sizes in favour of INT (Table 1 and Figure 2). Although there was a small negative effect of INT (*d* = -0.35) on shoulder pain, there was no significant interaction (P = 0.386) and the mechanistic inference was '*unclear*', suggesting the intervention had no significant or meaningful impact on perceptions of pain.

[Insert Figure 2 About Here]

[Insert Figure 3 About Here]

For comparative purposes, a modified version of Table 1 has been included as a Supplementary data file. This Table includes data for the two participants that were excluded due to lack of compliance with the intervention (n=15 for INT group). Had this been a planned intention to treat (ITT) analysis, these participants would have been included in the analyses regardless of compliance. While the Tables show small variations in the final effect size calculations, the main statistical effects and inferences are consistent and robust. The only noteworthy difference relates to PCS, where the overall effect size is greater, becomes statistically significant and, in terms of inference, changes from 'likely positive' to 'very likely positive' when the two participants are excluded.

Predictors of change in health-related quality of life

Changes in $\dot{V}O_2$ peak were strongly correlated with Δ MVPA (r = 0.66, P = 0.002) and Δ exercise self-efficacy (r = 0.66, P = 0.001). Changes in cardiorespiratory fitness, MVPA and exercise self-efficacy over the 6 weeks demonstrate moderate to large, significant ($P \leq 0.05$) associations with changes in various HRQOL outcomes (Table 2).

[Insert Table 2 About Here]

DISCUSSION

This study investigated the effect of a home-based upper body 6-week exercise intervention on MVPA, cardiorespiratory fitness (CRF) and indices of HRQOL in people with SCI. The main findings support our primary hypothesis that a 6-week home-based upper-body exercise intervention improves aspects of HRQOL in persons with SCI. Furthermore, intervention induced increases in ESE were positively associated with indicators of both physical and mental quality of life domains.

Change in physical activity, cardiorespiratory fitness and exercise self-efficacy

Results revealed that providing an arm-crank ergometer and a personalised progressive exercise programme increased MVPA and CRF compared to a lifestyle maintenance control group. These positive effects were observed in a substantially shorter intervention period (i.e. 6-weeks) compared to previous exercise intervention studies in persons with SCI, which were 12 weeks [45] and 9 months [15], respectively. We also adopted more rigorous methods than those of Mulroy et al. [45], where we used objective measures of MVPA and CRF. In addition, the intervention had a significant positive effect on participants ESE, that is, people with SCI who received the intervention demonstrated a significant increase in their perceived confidence to participate in exercise in the face of barriers such as a lack of access to a gym or exercise training facilities. Increasing ESE is a key intervention target as it is a modifiable predictor of physical activity behaviour in a variety of populations [46, 47] including people with SCI [8-10, 15].

Change in health-related quality of life

354 The intervention group demonstrated improvements in measures of both physical and
355 psychological quality of life. Indeed, the measure of physical functioning (PCS) improved
356 significantly in response to the intervention. Increases in vitality, a measure of how much
357 energy an individual perceives, was also observed in INT, but not CON (Figure 3). These
358 findings were coupled with reductions in perceptions of fatigue, adding evidence for the
359 positive effects of exercise on the physical and psychological quality of life for people with
360 SCI [15, 45]. The significant and robust adaptations were observed with no significant effects on
361 shoulder pain, which is in contrast to previous research where exercise has reduced pain [11, 45,
362 48]. The disparity may be explained by the low levels of shoulder pain reported at baseline
363 among participants in the current study. Still, the home-based arm-crank ergometry
364 intervention had positive effects on outcomes such as MVPA, CRF and HRQOL without any
365 associated increase in shoulder pain. Therefore, this intervention protocol presents a brief,
366 viable and implementable tool, particularly for those who are exiting intensive rehabilitation
367 support after SCI and need to transition to independent exercise.

368

369 Despite these beneficial effects, there was only a trend for a significant impact on emotional
370 quality of life (assessed via the MCS). Dijkers [21] conceptualisation of quality of life indicates
371 that the physical activity - quality of life relationship is driven by achievement domains such
372 as mental functioning, functional ability and social relationships. It appears that whilst our
373 intervention improved physical function it did not significantly influence the mental and
374 social achievement domains. This is not surprising given that the intervention was not
375 designed to target psychological constructs such as social and mental functioning (i.e.
376 isolated home-based exercise intervention). Future interventions for people with SCI would
377 benefit from integrating methods that target improvements in both mental and social
378 functioning. For example, this brief intervention could be supplemented by targeting patient's

feelings of autonomy by offering participants choice over the programme's duration and/or intensity and support feelings of connectedness with others via virtual or community exercise groups [49, 50]. However, confidence in one's ability to continue exercising in the face of barriers, which were enhanced in this study, are most relevant when initiating exercise behaviour [51], something this intervention achieved and is important to retain [52].

Although the impact of the intervention on health utility, as measured by QALY, was only approaching significance, the effect size was large and the inference 'likely positive'. The magnitude of this effect is above the threshold to be considered a minimally clinically important difference (MCID), as previously described by Kaplan [53]. In addition to targeting adaptations in social and mental functioning, future interventions should assess health utility as a primary outcome variable.

Relationships between changes in physical activity, fitness and health-related quality of life

A particular strength of this RCT is the ability to investigate relationships between change scores in objective markers of MVPA and CRF with changes in indices of physical and psychological quality of life. Results revealed that both MVPA and CRF were significantly negatively associated with fatigue severity. CRF was also positively related to PCS, MCS and global fatigue. MVPA was positively associated with QALY, but not with ESE. These relationships provide credence to the argument that the intervention-induced changes in MVPA and CRF had a positive impact on participant's physical and psychological quality of life.

In addition, CRF was significantly and positively related to change in exercise self-efficacy (r = 0.66, P = 0.001), which suggests that intervention-induced increases in CRF were positively associated with participant's beliefs that they can successfully overcome barriers to participate in exercise. This is important because ESE has stronger positive associations with more indices of physical and psychological quality of life than either CRF or MVPA. Furthermore, ESE is reportedly lower in people with paraplegia who have lower peak power output [54]. Therefore, interventions that achieve enhancements in CRF may also achieve a corresponding enhancement in ESE, physical and psychological quality of life.

Limitations

Although this intervention demonstrated important and robust effects, the relatively short duration (i.e. 6 weeks) and lack of follow-up assessments to investigate the longer-term impact, could be considered limitations. Moreover, the primary power calculation was based on a physiological outcome variable (i.e. fasting insulin concentration), potentially limiting the robustness of conclusions made using traditional inferential statistics (mixed-model ANOVA) on these secondary outcomes. However, standardised effect sizes and magnitude-based inferences were also calculated to help practitioners interpret the real-world relevance of upper-body exercise on these study outcomes.

The lack of compliance and subsequent withdrawal of two participants from the analysis could also be seen as a limitation, although we have been clear that this was a planned 'treatment exposure analysis', not an 'intention to treat' analysis. While these participants were contacted periodically over the 6 weeks, their compliance with exercise duration and/or intensity was poor. Given the trial design (i.e. remote home-based exercise intervention) this

non-compliance only became apparent upon downloading the wearable physical activity monitors after the post-intervention laboratory testing was completed. Thus, inclusion of these data could have resulted in erroneous interpretations of the efficacy of the intervention. Even with the exclusion of these participants, the attrition reported in this current study (~11%) was considerably less than previous exercise intervention studies conducted in persons with SCI (~46%) [55]. Furthermore, the data presented in the supplementary data file (modified Table 1) include the two 'excluded' participants and show remarkably similar effect sizes, statistical outcomes and inferences. Intuitively, the overall effect size for the physical component score is reduced when these two participants, who did not comply with the physical intervention, are included in the analysis.

While the small sample size is also a limitation, researchers should be aware of the considerable challenges associated with the identification and recruitment of inactive participants with chronic SCI [56]. Given the rather large number of statistical tests and comparisons, we urge caution in the interpretation of effect sizes for individual variables, but felt that this was more appropriate than reporting an average effect size for a diverse set of measures of physical and psychological quality of life. In some cases (i.e. FSS) the significant interaction effects were possibly reflective of the control group becoming worse over time. We wish to point out that *Post Hoc* analyses (within group paired t-tests) revealed statistically significant 'improvements' in the intervention group and no statistical significant changes over time in the control group. Nevertheless, it is important to emphasise that being randomly allocated to the control group may have detrimental effects on participants, an observation which is consistent with findings from other exercise RCTs in this population [15]. This trial employed a waiting list control [24] to facilitate a comparison against a 'true-world'

control group. However, perhaps other innovative solutions are required in the future to overcome such issues.

Implications and future directions

This home-based exercise intervention for inactive people with a SCI overcame known informational (i.e. 'lack of knowledge', 'lack of awareness') and systemic exercise (i.e. 'accessibility', 'financial cost') barriers [17-19, 57] and was effective at initiating MVPA sufficient to improve objective physical and psychological quality of life. Therefore, this programme could be implemented to bridge the gap between intensive supervised rehabilitation and independent exercise. Moreover, the SF-36 is one of the most widely employed measures of physical and psychological quality of life in the general population as well as in SCI and has been shown to be sensitive to changes in physical activity [58]. This study did not observe intervention effects for MCS, which includes social functioning and mental health subscales of the SF-36. Modifications could be made to the intervention to target these domains in order to maximise the beneficial outcomes. Future research could supplement this brief intervention with empirically-informed design and delivery to support adherence and maintenance to exercise regimes [59, 60], factors that can inhibit the efficacy of exercise interventions [61]. Such investigations would help to inform effective methods of supporting persons with SCI transition to physically active lifestyles following intensive clinical rehabilitation.

CONCLUSION

This short home-based upper-body exercise intervention is an effective way of enhancing indices of physical and psychological quality of life in people with SCI. Exercise self-

efficacy was a prominent outcome from the intervention, demonstrating stronger associations with more indices of physical and psychological quality of life than either MVPA or CRF. Future research should supplement this intervention with empirically-informed trial designs to support social and mental functioning, adaptive motivations and exercise maintenance.

SUPPLIERS

a. Lufkin, Sparks, MD, USA.

b. Detecto® BRW1000, Webb City, MO, USA.

c. MiniMP 5200, Servomex Ltd., Sussex, UK.

d. Monark 871E, Dalarna, Sweden.

e. Lode Angio, Groningen, Netherlands.

f. TrueOne® 2400, ParvoMedics, Salt Lake City, UT, USA.

g. T31, Polar Electro Inc., Lake Success, NY, USA.

h. Actiheart™, Cambridge Neurotechnology Ltd, Papworth, UK

i. GENEActiv, Activinsights, Cambridge, UK.

j. SPSS version 22, IBM, Armonk, NY, USA.

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660

Figure Legends

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram for HOMEX-SCI trial.

Figure 2. SF-36, physical component summary[1] **(A)** and mental component summary[1] **(B)**; and arithmetic fatigue severity mean[2] **(C)** and global fatigue[3] **(D)** at baseline and follow-up for the INT (solid black line and open diamond) and CON (dashed line and black triangle) groups. Means ± normalised confidence intervals (CIs) are shown. There were no significant differences at baseline ($P \geq 0.159$) between groups. P values are displayed for significant day x group interaction effects. # denotes values are different pre-post within INT group ($P \leq 0.05$).
[1] scaled summaries from the SF-36 questionnaire (higher scores indicate a more favourable health state).
[2] arithmetic mean from 9-item FSS (7 point scale; 1 = strongly disagree, 7 = strongly agree). Higher scores indicate greater fatigue severity, with cut-scores over 4 indicative of significant fatigue [62].
[3] global fatigue from FSS (11 point visual analogue fatigue scale (VAFS); 0 = worst, 10 = normal).

Figure 3: Standardised effect sizes (Cohens *d*) (±90% CI) and magnitude based inferences for all health related quality of life outcomes.
[1] SF-36, [2] Fatigue severity scale, [3] Wheelchair user shoulder pain index.
‡ Direction of effect was reversed in the Figure for consistency. Arithmetic mean from 9-item FSS went down, which indicates reduced fatigue severity.
Abbreviations: CON, lifestyle maintenance control group; INT, upper-body exercise intervention; MCS, mental component summary; PCS, physical component summary, QALY, quality-adjusted life years.

Running head: Exercise enhances SCI health-related quality of life

Title: Home-based exercise enhances health-related quality of life in persons with spinal cord injury: A randomized controlled trial

Abstract

Objective: To assess the influence of a home-based exercise intervention on indices of health-related quality of life (HRQOL) in persons with spinal cord injury (SCI).

Design: This was a randomized controlled trial (HOMEX-SCI; ISRCTN57096451). After baseline laboratory testing and a week of free-living physical activity monitoring, eligible participants were randomly assigned (2:1 allocation ratio) to a home-based moderate-intensity upper-body exercise intervention (INT, n = 13), or a lifestyle maintenance control group (CON, n = 8), for 6 weeks.

Setting: Home-based with short laboratory visits immediately before and after the intervention/control period.

Participants: Twenty-one inactive participants with chronic (> 1 year) SCI (injury level range, T4 – L5).

Intervention: Participants assigned to the exercise intervention group (INT) completed 4 x 45 min moderate-intensity (60-65% peak oxygen uptake [V̇O2 peak]) arm-crank exercise per week for 6 weeks. Participants assigned to the control group (CON) were asked to maintain their habitual physical activity behaviour.

Main Outcome Measures: Secondary outcome measures were assessed, including physical and emotional component scores (PCS and MCS) of health-related quality of life (SF-36), fatigue, global fatigue (FSS) and shoulder pain index (WUSPI). Cardiorespiratory fitness (CRF), objectively measured habitual moderate-to-vigorous physical activity (MVPA) and exercise self-efficacy (ESE) were also assessed at baseline and follow-up.

Results. Changes in the PCS (P = 0.017) of the SF-36, ESE (P = 0.011) and FSS (P = 0.036) were significantly different between the two groups, with moderate to large effect sizes (*d* =

0.75 – 1.37). Various HRQOL outcomes demonstrated ‘likely’ to ‘very likely’ positive inferences in favour of the INT group following the 6-week exercise intervention. Changes in ESE were significantly ($P < 0.01$) associated with changes in PCS ($r = 0.62$) and MCS ($r = 0.71$), FSS ($r = -0.71$) and global fatigue ($r = 0.57$).

Conclusions. A 6-week upper-body exercise intervention improved indices of HRQOL in persons with SCI. Improvements were associated with increases in ESE. While this intervention demonstrated a positive impact on perceived physical functioning, future interventions should aim to support social and mental functioning and exercise maintenance.

Key words: Spinal cord injury; exercise intervention; health and wellbeing; self efficacy; quality of life

Abbreviations:

CON- Lifestyle maintenance control group,

ESE- Exercise Self-Efficacy

ESES- Exercise Self-Efficacy Scale

FSS- fatigue severity scale

HOMEX-SCI- Home-based upper-body exercise randomized controlled trial,

HRQOL- Health-related quality of life

INT- Home-based moderate-intensity upper-body exercise intervention group,

MVPA- moderate-to-vigorous physical activity,

SCI- spinal cord injury,

SF36- short form 36 health survey,

CRF- cardiorespiratory fitness,

$\dot{V}O_{2peak}$ - peak oxygen uptake,

WUSPI- wheelchair user shoulder pain index

INTRODUCTION

Disability can negatively impact physical activity behaviour [1]. The reasons for the adoption of a more sedentary lifestyle are multifactorial, but the perceived psychosocial and environmental barriers to engage in physical activity are numerous for wheelchair users living with a spinal cord injury (SCI) [2, 3]. Consequently, persons with SCI are relatively inactive [4] and new ways to support the initiation of physical activity in this population are needed.

Besides an increased incidence of chronic diseases (e.g. cardiovascular disease, type 2 diabetes) [5], persons with SCI have significantly elevated levels of fatigue, anxiety, depression and poorer exercise self-efficacy (ESE) compared to non-disabled controls [6, 7]. This is important because physical activity can improve quality of life for people with SCI and ESE is considered a modifiable predictor of physical activity behaviour change, specifically in this population [8-12]. Therefore, it is essential to develop strategies capable of improving exercise self-efficacy in order to increase physical activity participation and accrue enhancements in quality of life.

Educational interventions, covering physical activity, nutrition and lifestyle management, have been shown to improve exercise self-efficacy and self-rated health, and result in fewer and less severe secondary conditions in persons with SCI [13, 14]. Following a 9-month, twice-weekly strength and arm-ergometry intervention, participants reported significantly higher levels of satisfaction with physical function, level of perceived health, overall quality of life and less pain than a control group [15]. However, these findings have not been demonstrated with shorter term, higher volume aerobic exercise training *per se*. Moreover, it has previously been suggested that upper-body exercise, primarily arm-crank ergometry as a training modality, might contribute to shoulder overuse injuries and trigger the onset of pain [16].

Therefore, the available evidence is currently inconclusive about whether upper-body arm-crank exercise is an effective treatment modality for improving health-related quality of life (HRQOL) in persons with SCI. Furthermore, a lack of access to gym facilities and exercise equipment, as well as poor information and support, have been identified as key barriers to exercise for adults with SCI [17-19]. Therefore, the provision of exercise equipment and a tailored exercise programme within a home setting could provide a mastery experience and help enhance ESE in people with SCI.

A recent meta-analysis on physical activity and wellbeing among individuals with SCI noted that most of the evidence to date has been from cross-sectional studies, with little consistency in the constructs and measures of HRQOL [20]. Therefore, the aim of this study was to test the hypothesis that a 6-week home-based upper-body exercise intervention would improve HRQOL component scores compared to a lifestyle maintenance control group, in persons with SCI. In keeping with Dijkers [21] conceptualisation of HRQOL and supported by previous research [10, 20, 22], it was hypothesized that physical activity behaviour would positively correlate with objective measures of physical and mental component scores (derived from the short-form 36 health survey). These summary component scores describe what the individual can achieve in both the physical and psychological domains. In addition, and grounded on the propositions of social cognitive theory [23], it was further hypothesized that exercise barrier self-efficacy would positively correlate with quality of life [10, 12].

METHODS

Study design

This randomised controlled trial (HOMEX-SCI; ISRCTN57096451) was approved by the National Research Ethics Service Committee. A detailed trial protocol has previously been

published [24] and is in accordance with current Consolidated Standards of Reporting Trials (CONSORT) guidelines Schulz [25]. It should be noted that the primary outcome measures related to biomarkers of cardiometabolic disease are reported elsewhere [26]. Data reported in this article are based on the secondary outcome measures associated with HRQOL.

Participants were initially recruited by displaying advertisements on national disability charity websites, online forums and social media networking sites. Members of our Patient and Public Involvement (PPI) group, who met the inclusion criteria, were notified directly via email. Written informed consent was obtained from all participants. After baseline laboratory testing and a week of free-living physical activity monitoring, eligible participants were randomly assigned (2:1 allocation ratio) to a home-based moderate-intensity upper-body exercise intervention (INT), or a lifestyle maintenance control group (CON), for 6 weeks. Minimisation was used to ensure balance between the two groups for baseline characteristics of; age, body mass, level of spinal cord lesion and physical activity level. All participants attended the Centre for DisAbility Sport and Health (DASH) laboratory at the University of Bath, on two occasions, for baseline (week 0) and follow-up testing (week 7). The same experimental procedures were performed during both baseline and follow-up testing. It should be noted that we did not plan an intention to treat (ITT) analysis but instead a treatment exposure analysis (TEA), where only participants that complied with the intervention were included in the final analyses.

Sample Size

The sample size was calculated for the primary outcome measure (i.e. fasting serum insulin concentration), as detailed in the previously published trial protocol [24]. It was estimated that nine participants would be required to detect a statistically significant change in insulin

sensitivity in the INT group, based on an estimated effect size (Cohen's *d*) of 1.1. The power was set at 0.8 and the alpha at 0.05. However, a 2:1 allocation ratio was adopted in anticipation of more dropouts in the intervention group (INT) compared to the control group (CON), where there were concerns that by the end of the study the INT group sample might not be sufficiently large to have adequate power for our planned statistical analyses. Consequently, a computer programme was used to calculate sample size adjustments for two groups with unequal size, to account for any consequences of unequal allocation on statistical power. Also, taking into account an expected drop-out rate of approximately 15%, we aimed to recruit at least 24 (INT: 16, CON: 8) participants with chronic paraplegia.

Participants

Participant eligibility criteria were as follows: aged between 18–65 years, inactive (habitual physical activity level; PAL <1.60); chronic (>1 year) spinal cord lesion below the second thoracic level; no immediate plans to alter diet and/or physical activity behaviour; weight stable (±3 kg over the previous 6 months) and; free from active medical issues [i.e. pressure sores, urinary tract infections and cardiovascular contra-indications for testing] or musculoskeletal complaints.

Trial day protocol

Anthropometric characteristics: supine height [a] and body mass [b] were measured at 0830 ± 1 hr. While participants remained in a 10 hr overnight fast, resting metabolic rate was measured in a supine position via indirect calorimetry from gaseous exchange [c], in accordance with best practice guidelines [27]. Participants then completed various HRQOL-related questionnaires: the short form-36 health survey (SF-36); the Wheelchair User's Shoulder Pain index

(WUSPI); the Fatigue Severity Scale (FSS) and the Exercise Self-Efficacy Scale (ESES). These questionnaires were completed, without any time pressures, in a well-lit, private setting by the participants themselves.

Participants performed a discontinuous, incremental sub-maximal arm-crank ergometry test on the same portable desktop ergometer [d] provided to them during the intervention. Following a short rest, peak oxygen uptake ($\dot{V}O_{2\ peak}$) and workload were measured at the point of volitional exhaustion during a continuous, incremental exercise protocol [24], performed on an electrically braked arm-crank ergometer [e]. During both of these exercise protocols, expired gases were continuously analysed using a calibrated computerised metabolic system [f]. Heart rate was also recorded using a heart rate monitor [g].

Objective measurement of physical activity

During the 7-days following baseline laboratory testing, participants wore a chest-mounted Actiheart™ device [h] to estimate free-living habitual physical activity. The Actiheart™ was individual calibrated for each participant using heart rate data collected at rest and across a range of exercise intensities during laboratory testing [24]. This method has been shown to be a valid measure of physical activity energy expenditure (PAEE) in wheelchair users [28]. Time spent performing moderate-to-vigorous physical activity [MVPA; $\geq$ 3.0 metabolic equivalents (METs)], PAL (total energy expenditure/RMR) and absolute PAEE were estimated. A further 7-day habitual physical activity monitoring period was repeated during the final week (week 6) of observation, for the INT and CON groups.

Home-based moderate-intensity aerobic exercise intervention

The intervention group performed moderate-intensity exercise four times per week on a portable desktop arm-crank ergometer set up in their own home. The exercise intensity was increased from ~60% $\dot{V}O_{2\ peak}$ during the first 3 weeks to ~65% $\dot{V}O_{2\ peak}$ for the final 3-weeks. To attain the desired exercise intensity, participants wore a Polar T31 heart rate monitor [g] during each exercise session and were shown how to manually adjust the resistance to achieve the prescribed target heart rate. Compliance with the intervention was monitored via a GENEActiv tri-axial accelerometer [i], worn on the wrist, and an activity diary where participants recorded the difficulty, total revolutions (RPM) and heart-rate during each exercise session.

Processing health-related quality of life measures

HRQOL was measured using the SF-36, with data scored using the RAND 36-item Health survey (Version 1.0) method [29]. Pre-coded numeric values for each item were transformed into a score, ranging from 0 to 100, while also accounting for items that were negatively scored. Items in the same scale were then averaged together to create 8 subscales (four represent physical quality of life (Physical Component Summary; PCS) and four represent emotional quality of life (Mental Component Summary; MCS). Using the original SF-36 [30] in persons with SCI is not without complications. The rehabilitation research community has raised concerns about the inclusion of three and two questions that refer to walking and stair climbing, respectively [31, 32]. Given that these five physical functioning items are insulting and irrelevant for persons with SCI, we replaced the words ‘walk’ and ‘climb’ with ‘go’ and ‘go up’, as previously recommended [33, 34]. Construct validity remains acceptable with this approach [33]. The SF-36 was also used to derive health utility through the calculation of

quality adjusted life years (QALY) [35]. Shoulder pain was measured using the sum of the 15-item WUSPI [36]. The raw WUSPI score was divided by the number of items completed, then multiplied by 15 to give the performance-corrected WUSPI score (PC-WUSPI). This was used to accommodate participants who were unable to undertake certain functions (e.g. item 13: driving?). Fatigue and self-efficacy were also measured using the FSS [37] and ESES [38], respectively.

Outcome measures

A total of seven outcome measures (scale of measurement) were assessed, as follows:

- Physical quality of life (PCS, SF-36)
- Emotional quality of life (MCS, SF-36)
- Quality adjusted life years (QALY)
- Fatigue severity (FSS)
- Global fatigue (FSS Visual Analogue Fatigue Scale)
- Shoulder pain (WUSPI)
- Exercise self-efficacy (ESES).

The main outcome variables of interest were physical quality of life and exercise self-efficacy. Shoulder pain was primarily recorded to assess any changes in shoulder-specific pain in the intervention group and was not intended as a secondary measure of HRQOL.

Statistical analyses

Responses within and between trials were analysed by two-way (group [intervention, control] x time [baseline, follow-up]) mixed-model analysis of variance (ANOVA). ANOVAs were

performed irrespective of any minor deviations from a normal distribution Maxwell [39] but with Greenhouse-Geisser corrections applied to intra-individual contrasts where $\varepsilon < 0.75$ and the Huynh-Feldt corrections applied for less severe asphericity Atkinson [40]. Where significant interaction effects were observed, paired and independent t-tests were applied to determine significant differences within and between groups. Magnitude-based inferences were used to provide an interpretation of the real-world relevance of the outcomes [41]. A value equivalent to a standardised difference in means of 0.20 was set as the smallest worthwhile effect threshold [42]. Effects were classified as unclear if the percentage likelihood that the true effect crossed both positive and negative smallest worthwhile effect thresholds were both greater than 5%. Otherwise, the effect was deemed clear, and was qualified with a probabilistic term using the following scale: <0.5%, most unlikely; 0.5-5%, very unlikely; 5-25%, unlikely; 25-75%, possible; 75-95%, likely; 95-99.5%, very likely; >99.5%, most likely [43]. Standardised effect sizes (Cohens *d*) were also calculated, based on the magnitude of correlation between trials, thresholds of >0.2 (small), >0.5 (moderate) and >0.8 (large) were used [44]. Pearson product moment correlation coefficients (*r*) were conducted on participants who complied with the intervention (n = 21) to assess the associations between change (Δ) scores for various outcomes (i.e. Δ MVPA vs. Δ PCS). The distributions of all Δ scores were analysed for normality of distribution using the Shapiro-Wilk test. Non-parametric Δ scores were log-transformed to allow the use of parametric statistics. Data from an ITT analysis (n = 23) is also presented for comparative purposes (Supplementary Table). Statistical analyses were performed using SPSS version 22 [j], with statistical significance set *a priori* of $\alpha \leq 0.05$.

RESULTS

Twenty-five participants were recruited into the study between September 2014 and May 2016, with follow-up assessments in a further 8 weeks. One participant was deemed too

active at baseline, one participant did not complete the trial due to illness and two participants were excluded from the analysis due to a lack of adherence to the INT (Figure 1). Baseline demographic characteristics for the participants included in the treatment-exposure analysis (n = 21) were; age 47 ± 8 years, time since injury 16 ± 11 years, injury lesion below the T4 level and 71% were male (n = 15). None of these baseline characteristics differed significantly between groups (P > 0.28). Over the 6-week period mean: subjective ratings of difficulty for the intervention group sessions was 7 ± 1 (1: easy, 10: hard); exercise session duration was 44 ± 1 min; power output was 46 ± 18 W and; heart rate was 144 ± 11 $b \cdot min^{-1}$.

[Insert Figure 1 About Here]

Participants were asked to eat *ad-libitum* during the 6-week period and the intervention did not positively influence body mass relative to the control group. Whereas there were significant (P < 0.05) interaction effects for objectively measured physical activity (MVPA and PAEE), cardiorespiratory fitness ($\dot{V}O_2$ peak) and exercise self-efficacy (Table 1). The standardised effect of the intervention on these outcomes ranged from moderate (d = 0.62) to large (d = 1.37) with mechanistic inferences of '*most likely*' and '*very likely*' positive.

[Insert Table 1 About Here]

Intervention effects on health-related quality of life

Changes in PCS were significantly different between the two groups (interaction effect; P = 0.017) with a moderate effect size and a '*very likely*' positive inference, in favour of the INT

group (Table 1 and Figure 2). There were also trends for an interaction effect in MCS (P = 0.055) and QALY (P = 0.056) with moderate (*d* = 0.76) and large (*d* = 0.82) effect sizes, respectively, for the INT relative to the CON group. The change in the arithmetic mean of the FSS was significantly different between groups (interaction effect; P = 0.036), with a significant reduction in the INT group (P = 0.027) (Table 1 and Figure 2). Lower scores on these 9-items indicate reduced fatigue severity. There was also a trend for an interaction effect (P = 0.084) in global fatigue measured using the 11-point visual analogue fatigue scale (VAFS; 0 = worst, 10 = normal). These measures of fatigue demonstrated large effect sizes in favour of INT (Table 1 and Figure 2). Although there was a small negative effect of INT (*d* = -0.35) on shoulder pain, there was no significant interaction (P = 0.386) and the mechanistic inference was '*unclear*', suggesting the intervention had no significant or meaningful impact on perceptions of pain.

[Insert Figure 2 About Here]

[Insert Figure 3 About Here]

For comparative purposes, a modified version of Table 1 has been included as a Supplementary data file. This Table includes data for the two participants that were excluded due to lack of compliance with the intervention (n=15 for INT group). Had this been a planned intention to treat (ITT) analysis, these participants would have been included in the analyses regardless of compliance. While the Tables show small variations in the final effect size calculations, the main statistical effects and inferences are consistent and robust. The only noteworthy difference relates to PCS, where the overall effect size is greater, becomes statistically significant and, in terms of inference, changes from 'likely positive' to 'very likely positive' when the two participants are excluded.

Predictors of change in health-related quality of life

Changes in $\dot{V}O_2$ peak were strongly correlated with Δ MVPA (r = 0.66, P = 0.002) and Δ exercise self-efficacy (r = 0.66, P = 0.001). Changes in cardiorespiratory fitness, MVPA and exercise self-efficacy over the 6 weeks demonstrate moderate to large, significant ($P \leq 0.05$) associations with changes in various HRQOL outcomes (Table 2).

[Insert Table 2 About Here]

DISCUSSION

This study investigated the effect of a home-based upper body 6-week exercise intervention on MVPA, cardiorespiratory fitness (CRF) and indices of HRQOL in people with SCI. The main findings support our primary hypothesis that a 6-week home-based upper-body exercise intervention improves aspects of HRQOL in persons with SCI. Furthermore, intervention induced increases in ESE were positively associated with indicators of both physical and mental quality of life domains.

Change in physical activity, cardiorespiratory fitness and exercise self-efficacy

Results revealed that providing an arm-crank ergometer and a personalised progressive exercise programme increased MVPA and CRF compared to a lifestyle maintenance control group. These positive effects were observed in a substantially shorter intervention period (i.e. 6-weeks) compared to previous exercise intervention studies in persons with SCI, which were 12 weeks [45] and 9 months [15], respectively. We also adopted more rigorous methods than those of Mulroy et al. [45], where we used objective measures of MVPA and CRF. In addition, the intervention had a significant positive effect on participants ESE, that is, people with SCI who received the intervention demonstrated a significant increase in their perceived confidence to participate in exercise in the face of barriers such as a lack of access to a gym or exercise training facilities. Increasing ESE is a key intervention target as it is a modifiable predictor of physical activity behaviour in a variety of populations [46, 47] including people with SCI [8-10, 15].

Change in health-related quality of life

354 The intervention group demonstrated improvements in measures of both physical and
355 psychological quality of life. Indeed, the measure of physical functioning (PCS) improved
356 significantly in response to the intervention. Increases in vitality, a measure of how much
357 energy an individual perceives, was also observed in INT, but not CON (Figure 3). These
358 findings were coupled with reductions in perceptions of fatigue, adding evidence for the
359 positive effects of exercise on the physical and psychological quality of life for people with
360 SCI [15, 45]. The significant and robust adaptations were observed with no significant effects on
361 shoulder pain, which is in contrast to previous research where exercise has reduced pain [11, 45,
362 48]. The disparity may be explained by the low levels of shoulder pain reported at baseline
363 among participants in the current study. Still, the home-based arm-crank ergometry
364 intervention had positive effects on outcomes such as MVPA, CRF and HRQOL without any
365 associated increase in shoulder pain. Therefore, this intervention protocol presents a brief,
366 viable and implementable tool, particularly for those who are exiting intensive rehabilitation
367 support after SCI and need to transition to independent exercise.

368

369 Despite these beneficial effects, there was only a trend for a significant impact on emotional
370 quality of life (assessed via the MCS). Dijkers [21] conceptualisation of quality of life indicates
371 that the physical activity - quality of life relationship is driven by achievement domains such
372 as mental functioning, functional ability and social relationships. It appears that whilst our
373 intervention improved physical function it did not significantly influence the mental and
374 social achievement domains. This is not surprising given that the intervention was not
375 designed to target psychological constructs such as social and mental functioning (i.e.
376 isolated home-based exercise intervention). Future interventions for people with SCI would
377 benefit from integrating methods that target improvements in both mental and social
378 functioning. For example, this brief intervention could be supplemented by targeting patient's

feelings of autonomy by offering participants choice over the programme's duration and/or intensity and support feelings of connectedness with others via virtual or community exercise groups [49, 50]. However, confidence in one's ability to continue exercising in the face of barriers, which were enhanced in this study, are most relevant when initiating exercise behaviour [51], something this intervention achieved and is important to retain [52].

Although the impact of the intervention on health utility, as measured by QALY, was only approaching significance, the effect size was large and the inference 'likely positive'. The magnitude of this effect is above the threshold to be considered a minimally clinically important difference (MCID), as previously described by Kaplan [53]. In addition to targeting adaptations in social and mental functioning, future interventions should assess health utility as a primary outcome variable.

Relationships between changes in physical activity, fitness and health-related quality of life

A particular strength of this RCT is the ability to investigate relationships between change scores in objective markers of MVPA and CRF with changes in indices of physical and psychological quality of life. Results revealed that both MVPA and CRF were significantly negatively associated with fatigue severity. CRF was also positively related to PCS, MCS and global fatigue. MVPA was positively associated with QALY, but not with ESE. These relationships provide credence to the argument that the intervention-induced changes in MVPA and CRF had a positive impact on participant's physical and psychological quality of life.

In addition, CRF was significantly and positively related to change in exercise self-efficacy (r = 0.66, P = 0.001), which suggests that intervention-induced increases in CRF were positively associated with participant's beliefs that they can successfully overcome barriers to participate in exercise. This is important because ESE has stronger positive associations with more indices of physical and psychological quality of life than either CRF or MVPA. Furthermore, ESE is reportedly lower in people with paraplegia who have lower peak power output [54]. Therefore, interventions that achieve enhancements in CRF may also achieve a corresponding enhancement in ESE, physical and psychological quality of life.

Limitations

Although this intervention demonstrated important and robust effects, the relatively short duration (i.e. 6 weeks) and lack of follow-up assessments to investigate the longer-term impact, could be considered limitations. Moreover, the primary power calculation was based on a physiological outcome variable (i.e. fasting insulin concentration), potentially limiting the robustness of conclusions made using traditional inferential statistics (mixed-model ANOVA) on these secondary outcomes. However, standardised effect sizes and magnitude-based inferences were also calculated to help practitioners interpret the real-world relevance of upper-body exercise on these study outcomes.

The lack of compliance and subsequent withdrawal of two participants from the analysis could also be seen as a limitation, although we have been clear that this was a planned 'treatment exposure analysis', not an 'intention to treat' analysis. While these participants were contacted periodically over the 6 weeks, their compliance with exercise duration and/or intensity was poor. Given the trial design (i.e. remote home-based exercise intervention) this

non-compliance only became apparent upon downloading the wearable physical activity monitors after the post-intervention laboratory testing was completed. Thus, inclusion of these data could have resulted in erroneous interpretations of the efficacy of the intervention. Even with the exclusion of these participants, the attrition reported in this current study (~11%) was considerably less than previous exercise intervention studies conducted in persons with SCI (~46%) [55]. Furthermore, the data presented in the supplementary data file (modified Table 1) include the two 'excluded' participants and show remarkably similar effect sizes, statistical outcomes and inferences. Intuitively, the overall effect size for the physical component score is reduced when these two participants, who did not comply with the physical intervention, are included in the analysis.

While the small sample size is also a limitation, researchers should be aware of the considerable challenges associated with the identification and recruitment of inactive participants with chronic SCI [56]. Given the rather large number of statistical tests and comparisons, we urge caution in the interpretation of effect sizes for individual variables, but felt that this was more appropriate than reporting an average effect size for a diverse set of measures of physical and psychological quality of life. In some cases (i.e. FSS) the significant interaction effects were possibly reflective of the control group becoming worse over time. We wish to point out that *Post Hoc* analyses (within group paired t-tests) revealed statistically significant 'improvements' in the intervention group and no statistical significant changes over time in the control group. Nevertheless, it is important to emphasise that being randomly allocated to the control group may have detrimental effects on participants, an observation which is consistent with findings from other exercise RCTs in this population [15]. This trial employed a waiting list control [24] to facilitate a comparison against a 'true-world'

control group. However, perhaps other innovative solutions are required in the future to overcome such issues.

Implications and future directions

This home-based exercise intervention for inactive people with a SCI overcame known informational (i.e. 'lack of knowledge', 'lack of awareness') and systemic exercise (i.e. 'accessibility', 'financial cost') barriers [17-19, 57] and was effective at initiating MVPA sufficient to improve objective physical and psychological quality of life. Therefore, this programme could be implemented to bridge the gap between intensive supervised rehabilitation and independent exercise. Moreover, the SF-36 is one of the most widely employed measures of physical and psychological quality of life in the general population as well as in SCI and has been shown to be sensitive to changes in physical activity [58]. This study did not observe intervention effects for MCS, which includes social functioning and mental health subscales of the SF-36. Modifications could be made to the intervention to target these domains in order to maximise the beneficial outcomes. Future research could supplement this brief intervention with empirically-informed design and delivery to support adherence and maintenance to exercise regimes [59, 60], factors that can inhibit the efficacy of exercise interventions [61]. Such investigations would help to inform effective methods of supporting persons with SCI transition to physically active lifestyles following intensive clinical rehabilitation.

CONCLUSION

This short home-based upper-body exercise intervention is an effective way of enhancing indices of physical and psychological quality of life in people with SCI. Exercise self-

efficacy was a prominent outcome from the intervention, demonstrating stronger associations with more indices of physical and psychological quality of life than either MVPA or CRF. Future research should supplement this intervention with empirically-informed trial designs to support social and mental functioning, adaptive motivations and exercise maintenance.

SUPPLIERS

a. Lufkin, Sparks, MD, USA.

b. Detecto® BRW1000, Webb City, MO, USA.

c. MiniMP 5200, Servomex Ltd., Sussex, UK.

d. Monark 871E, Dalarna, Sweden.

e. Lode Angio, Groningen, Netherlands.

f. TrueOne® 2400, ParvoMedics, Salt Lake City, UT, USA.

g. T31, Polar Electro Inc., Lake Success, NY, USA.

h. Actiheart™, Cambridge Neurotechnology Ltd, Papworth, UK

i. GENEActiv, Activinsights, Cambridge, UK.

j. SPSS version 22, IBM, Armonk, NY, USA.

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660

Figure Legends

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram for HOMEX-SCI trial.

Figure 2. SF-36, physical component summary[1] **(A)** and mental component summary[1] **(B)**; and arithmetic fatigue severity mean[2] **(C)** and global fatigue[3] **(D)** at baseline and follow-up for the INT (solid black line and open diamond) and CON (dashed line and black triangle) groups. Means ± normalised confidence intervals (CIs) are shown. There were no significant differences at baseline ($P \geq 0.159$) between groups. P values are displayed for significant day x group interaction effects. # denotes values are different pre-post within INT group ($P \leq 0.05$).
[1] scaled summaries from the SF-36 questionnaire (higher scores indicate a more favourable health state).
[2] arithmetic mean from 9-item FSS (7 point scale; 1 = strongly disagree, 7 = strongly agree). Higher scores indicate greater fatigue severity, with cut-scores over 4 indicative of significant fatigue [62].
[3] global fatigue from FSS (11 point visual analogue fatigue scale (VAFS); 0 = worst, 10 = normal).

Figure 3: Standardised effect sizes (Cohens *d*) (±90% CI) and magnitude based inferences for all health related quality of life outcomes.
[1] SF-36, [2] Fatigue severity scale, [3] Wheelchair user shoulder pain index.
‡ Direction of effect was reversed in the Figure for consistency. Arithmetic mean from 9-item FSS went down, which indicates reduced fatigue severity.
Abbreviations: CON, lifestyle maintenance control group; INT, upper-body exercise intervention; MCS, mental component summary; PCS, physical component summary, QALY, quality-adjusted life years.

Figure 1
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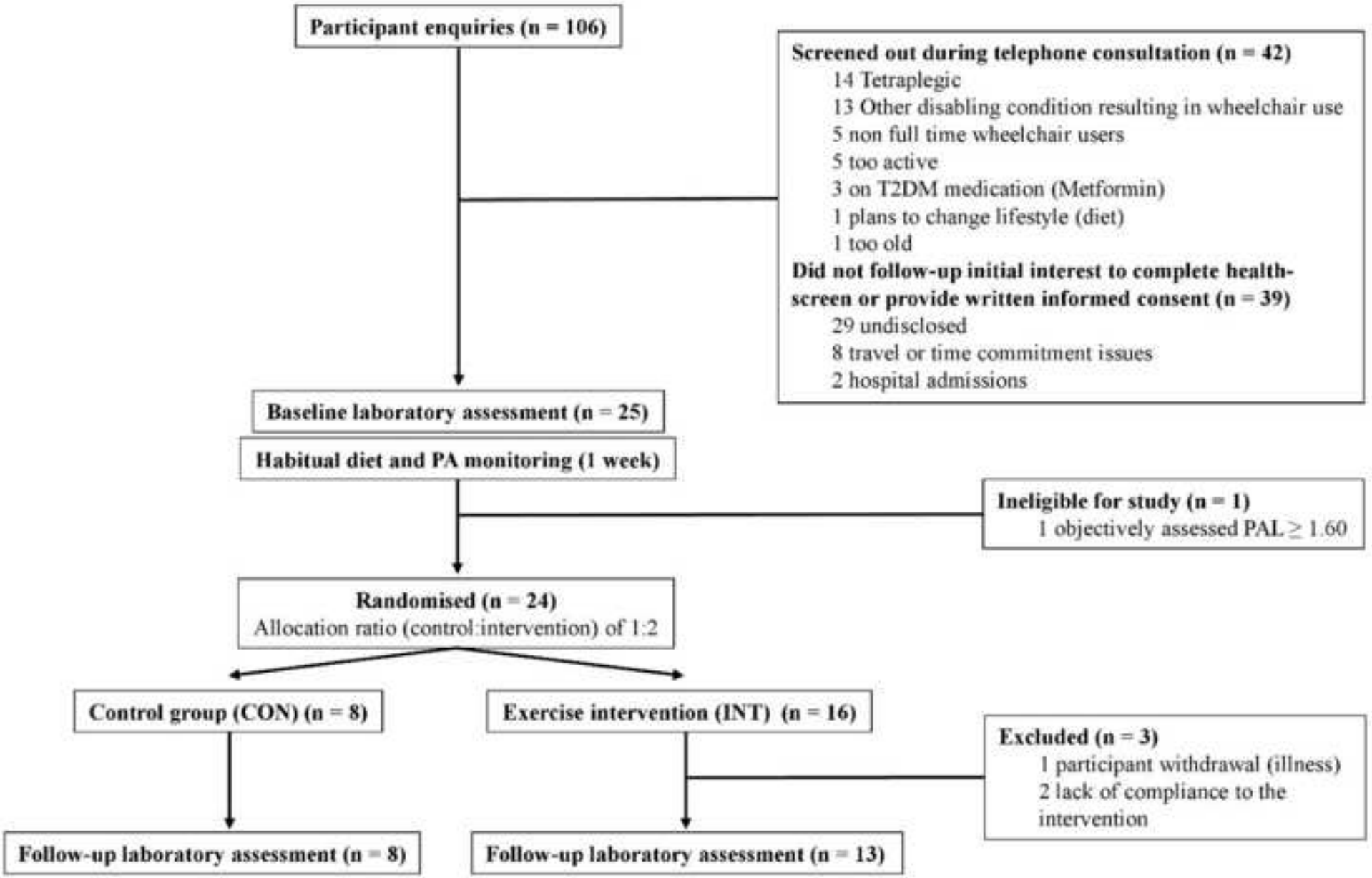

Figure 2

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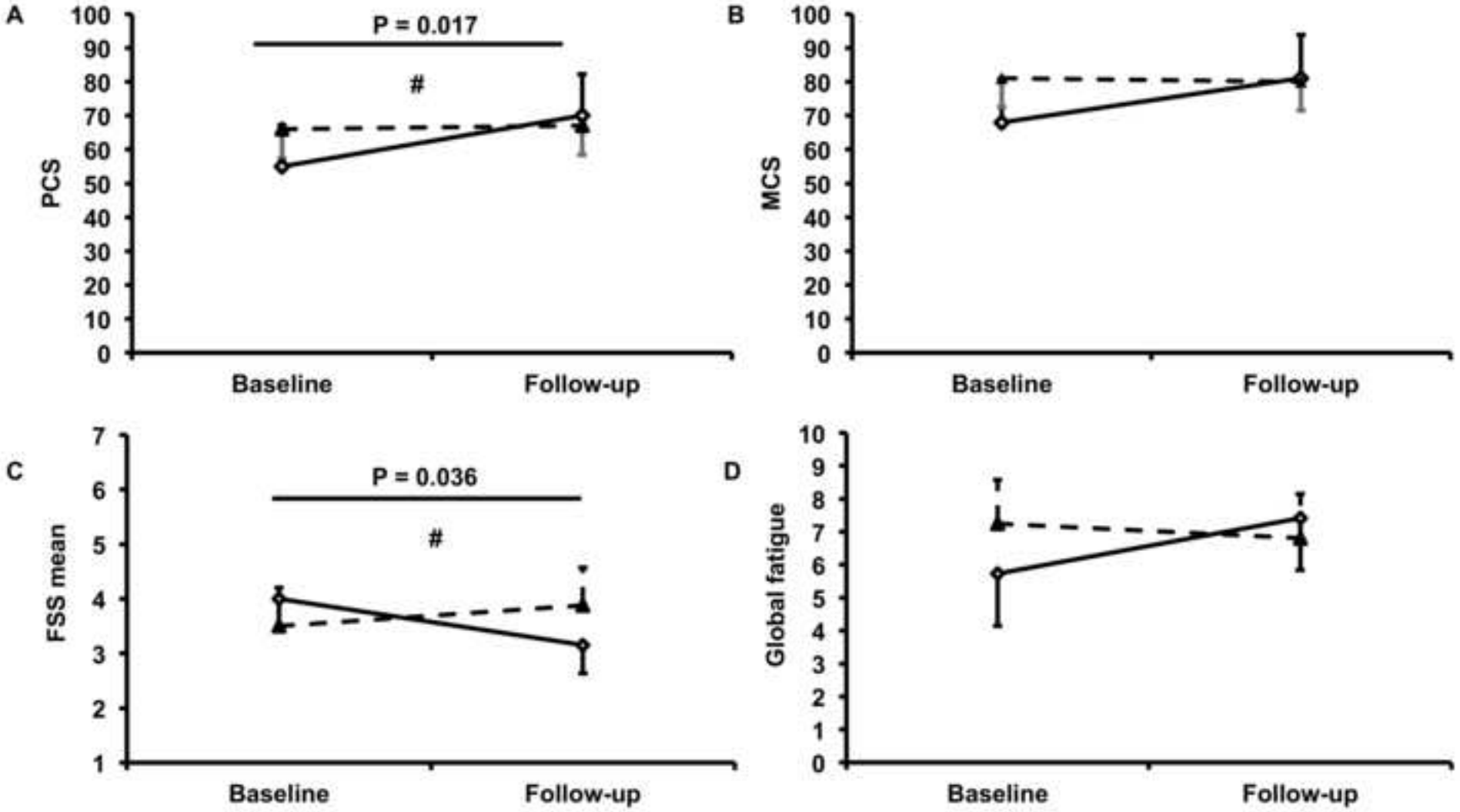

Figure 3

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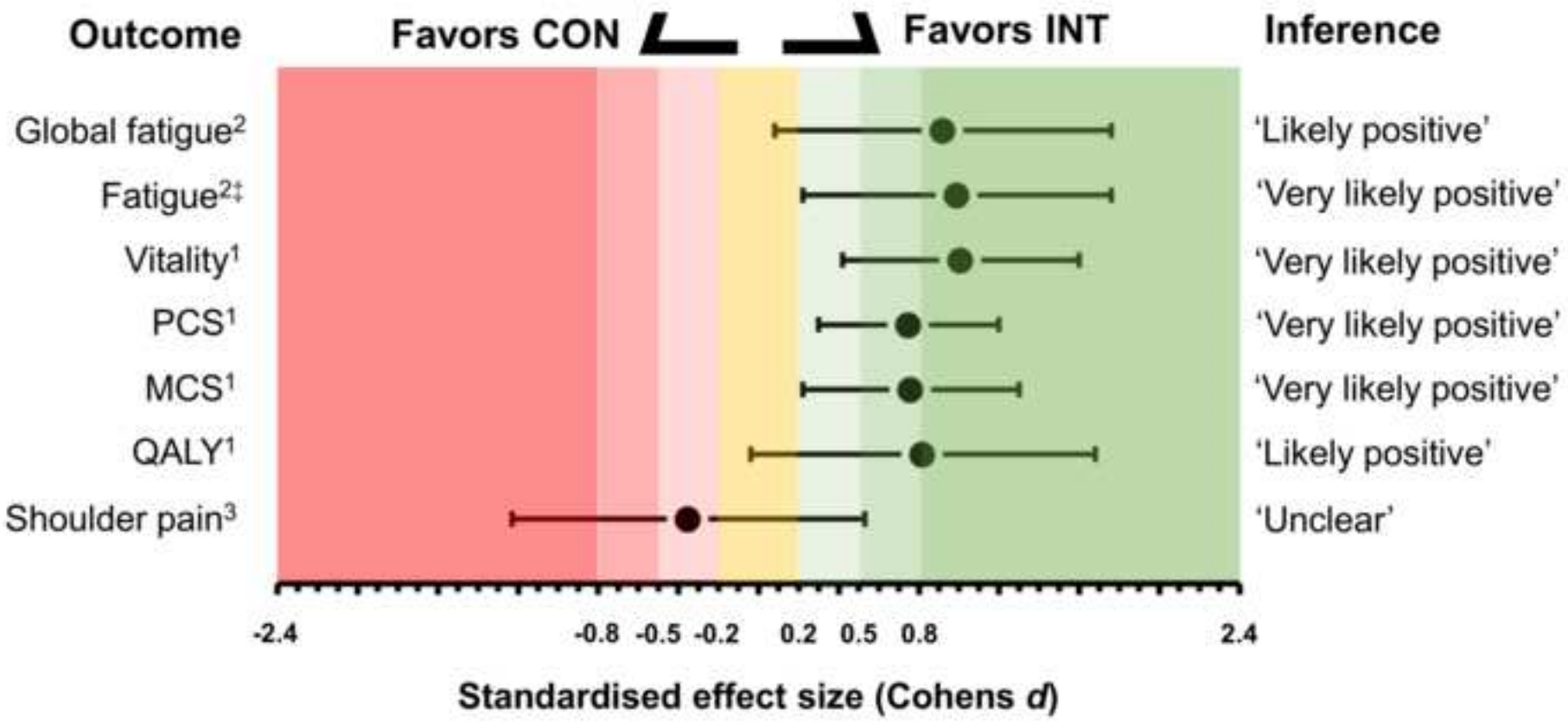

Table 1

Table 1. Changes in outcome measures in response to 6 weeks of lifestyle maintenance (CON) or moderate-intensity upper-body exercise (INT).

	CON (n = 8)			INT (n = 13)			Cohens *d* (90% CI)	Inference
	Baseline	Follow-up	Δ (90% CI)	Baseline	Follow-up	Δ (90% CI)		
Body mass (kg)	76.8 ± 11.3	76.1 ± 10.6	-0.7 (-1.9, 0.6)	76.8 ± 13.3	75.7 ± 13.8	-1.1 (-1.9, -0.2)	-0.03 (-0.15, 0.08)	*'Very likely trivial'*
PAEE (kcal·d^{-1})[1]	342 ± 171	340 ± 179	-2 (-21, 17)	**324 ± 161**	**433 ± 195#**	**109 (65, 153)**	**0.62 (0.36, 0.88)***	*'Very likely positive'*
MVPA (min·d^{-1})[1]	22 ± 30	19 ± 27	-3 (-7, 2)	**13 ± 13**	**30 ± 19#**	**17 (11, 23)**	**0.90 (0.56, 1.24)***	*'Most likely positive'*
$\dot{V}O_2$ peak (ml·kg^{-1}·min^{-1})	18.8 ± 6.2	18.3 ± 6.3	-0.5 (-1.0, 0.0)	**18.3 ± 4.9**	**21.7 ± 5.1#**	**3.4 (2.6, 4.1)**	**0.68 (0.48, 0.75)***	*'Most likely positive'*
Exercise self-efficacy	33 ± 5	29 ± 8	-4 (-9, 1)	**31 ± 4**	**35 ± 4#**	**4 (1, 7)**	**1.37 (0.41, 2.32)***	*'Very likely positive'*
PCS	66 ± 9	67 ± 11	1 (-4, 7)	**55 ± 20**	**70 ± 20#**	**15 (8, 21)**	**0.75 (0.30, 1.20)***	*Very likely positive'*
MCS	81 ± 12	80 ± 8	-1 (-6, 4)	68 ± 23	81 ± 19	13 (4, 22)	0.76 (0.21, 1.30)	*Very likely positive'*
QALY	0.741 ± 0.097	0.701 ± 0.076	-0.041 (-0.138, 0.056)	0.689 ± 0.128	0.747 ± 0.128	0.058 (0.016, 0.101)	0.82 (-0.04, 1.68)	*'Likely positive'*
FSS	3.5 ± 1.1	3.9 ± 1.4	0.4 (-0.1, 0.8)	**4.0 ± 1.1**	**3.2 ± 1.2#**	**-0.8 (-1.2, -0.3)**	**-0.99 (-1.75, -0.22)***	*'Very likely negative'*
Global fatigue	7.3 ± 1.7	6.8 ± 1.9	-0.5 (-1.8, 0.9)	5.7 ± 2.7	7.4 ± 2.2	1.7 (0.4, 3.0)	0.92 (0.08, 1.76)	*'Likely positive'*
WUSPI	19 ± 21	14 ± 15	-5 (-16, 6)	13 ± 11	13 ± 13	0 (-4, 4)	0.35 (-0.53, 1.24)	*'Unclear'*

*Values are means ± SD. Change scores (Δ) and standardised effect sizes are shown with 90% confidence intervals. None of the above variables differed significantly between groups at baseline (P ≥ 0.28). * denotes a day × group interaction (P ≤ 0.05) and # denotes values are different pre-post within INT group (P ≤ 0.05).*

[1] *CON (n = 7) and INT (n = 12). Missing data are the result of monitor failure.*

Abbreviations: FSS, fatigue severity scale; MCS, mental component summary; MVPA, moderate-to-vigorous physical activity (≥ 3.0 METs); PAEE, physical activity energy expenditure; PCS, physical component summary; QALY, quality adjusted life years; WUSPI, wheelchair user shoulder pain index.

Table 2. Pearson correlation coefficients between changes in (Δ) cardiorespiratory fitness, moderate-to-vigorous physical activity, exercise self-efficacy, SF-36 components, fatigue and shoulder pain from baseline to follow-up. Analyses are based on the treatment exposure analysis (n = 21).

Outcome	Δ $\dot{V}O_2$ peak ($ml \cdot kg^{-1} \cdot min^{-1}$)	Δ MVPA ($min \cdot day^{-1}$)	Δ Exercise self-efficacy[b]
Δ PCS	**0.52***	0.41	**0.62†**
Δ MCS[a]	**0.47***	0.40	**0.71†**
Δ QALY[b]	0.44	**0.50***	-0.17
Δ FSS	**-0.59†**	**-0.55***	**-0.71†**
Δ Global fatigue	**0.52***	0.22	**0.57†**
Δ WUSPI[b]	0.31	0.21	-0.02

Abbreviations: FSS, fatigue severity scale; MCS, mental component summary; MVPA, moderate-to-vigorous physical activity (≥ 3.0 METs); PCS, physical component summary; QALY, quality adjusted life years; WUSPI, wheelchair user shoulder pain index.

[a] *positively skewed so was log-transformed prior to parametric analysis.*

[b] *negatively skewed so was reflected prior to log-transformation*

** $P < 0.05$, † $P < 0.01$*

Supplementary Table 1. Changes in outcome measures in response to 6 weeks of lifestyle maintenance (CON) or moderate-intensity upper-body exercise (INT), including participants (n = 2) excluded from the main analysis due to non-compliance.

	CON (n = 8)			INT (n = 15)			Cohens *d* (90% CI)	Inference
	Baseline	Follow-up	Δ (90% CI)	Baseline	Follow-up	Δ (90% CI)		
Body mass (kg)	76.8 ± 11.3	76.1 ± 10.6	-0.7 (-1.9, 0.6)	78.0 ± 13.0	77.2 ± 13.5	-0.8 (-1.6, -0.1)	-0.02 (-0.13, 0.09)	*'Very likely trivial'*
PAEE (kcal·d^{-1})[1]	342 ± 171	340 ± 179	-2 (-21, 17)	**345 ± 171**	**439 ± 188#**	**94 (46, 142)**	**0.52 (0.25, 0.80)***	*'Very likely positive'*
MVPA (min·d^{-1})[1]	22 ± 30	19 ± 27	-3 (-7, 2)	**16 ± 15**	**31 ± 19#**	**15 (9, 22)**	**0.80 (0.45, 1.14)***	*'Most likely positive'*
$\dot{V}O_2$ peak (ml·kg^{-1}·min^{-1})	18.8 ± 6.2	18.3 ± 6.3	-0.5 (-1.0, 0.0)	**17.8 ± 4.9**	**20.7 ± 5.5#**	**2.9 (2.1, 3.8)**	**0.60 (0.44, 0.76)***	*'Most likely positive'*
Exercise self-efficacy	33 ± 5	29 ± 8	-4 (-9, 1)	**32 ± 5**	**35 ± 4#**	**3 (1, 6)**	**1.25 (0.32, 2.19)***	*'Very likely positive'*
PCS	66 ± 9	67 ± 11	1 (-4, 7)	60 ± 23	71 ± 19	11 (4, 18)	0.52 (0.05, 0.98)	*'Likely positive'*
MCS	81 ± 12	80 ± 8	-1 (-6, 4)	70 ± 23	82 ± 18	12 (4, 20)	0.72 (0.21, 1.22)	*'Very likely positive'*
QALY	0.741 ± 0.097	0.701 ± 0.076	-0.041 (-0.138, 0.056)	0.716 ± 0.130	0.754 ± 0.125	0.038 (-0.004, 0.08)	0.65 (-0.21, 1.51)	*'Unclear'*
FSS	3.5 ± 1.1	3.9 ± 1.4	0.4 (-0.1, 0.8)	**3.9 ± 1.2**	**3.1 ± 1.1#**	**-0.8 (-1.2, -0.3)**	**-0.92 (-1.54, -0.29)***	*'Very likely negative'*
Global fatigue	7.3 ± 1.7	6.8 ± 1.9	-0.5 (-1.8, 0.9)	6.0 ± 2.7	7.4 ± 2.3	1.4 (0.1, 2.6)	0.75 (-0.05, 1.55)	*'Likely positive'*
WUSPI	19 ± 21	14 ± 15	-5 (-16, 6)	11 ± 10	12 ± 12	1 (-3, 5)	0.44 (-0.49, 1.38)	*'Unclear'*

*Values are means ± SD. Change scores (Δ) and standardised effect sizes are shown with 90% confidence intervals. * denotes a day × group interaction (P ≤ 0.05) and # denotes values are different pre-post within INT group (P ≤ 0.05).*

[1] *CON (n = 7) and INT (n = 13). Missing data are the result of monitor failure and insufficient wear time criteria.*

Abbreviations: FSS, fatigue severity scale; MCS, mental component summary; MVPA, moderate-to-vigorous physical activity (≥ 3.0 METs); PAEE, physical activity energy expenditure; PCS, physical component summary; QALY, quality adjusted life years; WUSPI, wheelchair user shoulder pain index.

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CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5-6
	2b	Specific objectives or hypotheses	6
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6-7
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	9-10
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	10
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	7-8
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	7
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	7
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	NA

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	7
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	11-12
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	12
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	12
	13b	For each group, losses and exclusions after randomisation, together with reasons	12
Recruitment	14a	Dates defining the periods of recruitment and follow-up	12
	14b	Why the trial ended or was stopped	12
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	12, Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	12
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	12-13,Table 1
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	NA
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	14, Table 2
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	NA
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	19
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	20
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	19
Other information			
Registration	23	Registration number and name of trial registry	Title Page
Protocol	24	Where the full trial protocol can be accessed, if available	Ref 15
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Title Page

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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