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Running head: Reducing sitting time after stroke

Title: Reducing sitting time after stroke. A Phase II safety and feasibility randomised controlled trial.

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Preliminary data were presented as part of poster at the European Stroke Organisation Conference, Glasgow, United Kingdom, April 17-19 2015. Main results were presented at Stroke 2015 (a combined conference of the Stroke Society of Australasia and Smartstrokes NSW). Melbourne, Australia September 1-5 2015.

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There are no conflicts of interest to declare.

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Trial registration

The trial was registered with the Australian and New Zealand Trial Registry (ACTRN12612000958886).

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Abstract

Objective

To test the safety, feasibility and effectiveness of reducing sitting time in stroke survivors.

Design

Randomised controlled trial with attention-matched control and blinded assessments.

Setting

Community

Participants

Thirty-five stroke survivors (22 male, mean age 66.9 ± 12.7 years).

Interventions

Four counselling sessions over seven weeks with a message of 'sit less, move more' (intervention group) or 'calcium for bone health' (attention-matched control group).

Main outcome measures

Safety (adverse events, increases in pain, spasticity or fatigue) and feasibility (adherence to trial protocol). Secondary measures included time spent sitting (including in prolonged bouts ≥30mins), standing, and stepping as measured by the thigh-worn activPAL3 activity monitor (7 days, 24hrs/day protocol) and time spent in physical activity of at least moderate intensity as measured by the actigraph GT3x+. The Multi-Media Activity Recall for Children and Adults (MARCA) was used to describe changes in use-of-time.

Results

Thirty-three participants completed the full protocol. Four participants reported falls during the intervention period with no other adverse events. From a baseline average of 640.7 (SD 99.6) min/day, daily sitting time reduced on average by 30.0 (SD 50.6) min/day (95% CI 5.8 to 54.6) in the intervention group and 40.4 (SD 92.5) min/day in the control group (95% CI 13.0 to 93.8). Participants in both groups also reduced their time spent in prolonged sitting bouts (≥30 minutes) and increased time spent standing and stepping.

Conclusions

Our protocol was both safe and feasible. Participants in both groups spent less time sitting and more time standing and stepping post-intervention, but outcomes were not superior for intervention participants. Attention-matching is desirable in clinical trials, and may have contributed to the positive outcomes for control participants.

Key words:

stroke, sedentary behaviors**,** sitting time**,** physical activity, objective activity monitoring

Introduction

Between 1990 and 2010 worldwide prevalence rates for stroke increased by 84% (by 27% in high income countries), making stroke the third leading cause of disability. [1] Up to a third of people who survive a first stroke will suffer a recurrent stroke within five years, with this figure increasing to 43% for people surviving 10 years or more. [2] Both lack of adequate levels of physical activity and high sedentariness (i.e. too much sitting) in this population are likely contributing factors to recurrent stroke rates. Lack of adequate physical activity - less than 150 minutes a week of moderate to vigorous intensity physical activity (MVPA) - is the second highest population attributable risk factor for stroke, [3] while spending long periods of the day sitting down, particularly in long bouts of uninterrupted sitting, is an independent risk factor for cardiovascular disease morbidity and mortality in otherwise healthy adults, even after taking into account the time spent in moderate to vigorous intensity physical activity. [4, 5] Studies have shown that people with stroke are typically both highly sedentary and physically inactive, [6-11] placing them at the greatest risk of the consequences arising from these conditions. In a recently completed observational study utilising high precision activity monitors, people with stroke were more sedentary and less activity than age-matched controls, spending 75% of their waking hours sitting down each day and less than five minutes a day in MVPA. [6]

Experimental studies [12] and epidemiological studies [13] have shown that breaking up sitting time with periods of light intensity physical activity (such as walking at a comfortable pace) leads to reductions in cardiovascular disease risk factors [12] and mortality[13]. Therefore,

interventions aimed at reducing daily sitting time may be a promising new target for reducing recurrent stroke risk. However, there are many reasons why people with stroke spend long periods sitting down, including mobility impairments, post-stroke fatigue, pain and spasticity. This means that people with stroke may find it difficult to sit less each day. Furthermore, encouraging people with stroke to move more each day may lead to increased exposure to risk of falls.

The aim of this pilot randomised controlled trial was to assess the safety, feasibility and effectiveness of an intervention to reduce sitting time in people with stroke. Our primary hypotheses were that the intervention would be both safe (not lead to adverse events including falls, negative changes in pain, spasticity and fatigue) and feasible (have a high adherence to the measurement protocol, in particular activity monitor wear time). Our secondary hypotheses were that the intervention would lead to a reduction in sitting time, prolonged sitting time (bouts ≥30 min duration [14]and increases in standing and stepping time, as well as time spent in MVPA. We considered a 30-min/day reduction in sitting time as the minimal clinically important difference. In healthy, inactive adults, replacing one hour a day of self-reported sitting with light intensity activity has been linked to lower all-cause mortality[13]. As the dose-response relationship between sedentary physical activity and health is non-linear [13] it is possible that even smaller reductions in sitting time will have health benefits for people who are both more sedentary (spend more time sitting) and more inactive (spend less time in MVPA), particularly when measured accurately and objectively as opposed to self-report.

Method

This was a pilot randomised controlled trial with an attention-matched control group, concealed allocation and blinded assessment of outcome. The trial was registered with the Australian and New Zealand Trial Registry (xxxx). Participants were unaware of the intervention of interest. They were told only that this was a trial of 'healthy living after stroke'. A 1:1 randomisation sequence was prepared by a statistician independent of the project. A research assistant independent of the project prepared a set of sequentially numbered, opaque, sealed envelopes with the group allocation inside. Participants were recruited from outpatient clinics, databases of participants from previous trials, stroke exercise classes and social media. Research staff repeatedly visited outpatient clinics and stroke exercise classes to identify potential participants. Flyers were also placed in clinics, and frequent phone calls were made to therapy staff within these centres to assist in recruitment. A trained assessor who was unaware of group allocation assessed participants at baseline (pre-intervention) and post-intervention. Ethical approval was obtained from the relevant ethics committees and participants provided written, informed consent. As the primary outcomes were safety and feasibility, we did not power the trial to detect statistically significant changes in sitting time. Changes in sitting time were interpreted in light of what we considered the minimal clinically important difference in daily sitting time (30 min/day).[13]

Participants

We recruited people living at home after stroke. Inclusion criteria were: at least six months since last stroke (to minimise the impact of spontaneous neurological recovery after stroke); living at home for at least three months since last hospital discharge; some residual walking and/or balance deficits (self-reported); and, sufficient cognitive and language ability to provide informed consent and participate in the motivational interviewing sessions.

Intervention

Participants were randomly assigned to the intervention or control group. Participants in the intervention group received a series of four counselling sessions with the main message being to 'sit less and move more', with encouragement to regularly break up sitting time with short bursts of light intensity activity (standing, walking at a comfortable pace). Interventions specifically targeted at reducing sitting time have been found to be more effective than those aimed at general lifestyle advice, or advice to increase MVPA. [15] The counselling sessions were provided by two researchers (xx and xx) both of whom were formally trained in motivational interviewing techniques through accredited courses. Motivational interviewing is a form of goal-directed counselling that aims to strengthen a person's own motivation and commitment to change and is particularly effective in eliciting behaviour change for people who are reluctant or ambivalent about change. [16] The first session was provided face-to-face in the participant's home. At this first session, participants were presented with an individualised written report which provided feedback regarding daily sedentary time and breaks in sedentary time based on the baseline hip-worn accelerometer data (see below). This report was used as the starting point for discussions. The counselling sessions used key

motivational interviewing techniques (decisional balance sheets, importance and confidence rulers) to initiate and reinforce change talk. Action plans, goals and strategies were elicited from the participants, rather than imposed by the counsellors. Follow-up counselling sessions were delivered by phone and occurred one, three and seven weeks after the initial session. We chose to deliver the intervention via a face-to-face home visit and follow-up telephone calls, rather than in groups to avoid transport being a barrier to participation. [17] In order to match the groups for attention, control group participants received the same schedule of interviews, with a placebo message of increasing calcium for bone health. Data from a food frequency questionnaire were used to create personalised feedback for control participants.[18] The food frequency questionnaire was used to reinforce the credibility of the attention-matched control group and data were not analysed.

Outcome measures

Baseline measures were collected at the first face-to-face appointment and included stroke type (Oxfordshire Stroke Classification [19]), stroke severity (National Institutes of Stroke Scale, score 0 to 42 with higher scores indicating more severe stroke) side of stroke, height, weight, walking speed (self-selected, measured over the middle 5 m of a 9 m walkway), use of walking aids, living arrangements (alone/with spouse), degree of independence in activities of daily living (self-reported as independent or requiring some assistance in daily tasks such as showering, dressing and cooking), and cognitive function (Montreal Cognitive Assessment, score range 0 to 30, scores <22 indicate cognitive dysfunction [20]). All participants completed a food frequency questionnaire. [18] At this appointment, participants

were fitted with three activity monitors and provided with instructions regarding keeping diaries of sleep/wake time and when monitors should be removed. Participants wore all three monitors for seven days at baseline and again one week after the final counselling session (post-intervention).

Safety was assessed by recording changes in self-reported pain and spasticity (visual analogue scale, anchored at 0 [no pain/spasticity] and 10 [severe pain/spasticity]), and fatigue (Checklist Individual Strength, score 8 to 56, higher scores indicating greater fatigue symptoms [21]). Falls incidence and any other adverse events were ascertained by asking structured questions ("have you fallen or tripped over in the last 2 months") at each assessment point. While simple recall of falls can underestimate falls incidence, it does not underestimate injurious falls (specificity 87-100%) [22].

Feasibility was assessed via adherence to counselling sessions (actively engaged in all scheduled counselling sessions) and completion of all assessments at baseline and post-intervention, including activity monitor wear time.

Time spent sitting, standing and stepping was measured using the activPAL3 device (PAL Technologies Ltd), which was waterproofed and attached to the participants' anterior thigh on the non-hemiparetic leg. Participants wore this monitor continuously (24 hours/day) for seven days including during showering/bathing and water-based activities. The activPAL3 contains an inclinometer and a tri-axial accelerometer. In studies of both healthy adults and people with stroke it has been shown to be 99-100% accurate in classifying sitting/lying and standing postures [23, 24] The activPAL3 data were processed using activPAL3 software (version 7.2.32). Sleep/wake diaries were entered into a Microsoft Access database. A

189 custom built SAS program linked activPAL3 data to the sleep wake diaries to identify and
190 remove sleep and non-wear time. This program also identified periods of prolonged,
191 uninterrupted sitting of ≥ 30 minutes duration.

192

193 *Physical activity* was measured using the Actigraph GT3+ triaxial accelerometer, which was
194 worn on an elastic waist belt and positioned over the non-hemiparetic hip. Participants were
195 asked to wear the monitor 24 hours a day for seven days, removing it for showering/bathing
196 or any other water-based activities. Participants also wore the Sensewear arm band around
197 their non-hemiparetic upper arm. In this trial, the Sensewear arm band was used purely to
198 determine non-wear time for the Actigraph. As the Sensewear arm band switches off when
199 not in contact with the skin and also had to be removed for water-based activities, we made
200 the assumption (backed up by review of participant diaries) that the Actigraph and Sensewear
201 monitors were always removed at the same time. Actigraph data were processed by Actilife
202 software (version 6.3.2), and periods of sleep (matched to activPAL data) and non-wear (as
203 detected by the Sensewear arm band) were removed using custom filters. In line with the
204 most commonly used cut-points for classification of activity intensity of older adults [25]
205 activity of at least moderate intensity was defined as ≥1952 counts per minute. [26]

206

207 *Use of time* was measured using the Multimedia Activity Recall for Children and Adults
208 (MARCA) [27] This computerised use of time tool asks participants to recall their previous day
209 from midnight to midnight and classifies activities according to a pre-determined list of 520
210 separate items. Activities are then classified into time spent in various 'superdomains' such as
211 transport, screen time and chores. The superdomains are further categorised into 'macro-
212 domains', for example active and passive transport, computer and TV time. Participants were

phoned at a pre-determined time during the week they were wearing the monitors at baseline, and post-intervention and the MARCA was administered by interview, which took approximately 20 minutes. In a previous observational study, agreement between repeated administration of the MARCA on the same day, ranged from 0.834 (95% confidence interval [C] 0.681 to 0.918) and 0.946 (95% CI 0.890 to 0.974) for the different MARCA superdomains [6] The MARCA has been validated against doubly-labelled water in young adults, with a correlation of r = 0.70 for daily energy expenditure. [28]

Statistical Analyses

Paired t-tests (or Wilcoxon Signed Rank tests where data were not normally distributed) were used to examine within group differences between baseline and post-intervention in safety and feasibility measures (pain, spasticity, fatigue, monitor wear-time and falls). To adjust for waking hours, activPAL3 and Actigraph derived activity variables (time spent in sitting, prolonged sitting, standing, stepping and MVPA) were standardised to a 16-hour/day waking wear time period. Paired t-tests (or Wilcoxon Signed Rank tests where data were not normally distributed) were used to examine within group differences between baseline and post-intervention in activity variables. Univariate analyses of variance (with adjustment for multiple comparisons) were used to examine between group differences in change scores (post-intervention minus baseline) in time spent sitting, standing, stepping and in MVPA. Independent t-tests were used to examine between group differences in MARCA-derived variables between intervention and control groups. Sequential Bonferroni corrections were applied to account for multiple comparisons. All analyses were by intention to treat.

Results

Participants were recruited between February 2013 and February 2014 with final data collected in May 2014. Figure 1 presents the flow of participants through the trial. Table 1 presents baseline characteristics of the 35 participants. Four (n=2 intervention and n=2 control) participants reported falls during the intervention period. None of the falls were injurious. There were no other adverse events reported. Pain, spasticity and fatigue did not change between baseline and post-intervention for either group (Table 2). Compliance with wearing the activity monitors was high. At baseline n=23 and n=31 participants had seven days of valid data from the activPAL3 and the GT3x+ monitors respectively. All other participants had at least four days of wear time for both monitors, with the exception of three participants for whom the GT3x+ monitor did not record any valid data on any days. At post-intervention, n=33 and n=25 had seven days of valid data from the activPAL3 and the GT3x+ monitors respectively. All other participants had at least four valid wear days for both the activPAL3 and GT3x+ monitors, with the following exceptions; two participants (both in the control group) did not complete the post-intervention assessment for reasons of ill health not related to the trial, and a further three participants did not have any valid wear days for the GT3x+ monitor. Table 2 presents average wear days and monitored hours for all participants. There was 100% compliance with counselling sessions – that is all participants engaged in all scheduled counselling sessions.

At baseline participants spent an average of 640.7 (SD 99.6) min/day sitting, 436.2 (SD147.0) min/day in prolonged sitting (un-interrupted sitting bouts of ≥30 mins), 153.6 (SD 63.9) min/day standing, 59.3 (SD 36.8) min/day stepping and 7.4 (SD 8.6) min/day in MVPA. Table 3 presents baseline and follow-up values for intervention and control groups (unadjusted for wear-time). Table 4 presents data standardised to a 16-hour waking wear time, including within-group and between group effects. Here, daily sitting time reduced on average by 30.0 (SD 50.6) min/day (95% CI 5.8 to 54.6) in the intervention group and 40.4 (SD 92.5) min/day (95% CI 13.0 to 93.8) in the control group. Prolonged sitting time reduced on average by 36.1 ± 65.0 min/day (95% CI 4.8 to 67.5) in the intervention group and 44.2 ± 134.2 min/day (95% CI 33.3 to 121.7) in the control group. Reductions in sitting time were replaced with increases in time spent standing (intervention 22.5 [SD 35.5] min/day, control 33.8 [SD 59.0] min/day) and stepping (intervention 7.8 [SD 19.2] min/day, control 6.6 [SD 9.9] min/day). No differences were statistically significant following sequential Bonferroni adjustments. On average, both intervention and control group participants exceeded the target of reducing sitting time by at least 30 min/day, with effect sizes of 0.62 and 0.46 respectively. At less than 10 min/day, average time spent in MVPA (GT3X+ data) remained very low for all participants at baseline and post-intervention. Regarding reported use of time (MARCA data), participants reported reductions in sedentary activities, in particular TV viewing (-46 min/day and -38 min/day for the intervention and control groups respectively), but there were no significant between group differences in any of the domains (Table 5).

Discussion

Stroke survivors are both sedentary (spending large proportions of their day sitting down), and physically inactive. Previous research has largely focused on encouraging stroke survivors to increase their time in physical activity of at least moderate intensity. This is the first clinical trial to investigate an intervention aimed at encouraging stroke survivors to replace sitting time with light intensity activity – i.e. 'sit less and move more'. Our protocol was both safe and feasible, with no adverse events (apart from four non-injurious falls, two in the control and two in the intervention group) and high compliance. On average, participants in both groups reduced their sitting time by at least 30 min/day and replaced sitting time with standing and stepping. However, there was considerable intra-individual variability in the magnitude of change, and, participants in the intervention group did not show superior outcomes relative to the control group.

The trial was not powered to detect statistically significant intervention effects. However, the attention-matched control group may have played a role in the lack of between group differences. Participants in the control arm of the trial received the same number of counselling sessions as intervention participants. In an attempt to further reduce bias, participants were unaware of the intervention of interest; they were told the trial was about 'healthy living after stroke', and that they would receive counselling based on either diet or exercise. While the content of the counselling sessions in the control group focussed on a dietary message, anecdotally many participants reported changing physical activity habits, for example going for more regular walks or recommencing gym programs. The activity monitors worn by all participants did not provide any real-time feedback, however, it is possible that they could have impacted on activity levels in all participants. Determining the key active elements in any intervention is important.

Currently, the evidence for the effectiveness of behaviour change interventions and self-management programs for increasing physical activity in people with stroke is limited. [29] Very few high quality trials have been conducted to date, and there is little similarity in the content of the interventions delivered. [29] We chose to use a motivational interviewing intervention to target behaviour change in this study. While one previous study found this approach to be effective in increasing physical activity in people after stroke,[30] more high quality trials are needed to evaluate the relative effectiveness of different behaviour change interventions for people with stroke.

The barriers for people with stroke to exercise regularly at moderate intensity are often insurmountable,[17, 31] and efforts to address this have been largely ineffective. [32, 33] Reducing daily sitting time may be a more achievable target with significant health benefits. We recently modelled the impact of replacing sitting with standing or stepping time or both, using accelerometer (activPAL3) based measures of sitting time in a large sample of healthy adults [34]. Replacing two hour/day of sitting with either standing or stepping was associated with important reductions in cardiovascular disease risk.[34] Furthermore, experimental work in healthy adults has demonstrated that reductions in sitting time leads to clinically worthwhile reductions in cardiovascular disease risk factors such as improved glucose metabolism, reduced insulin resistance and decreased blood pressure, at least in the short term. [12, 35]However, the longer term benefits of changes in sitting time are not known.

Limitations

The lack of difference between intervention and control participants suggests the intervention requires development. We did not formally evaluate the degree to which our intervention adhered to motivational interviewing principles, or if there were any differences related to the two individual counsellors delivering the intervention. This may also have contributed to the fact that the intervention expected to change behaviour the most, was not more effective. Furthermore, seasonal variations in habitual physical activity levels have also been well documented [36]and may have played a role in this trial as data were collected across an 15-month time period. While both modelling of epidemiological data [13] and experimental work[12] suggest that changes in sitting time may lead to clinically meaningful reductions in cardiovascular disease risk, this requires testing in large-scale clinical trials. The study was not powered to detect a difference in safety measures between groups, and therefore we cannot exclude the possibility of modest harms. Future trials should carefully monitor fall rates and fear of falling. Accelerometers such as the Actigraph GT3x+ tend to underestimate step counts in people with slow walking speeds. [37] This may have affected the accuracy of the absolute values of physical activity in some of our participants, but is not likely to have affected estimations of change over time. Finally, while all participants self-reported they had residual walking or balance deficits, 17% of participants recorded no symptoms on the National Health Institute of Stroke Severity Scale indicating minimal to no disability.

Conclusion

This is the first clinical trial to demonstrate that it is possible for people with stroke to sit less each day. We have demonstrated that the clinical trial protocol is both safe and feasible and leads to reductions in daily sitting time. However, the health benefits associated with sitting less each day remain unclear.

Suppliers

PAL Technologies Ltd. 50 Richmond St Glasgow G1 1XP, Scotland, United Kingdom (activPAL monitors).

Actigraph LLC. 49 E Chase Street Pensacola, Florida 32502, United States of America (GT3x+ monitors).

Temple Healthcare Pty Ltd. PO Box 299 Bowral 2576, New South Wales, Australia (sensewear am band monitors).

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Running head: Reducing sitting time after stroke

Title: Reducing sitting time after stroke. A Phase II safety and feasibility randomised controlled trial.

Abstract

Objective

To test the safety, feasibility and effectiveness of reducing sitting time in stroke survivors.

Design

Randomised controlled trial with attention-matched control and blinded assessments.

Setting

Community

Participants

Thirty-five stroke survivors (22 male, mean age 66.9 ± 12.7 years).

Interventions

Four counselling sessions over seven weeks with a message of 'sit less, move more' (intervention group) or 'calcium for bone health' (attention-matched control group).

Main outcome measures

Safety (adverse events, increases in pain, spasticity or fatigue) and feasibility (adherence to trial protocol). Secondary measures included time spent sitting (including in prolonged bouts ≥30mins), standing, and stepping as measured by the thigh-worn activPAL3 activity monitor (7 days, 24hrs/day protocol) and time spent in physical activity of at least moderate intensity as measured by the actigraph GT3x+. The Multi-Media Activity Recall for Children and Adults (MARCA) was used to describe changes in use-of-time.

Results

Thirty-three participants completed the full protocol. Four participants reported falls during the intervention period with no other adverse events. From a baseline average of 640.7 (SD 99.6) min/day, daily sitting time reduced on average by 30.0 (SD 50.6) min/day (95% CI 5.8 to 54.6) in the intervention group and 40.4 (SD 92.5) min/day in the control group (95% CI 13.0 to 93.8). Participants in both groups also reduced their time spent in prolonged sitting bouts (≥30 minutes) and increased time spent standing and stepping.

Conclusions

Our protocol was both safe and feasible. Participants in both groups spent less time sitting and more time standing and stepping post-intervention, but outcomes were not superior for intervention participants. Attention-matching is desirable in clinical trials, and may have contributed to the positive outcomes for control participants.

Key words:

stroke, sedentary behaviors**,** sitting time**,** physical activity, objective activity monitoring

Introduction

Between 1990 and 2010 worldwide prevalence rates for stroke increased by 84% (by 27% in high income countries), making stroke the third leading cause of disability. [1] Up to a third of people who survive a first stroke will suffer a recurrent stroke within five years, with this figure increasing to 43% for people surviving 10 years or more. [2] Both lack of adequate levels of physical activity and high sedentariness (i.e. too much sitting) in this population are likely contributing factors to recurrent stroke rates. Lack of adequate physical activity - less than 150 minutes a week of moderate to vigorous intensity physical activity (MVPA) - is the second highest population attributable risk factor for stroke, [3] while spending long periods of the day sitting down, particularly in long bouts of uninterrupted sitting, is an independent risk factor for cardiovascular disease morbidity and mortality in otherwise healthy adults, even after taking into account the time spent in moderate to vigorous intensity physical activity. [4, 5] Studies have shown that people with stroke are typically both highly sedentary and physically inactive, [6-11] placing them at the greatest risk of the consequences arising from these conditions. In a recently completed observational study utilising high precision activity monitors, people with stroke were more sedentary and less activity than age-matched controls, spending 75% of their waking hours sitting down each day and less than five minutes a day in MVPA. [6]

Experimental studies [12] and epidemiological studies [13] have shown that breaking up sitting time with periods of light intensity physical activity (such as walking at a

comfortable pace) leads to reductions in cardiovascular disease risk factors [12] and mortality[13]. Therefore, interventions aimed at reducing daily sitting time may be a promising new target for reducing recurrent stroke risk. However, there are many reasons why people with stroke spend long periods sitting down, including mobility impairments, post-stroke fatigue, pain and spasticity. This means that people with stroke may find it difficult to sit less each day. Furthermore, encouraging people with stroke to move more each day may lead to increased exposure to risk of falls.

The aim of this pilot randomised controlled trial was to assess the safety, feasibility and effectiveness of an intervention to reduce sitting time in people with stroke. Our primary hypotheses were that the intervention would be both safe (not lead to adverse events including falls, negative changes in pain, spasticity and fatigue) and feasible (have a high adherence to the measurement protocol, in particular activity monitor wear time). Our secondary hypotheses were that the intervention would lead to a reduction in sitting time, prolonged sitting time (bouts ≥30 min duration [14]and increases in standing and stepping time, as well as time spent in MVPA. We considered a 30-min/day reduction in sitting time as the minimal clinically important difference. In healthy, inactive adults, replacing one hour a day of self-reported sitting with light intensity activity has been linked to lower all-cause mortality[13]. As the dose-response relationship between sedentary physical activity and health is non-linear [13] it is possible that even smaller reductions in sitting time will have health benefits for people who are both more sedentary (spend more time sitting) and more inactive (spend less time in MVPA), particularly when measured accurately and objectively as opposed to self-report.

Method

This was a pilot randomised controlled trial with an attention-matched control group, concealed allocation and blinded assessment of outcome. The trial was registered with the Australian and New Zealand Trial Registry (xxxx). Participants were unaware of the intervention of interest. They were told only that this was a trial of 'healthy living after stroke'. A 1:1 randomisation sequence was prepared by a statistician independent of the project. A research assistant independent of the project prepared a set of sequentially numbered, opaque, sealed envelopes with the group allocation inside. Participants were recruited from outpatient clinics, databases of participants from previous trials, stroke exercise classes and social media. Research staff repeatedly visited outpatient clinics and stroke exercise classes to identify potential participants. Flyers were also placed in clinics, and frequent phone calls were made to therapy staff within these centres to assist in recruitment. A trained assessor who was unaware of group allocation assessed participants at baseline (pre-intervention) and post-intervention. Ethical approval was obtained from the relevant ethics committees and participants provided written, informed consent. As the primary outcomes were safety and feasibility, we did not power the trial to detect statistically significant changes in sitting time. Changes in sitting time were interpreted in light of what we considered the minimal clinically important difference in daily sitting time (30 min/day).[13]

Participants

We recruited people living at home after stroke. Inclusion criteria were: at least six months since last stroke (to minimise the impact of spontaneous neurological recovery after stroke); living at home for at least three months since last hospital discharge; some residual walking and/or balance deficits (self-reported); and, sufficient cognitive and language ability to provide informed consent and participate in the motivational interviewing sessions.

Intervention

Participants were randomly assigned to the intervention or control group. Participants in the intervention group received a series of four counselling sessions with the main message being to 'sit less and move more', with encouragement to regularly break up sitting time with short bursts of light intensity activity (standing, walking at a comfortable pace). Interventions specifically targeted at reducing sitting time have been found to be more effective than those aimed at general lifestyle advice, or advice to increase MVPA. [15] The counselling sessions were provided by two researchers (xx and xx) both of whom were formally trained in motivational interviewing techniques through accredited courses. Motivational interviewing is a form of goal-directed counselling that aims to strengthen a person's own motivation and commitment to change and is particularly effective in eliciting behaviour change for people who are reluctant or ambivalent about change. [16] The first session was provided face-to-face in

the participant's home. At this first session, participants were presented with an individualised written report which provided feedback regarding daily sedentary time and breaks in sedentary time based on the baseline hip-worn accelerometer data (see below). This report was used as the starting point for discussions. The counselling sessions used key motivational interviewing techniques (decisional balance sheets, importance and confidence rulers) to initiate and reinforce change talk. Action plans, goals and strategies were elicited from the participants, rather than imposed by the counsellors. Follow-up counselling sessions were delivered by phone and occurred one, three and seven weeks after the initial session. We chose to deliver the intervention via a face-to-face home visit and follow-up telephone calls, rather than in groups to avoid transport being a barrier to participation. [17] In order to match the groups for attention, control group participants received the same schedule of interviews, with a placebo message of increasing calcium for bone health. Data from a food frequency questionnaire were used to create personalised feedback for control participants.[18] The food frequency questionnaire was used to reinforce the credibility of the attention-matched control group and data were not analysed.

Outcome measures

Baseline measures were collected at the first face-to-face appointment and included stroke type (Oxfordshire Stroke Classification [19]), stroke severity (National Institutes of Stroke Scale, score 0 to 42 with higher scores indicating more severe stroke) side of stroke, height, weight, walking speed (self-selected, measured over the middle 5 m

of a 9 m walkway), use of walking aids, living arrangements (alone/with spouse), degree of independence in activities of daily living (self-reported as independent or requiring some assistance in daily tasks such as showering, dressing and cooking), and cognitive function (Montreal Cognitive Assessment, score range 0 to 30, scores <22 indicate cognitive dysfunction [20]). All participants completed a food frequency questionnaire. [18] At this appointment, participants were fitted with three activity monitors and provided with instructions regarding keeping diaries of sleep/wake time and when monitors should be removed. Participants wore all three monitors for seven days at baseline and again one week after the final counselling session (post-intervention).

Safety was assessed by recording changes in self-reported pain and spasticity (visual analogue scale, anchored at 0 [no pain/spasticity] and 10 [severe pain/spasticity]), and fatigue (Checklist Individual Strength, score 8 to 56, higher scores indicating greater fatigue symptoms [21]). Falls incidence and any other adverse events were ascertained by asking structured questions ("have you fallen or tripped over in the last 2 months") at each assessment point. While simple recall of falls can underestimate falls incidence, it does not underestimate injurious falls (specificity 87-100%) [22].

Feasibility was assessed via adherence to counselling sessions (actively engaged in all scheduled counselling sessions) and completion of all assessments at baseline and post-intervention, including activity monitor wear time.

Time spent sitting, standing and stepping was measured using the activPAL3 device (PAL Technologies Ltd), which was waterproofed and attached to the participants'

anterior thigh on the non-hemiparetic leg. Participants wore this monitor continuously (24 hours/day) for seven days including during showering/bathing and water-based activities. The activPAL3 contains an inclinometer and a tri-axial accelerometer. In studies of both healthy adults and people with stroke it has been shown to be 99-100% accurate in classifying sitting/lying and standing postures [23, 24] The activPAL3 data were processed using activPAL3 software (version 7.2.32). Sleep/wake diaries were entered into a Microsoft Access database. A custom built SAS program linked activPAL3 data to the sleep wake diaries to identify and remove sleep and non-wear time. This program also identified periods of prolonged, uninterrupted sitting of ≥ 30 minutes duration.

Physical activity was measured using the Actigraph GT3+ triaxial accelerometer, which was worn on an elastic waist belt and positioned over the non-hemiparetic hip. Participants were asked to wear the monitor 24 hours a day for seven days, removing it for showering/bathing or any other water-based activities. Participants also wore the Sensewear arm band around their non-hemiparetic upper arm. In this trial, the Sensewear arm band was used purely to determine non-wear time for the Actigraph. As the Sensewear arm band switches off when not in contact with the skin and also had to be removed for water-based activities, we made the assumption (backed up by review of participant diaries) that the Actigraph and Sensewear monitors were always removed at the same time. Actigraph data were processed by Actilife software (version 6.3.2), and periods of sleep (matched to activPAL data) and non-wear (as detected by the Sensewear arm band) were removed using custom filters. In line with the most commonly used cut-points for classification of activity intensity of older

adults [25] activity of at least moderate intensity was defined as ≥1952 counts per minute. [26]

Use of time was measured using the Multimedia Activity Recall for Children and Adults (MARCA) [27] This computerised use of time tool asks participants to recall their previous day from midnight to midnight and classifies activities according to a pre-determined list of 520 separate items. Activities are then classified into time spent in various 'superdomains' such as transport, screen time and chores. The superdomains are further categorised into 'macro-domains', for example active and passive transport, computer and TV time. Participants were phoned at a pre-determined time during the week they were wearing the monitors at baseline, and post-intervention and the MARCA was administered by interview, which took approximately 20 minutes. In a previous observational study, agreement between repeated administration of the MARCA on the same day, ranged from 0.834 (95% confidence interval [C] 0.681 to 0.918) and 0.946 (95% CI 0.890 to 0.974) for the different MARCA superdomains [6] The MARCA has been validated against doubly-labelled water in young adults, with a correlation of r = 0.70 for daily energy expenditure. [28]

Statistical Analyses

Paired t-tests (or Wilcoxon Signed Rank tests where data were not normally distributed) were used to examine within group differences between baseline and

post-intervention in safety and feasibility measures (pain, spasticity, fatigue, monitor wear-time and falls). To adjust for waking hours, activPAL3 and Actigraph derived activity variables (time spent in sitting, prolonged sitting, standing, stepping and MVPA) were standardised to a 16-hour/day waking wear time period. Paired t-tests (or Wilcoxon Signed Rank tests where data were not normally distributed) were used to examine within group differences between baseline and post-intervention in activity variables. Univariate analyses of variance (with adjustment for multiple comparisons) were used to examine between group differences in change scores (post-intervention minus baseline) in time spent sitting, standing, stepping and in MVPA. Independent t-tests were used to examine between group differences in MARCA-derived variables between intervention and control groups. Sequential Bonferroni corrections were applied to account for multiple comparisons. All analyses were by intention to treat.

Results

Participants were recruited between February 2013 and February 2014 with final data collected in May 2014. Figure 1 presents the flow of participants through the trial. Table 1 presents baseline characteristics of the 35 participants. Four (n=2 intervention and n=2 control) participants reported falls during the intervention period. None of the falls were injurious. There were no other adverse events reported. Pain, spasticity and fatigue did not change between baseline and post-intervention for either group (Table 2). Compliance with wearing the activity monitors was high. At baseline n=23 and

n=31 participants had seven days of valid data from the activPAL3 and the GT3x+ monitors respectively. All other participants had at least four days of wear time for both monitors, with the exception of three participants for whom the GT3x+ monitor did not record any valid data on any days. At post-intervention, n=33 and n=25 had seven days of valid data from the activPAL3 and the GT3x+ monitors respectively. All other participants had at least four valid wear days for both the activPAL3 and GT3x+ monitors, with the following exceptions; two participants (both in the control group) did not complete the post-intervention assessment for reasons of ill health not related to the trial, and a further three participants did not have any valid wear days for the GT3x+ monitor. Table 2 presents average wear days and monitored hours for all participants. There was 100% compliance with counselling sessions – that is all participants engaged in all scheduled counselling sessions.

At baseline participants spent an average of 640.7 (SD 99.6) min/day sitting, 436.2 (SD147.0) min/day in prolonged sitting (un-interrupted sitting bouts of ≥30 mins), 153.6 (SD 63.9) min/day standing, 59.3 (SD 36.8) min/day stepping and 7.4 (SD 8.6) min/day in MVPA. Table 3 presents baseline and follow-up values for intervention and control groups (unadjusted for wear-time). Table 4 presents data standardised to a 16-hour waking wear time, including within-group and between group effects. Here, daily sitting time reduced on average by 30.0 (SD 50.6) min/day (95% CI 5.8 to 54.6) in the intervention group and 40.4 (SD 92.5) min/day (95% CI 13.0 to 93.8) in the control group. Prolonged sitting time reduced on average by 36.1 ± 65.0 min/day (95% CI 4.8 to 67.5) in the intervention group and 44.2 ± 134.2 min/day (95% CI 33.3 to 121.7) in the control group. Reductions in sitting time were replaced with increases in time spent standing (intervention 22.5 [SD 35.5] min/day, control 33.8

[SD 59.0] min/day) and stepping (intervention 7.8 [SD 19.2] min/day, control 6.6 [SD 9.9] min/day). No differences were statistically significant following sequential Bonferroni adjustments. On average, both intervention and control group participants exceeded the target of reducing sitting time by at least 30 min/day, with effect sizes of 0.62 and 0.46 respectively. At less than 10 min/day, average time spent in MVPA (GT3X+ data) remained very low for all participants at baseline and post-intervention. Regarding reported use of time (MARCA data), participants reported reductions in sedentary activities, in particular TV viewing (-46 min/day and -38 min/day for the intervention and control groups respectively), but there were no significant between group differences in any of the domains (Table 5).

Discussion

Stroke survivors are both sedentary (spending large proportions of their day sitting down), and physically inactive. Previous research has largely focused on encouraging stroke survivors to increase their time in physical activity of at least moderate intensity. This is the first clinical trial to investigate an intervention aimed at encouraging stroke survivors to replace sitting time with light intensity activity – i.e. 'sit less and move more'. Our protocol was both safe and feasible, with no adverse events (apart from four non-injurious falls, two in the control and two in the intervention group) and high compliance. On average, participants in both groups reduced their sitting time by at least 30 min/day and replaced sitting time with standing and stepping. However, there was considerable intra-individual variability in

the magnitude of change, and, participants in the intervention group did not show superior outcomes relative to the control group.

The trial was not powered to detect statistically significant intervention effects. However, the attention-matched control group may have played a role in the lack of between group differences. Participants in the control arm of the trial received the same number of counselling sessions as intervention participants. In an attempt to further reduce bias, participants were unaware of the intervention of interest; they were told the trial was about 'healthy living after stroke', and that they would receive counselling based on either diet or exercise. While the content of the counselling sessions in the control group focussed on a dietary message, anecdotally many participants reported changing physical activity habits, for example going for more regular walks or recommencing gym programs. The activity monitors worn by all participants did not provide any real-time feedback, however, it is possible that they could have impacted on activity levels in all participants. Determining the key active elements in any intervention is important.

Currently, the evidence for the effectiveness of behaviour change interventions and self-management programs for increasing physical activity in people with stroke is limited. [29] Very few high quality trials have been conducted to date, and there is little similarity in the content of the interventions delivered. [29] We chose to use a motivational interviewing intervention to target behaviour change in this study. While one previous study found this approach to be effective in increasing physical activity

in people after stroke,[30] more high quality trials are needed to evaluate the relative effectiveness of different behaviour change interventions for people with stroke.

The barriers for people with stroke to exercise regularly at moderate intensity are often insurmountable,[17, 31] and efforts to address this have been largely ineffective. [32, 33] Reducing daily sitting time may be a more achievable target with significant health benefits. We recently modelled the impact of replacing sitting with standing or stepping time or both, using accelerometer (activPAL3) based measures of sitting time in a large sample of healthy adults [34]. Replacing two hour/day of sitting with either standing or stepping was associated with important reductions in cardiovascular disease risk.[34] Furthermore, experimental work in healthy adults has demonstrated that reductions in sitting time leads to clinically worthwhile reductions in cardiovascular disease risk factors such as improved glucose metabolism, reduced insulin resistance and decreased blood pressure, at least in the short term. [12, 35]However, the longer term benefits of changes in sitting time are not known.

Limitations

The lack of difference between intervention and control participants suggests the intervention requires development. We did not formally evaluate the degree to which our intervention adhered to motivational interviewing principles, or if there were any differences related to the two individual counsellors delivering the intervention. This may also have contributed to the fact that the intervention expected to change behaviour the most, was not more effective. Furthermore, seasonal variations in

habitual physical activity levels have also been well documented [36]and may have played a role in this trial as data were collected across an 15-month time period. While both modelling of epidemiological data [13] and experimental work[12] suggest that changes in sitting time may lead to clinically meaningful reductions in cardiovascular disease risk, this requires testing in large-scale clinical trials. The study was not powered to detect a difference in safety measures between groups, and therefore we cannot exclude the possibility of modest harms. Future trials should carefully monitor fall rates and fear of falling. Accelerometers such as the Actigraph GT3x+ tend to underestimate step counts in people with slow walking speeds. [37] This may have affected the accuracy of the absolute values of physical activity in some of our participants, but is not likely to have affected estimations of change over time. Finally, while all participants self-reported they had residual walking or balance deficits, 17% of participants recorded no symptoms on the National Health Institute of Stroke Severity Scale indicating minimal to no disability.

Conclusion

This is the first clinical trial to demonstrate that it is possible for people with stroke to sit less each day. We have demonstrated that the clinical trial protocol is both safe and feasible and leads to reductions in daily sitting time. However, the health benefits associated with sitting less each day remain unclear.

Suppliers

PAL Technologies Ltd. 50 Richmond St Glasgow G1 1XP, Scotland, United Kingdom (activPAL monitors).

Actigraph LLC. 49 E Chase Street Pensacola, Florida 32502, United States of America (GT3x+ monitors).

Temple Healthcare Pty Ltd. PO Box 299 Bowral 2576, New South Wales, Australia (sensewear am band monitors).

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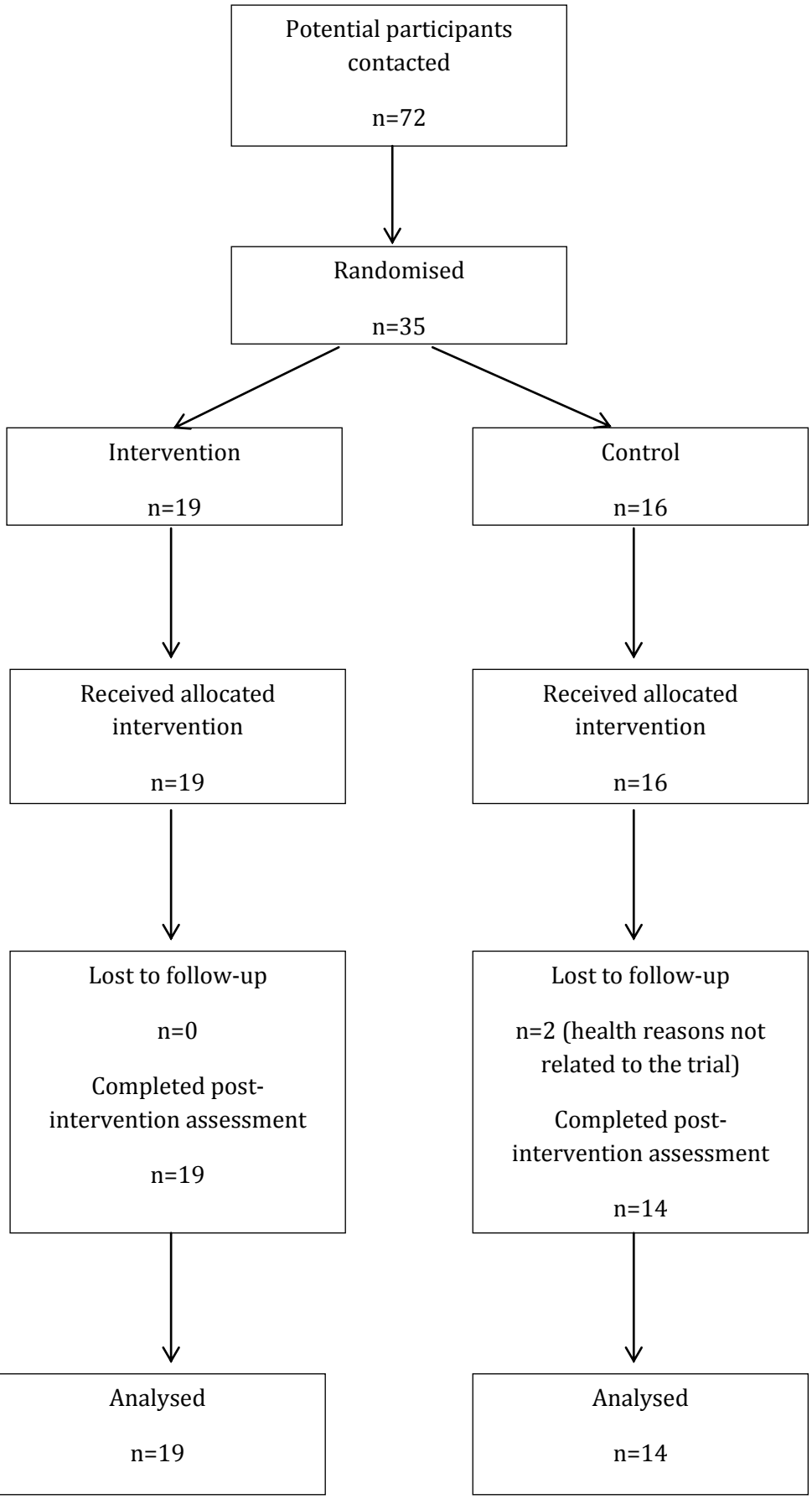
Figure 1 CONSORT statement flow chart



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1 **Table 1 Participant characteristics**

Characteristic N(%) or mean (SD)	**Whole sample (n=33)**	**Intervention (n=19)**	**Control (n=14)**
Age (years)	66.9 (12.7)	65.4 (12.3)	67.8 (13.8)
Males	22 (62.9)	13 (68.4)	9 (64.3)
First stroke	28 (80.0)	12 (63.2)	14 (100)
Stroke type*			
TACI	6 (17.1)	5 (26.3)	1 (7.1)
PACI	13 (37.1)	9 (47.4)	3 (21.4)
LACI	7 (20)	3 (15.8)	4 (28.6)
Haemorrhage	9 (25.7)	2 (10.5)	6 (42.9)
Stroke severity (NIHSS)(score)			
No symptoms (0)	6 (17.1)	3 (15.8)	3 (21.4)
Mild (1 to 4)	20 (57.1)	11 (57.9)	7 (50.0)
Moderate/severe (>4)	9 (25.7)	5 (26.3)	4 (28.6)
Time since stroke (years)	3.2 (3.4)	2.8 (2.6)	4.1 (4.3)
Living arrangement			
Spouse/other	27 (77.1)	14 (73.7)	12 (85.7)
Alone	8 (22.9)	5 (26.3)	3 (14.3)
Independence in ADLs			
Independent	23 (65.7)	14 (73.7)	7 (50.0)

Requires assistance	12 (34.3)	5 (26.3)	7 (50.0)
Use of walking aid			
No aids	23 (65.7)	13 (68.4)	9 (64.3)
Walking stick	10 (28.6)	5 (26.3)	4 (28.6)
Frame	2 (5.7)	1 (5.3)	1 (7.1)
Walking speed (m/s)	0.81 (0.41)	0.80 (0.36)	0.82 (0.51)
BMI (kg/m^2)	28.6 (4.8)	29.3 (5.8)	27.5 (3.0)
MoCA (score)	24.2 (3.6)	24.0 (4.2)	24.4 (2.7)

*Oxfordshire Stroke Classification. TACI = total anterior circulation infarct, PACI = partial anterior circulation infarct, LACI = lacunar infarct, NIHSS = National Institutes of Health Stroke Scale, ADL = activities of daily living, BMI = body mass index, MoCA = Montreal Cognitive Assessment

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1 **Table 2 Safety and feasibility measures**

	Intervention		Control	
Outcomes mean (SD)	**Baseline (n=19)**	**Post-intervention (n=19)**	**Baseline (n=14)**	**Post-intervention (n=14)**
Pain (cm, VAS)	3.4 (2.8)	3.2 (3.1)[¥]	3.7 (3.5)	3.4 (3.3)[¥]
Spasticity (cm, VAS)	3.0 (2.8)	2.4 (2.4)[¥]	3.6 (3.2)	3.8 (2.7)[¥]
Fatigue (score, CIS)	34.1 (9.3)	32.3 (8.3)[¥¥]	32.9 (11.7)	35.3 (10.7)[¥¥]
Number falls[§]				
None		16 (84.2)		11 (78.6)
One		1 (5.3)		1 (7.1)
Two		1 (5.3)		1 (7.1)
Missing		1 (5.3)		1 (7.1)
Valid wear days activPAL3 (n)	6.1 (0.8)	6.9 (0.2)	5.6 (0.9)	6.9 (0.4)
Waking wear hours[§§] activPAL3 (hr/day)	14.4 (1.2)	14.1 (1.3)	14.1 (1.2)	14.0 (1.6)
Valid wear days GT3x+ (n)	6.5 (0.9)	6.6 (0.8)	6.7 (0.6)	6.8 (0.6)

Waking wear hours[§§] GT3x+ (hr/day)	14.6 (1.1)	14.1 (1.4)	14.5 (1.5)	14.2 (1.4)

VAS = visual analogue scale, CIS = Checklist Individual Strength, [¥]No significant difference, Wilcoxon Signed Rank Test, [¥¥] significant difference, paired t-test, [§]Number of falls reported during the intervention period, [§§]waking hours monitored

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1 **Table 3 Sitting time and physical activity. Mean (SD) of intervention and control groups, not adjusted for wear time.**

	Groups			
	Intervention (n=19)		Control (n=14)	
Outcomes mean (SD)	**Baseline**	**Post-Intervention**	**Baseline**	**Post-Intervention**
Total sitting time (min /day)	645.8 (99.9)	609.7 (121.0)	633.8 (102.5)	589.9 (111.5)
Sitting time accumulated in bouts ≥30 mins (min/day)	431.1 (155.7)	396.0 (177.3)	443.2 (139.8)	396.4 (162.6)
Standing time (min/day)	154.8 (66.8)	171.3 (73.9)	151.9 (62.1)	183.5 (90.8)
Stepping time	59.6 (40.6)	64.3 (45.0)	59.0 (32.4)	65.5 (42.3)

(min/day)				
MVPA (≥ 1952 cpm)	8.2 (10.5)	6.6 (9.5)	6.6 (5.9)	9.9 (10.4)
min/day				

MVPA = moderate to vigorous physical activity

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Table 4 Sitting time and physical activity, standardised to 16 hour-day waking wear time. Mean (SD) of intervention and control groups, differences within groups and mean (95% CI) of difference between groups.

	Groups				Difference within groups		Difference between groups in change scores
	Intervention (n=19)		Control (n=14)		Post-intervention - Baseline mean difference (95% CI) [§]		Intervention – Control mean difference (95% CI) [§§]
Outcomes mean (SD)	**Baseline**	**Post-Intervention**	**Baseline**	**Post-Intervention**	**Intervention (n=19)**	**Control (n=14)**	
Total sitting time (min/day)	722.3 (107.5)	692.1 (124.8)	720.7 (99.5)	680.2 (133.1)	-30.2 ± 50.6 (-54.6 to -5.8)	-40.4 ± 92.5 (-93.8 to 13.0)	-10.2 (-62.2 to 41.9) p=0.693

					p=0.018	p=0.126	
Sitting time accumulated in bouts ≥30 mins, (min/day)	484.4 (186.6)	448.2 (206.4)	501.9 (146.7)	457.7 (188.5)	-36.1 ± 65.0 (-67.5 to -4.8) p=0.026	-44.2 ± 134.2 (-121.7 to 33.3) p=0.24	-8.1 (-81.4 to 65.1) p=0.821
Standing time (min/day)	171.0 (71.2)	193.4 (79.7)	171.9 (67.1)	205.7 (93.5)	22.4 ± 35.5 (5.4 to 39.6) p=0.013	33.8 ± 59.3 (0.3 to 67.9) p=0.051	-11.3 (-45.5 to 22.9) p=0.504
Stepping time (min/day)	66.8 (48.8)	74.5 (57.8)	67.5 (38.1)	74.1 (45.3)	7.8 ± 19.2 (-1.5 to 17.0) p=0.096	6.6 ± 36.9 (-14.6 to 27.9) p=0.516	1.2 (-19.3 to 21.7) p=0.907
MVPA (≥ 1952	8.8 (11.2)	7.7 (11.4)	7.2 (6.3)	10.9 (11.0)	-0.6 ± 10.9 (-6.4	4.1 ± 9.7 (-	-3.8 (-11.8 to 4.1)

cpm) min/day		to 5.3) p=0.842	1.9 to 10.3) p=0.161	p=0.332

[§]Paired t-test [§§]univariate analysis of variance, MVPA = moderate to vigorous intensity physical activity. Sitting, prolonged sitting, standing, and stepping were derived from activPAL3 data; MVPA was derived from GT3X+ data.

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Table 5 Use of time data measured by the MARCA

	Control		Intervention		Difference between groups in change scores	
Activity, min/day mean (SD)	**Baseline**	**Post-intervention**	**Baseline**	**Post-intervention**	**Intervention – Control mean difference (95% CI) §**	**P**
Total sitting time	679 (167)	667 (217)	668 (136)	593 (170)	63	0.28
Television	221 (157)	183 (133)	303 (183)	257 (120)	8	0.13
Passive Transport	36 (41)	62 (58)	50 (64)	42 (49)	34	0.10
Reading	45 (61)	75 (69)	47 (78)	51 (92)	26	0.42
Sit and talk	87 (109)	58 (51)	50 (62)	72 (92)	26	0.42

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