Minimum number of days required for a reliable estimate of daily step count and energy expenditure, in people with MS who walk unaided.

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Abstract

**Background and purpose:** The purpose of this study was to examine the minimum number of days needed to reliably estimate daily step count and energy expenditure (EE), in people with multiple sclerosis (MS) who walked unaided.

**Methods:** Seven days of activity monitor data were collected for 26 participants with MS (age = 44.5 ± 11.9 years; time since diagnosis = 6.5 ± 6.2 years; Patient Determined Disease Steps = ≤ 3). Mean daily step count and mean daily EE (kcal) were calculated for all combinations of days (127 combinations), and compared to the respective 7-day mean daily step count or mean daily EE using intra-class correlations (ICC), the Generalizability Theory and Bland-Altman.

**Results:** For step count, ICC values of 0.94 – 0.98 and a G-coefficient of 0.81 indicate a minimum of any random 2-day combination is required to reliably calculate mean daily step count. For EE, ICC values of 0.96 – 0.99 and a G-coefficient of 0.83 indicate a minimum of any random 4-day combination is required to reliably calculate mean daily EE. For Bland-Altman analyses all combinations of days, bar single day combinations, resulted in a mean bias within ± 10%, when expressed as a percentage of the 7-day mean daily step count or mean daily EE.

**Conclusions:** A minimum of 2 days for step count and 4 days for EE, regardless of day type, is needed to reliably estimate daily step count and daily EE, in people with MS who walk unaided.

**Keywords:** Accelerometry, chronic disease, physical activity, pedometry.
Introduction

Multiple sclerosis (MS) is a chronic autoimmune disease which can result in symptoms such as fatigue, depression, loss of mobility, balance and coordination, and neurological dysfunction [1-3]. These symptoms have an overall impact on activities of daily living (ADL) and physical functioning [4], and therefore any treatment and/or intervention which may lessen the impact of these symptoms may improve overall quality of life (QOL) in people with MS [5].

One such treatment is engaging in regular physical activity (PA) [6]. Recently the numerous health benefits of PA participation, such as reduced risk of sedentary related disease onset [7], increased muscular strength [7], and increased psychological wellbeing [8], have been found among people with MS [9-12]. However, current research [13-17] indicates that people with MS are substantially more inactive than their non-diseased counterparts.

The accurate selection of objective measures of PA are vital to a better understanding of PA and MS [18]. PA has previously been defined as “any bodily movement produced by skeletal muscles that result in EE” and therefore accelerometer outputs of both step count and energy expenditure may be useful ways of estimating free living PA [19]. The use of step count as an output is consistent with the use of walking as a primary monitoring outcome of PA in MS research due to its link with disease progression and disability level [20, 21]. Research [22] has found that accelerometers measure both PA and walking mobility in people with MS, whilst also providing an objective measurement outcome sensitive to detecting differences in PA [1]. Furthermore, accelerometer step count has been found to be a reliable measure of PA in people with MS [23]. Additionally, people with MS may use activity modifications, such
as a decrease in step count, to conserve EE when performing everyday activities [24]. Therefore, EE is also a parameter of interest when investigating PA levels in people with MS.

When measuring step count or EE in a free-living environment the number of days required for monitoring is of importance to ensure a reliable estimate of the variable of interest is collected [18, 23]. People with MS already have significant constraints on everyday living due to MS symptoms; therefore PA measurement should be for as short a possible time as to be accurate, while not overly impacting on the person’s life. Whilst a 7-day monitoring period is commonly used to assess PA in people with MS [25], monitor wearing compliance has ranged from one to seven days [26]. Previous research [23] has investigated the number of days of pedometer monitoring required to accurately predict daily step count in adults with multiple sclerosis, indicating a minimum of 3 days is necessary. However, it was unclear how many participants performed habitual walking behaviour aided or un-aided. People with MS who perform gait unaided are of particular interest as they are typically the targets of PA interventions, and undertake habitual walking behaviour similar to a non-diseased population, whilst concurrently managing the symptoms of MS. Also, whilst previous research [23] recommended a 3-day monitoring period, this cannot be assumed when measuring PA utilising EE as a monitoring outcome, as people with MS adopt alternate EE and step count strategies when performing the same task [24]. In doing so people with MS may slow down the pace at which they move, or in fact move less.

Lastly, in previous research [23] pedometers and accelerometers utilised to measure step count and/or EE were not worn 24 hours a day. This may lead to missed data due to non-wear time. Also, gait behaviour within an MS population can fluctuate from day-to-day, and from one time of a day to another [27]. Therefore, to achieve a thorough reflection of step count
and EE in MS population, participants should wear the chosen accelerometer or pedometer for all waking hours. The SenseWear Armband® (SWA) can be worn 24 hours a day and is lightweight and unobtrusive during ADL’s. The SWA has been identified to provide adequate step count data in people with MS and a valid estimate of EE during everyday activities [28]. For this reason, the SWA has achieved many of the recommendations previously set forward for capturing walking behaviour and EE in people with MS [27].

To this end, the purpose of this study was to investigate the minimum number of days needed to reliably estimate daily step count and EE, using the SWA, in people with MS who walk unaided.

Methods

Data utilised within this study was collected via the “Step It Up” [29] study protocol within a larger randomised controlled trial study. The study was performed in agreement with the Declaration of Helsinki and approved by the Health Service Executive Mid-West Research Ethics Committee, the Galway University Hospitals Clinical Research Ethics Committee and the University of Limerick, Faculty of Education and Health Sciences Research Ethics Committee.

Participants and Protocol
Participants completing the “Step It Up” [29] research study were recruited via (1) social media, email and postal communications of the MS Society of Ireland and (2) via neurology clinics in three urban locations in the west and south of Ireland. Participants which expressed interest were screened for selection criteria. Inclusion criteria included: (1) physician-confirmed formal diagnosis of MS, (2) aged 18 years or more, (3) Patient Determined Disease Steps score of ≤ 3 (participant has gait disability, but can work entire day [30]), (4) a sedentary lifestyle (<30 minutes of moderate to strenuous exercise one day or more per week over the last six months) and (5) willing to give written informed consent. Exclusion criteria included: (1) pregnancy, (2) MS relapse in the last 12 weeks and (3) changes to MS medication or steroid treatment in the last 12 weeks. This resulted in SWA data for a total of 68 participants, all of which undertook one of two 10- week exercise based interventions. Whilst numerous outcome measures were recorded within the “Step It Up” [29] protocol, for this analysis only daily step count and daily EE recorded over a 7-day period pre-intervention (week 1) were utilised. Daily step count and daily EE data were recorded via the SWA, which participants were asked to wear day and night for a 7-day period. For the current analysis SWA step count and EE data were visually screened post data collection and only participants with 7 valid days of step count and EE data were included. A valid day was a 24 hour period in which there were 10+ hours of awake, recorded SWA activity, criteria previously used within MS populations [31]. Awake hours were identified as the hours between two extended periods of sedentary behaviour (typically 6 to 10 hours), in which a participant displayed both step count and EE data for a minimum of 30 minutes. Therefore, due to SWA failure (n = 4) and participants not having 7 valid days of step count and EE data (n = 38), a total of 26 participants were included in the final analysis (age = 44.5 ± 11.9 years). Participants in the final sample had been diagnosed with MS for 6.5 ± 6.2 years and
the majority had relapsing–remitting MS (relapsing–remitting, n = 21; benign, n = 2; primary progressive, n = 1; secondary progressive, n = 1; unknown, n = 1).

Additionally, the SWA provides two measures of EE. The first EE measure is the conversion of counts, via prediction equations, to metabolic equivalents (METs). The second EE measure is kilocalories per day (kcals per day). Within this study EE was estimated using kcals per day as Coote and O'Dwyer [28] found that kilocalorie estimates provided a more accurate estimate of PA than METS, using the SWA, in people with MS performing ADL’s.

Lastly, preceding the main investigation the 7 valid days of step count and EE data collected were categorised by day type (Monday – Sunday) and analysed to investigate if there was a significant difference in daily step count or daily EE due to day type. Within this preceding analysis, 1 of the 26 participants with 7 valid days had two re-occurring days (i.e. Monday twice), due to non-consecutive SWA wear. This participant was therefore omitted from the preceding investigation (n = 25).

**Data Analysis**

Data analysis methods are similar to those previously used [23, 32, 33] and therefore are summarised below. For the preceding investigation daily step count and daily EE over the 7-day period was calculated for those only with 7 consecutive valid days representing Monday – Sunday (n = 25). A one-way repeated measures analysis of variance (ANOVA) was performed to investigate if a significant difference lay in daily step count or daily EE, due to day type, across the 7-day period. Hereafter, analysis was performed on all participants with
7 valid, consecutive and non-consecutive days (n = 26). Coefficient of Variance (CoV) was used to calculate daily step count and daily EE variability within participant (CoV\textsuperscript{w}) and between participants (CoV\textsuperscript{b}), expressed as a percentage. Mean daily step count and mean daily EE were calculated for all possible day combinations (1 day to 7 day combinations), resulting in 127 mean daily values for each parameter (step count and EE). A two way random effects model was utilised for intra-class correlations (ICCS’s) calculation between all possible mean daily step counts and mean daily EE values from all combinations of days, compared to criterion mean daily step count and mean daily EE derived from the valid 7-day period. All statistical analysis was conducted using SPSS version 21.0. Furthermore, the minimum number of days needed to calculate a reliable estimate of mean daily step count and mean daily EE was estimated in MATLAB™ (Mathworks, Cambridge, UK) utilising the Generalizability Theory [34]. Explained in detail elsewhere [34], briefly within the Generalizability Theory firstly we performed an extended two-way repeated measures ANOVA (G-study) in which the amount of variance contributed by each factor (participant and day) and the interaction effect (participant × day) were outlined. Secondly, G-coefficients were calculated using a fully crossed D-study design (participant × day) to derive the minimum number of days needed to calculate a reliable estimate of mean daily step count and mean daily EE. For both ICC values and G-coefficients, following previous literature [23, 32, 33], a threshold of 0.80 was utilised as the minimum cut-off to calculate the reliable amount of days needed. Lastly, a comparison of methods was assessed by calculating the paired difference of the methods, and the mean of the methods [35]. The criterion method was the mean daily step count and mean daily EE derived from the 7-day period, while the comparison methods were the mean daily step count and mean daily EE values derived from single and multiple day combinations (n = 127 for each parameter). Bland-Altman plots provide mean bias values (criterion – comparison) and 95% confidence intervals (95% CI = ±
1.96 × SD) [36]. These were calculated in both standard units (steps and kcal) and also as a percentage of the criterion and represented in table format.

**Results**

There were no significant differences for age ($p = .521$) or years since diagnosis ($p = .984$) between the subgroup used in this analysis ($n = 26$) and the overall group within the ‘Step it Up’ research study ($n = 68$) [29]. Participants daily and weekly mean steps and EE values are outlined in Table 1. The one-way repeated measures ANOVA indicated no significant difference in mean daily step count ($F(6,144) = 1.483, p > 0.05$) or mean daily EE ($F(6,144) = .987, p > 0.05$) across the consecutive 7-day period, regardless of whether they were weekend or week days.

**Table 1. Daily and weekly mean daily steps and mean daily EE for participants with 7 consecutive valid days, Monday – Sunday ($n = 25$).**

<table>
<thead>
<tr>
<th></th>
<th>Steps (steps per day)</th>
<th>EE (kcal per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monday</strong></td>
<td>8,529 (3,854; 7,019 – 10,040)</td>
<td>2,271 (570; 2,048 – 2,494)</td>
</tr>
<tr>
<td><strong>Tuesday</strong></td>
<td>8,377 (3,676; 6,935 – 9,816)</td>
<td>2,251 (593; 2,019 – 2,484)</td>
</tr>
<tr>
<td><strong>Wednesday</strong></td>
<td>8,083 (4,243; 6,420 – 9,747)</td>
<td>2,182 (607; 1,944 – 2,420)</td>
</tr>
<tr>
<td><strong>Thursday</strong></td>
<td>8,566 (3,574; 7,165 – 9,967)</td>
<td>2,265 (525; 2,060 – 2,471)</td>
</tr>
<tr>
<td><strong>Friday</strong></td>
<td>8,420 (3,537; 7,033 – 9,807)</td>
<td>2,208 (666; 1,946 – 2,468)</td>
</tr>
<tr>
<td><strong>Saturday</strong></td>
<td>9,008 (4,067; 7,413 – 10,602)</td>
<td>2,419 (559; 2,200 – 2,638)</td>
</tr>
<tr>
<td><strong>Sunday</strong></td>
<td>7,304 (3,345; 5,993 – 8,615)</td>
<td>2,199 (358; 2,059 – 2,339)</td>
</tr>
<tr>
<td><strong>Week (all days)</strong></td>
<td>8,327 (3,487; 7,077 – 9,576)</td>
<td>2,256 (421; 2,091 – 2,421)</td>
</tr>
</tbody>
</table>
There were no significant differences in mean daily step count or mean daily EE between participants with consecutive or non–consecutive data (Step count: \(t(49) = .01, p > 0.05\), EE: \(t(49) = -0.45, p > 0.05\)). Therefore, Day 1 was representative of the first valid day of data, Day 2 the second day of valid data etc. Mean CoV\(^w\) for daily step count was 27.1 % (SD = 9.2 %; Range = 8.9 – 49.3 %), with mean CoV\(^b\) = 47.9 % (SD = 5.6 %; Range = 41.2 – 57.0 %). Mean CoV\(^w\) for daily EE was 16.0 % (SD = 5.9 %; Range = 7.5 – 27.0 %), with mean CoV\(^b\) = 23.6 % (SD = 6.1 %; Range = 19.0 – 37.1 %). Mean, median and range of ICC values for 1 day, 2 day, 3 day, 4 day, 5 day and 6 day combinations are outlined in Table 2.

Table 2. Intra-class correlation values for combinations of days (1-6) and the criterion 7-day.

<table>
<thead>
<tr>
<th>Combinations of days</th>
<th>Step Count</th>
<th>Energy Expenditure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Median</td>
</tr>
<tr>
<td>1 Day</td>
<td>0.83</td>
<td>0.84</td>
</tr>
<tr>
<td>2 Days</td>
<td>0.96</td>
<td>0.96</td>
</tr>
<tr>
<td>3 Days</td>
<td>0.98</td>
<td>0.98</td>
</tr>
<tr>
<td>4 Days</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td>5 Days</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td>6 Days</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

G-study results indicated that the majority of the variance in both mean daily step count and mean daily EE were as a result of variance within the participant term (67.5% and 48.8%), whilst the variance between days accounted for minimal variance in both mean daily step
count (1.4%) and mean daily EE (11.0%) (Table 3). The remaining variance (31.1% for mean daily step count and 40.2% for mean daily EE) was due to the interaction effect between the participant and day terms and is deemed as non-specific variance.

Table 3. G-Study results representing variance component estimates and relative magnitude of error for each term and the interaction effect.

<table>
<thead>
<tr>
<th>Term</th>
<th>Step Count Variance</th>
<th>Relative Magnitude of Error (%)</th>
<th>Energy Expenditure Variance</th>
<th>Relative Magnitude of Error (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>12,039,320.97</td>
<td>67.5</td>
<td>152,281.81</td>
<td>48.8</td>
</tr>
<tr>
<td>D</td>
<td>243,365.11</td>
<td>1.4</td>
<td>34,533.74</td>
<td>11.0</td>
</tr>
<tr>
<td>P x D</td>
<td>5,560,327.97</td>
<td>31.1</td>
<td>125,468.85</td>
<td>40.2</td>
</tr>
<tr>
<td>Total</td>
<td>17,840,014.05</td>
<td>100</td>
<td>312,284.40</td>
<td>100</td>
</tr>
</tbody>
</table>

\(P = \text{participant term}, D = \text{day term}, P \times D = \text{participant} \times \text{day interaction effect}\)

G-coefficients ranged from 0.68 – 0.94 for step count and 0.55 – 0.89 for EE. Step count derived from selecting any random single day (0.68) was the only combination, within the step count parameter, to fall below 0.80. Therefore, a minimum of any 2 days of the week (G-coefficients \(\geq 0.80\)) was indicated as a reliable estimate of mean daily step count. EE derived from selecting any random single day (0.55), any random 2-day combination (0.71) and any random 3-day combination (0.79) fell below 0.80. Therefore, a minimum of any random 4-day combination (G-coefficients \(\geq 0.80\)) was indicated as a reliable estimate of mean daily EE (Figure 1).
Figure 1. G-coefficients (●) and minimum ICC values (×) when comparing 1–7 day combinations to a 7–day mean for (a) mean daily step count and (b) mean daily EE. Dashed line represents a D-study coefficient of 0.80.

Bland-Altman results indicate the greatest agreement between methods for both parameters (step count and EE) is any 6-day combinations versus the 7-day criterion, with a mean bias range of -171 to 177 for step count, and a mean bias range of -28 to 71 kcal for EE (Table 4). Ranges were represented as there were multiple results for each combination of days (single day = 7 results, 2 Day combinations = 21 results etc.). All combinations of days result in a mean bias within ±10% when expressed as a percentage of the criterion, bar single day combinations.
Table 4. Range of Bland-Altman mean bias and range of 95% CI represented in steps and kcal for combinations of days (1-6) compared to the respective criterion 7-day mean for daily step count and mean daily EE.

<table>
<thead>
<tr>
<th>Combinations of Days</th>
<th>Step Count (steps)</th>
<th>Energy Expenditure (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Bias (%)</td>
<td>95% CI Range (%)</td>
</tr>
<tr>
<td>Single Day</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-1062 to 1028</td>
<td>± 3815 to ± 4865</td>
</tr>
<tr>
<td></td>
<td>(-12.1 to 11.7)</td>
<td>(± 43.6 to ± 55.6)</td>
</tr>
<tr>
<td>2 Days</td>
<td>-751 to 798</td>
<td>± 1943 to ± 3342</td>
</tr>
<tr>
<td></td>
<td>(-8.6 to 9.1)</td>
<td>(± 22.2 to ± 38.2)</td>
</tr>
<tr>
<td>3 Days</td>
<td>-565 to 551</td>
<td>± 1416 to ± 2433</td>
</tr>
<tr>
<td></td>
<td>(-6.5 to 6.3)</td>
<td>(± 16.2 to ± 27.8)</td>
</tr>
<tr>
<td>4 Days</td>
<td>-414 to 423</td>
<td>± 1062 to ± 1825</td>
</tr>
<tr>
<td></td>
<td>(-4.7 to 4.8)</td>
<td>(± 12.1 to ± 20.9)</td>
</tr>
<tr>
<td>5 Days</td>
<td>-319 to 300</td>
<td>± 777 to ± 1337</td>
</tr>
<tr>
<td></td>
<td>(-3.6 to 3.4)</td>
<td>(± 8.9 to ± 15.3)</td>
</tr>
<tr>
<td>6 Days</td>
<td>-171 to 177</td>
<td>± 636 to ± 811</td>
</tr>
<tr>
<td></td>
<td>(-2.0 to 2.0)</td>
<td>(± 7.3 to ± 9.3)</td>
</tr>
</tbody>
</table>

Discussion

The aim of this study was to identify the minimum number of days needed to reliably estimate daily step count and daily EE, using the SWA, in an MS population who walk
unaided. We found there was no significant difference when examining the effect of day type on daily step count or daily EE therefore used any combination of days from 7 days of 24 hour monitoring in our analysis. The current research indicates a minimum of two days is necessary to reliably estimate daily step count and a minimum of any random 4-day combination is necessary for a reliable estimate of daily EE in this ambulatory sample of people with MS.

The finding that there was no effect of day type on daily step count is supported by previous research [23] which identified that day type had little effect on the reliability of calculating mean daily step count. Almeida, Wasko [37] also found no significant difference in total energy expenditure (TEE) due to day type, in women with rheumatoid arthritis, suggesting that participants did not undertake marked differences in PA during their weekend compared to their weekdays, due to a moderate level of disability. This may support that those with moderate disability due to a chronic disease display relatively consistent levels of PA, as identified by EE, step or activity count, across all days of the week [23].

Our finding for mean daily step count (8327) confirms the relative inactivity of this population and confirms that the patients in this analysis were representative of the wider MS population with a PDDS ≤ 3. Whilst participants recruited with the “Step it Up” research study were required to have a sedentary lifestyle, this was defined by the amount of time spent performing moderate to strenuous exercise. As mean daily step count within the current study was similar to that previously reported [25, 38], it appears people with MS, and a PDDS ≤ 3, may maintain a somewhat active profile, despite not engaging in higher intensity exercise. Mean daily EE calculated via the consecutive and non-consecutive 7-day criterion
were also similar to those found when investigating daily TEE in other chronic disease populations such as diabetes and rheumatoid arthritis [37, 39].

The key investigation in our research was to examine the minimum number of days needed to reliably estimate daily step count and daily EE using the SWA, in people with MS who walk unaided as these are the target of health promoting PA interventions. The current research indicates a minimum of two days is necessary to reliably estimate daily step count. This was supported by both single day ICC values and the single day G – coefficient, as values fell below the recommended 0.80 threshold [33]. This is in agreement with previous research in older adults [40], however is in contrast to Motl, Zhu [23] who suggested a minimum of three days is required in an MS population and recruited an MS population whom performed gait with or without the use of a cane and utilised a pedometer for data collection. However, the participants in the current study all performed habitual walking behaviour unaided and a multisensory accelerometer based device was utilised for data collection. This may account for the contrast in results found.

For EE, ICC results within the current study indicate a minimum of any random 2-day combination is needed for a reliable estimate of EE. This is supported within a diseased population where ICC values for a random single day compared to the 7-day criterion fell below 0.80, when monitoring daily TEE in women with rheumatoid arthritis [37]. However, on performing the generalisability theory analysis, G - coefficients from combinations less than 4 days fell below 0.80, indicating a minimum of any random 4-day combination is necessary for a reliable estimate of daily EE. The generalisability theory identifies where variance lies within the data, any variance interaction, and this is then factored into G-coefficient calculation [41]. Also, the generalisability theory has previously been identified as
superior to the ICC [41]. Therefore, within the current analysis G-coefficients were given more credence than ICC results and a minimum of any random 4-day combination was regarded as necessary for a reliable estimate of daily EE. Whilst there is limited research investigating the number of days required for a reliable estimate of EE in people with MS, this result is comparable to similar research performed within a healthy population (3-5 days required to calculate a reliable estimate of mean daily EE) [42], and a population with chronic disease (4 days required to calculate a reliable estimate of mean daily EE) [37].

Lastly, Bland-Altman results indicated that all combinations of days, bar single day combinations, resulted in a mean bias of $\leq 10\%$ compared to the criterion 7-day mean, for both step count and EE. When guided by ICC and G-coefficient results selecting a 2-day combination for step count results in a 95% CI range of $\pm 1943$ to $\pm 3342$ steps, compared to the criterion 7-day mean, whilst for EE selecting a 4-day combination results in a 95% CI range of $\pm 158$ to $\pm 313$ kcal, compared to the criterion 7-day mean. Reliable step count devices have been identified to have a 95% CI of $\pm 1801$ steps over a three day period in those with a neurological condition [42] and therefore the results represented by the Bland-Altman analysis may be representative of the population.

Study Limitations

Whilst this study contributes significantly to the research questions posed by Motl, Learmonth [18] there are limitations. Firstly, our subgroup ($n = 26$) is smaller than that previously used in studies investigating PA and step count in people with MS [15, 22, 23]. Secondly, whilst our sub-group was representative of our larger group ($n = 68$) in terms of both age and years since diagnosis, it includes only those with minimal to moderate disability.
(PDDS ≤ 3). Further research should investigate the number of days necessary for a reliable estimate of step count, in people with MS with more activity limitations.

**Conclusions**

It is vital that we are able to accurately quantify habitual walking behaviour and EE in people with MS, to gain a better understanding of the amount of PA this population undertakes on a daily basis. These results indicate that a minimum of 2 days for step count and a minimum 4 days for EE, regardless of day type, is needed to reliably estimate daily values, using the SWA, in an MS population with unaided walking gait. This may minimise the number of data collection days required in future studies, when researching PA in people with MS utilising a 24-hour activity monitor such as the SWA. This may not only reduce the burden placed upon participants, but also improve adherence within these studies.

**Conflicts of Interest**

The “Step it Up” study is funded by the Health Research Boards, HRA_PHR/2013/264.
References
