Research article

Sedentary behaviour and physical activity patterns in adults with traumatic limb fracture

Christina L. Ekegren1,2,3,*, Rachel E. Climie2, William G. Veitch1, Neville Owen2,4, David W. Dunstan2,5, Lara A. Kimmel1,3 and Belinda J. Gabbe1,6

1 Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia
2 Baker Heart and Diabetes Institute, Melbourne, Australia
3 The Alfred, Melbourne, Australia
4 Swinburne University of Technology, Melbourne, Australia
5 Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia
6 Health Data Research UK, Swansea University, Swansea, UK

* Correspondence: Email: christina.ekegren@monash.edu; Tel: +613 9903 0939.

Abstract: Objective: To describe patterns of sedentary behaviour and physical activity in adults two weeks post-hospital discharge following an upper or lower limb fracture, and identify associated predictive factors. Design: Observational study. Setting: Level 1 Trauma Centre. Participants: Adults aged 18–69 years with an isolated upper (UL) or lower (LL) limb fracture. Main Outcome Measures: Sitting time and steps measured via a triaxial accelerometer and inclinometer-based device (activPAL) (anterior thigh); and moderate-intensity physical activity (MPA) measured via triaxial accelerometer (ActiGraph) (hip) for ten days. Results: Of 83 participants, 63% were men and 55% had sustained LL fractures; mean (SD) age was 41 (14) years. Participants sat for a mean (SD) of 11.07 (1.89) h/day, took a median (IQR) of 1575 (618–3445) steps/day and had only 5.22 (1.50–20.78) mins/day of MPA. Multivariable regression analyses showed participants with LL fracture, had increased adjusted mean sitting time of 2.5 h/day relative to UL fracture (β = 2.5 hours, p < 0.001). For each day since surgery/injury there was reduced adjusted mean sitting time of 4 mins/day (β = −0.06 hours, p = 0.048). LL fracture was associated with 80% fewer steps/day (Ratio of Geometric Means (RGM) = 0.20, p < 0.001) and 89% less MPA (RGM = 0.11, p < 0.001) relative to UL fracture. Older age was associated with 59–62% less MPA relative to the youngest participants (RGM = 0.38–0.41, p = 0.01). There was no association between the predictive variables sex, BMI and pre-injury physical activity and any outcome. Conclusions: At two weeks post-hospital discharge, participants were engaged in high
amounts of sitting and were physically inactive. Injury location was the strongest predictor of outcome, indicating that patients with LL fracture are most in need of encouragement to reduce sitting time and gradually increase activity, within the bounds of clinical safety.

**Keywords:** sitting; orthopaedic; injury; trauma; recovery

### 1. Introduction

Fractures are the most common form of hospitalised trauma in every age group [1], contributing the largest proportion of hospitalisations from injuries sustained at work [2], on the road [3], or while playing sport [4]. It is estimated that one in every two men and three women will experience a traumatic fracture before the age of 65, most commonly as a result of falls and road crashes [1,5]. Many people experience ongoing pain and activity restrictions following fracture, and almost one third of adults with a lower limb fracture fail to return to work 12 months post-injury [6,7]. The resulting healthcare and productivity costs, have been estimated at $9,800 to $23,100 USD per working-age adult in the six months following a single limb fracture [8].

During recovery from fracture, mobility restrictions, pain, fatigue, or medication side-effects may cause an initial reduction in physical activity (i.e. bodily movement produced by skeletal muscle resulting in energy expenditure [9]), and an increase in sedentary behaviour (i.e. waking behaviour characterized by low energy expenditure while sitting, reclining or lying [10]) [11,12]. In the short term, this change in behaviour can lead to impaired glucose control and fat metabolism [13,14], precipitate a decline in physical capacity (e.g. muscle strength and cardiovascular fitness), lead to a loss of bone density, and potential re-fracture [15–17]. Other factors may also influence post-injury activity behaviour, such as fear-avoidance, loss of motivation or loss of routine [18]. These limitations may persist in the long-term such that, even after bony injuries are healed and physical capacity has returned, the diminished activity behaviours can become ingrained [19].

There is mounting evidence that long-term physical inactivity (i.e. failure to meet Physical Activity Guidelines) and also sedentary behaviour (e.g. high levels of sitting) are related to all-cause mortality, cancer, heart disease and type 2 diabetes [20,21]. There is also preliminary evidence of a heightened prevalence of chronic disease in people who have experienced serious injury [22], and a six-fold increase in mortality risk two years following major trauma [23]. One hypothesis for this is that a dramatic change in patients’ activity levels can precipitate certain risk factors for chronic disease, such as hyperlipidaemia and hypertension [22].

Recent systematic reviews on this topic have demonstrated that orthopaedic injury does have an impact on physical activity levels and sedentary behavior [11,12]. However, previous studies have either relied on self-reported physical activity measures (e.g. the International Physical Activity Questionnaire (IPAQ) or the Community Healthy Activities Model Program for Seniors (CHAMPS) Physical Activity Questionnaire) which are susceptible to over-reporting [24,25], have focused solely on hip fracture in older adults, failed to include pre-injury measures of activity, or not included the measurement of sedentary behavior [11]. At present, despite the potential for broader adverse health outcomes following fracture in working-age adults, there are no objective data capturing activity levels and patterns of sitting time within this high-risk group [11]. These data are needed to provide a more accurate and unbiased understanding of post-fracture activity levels and to better identify
associated factors.

The aims of this study were to describe patterns of sedentary behaviour and physical activity in working-age adults two-weeks post hospital discharge following an upper or lower limb fracture, and to identify factors associated with these patterns.

2. Methods

2.1. Participants

All patients aged 18–69 years admitted to a major trauma centre with a new isolated upper limb (UL) or lower limb (LL) fracture (confirmed by X-Ray), a hospital length of stay >24 hours and home discharge, were eligible for inclusion. Patients with a pathological fracture related to metastatic disease, cognitive deficits or a language other than English were excluded. Ethical approval was obtained from the Alfred Health and Monash University human research ethics committees. All participants were recruited during their inpatient stay and provided written informed consent before participating in the study. The rights of participants were protected.

2.2. Procedures

Data collection commenced approximately two weeks post-hospital discharge when participants returned to the hospital for their outpatient review. Participants completed a questionnaire pertaining to their demographics, self-reported height and weight, self-reported physical activity for the week preceding injury (IPAQ, Short Form (SF) [26]) and current weight-bearing status. During the appointment, each participant received two activity monitors, waterproof adhesive patches, an activity log, and a postage-paid satchel for returning the devices to investigators. Details of participants’ injury and surgical management were obtained from hospital medical records.

Time spent sitting was collected using the validated activPAL3™, a triaxial accelerometer and inclinometer-based device (PAL Technologies Limited, Glasgow, UK) [27]. Step count was collected using the activPAL based on evidence of the activPAL’s accuracy across a wide range of walking speeds, including slow speeds and when using gait aids [28–30]. The monitor was secured to the anterior thigh (uninjured limb for LL fracture patients) [29] with a waterproof patch and worn continuously (24 hour/day) for 10 days following the outpatient appointment. Physical activity was measured using an ActiGraph GTX3+ triaxial accelerometer (ActiGraph LLC, Pensacola, FL, USA) during the same 10 day period [31]. Data were sampled at 30Hz and counts per minute (cpm) were determined using ActiGraph’s proprietary software, ActiLife (Version 6.13.3). Participants used a diary to report their sleep/wake times as well as whether devices were removed for more than 15 minutes during the day. This information was used to verify non-wear/sleep time [32].

2.3. Data processing

Monitor data were processed in SAS™ 9.3 (SAS Institute Inc., Cary, NC, USA). The algorithm outlined by Winkler et al. [32] was used to determine sleep/non wear bouts for ActivPAL data. To allow for potentially very low activity levels in this population, the “any one activity that accounts for >95% of waking wear time” condition described by Winkler et al. [32] was removed from
consideration and the threshold for invalid days was lowered from 500 to 100 steps/day. For ActiGraph data, valid days were determined using the Choi algorithm [33]. For each day of data collection, heat maps of data were visually inspected for any potential classification errors (e.g. sleep time as waking time). Finally, any potential errors were checked against the patient diaries and the most plausible classification chosen and applied [34]. Where participants had at least four valid days (with ≥600 minutes of waking wear time/day) [35], total daily sitting time (hours/day), percentage of the day spent sitting (sitting time/total waking time), steps (n), and moderate- (1952 cpm–5724 cpm) (MPA) and vigorous-intensity (≥5725 cpm) physical activity (VPA) (mins/day) were calculated and then averaged across all valid days [36]. Accelerometry cut points were deemed appropriate for the pre-injury health status and age range of our participants (i.e. healthy adults, aged 18–69 years) [36].

2.4. Statistical analysis

Characteristics of the sample and activity data were summarised descriptively using frequencies and percentages for categorical data, and means and standard deviations (SD) for continuous data or medians and interquartile ranges (IQR) if data were skewed. Age followed a bimodal distribution and was subsequently categorised. Body mass index (BMI) was calculated as weight (kg)/height (m²), and categorised according to accepted cut points [37]. Pre-injury physical activity data was reported as low, moderate and high, in accordance with IPAQ-SF scoring protocols [26].

Separate multivariable linear regression models were fitted for the three main outcomes: (i) sitting time; (ii) steps; and (iii) MPA. Based on previous literature, the potential predictive variables included were age, sex, UL vs. LL fracture, BMI, pre-injury physical activity, and days elapsed since surgery (or from injury where fracture was non-operatively managed) to the start of activity monitoring [38–40]. Variables showing a significant (p < 0.25) association on preliminary univariate analyses, in addition to those deemed clinically important (age and sex), were entered into each model [41]. Non-significant variables were identified using Wald tests, and were removed from the model individually in a backward stepwise approach (p < 0.05) [41]. The reduced models were compared with the initial model using likelihood ratio tests and the remaining variable coefficients assessed to ensure that they had not substantially changed, indicating potential confounding. This process was repeated until a parsimonious final model was achieved. Variables excluded from the initial model were then included to ensure that important variables had not been missed. Residual plots were inspected to evaluate model assumptions (i.e. normal distribution of residuals and equal variances) [42]. As steps and MPA outcomes were not normally distributed, a log transformation was used with the effect estimated as a ratio of geometric means (RGM) [43]. With age, BMI and pre-injury physical activity treated as three-level categorical variables, the estimated models used 9 degrees of freedom. Thus, a sample size of 72 would allow for 8 subjects per variable (SPV), well exceeding the minimum SPV required for accurate estimation of regression coefficients, confidence intervals and adjusted R² values [44]. All analyses were performed using Stata Version 15 (StataCorp LLC, college Station, TX, USA).

3. Results

Out of the 120 participants recruited, 83 returned valid activPAL data (n = 78) and/or valid Actigraph data (n = 77) and were included in the final analysis. For activPAL data, 125 invalid days
(i.e. <600 mins waking wear time and/or <100 steps per day) were removed from analysis leaving 706 valid days. For ActiGraph data, 176 invalid days (<600 mins waking wear time) were removed, leaving 699 valid days. There were no significant differences in demographics between included and non-included participants (Table S1 of Supplementary). There were a range of reasons for non-inclusion, such as loss of interest in participating (n = 14), ineligibility (n = 11), non-attendance at outpatient appointment (n = 8) and <4 valid days (n = 4).

For included participants, the mean (SD) time from surgery (or from injury for those managed non-operatively, n = 10) to the start of activity monitoring was 17 (5) days (Table 1). Most participants were men (63%), almost half (43%) were aged 18-34 years (mean (SD) age 41 (14) years) and over half (51%) were overweight or obese (BMI median (IQR): 25 (22–28)). Of the 46 participants with lower limb fractures (55%), most were non-weight bearing on the affected limb (65%), and mostly using crutches to ambulate. Twenty-eight percent of all participants had ankle fractures, with forearm/wrist fractures the next most common (18%). Most participants (63%) reported a high level of physical activity in the week preceding injury.

### Table 1. Characteristics of included participants (n = 83).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>52 (62.7)</td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
</tr>
<tr>
<td>18–34</td>
<td>36 (43.4)</td>
</tr>
<tr>
<td>35–49</td>
<td>21 (25.3)</td>
</tr>
<tr>
<td>50–69</td>
<td>26 (31.3)</td>
</tr>
<tr>
<td>Injury group</td>
<td></td>
</tr>
<tr>
<td>Upper limb fracture</td>
<td>37 (44.6)</td>
</tr>
<tr>
<td>Lower limb fracture</td>
<td>46 (55.4)</td>
</tr>
<tr>
<td>Non weight bearing</td>
<td>30 (65.2)</td>
</tr>
<tr>
<td>Partial weight bearing/weight bearing as tolerated*</td>
<td>16 (34.8)</td>
</tr>
<tr>
<td>Fracture type</td>
<td></td>
</tr>
<tr>
<td>Ankle</td>
<td>23 (27.7)</td>
</tr>
<tr>
<td>Forearm/wrist</td>
<td>15 (18.1)</td>
</tr>
<tr>
<td>AC/Scapula/clavicle</td>
<td>11 (13.3)</td>
</tr>
<tr>
<td>Tibia/fibula</td>
<td>10 (12.0)</td>
</tr>
<tr>
<td>Humerus</td>
<td>8 (9.6)</td>
</tr>
<tr>
<td>Foot</td>
<td>6 (7.2)</td>
</tr>
<tr>
<td>Patella</td>
<td>4 (4.8)</td>
</tr>
<tr>
<td>Elbow</td>
<td>3 (3.6)</td>
</tr>
<tr>
<td>Hip</td>
<td>3 (3.6)</td>
</tr>
<tr>
<td>Body mass index categories</td>
<td></td>
</tr>
<tr>
<td>Normal or underweight (&lt;25 kg/m²)</td>
<td>41 (49.4)</td>
</tr>
<tr>
<td>Overweight (≥25 kg/m²–&lt;30 kg/m²)</td>
<td>31 (37.4)</td>
</tr>
<tr>
<td>Obese (≥30 kg/m²)</td>
<td>11 (13.3)</td>
</tr>
<tr>
<td>Pre-injury physical activity (IPAQ-SF category)</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>7 (8.4)</td>
</tr>
<tr>
<td>Moderate</td>
<td>24 (28.9)</td>
</tr>
</tbody>
</table>
The mean (SD) sitting time was 11.07 (1.89) hours per day with participants spending 41%–98% of their waking hours sitting (median 79%) (Figure 1 and Table S2 of Supplementary). Participants with lower limb fractures spent more time sitting than those with upper limb fractures. Overall, participants took a median (IQR) of 1575 (618–3445) steps per day, but participants with lower limb fractures, took only 647 (344–1140) steps per day. Participants overall spent only 5.22 (1.50–20.78) minutes per day engaging in moderate intensity physical activity, while for those with lower limb fractures this was less than 2 minutes per day (Figure 1 and Table S2 of Supplementary). No vigorous-intensity physical activity was recorded for 78% of participants and the remainder recorded very low values (<3 mins). Therefore this variable was not further examined.

![Figure 1](image)

**Figure 1.** Sitting time and physical activity patterns of study population.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-injury physical activity (IPAQ-SF category)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>52 (62.7)</td>
</tr>
<tr>
<td>Days since fracture/surgery (mean, SD)</td>
<td></td>
</tr>
<tr>
<td>To activPAL start</td>
<td>16.7 (5.0)</td>
</tr>
<tr>
<td>To actigraph start</td>
<td>16.5 (4.3)</td>
</tr>
</tbody>
</table>

*Note: Non-weight bearing: patient is not permitted to bear any weight on the affected limb (i.e. must use crutches to hop on the unaffected limb); partial weight-bearing: patient is allowed to bear some weight on the affected limb (i.e. must use crutches to walk); weight bearing as tolerated: patient is allowed to bear as much weight on the limb as they can tolerate (i.e. can walk with or without crutches). AC: acromioclavicular joint.*
Multivariable regression analyses showed that for participants with LL fracture, there was an increase in adjusted mean sitting time of 2.5 hours per day relative to participants with UL fracture ($\beta = 2.5$ hours, $p < 0.001$), while for each day since surgery/injury there was a reduction in adjusted mean sitting time of approximately four minutes per day ($\beta = -0.06$ hours, $p = 0.048$; Table 2). These variables accounted for 44% of the variance in sitting time (adjusted $R^2$). Lower limb fracture was associated with 80% fewer steps per day relative to UL fracture (RGM = 0.20, $p < 0.001$), accounting for 60% of the variance. Finally, LL fracture was associated with 89% less time spent in MPA relative to UL fracture (RGM = 0.11, $p < 0.001$), and older age was associated with 59-62% less time spent in MPA relative to participants in the youngest age group (RGM = 0.38–0.41, $p = 0.01$), accounting for 44% of the variance. There was no association between the predictive variables sex, BMI and pre-injury physical activity and any outcome ($p > 0.05$ for all).

Table 2. Multivariable analysis for independent predictors of sitting time, steps and moderate-intensity physical activity.

<table>
<thead>
<tr>
<th></th>
<th>Sitting time (hours/day) (n = 78)</th>
<th>Steps (n/day) (n = 78)</th>
<th>Moderate-intensity physical activity (mins/day) (n = 77)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td>$\beta$ (95% CI)</td>
<td>$\beta$ (95% CI)</td>
<td>$\beta$ (95% CI)</td>
</tr>
<tr>
<td>18-34</td>
<td>–</td>
<td>–</td>
<td>Ref</td>
</tr>
<tr>
<td>35-49</td>
<td>0.38 (0.18, 0.79)</td>
<td>–</td>
<td>0.01</td>
</tr>
<tr>
<td>50-69</td>
<td>0.41 (0.20, 0.82)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Injury group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Limb</td>
<td>Ref</td>
<td>&lt;0.001</td>
<td>Ref</td>
</tr>
<tr>
<td>Lower Limb</td>
<td>2.50 (1.86, 3.14)</td>
<td>0.20 (0.15, 0.27)</td>
<td>0.11 (0.06, 0.20)</td>
</tr>
<tr>
<td>Days since fracture/surgery</td>
<td>$-0.06$</td>
<td>0.048</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>($-1.13$, $-0.001$)</td>
<td>-</td>
<td>–</td>
</tr>
</tbody>
</table>

*Note: Missing data n = 1 (0 mins moderate physical activity recorded). $\beta$: beta coefficient; CI: confidence interval; RGM: ratio of geometric means.

4. Discussion

In this study we aimed to characterise patterns of sitting time and physical activity in adults following isolated limb fracture, and to identify factors associated with these patterns. Approximately two weeks post-hospital discharge, the working-age adults included in the current study were engaged in high amounts of sitting time, took few steps and engaged in little physical activity. Compared to participants with UL fractures, participants with LL fractures spent more time sitting, took fewer steps and were less physically active. Older participants also had lower levels of physical activity. As expected, participants spent less time sitting as time passed following surgery or injury.

Relative to population norms, our participants were highly sedentary. The US National Health and Nutrition Examination Survey (NHANES) reported mean daily sedentary time (accelerometry $<100$ cpm) in 6329 adults aged 20–85 years of up to 9.3 hours/day [45]. This upper limit, recorded in the oldest adults (70–85 years), was similar to sitting time for patients in our study with upper limb fractures, which is striking considering the much younger age of our participants. Notably, participants in our study with LL fractures recorded almost three hours per day more sitting time than...
Our participants also took very few steps relative to population values. Participants in the Australian-based Tasped study (n = 2576, mean age 59 years) recorded, via pedometers, an average of 7774–8925 steps per day [46]. Our overall median step count was substantially lower (~1500 steps per day) and was <700 steps per day in participants with LL fractures. For MPA, participants with upper limb fracture compared favourably with women of a similar age from the NHANES study, who recorded approximately 15 to 20 minutes of MPA per day (Actigraph 2020–5999 cpm) [47]. However, participants in our study with LL fractures recorded substantially less daily MPA than even the least active NHANES participants (women aged 70+ years), who recorded approximately 5 mins/day of MPA.

Previous studies of device-measured activity in older adults with hip fractures have also demonstrated high levels of sedentary time (up to 99% of the day) [38,48] minimal steps (as few as 36 steps/day) [48] and limited MPA (as little as 1.8 mins/day) [38,40], both in the early stage of recovery [48] and up to six months post fracture [38]. However, adolescents with LL fracture, have been shown to undertake over 20 minutes of MPA within the first month post-injury, suggesting a significant effect of age, and possibly physical health on post-injury physical activity [39].

Notably, patients’ pre-injury physical activity levels were not associated with post-injury activity levels, suggesting that, regardless of patients’ motivation to be active, or previous exercise habits, it is the injuries themselves, and the mobility restrictions that they cause, that are the main barrier to activity. This is supported by our finding that patients with LL fractures were significantly less active than those with UL fracture, and indicates that patients with more physically limiting injuries, such as tibial fractures, may need more education from clinicians in the early stage of recovery, particularly in relation to breaking up prolonged bouts of sitting. However, considering that people with UL fractures also recorded high levels of sitting time and few steps, there are other factors, such as pain, fatigue, medication side-effects or impaired haemodynamics that may contribute to inactivity following fracture [48]. Patients with both upper and LL fractures spent less time sitting as time passed, suggesting that some of these factors may be less influential as patients recover. While we did not collect data on mobility, pre-injury function or pain as potential correlates of physical activity and sitting time, these would be valuable to monitor in future research.

We do not yet know the long-term impact of this acute reduction in patients’ activity levels. However, there is evidence that lack of daily physical activity and high volumes of sedentary time, even for just a few weeks, can have an immediate impact on physical function and overall health. In healthy, previously active young adults, less than three weeks of bed rest was sufficient to cause significant muscle wasting and weakness [15]. In middle-aged adults substantial reductions in cardiovascular capacity have occurred after as little as 10 days of bed rest [16]. In both healthy and clinical populations, uninterrupted bouts of sitting are detrimental to glucose control, fat metabolism and blood pressure, which are all associated with chronic diseases such as diabetes and stroke [49]. Furthermore, while necessary for bone healing in some patients, immobility following fracture significantly reduces bone density which is known to increase the risk of future fracture [17].

Future research should investigate whether these changes are avoidable with early intervention. For example, for patients who are unable to walk without supervision, breaking up sitting time with regular standing breaks could provide a feasible alternative. Such interruptions to prolonged sitting, even for as little as one minute, have been shown to have positive effects on cardio-metabolic health markers, such as BMI and waist circumference in general and clinical populations [49]. For patients
using gait aids, who have difficulty walking long distances, short bursts of ambulation are a safe and viable option. These light activity bouts can have important cardio-metabolic effects, including lowered blood glucose and insulin, and reductions in blood triglycerides [50,51]. In the long-term, these simple interventions may even reduce the risk of chronic diseases such as type 2 diabetes and heart disease [20].

As demonstrated in previous physical activity research, there is the potential for sampling bias towards those with an interest in, or high levels of, physical activity [52]. Considering that the majority of our participants reported high levels of pre-injury physical activity, this is likely to be the case in the current study. However, this may also indicate that physical inactivity and high volumes of sitting are even higher in the wider orthopaedic population. Another limitation is that the Actigraph has not previously been validated for measurement of physical activity in the fracture population and further methodological research is needed in this population. However, we did use the activPAL rather than Actigraph to measure steps, which has been shown to have higher accuracy at slow walking speeds and when using gait aids [29]. It is also a limitation that certain activities commonly performed by patients recovering from fractures, such as swimming and stationary cycling, were not able to be measured with our devices. Finally, there is evidence of only fair agreement between self-reported and device-measured physical activity levels in patients with fractures, calling into question the accuracy of patients’ pre-injury physical activity levels [25]. However, there are currently few feasible options for capturing device-based pre-injury physical activity levels. Despite these limitations there were numerous strengths to our study, including the large sample size for studies of this kind, device-based measurement of physical activity and sitting time via gold-standard measures and investigation of a population not previously studied.

Acknowledgments

Parneet Sethi, Pamela Simpson, Jennifer Gong and Anthony Tsay are thanked for their assistance with this project. We gratefully acknowledge the participants of this research for contributing their time and effort. This project was funded by a Monash University Faculty of Medicine, Nursing and Health Sciences Strategic Grant. The funder had no involvement in the study design, data collection, analysis and interpretation of data, the writing of the report or the decision to submit the article for publication. CE was supported by a National Health and Medical Research Council of Australia (NHMRC) Early Career Fellowship (1106633). BG was supported by an Australian Research Council Future Fellowship (FT170100048). NO was supported by a NHMRC Program Grant (569940), a Senior Principal Research Fellowship (1003960) and by the Victorian Government’s Operational Infrastructure Support program. DD was supported by a NHMRC Senior Research Fellowship (1078360) and the Victorian Government’s Operational Infrastructure Support Program.

Conflict of interest

All authors declare no conflicts of interest in this paper.
References


© 2019 the Author(s), licensee AIMS Press. This is an open access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0)