

# The emergence of sedentary behaviour physiology and its effects on the cardiometabolic profile in young and older adults

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Received: 12 March 2015 / Accepted: 20 August 2015 / Published online: 28 August 2015  
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**Abstract** It has recently emerged that sedentary behaviour is independent of a lack of physical activity as individuals can be sufficiently active, based on the recommended physical activity guidelines, but also spend the majority of their waking hours engaging in sedentary behaviour. Individuals who follow this pattern of physical activity and sedentary behaviour are known as ‘active couch potatoes’. Sedentary behaviour has been found to have detrimental effects on cardiometabolic markers associated with cardiovascular disease. Since the positive effects of moderate-to-vigorous intensity physical activity do not necessarily negate the deleterious effects of sedentary behaviour on cardiometabolic markers, it is postulated that engaging in light physical activity is an intervention that will successfully reduce levels of sedentary behaviour and may hence improve health markers of quality of life. We propose that such lifestyle changes may be particularly relevant to older populations as these engage in sedentary behaviour for the majority of their waking hours, thereby adding to the negative aging effect on cardiometabolic markers.

**Keywords** Cardiometabolic · Older adults · Physical activity · Sedentary behaviour

## Introduction

The 2012 Health Survey for England found 67 % of males and 55 % of females aged 16 years and over met the recommended physical activity guidelines (Craig 2013; Craig et al. 2009). However, the average time spent performing sedentary behaviour (SB) was still 10 h day<sup>-1</sup> (Craig 2013). Whilst these surveys provide valuable information, they have their limitations, as they are highly reliant on the participant’s recall ability. Indeed, it is now thought that the prevalence of SB is even higher than previously reported, with recent accelerometer-derived survey data presenting that as few as 10 % of the population in fact do meet the recommended physical activity guidelines (Craig et al. 2009). SB is associated with an increased risk of developing factors associated with cardiovascular disease (CVD) (Healy et al. 2008b), such as type 2 diabetes mellitus (Oggioni et al. 2014) and atherosclerosis (Laufs et al. 2005). By 2025, it is predicted that five million Britons will be type 2 diabetics (Diabetes UK 2012).

Government health interventions have focused on improving physical health status by increasing bouts of moderate-to-vigorous physical activity (MVPA). The National Health Service (NHS) recommends 19–64+-year-old adults should engage in 150 min of MVPA per week, which is commonly divided into five 30-min bouts a week (National Health Service 2013b). However, individuals who meet the physical activity guidelines still display cardiometabolic risk factors associated with CVD, and this is thought to be linked to their amount of

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SB, irrespective of the amount of MVPA undertaken (Healy et al. 2008b). Therefore, the research community has shifted focus towards physical activity and SB levels during the remaining 15.5 h of daily waking time (Hamilton et al. 2008). As the independent physiological characteristics of SB and MVPA have become apparent, a new physical activity population known as ‘active couch potatoes’ has emerged (Gennuso et al. 2013; Healy et al. 2008b; Peddie et al. 2013). With life expectancy increasing, populations aged 60 years and older are projected to account for 25 % of the UK population by the year 2035 (Office for National Statistics 2012). Aging is associated with an increase in SB (Harvey et al. 2013) and studies examining the association between SB and CVD risk are warranted as the prevalence of CVD cases in the UK is greatest in populations aged 65 years and over (British Heart Foundation 2014).

This literature review aims to discuss the emergence of the ‘active couch potato’ lifestyle, and how the independent effects of SB and MVPA on cardiometabolic markers, associated with CVD, develop throughout the age spectrum.

### Defining sedentary behaviour

The definition of SB has been inconsistent throughout the literature due to different SB activities and the methods used to determine these SBs. Most studies classify SB as  $\leq 1.5$  metabolic equivalent tasks (METs) (Ainsworth et al. 2000; Owen et al. 2010; Pate et al. 2008; Rowlands et al. 2013; Tremblay et al. 2010); however, certain light intensity physical activities (LIPAs) (standing) can elicit similar MET values (Ainsworth et al. 2000). ‘Sedentary’ originates from ‘*sedere*’, Latin for ‘to sit’. Therefore, the definition of SB should not only include the MET threshold ( $\leq 1.5$  METs) but also acknowledge postural positions (sitting, lying, TV viewing, driving) (Tremblay et al. 2010).

Tremblay et al. (2010) further suggested that, similar to the measurement of physical activity using the (frequency, intensity, time, type (FITT), SB should be recorded by using (SB frequency, interruptions in SB, time duration of each SB, type of SB (SITT). SITT is recommended as SB does not have large variations in intensity and the

number of interruptions in SB appears to be an important determinant of health status.

### The effects of sedentary behaviour can be measured independent of those of moderate-to-vigorous physical activity

Generally speaking, physical activity may be considered as any activity of daily living that leads to the expenditure of energy, over and above the levels required for maintaining basal metabolic activities; threshold is usually considered as anything at least 1.5 times greater than resting metabolic rate (Mansoubi et al. 2015). The misclassification of SB under the umbrella of physical activity stems from the data collection methods of early epidemiological research. The Harvard Alumni study (Paffenbarger et al. 1986) used self-reports to gain insight into physical activity levels by recording the frequency of stair climbing, city blocks (0.13 km) walked, and sports played. Individuals who failed to expend more than 2000 kcal week<sup>-1</sup> through exercise were classed as sedentary even though there were no questions relating to SB. This assumption that too little MVPA equates to large amounts of SB may have come about through self-reports because it is easier for participants to recall more strenuous bouts of activity they have performed (Kriska 2000), rather than how much time they have spent performing SB. Additionally, it can be difficult to quantify the frequency and length of SB due to the focus of questions only relating to MVPA (e.g. “Ask only about activities that are at least the intensity of walking, but include walking.”—Stanford 7-day recall instructions (Sallis 1985)). Therefore, it is easy to understand how early physical activity research has influenced government health initiatives to focus on increasing MVPA to improve overall health, rather than aiming to reduce SB time.

Conversely, SB and MVPA cause quantifiably different cardiometabolic responses which do not correspond to the physical activity spectrum. SB was found to decrease lipoprotein lipase (LPL) activity (relative to ambulatory controls) by 55 %, in oxidative fibres, whereas voluntary running (56 m min<sup>-1</sup>) caused no increase in relative LPL activity in oxidative fibres (Bey and Hamilton 2003). In the singular physical activity spectrum, it would be expected that the decline in LPL from SB would be equally and oppositely matched by the benefits of MVPA. Therefore, in terms of

physiological response, the physical activity spectrum should be bi-axial. The *y*-axis should range from high SB to low SB, and the *x*-axis should range from insufficient MVPA to sufficient MVPA, subsequently allowing for the acknowledgment of the active couch potato lifestyle.

In light of this independence between SB and MVPA, Healy et al. (2008b) found populations (aged  $47.3 \pm 13.1$  years) that met the recommended physical activity guidelines still displayed associations between increased SB and CVD risk factors. This effect was more noticeable in their female sub-population (triglyceride increase, from lowest to highest quartile of TV viewing hours: female  $0.06 \text{ mmol l}^{-1}$ , CI 95 %  $0.04$ – $0.09$ ,  $p < 0.001$ ; male  $-0.001 \text{ mmol l}^{-1}$ , CI 95 %  $-0.03$ – $0.03$ ,  $p = 0.511$ ). The greater association in females may be due to sex differences in fuel homeostasis as 6 days of bed rest causes a 570 % increase in female lipogenesis activity compared to no difference from baseline in males (Blanc et al. 2000b). In terms of similar observations in older persons, Bankoski et al. (2011) found that individuals aged 60 years and older were more likely to suffer from metabolic syndrome if they engaged in longer bouts of SB and had a greater percentage of time spent performing SB per day, independent of any physical activity they undertook in parallel. Healy et al. (2008b) also highlight this example of an active couch potato who is classified as ‘active’ under the current physical activity guidelines (National Health Service 2013b) but spends the majority of their waking hours engaging in SB. In older active couch potatoes ( $74.6 \pm 6.4$  years), positive associations between increased SB and fasting plasma glucose concentration, but no negative association between increased MVPA and fasting plasma glucose concentration or interaction between SB and MVPA plasma glucose concentration, were found (Gennuso et al. 2013). The lack of interaction between SB and MVPA highlights that the two are independent of each other throughout the aging process.

The findings of Gennuso et al. (2013) are supported in acute environments as the active couch potato lifestyle appeared to elicit effects on glucose regulation that were similar to the effects of prolonged SB (Peddie et al. 2013). During a 9-h period, young participants (18–40 years) consumed a glucose solution at 3-h intervals. Participants engaged in either 9 h of prolonged sitting, 30 min of MVPA then 8.5 h of sitting (active couch potato), or sitting interrupted every 30 min by 1 min 40 s of walking (LIPA). Overall, plasma glucose incremental

area under the curve (iAUC) was similar for prolonged sitting and active couch potato groups ( $48.8 \text{ mmol l}^{-1} 9 \text{ h}^{-1}$  vs  $47.2 \text{ mmol l}^{-1} 9 \text{ h}^{-1}$ , respectively) while interrupted sitting produced lower plasma glucose concentrations ( $29.9 \text{ mmol l}^{-1} 9 \text{ h}^{-1}$ ) (Peddie et al. 2013), consequently highlighting that the physical activity guidelines may not ameliorate the deleterious consequences of SB. The UK, Canada, and Australia have recently updated the physical activity guidelines to recommend a reduction in SB. Although evidence of the effects of SB is increasing (see Table 1 for summary), no guidance is currently given as to the maximum amount of daily SB, how often SB should be interrupted, and methods to reduce SB.

### Benefits of LIPA

Interrupting long bouts of SB appears to be an important determinant of physical well-being. Irrespective of total SB, MVPA time, and age, individuals (40–87 years) who broke up SB on 673 occasions with LIPA (average break duration 4.50 min), over 5 days of accelerometer wear time, had a  $0.88 \text{ mmol l}^{-1}$  ( $p < 0.05$ ) decline in 2-h plasma glucose concentration compared to individuals who only had 506 breaks in SB. Reductions in triglycerides, body mass index (BMI), and waist circumference were also related to an increase in SB breaks (Healy et al. 2008a). This is further supported by a crossover study which found 2-h plasma glucose concentration, again independent of age, was decreased in middle-aged to older adults (45–65 years) when SB was interrupted every 20 min with 2 min of LIPA ( $1.7 \text{ mmol l}^{-1} 1 \text{ h}^{-1}$  decline) or MVPA ( $2.0 \text{ mmol l}^{-1} 1 \text{ h}^{-1}$  decline) compared to prolonged sitting (Dunstan et al. 2012). It appears that physical activity and SB plays an important role in the glucose insulin axis as 53 % of the variance in 2-h plasma glucose concentration can be explained by SB ( $r^2 = 0.18$ ), LIPA ( $r^2 = 0.17$ ) and MVPA ( $r^2 = 0.18$ ) (Healy et al. 2007). Therefore, because LIPA can be easily accumulated and prevents the deleterious effects of SB on additional cardiometabolic markers (e.g. LPL) (Bey and Hamilton 2003; Healy et al. 2008a), physical activity interventions should aim to interrupt SB with LIPA.

The optimum length of SB bouts and LIPA interruptions has not yet been determined. Beneficial associations with interruptions in SB and plasma glucose concentration were still visible in young persons ( $25.9 \pm 5.3$

**Table 1** Sample of studies examining the effects of SB on markers of cardiometabolic health in older persons

Author	Age group (years)	Measure of SB/PA	Measurement type	Outcome variable	Result
Bankoski et al. (2011)	71.0±8.0	Total SB time SB bouts SB breaks SB intensity	ActiGraph AM-7164 accelerometer	Metabolic syndrome	(**) 3.10 ↑ in metabolic syndrome development odds ratio (OR) from lowest to highest quartile of S time of total wear time
Gennuso et al. (2013)	74.6±6.5	Total SB time	ActiGraph AM-7164 accelerometer	Fasting plasma glucose C-reactive protein	(**) 4 mg dl <sup>-1</sup> ↑ from lowest to highest quartile of SB hours 0.10 mg dl <sup>-1</sup> ↑ from lowest to highest quartile of SB hours
Healy et al. (2008a)	40–87	SB breaks	Actigraph WAM-7164	2-h plasma glucose Triglycerides BMI Waist circumference	(**) $r^2=0.14$ with ↑ in SB breaks (**) $r^2=0.13$ with ↑ in SB breaks (**) $r^2=0.05$ with ↑ in SB break (**) $r^2=0.26$ with ↑ in SB breaks (all independent of age)
Dunstan et al. (2012)	45–65	MIPA or LIPA breaks in SB every 20 min for 2 min	NA	2-h plasma glucose	(N/A) LIPA ↓ 2-h plasma glucose by 1.7 mmol l <sup>-1</sup> , independent of age (N/A) MIPA ↓ 2-h plasma glucose by 2.0 mmol l <sup>-1</sup> , independent of age
Healy et al. (2007)	30–87	Total SB time Total LIPA time Total MIPA time	ActiGraph WAM 7164	2-h plasma glucose	(**) Total SB time ↑ 2-h plasma glucose ( $r^2=0.18$ ), adjusted for age (**) Total LIPA time ↓ 2-h plasma glucose ( $r^2=0.17$ ), adjusted for age (**) Total MIPA time ↓ 2-h plasma glucose ( $r^2=0.18$ ), adjusted for age
Latouche et al. (2013)	45–65	MIPA or LIPA breaks in SB every 20 min for 2 min Bed ridden	NA	Dynein light chain 1 gene	(N/A) 1.6-fold ↑ with ↑ intensity breaks in SB
Yamanouchi et al. (1992)	62–87	SB breaks	NA	Glucose infusion rate	(N/A) Glucose infusion rate 12.2 % ↓ in bed ridden compared to controls
Carson et al. (2014)	20–79	SB breaks	Actical accelerometer	HDL-C Triglycerides plasma glucose	(**) 10 extra SB breaks per day: 0.01 mmol l <sup>-1</sup> ↑ HDL-C 3.72 % ↓ 0.57 % ↓ (**) (all independent of age)
Fatouros et al. (2005)	69.8±3.8	6 months detraining	Subjective	Leptin	(N/A) 0.4 ng ml <sup>-1</sup> ↑ above pre-training baseline

Please note that (\*\*) indicates that results were statistically significant after adjustment for MVPA. Where (N/A) is used, indicates a study where the study design did not allow MVPA adjustments

N/A not applicable, ↑ increase, ↓ decrease

years) when SB bouts were increased to 30 min and interruption length was decreased to 1 min 40 s (plasma glucose iAUC: interrupted,  $29.9 \text{ mmol l}^{-1} 9 \text{ h}^{-1}$ , prolonged sitting,  $48.8 \text{ mmol l}^{-1} 9 \text{ h}^{-1}$ , active couch potato (30 min continuous MVPA followed by 8.5 h sitting),  $47.2 \text{ mmol l}^{-1} 9 \text{ h}^{-1}$ ) (Peddie et al. 2013). This shows that benefits in SB breaks still exist with relatively increased SB time and decreased SB interruption length. However, Peddie et al. (2013) interruption intervention caused a lower plasma glucose iAUC per hour compared to Dunstan et al. (2012) ( $3.32 \text{ mmol l}^{-1} 1 \text{ h}^{-1}$ ,  $5.10 \text{ mmol l}^{-1} 1 \text{ h}^{-1}$ , respectively). This discrepancy in findings may be explained by Dunstan et al. (2012) using an older population compared with Peddie et al. (2013) (55 and 25 years, respectively); glucose regulation declines with age (Gong and Muzumdar 2012). As a result, physical activity guidelines may require different SB recommendations for different age groups.

### Sedentary behaviour and physical activity: impact on glucose regulation

The interaction between SB and glucose regulation has been a popular topic due to the adverse effects hyperglycaemia has on the cardiovascular system. Newly recommended physical activity guidelines aimed at reducing SB by increasing LIPA could be crucial to the prevention of type 2 diabetes mellitus and subsequent CVD as SB and LIPA explain 35 % of the variance in 2-h plasma glucose concentration (Healy et al. 2007). However, relationships between SB and fasting plasma glucose are not commonly found in both self-report and objectively measured SB/physical activity studies (Dunstan et al. 2007; Healy et al. 2007, 2008a). This suggests that SB and physical activity influence glucose regulation through skeletal muscle related mechanisms as 2-h plasma glucose is characterised as a measure of skeletal muscle insulin resistance, whereas fasting plasma glucose is more reflective of hepatic insulin resistance with sustained skeletal muscle insulin sensitivity (Abdul-Ghani et al. 2006).

It is thought that a reduction in facilitated glucose diffusion into skeletal muscle cells is brought about through a downregulation of the glucose transporter, glucose transporter type-4 (GLUT-4). In the *vastus lateralis*, aging explains 7.8 and 26.0 % of the variance in the decline in GLUT-4 concentration in males and females, respectively (Houmard et al. 1995). In addition, the aging effect on GLUT-4 concentration also appears

to be fibre type dependent, as a reduction in GLUT-4 is found with aging in fast twitch fibres but not in slow twitch fibres of the *vastus lateralis* (Gaster et al. 2000). This decline in fast twitch GLUT-4 concentration may, in fact, be due to decreased participation in free-living physical activity. In line with the above observations and inference, moderate intensity physical activity (MIPA) in older populations is found to increase GLUT-4 concentration, as it does in their younger counterparts (Cox et al. 1999). In support of the SB-GLUT-4 relationship, data shows that seven young endurance runners aged 33 years displayed a 17.5 % reduction in gastrocnemius GLUT-4 concentration and a decrease in glucose disposal rates ( $1.9 \text{ mg kg FFM}^{-1} \text{ min}^{-1}$  decline), despite an increased insulin concentration of  $4.2 \text{ } \mu\text{m ml}^{-1}$ , after 6 days of bed rest (Vukovich et al. 1996). Thus, the relationship between free-living SB and GLUT-4 which has been exhibited in young populations is likely to be present in older persons, though the latter is yet to be determined and requires further research. The evidence thus far suggests that longitudinal physical activity intervention in aged participants (60–72 years) causes an increase in *vastus lateralis* GLUT-4 concentration (Biensø et al. 2015). It appears that this effect could also be found in acute bouts of physical activity. Breaking up SB with LIPA or MIPA increases the expression of the gene that encodes for dynein light chain 1 (DNLL1). DNLL1 plays a role in the transcription of GLUT-4 in middle aged to older adults (Latouche et al. 2013) and is thought to be part of a mechanism for GLUT-4-induced reduction in plasma glucose during SB breaks.

Insulin concentration may increase to compensate for the reduction in glucose uptake via the GLUT-4 pathway but consequently cause a decline in skeletal muscle insulin sensitivity. It should be noted that physical activity causes an increase in GLUT-4 translocation (Lund et al. 1995) and subsequently an increase in glucose clearance rate, independent of insulin (Lund et al. 1995). This increase in GLUT-4 translocation with physical activity (seen in the study of Lund et al. (1995)) may explain why interrupting SB with bouts of physical activity lowers plasma glucose concentrations compared with prolonged sitting (Healy et al. 2008a; Peddie et al. 2013). On the other hand, 30 min of MIPA followed by 8.5 h of prolonged sitting produced plasma glucose iAUC results that were similar to



9 h of prolonged sitting (Peddie et al. 2013). Based on the discussions above, this short bout of MIPA should have increased GLUT-4 concentration and hence impacted on the iAUC. However, this short bout of physical activity may not have been enough to sustain an increased concentration of GLUT-4 over the remaining 8.5 h of SB as GLUT-4 is predicted to have a half-life of just 8–10 h (Host et al. 1998).

Recently, Bailey and Locke (2014) found that SB breaks every 20 min with 2 min of light intensity walking reduced postprandial plasma glucose concentration (iAUC  $18.5 \text{ mmol l}^{-1} 5 \text{ h}^{-1}$ , reduction of  $3.5 \text{ mmol l}^{-1} 5 \text{ h}^{-1}$ ) compared to prolonged sitting in young persons ( $24.0 \pm 3.0$  years). However, it was found that interrupting SB every 20 min with 2 min of standing (a LIPA) did not cause any beneficial decline in postprandial plasma glucose concentration (iAUC  $22.2 \text{ mmol l}^{-1} 5 \text{ h}^{-1}$ ) compared to prolonged sitting (iAUC  $22.0 \text{ mmol l}^{-1} 5 \text{ h}^{-1}$ ). Therefore, physical activity interventions should aim to interrupt SB with a physical activity that is a movement-based LIPA. In addition, objective measures of physical activity should distinguish between breaks in SB caused by standing and walking to increase the validity of epidemiological studies examining the association between physical activity, SB and cardiometabolic health.

Whilst glucose regulation declines with aging (Gong and Muzumdar 2012), exercise interventions can protect against the aging process. Bed-ridden, master athletes (aged 62–87 years) and healthy aging adults ( $76 \pm 2$  years) glucose infusion rates were compared to that of healthy young individuals and young athletes ( $20 \pm 1$  years). In the older sub-population, glucose infusion rates were higher in master athletes and lower in bed-ridden individuals compared with that in healthy aged individuals. Compared to young individuals, the healthy aged sub-population had lower glucose infusion rates whereas master athletes had similar glucose infusion rates (Yamanouchi et al. 1992). Managing physical activity and SB is crucial in aging populations to manage glucose regulation as the prevalence of diabetes mellitus is nearly sevenfold greater in adults over 60 years compared to young populations (20 years) (Shaw et al. 2010). Although it is evident that frequent MVPA can protect against the effects of aging on glucose control (Yamanouchi et al. 1992), it can be difficult for elderly populations to accumulate the recommended levels of MVPA. Therefore, future intervention studies, similar to the work of Peddie et al. (2013), Healy et al. (2008a),

and Bailey and Locke (2014) should be conducted using aging populations, whose waking hours are predominantly spent performing SB (Harvey et al. 2013), to examine the potential benefits of LIPA breaks.

### Sedentary behaviour and physical activity: impact on cholesterol and LPL

Low-density lipids (LDL-C; normative value  $< 3 \text{ mmol l}^{-1}$ ), high-density lipids (HDL-C; normative value  $> 1 \text{ mmol l}^{-1}$ ), and triglycerides (normative value  $1.7 \text{ mmol l}^{-1}$ ) are collectively known as total cholesterol (normative value  $< 5 \text{ mmol l}^{-1}$ ) (National Health Service 2013a). Decreasing LDL-C by  $1 \text{ mmol l}^{-1}$  reduces the relative risk of cardiovascular events by 22 % in populations aged 65–74 years, and by 16 % in individuals over 75 years (Baigent et al. 2010). In conjunction, a  $0.78 \text{ mmol l}^{-1}$  increase in triglyceride concentration can increase the relative risk of CVD by 15 % in males, and 9 % in females in persons aged  $50.8 \pm 6.7$  years, respectively (Cui et al. 2001). Meanwhile, HDL-C has been shown to have a protective effect as a  $0.55 \text{ mmol l}^{-1}$  increase in HDL-C is associated with a decreased risk of coronary events by a factor of 1.70 and 1.95 in elderly (80 years) males and females, respectively (Aronow and Ahn 1996). These findings are likely linked to HDL-C role in transporting excessive cholesterol from peripheral tissues to the liver in a process known as reverse cholesterol transport (Sviridov and Nestel 2002), whereas LDL-C and triglycerides contribute to the pathogenesis of atherosclerosis. Increasing concentration of LDL-C can cause an accumulation within the arterial intima (Björnheden et al. 1996). These LDL-C particles become oxidised and bind to receptors on endothelial and smooth muscle cells causing apoptosis of smooth muscle cells (Björkerud and Björkerud 1996), impaired nitric oxide (NO) synthesis (Keaney et al. 1996) and oxidative stress (Cominacini et al. 2000). Macrophage secretion into the intimal space occurs to take up the oxidised LDL-C particles and consequently differentiate into foam cells (Rios et al. 2013). Triglyceride-rich very-LDL-C remnants, resulting from partial hydrolysis of triglycerides by LPL, bond to cholesterol esters from HDL-C via cholesteryl ester transfer proteins. These

cholesterol-enriched, triglyceride-poor species accumulate and are up taken by macrophages subsequently, forming foam cells (Talayero and Sacks 2011). LPL not only interacts with triglycerides during the pathogenesis of atherosclerosis but also promotes retention of LDL-C within the intimal space by binding LDL-C to proteoglycans, found on smooth muscle cells. This retention allows more time for LDL-C particle modification and subsequently promotes uptake by macrophages (Li et al. 2014).

However, whether LPL is antiatherogenic or proatherogenic is dependent on the cell/tissue that is expressing the enzyme (Mead and Ramji 2002). Skeletal muscle, plasma, and adipose tissue LPL is responsible for the clearance of lipoprotein particles and is therefore antiatherogenic, whereas endothelial LPL is proatherogenic (Clee et al. 2000; Mead et al. 1999; Mead and Ramji 2002). Changes in LPL concentration provide the best representation of the independence between physical activity and SB effects on cardiometabolic markers of health status. As shown in Sprague–Dawley rats, 6 h of SB was found to decrease LPL activity (relative to ambulatory controls) by 55 %, in postural oxidative fibres (soleus) while HDL-C concentration declined by 22 %. On the other hand, voluntary running (56 m min<sup>-1</sup>) caused no increase in relative LPL activity in oxidative fibres. Interestingly, in glycolytic muscles (*vastus lateralis*), voluntary running caused an increase in relative LPL activity above that of ambulatory controls (Bey and Hamilton 2003). The same authors (Bey et al. 2001) also reported a decrease in LPL activity in the *soleus* but not in the *tibialis anterior* with aging in two strains of rat. It was stipulated that this aging effect was visible in the *soleus* because it is a weight-bearing muscle and LPL activity is dependent on muscle contractile activity (Hamilton et al. 1998). This apparent aging effect on LPL activity in oxidative muscles was suggested to be due to a reduction in ambulatory movement with aging and thus a reduction in postural muscle contractile activity (Hennig and Lomo 1985). Therefore, the replacement of SB with LIPA may increase skeletal muscle LPL (antiatherogenic), subsequently reducing CVD risk in human populations.

In aging adults (74.2±0.5 years), individuals who engaged in more than 5 h per day of LIPA had a mean 0.23 mmol l<sup>-1</sup> (CI 95 % 0.07–0.39, *p*=0.002) increase in HDL-C concentration and a lower ratio of total cholesterol to HDL-C (−0.92, CI 95 % −1.36 to −0.48, *p*=

0.003) with a trend towards lower concentrations of LDL-C and triglycerides (Pescatello et al. 2000). Assessment of physical activity in this study was done using the Yale Physical Activity Survey, which despite being validated for use with elderly adults (Dipietro et al. 1993), may not necessarily provide an exact quantitative measurement of physical activity, or indeed, SB. It is possible that the use of a direct and objective measure of physical activity might have produced greater data reliability and hence improved the degree of statistically significant results, and/or greater associations between LIPA and HDL-C. Objective measures of physical activity and SB from 4935 Canadians (20–79 years) found an increase of ten breaks in SB per day (break in SB were greater than 1 min and classed as LIPA or MVPA) was associated with a 0.01 mmol l<sup>-1</sup> (CI 95 % 0.00–0.02) increase in HDL-C concentration and a 0.04 mmol l<sup>-1</sup> (CI 95 % −0.06 to −0.01) decline in triglyceride concentration, independent of age. However, an increase in SB breaks was not associated with a decline in LDL-C. Conversely, a 0.21 mmol l<sup>-1</sup> (CI 95 % −0.38–0.04) decline in LDL-C was associated with an hourly increase in MVPA (Carson et al. 2014). As a result, reducing SB by increasing LIPA appears to be partly beneficial in the management of cholesterol and LPL.

### Sedentary behaviour and physical activity: impact on Ghrelin–leptin–adiponectin axis

Ghrelin, leptin, and adiponectin were once considered to be single action hormones, mediating metabolism and hunger. However, their role in vascular function has become apparent and may forge the link between SB, obesity and CVD. Ghrelin (hunger hormone) and adiponectin (glucose regulation and fatty acid breakdown) appear to play a preventative role in CVD and type 2 diabetes mellitus risk (Nagaya et al. 2004; Spranger et al. 2003). Leptin, known as the satiety hormone, is a product of the *OB* gene and is a regulator of several physiological processes. Leptin is thought to play a role in the pathogenesis of atherosclerosis due to leptin receptor gene deficient rats becoming morbidly obese but immune to atherosclerosis (Nishina et al. 1994). Leptin has a positive association with body fat mass and obese individuals display an exponential rise in circulating plasma leptin concentrations, more than likely due to the onset of leptin resistance (Wang et al.

2001). Normative values in normal weight populations ( $6.60\text{--}18.8\text{ ng ml}^{-1}$ ) are lower than those of obese populations ( $28.6\text{--}34.8\text{ ng ml}^{-1}$ ) highlighting the association between circulating plasma leptin concentration and fat mass in younger population aged  $34.8\pm 4.6$  years (Kazmi et al. 2013). Interestingly, elderly populations also display higher fasting serum leptin levels than their younger counterparts ( $4.30\pm 1.90$  and  $1.25\pm 0.40\text{ ng ml}^{-1}$ , respectively (Di Francesco et al. 2006)). Thus, it is probable that older persons may show greater sensitivity to fluctuations in this hormone.

Due to leptin regulating the differentiation of bone marrow osteoprogenitor cells, it is thought that high concentrations of leptin binding to endothelial leptin receptors could cause calcification of the intimal wall (Parhami et al. 2001). A 10 % rise in plasma leptin concentration was associated with a 1.5 % decline in arterial compliance; on the other hand, no association was found between leptin concentration and flow-mediated dilation (FMD) in healthy, normal weight adolescents (Singhal et al. 2002). This suggests endothelial dilators are not initially affected by increased leptin concentrations. However, leptin has also been associated with an increase in oxidative stress (Wang et al. 2013), which can cause nitric oxide synthase (eNOS) uncoupling and subsequently, downregulation of NO (Förstermann and Münzel 2006). This mechanism may explain why negative associations between leptin concentration and endothelial dependent vasodilation exist in older populations (Gonzalez et al. 2013) due to oxidative stress being a mediator of declined FMD in populations older than 60 years (Franzoni et al. 2005; Taddei et al. 2001). Therefore, the effects of calcification appear to occur before the effects of oxidative stress in the development of vascular dysfunction and subsequently, CVD.

Taken together, both mechanisms could decrease vessel compliance and increase total peripheral resistance, which based on Darcy's law, decreases blood flow. A decline in blood flow increases the likelihood of fatty plaque build-up leading to the formation of atherosclerotic lesions at arterial bifurcation sites (VanderLaan et al. 2004).

In a controlled study, SB was simulated through 7 days of head down bed rest with 16 participants ( $32.4\pm 1.9$  years). The 7 days of bed rest caused 40

and 20 % increments in male and female plasma leptin concentrations, respectively (Blanc et al. 2000a). Similarly, in an intervention study, 6 months of detraining following a resistance training intervention in elderly individuals ( $69.8\pm 5.1$  years) caused an increase in leptin concentrations that exceeded pre-LIPA and MIPA resistance training concentrations. However, in the same study, with vigorous intensity physical activity (VIPA) training, at the end of the detraining, leptin concentrations were still comparatively improved than at pre-training levels, which suggests a physical activity intensity threshold (Fatouros et al. 2005). Therefore, further studies are warranted to explain the relationship between SB/physical activity and plasma leptin concentrations.

## Conclusions

The body of literature surrounding SB is rapidly expanding, and it has made the critical discovery that the cardiometabolic effects of SB are distinct from MVPA. Therefore, individuals can be sufficiently active, based on the physical activity guidelines, but still sedentary for the remainder of the day. Epidemiological and crossover studies have shown a relationship between SB and cardiometabolic markers associated with CVD. However, the objective measurement of physical activity and SB is still a new concept. Future studies need to ensure that objective measurements of physical activity and SB are able to distinguish sitting/lying from standing, and distinguish standing from LIPA that require movement. Although the use of pre-determined physical activity intensity thresholds, such as those derived by Freedson et al. (1998), are useful for between study comparisons, new research is needed to determine population-specific thresholds, as no two populations are the same, physiologically. The need for population specific accelerometer cut-off points is especially important in aging studies as most pre-determined cut-off points were created using young or middle-aged adults and therefore can cause misclassification of time spent in different physical activity intensities.

A threshold between sedentary populations and active couch potatoes has been established. However, what is not known is when an active couch potato becomes sufficiently active to counteract the effects of SB. A maximum threshold of SB needs to be established where the effects of SB on CVD risk are greatly reduced in individuals who report levels of SB that are below this



maximum threshold. In older adults, engaging in more than 7 h of SB per day is associated with an increased risk of all-cause mortality (Chau et al. 2013). However, further confirmation of this possible threshold is required using more refined methodologies.

Laboratory-controlled interventions have shown that breaking up SB with LIPA is a successful method to control cardiometabolic markers associated with CVD, such as glucose regulation. Further studies are warranted to establish links between SB breaks and other cardiometabolic markers as well as determining the optimum length of SB bouts and SB breaks to reduce CVD risk. More importantly, intervention studies that use aging populations are required as older populations are likely to engage in a greater amount of SB time than their young counterparts do.

Overall, SB research is still in the early stages of development, and more specifically, has not been implemented throughout the spectrum of ages, in particular, the older segment of the population (e.g. populations aged 75+). It is important that future research has a strong methodological framework in both epidemiological and intervention studies before any conclusions are implemented into the national health care initiatives.

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