Managing sedentary behavior to reduce the risk of diabetes and cardiovascular disease

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Published as: Dempsey, P. C., Owen, N., Biddle, S. J. H., & Dunstan, D. W. (2014). Managing sedentary behaviour to reduce the risk of diabetes and cardiovascular disease. *Current Diabetes Reports, 14*(9). doi:10.1007/s11892-014-0522-0

Abstract: (142 words)

Modern human environments are vastly different to those of our forebears. Rapidly advancing technology in transportation, communications, workplaces and home entertainment confer a wealth of benefits, but increasingly come with costs to human health. Sedentary behaviour – too much sitting as distinct from too little physical activity – contributes adversely to cardiometabolic health outcomes and premature mortality. Findings from observational epidemiology have been synthesised in meta-analyses and evidence is now shifting into the realm of experimental trials with the aim of identifying novel mechanisms and potential causal relationships. We discuss recent observational and experimental evidence that makes a compelling case for reducing and breaking up prolonged sitting time in both the primary-prevention and disease management contexts. We also highlight future research needs, the opportunities for developing targeted interventions, and the potential of population-wide initiatives designed to address too much sitting as a health risk.

Keywords:

Sitting time; Sedentary behaviour; Breaks in sedentary time; TV viewing time; Physical activity; Physical inactivity; Type 2 diabetes; Cardiovascular disease; Cardiometabolic risk; Mortality

Word count: 5009 words and 2 figures

INTRODUCTION

Globally, an estimated 382 million people have type 2 diabetes (T2D), a figure projected to rise to 592 million by 2035 [1]. Although diabetes management generally focuses on the significant risk of microvascular complications, cardiovascular disease (CVD) is the major complication for T2D patients, ultimately being the cause of death for about half of those with T2D, while accounting for some 30% of all-cause mortality [1, 2]. Unless a concerted effort to stem the tide of T2D can be mounted, these morbidity and mortality statistics are markers of a rapidly increasing public health problem over the coming decades, particularly in developing countries.

Increases in T2D worldwide and the huge burden of CVD are modern phenomena relative to human evolutionary history. Thus, in theory, they are reversible afflictions. Rapidly advancing technologies, such as in transportation, communications, workplace productivity and home entertainment provide numerous benefits, but have significantly reduced the need to be active [3]. Indeed, Lee and colleagues [4] recently presented estimates that 6–10% of all deaths from non-communicable diseases (T2D 7%; CVD 6%) worldwide can be attributed to physical inactivity, statistics now higher than those ascribed to smoking, making physical inactivity the fourth leading cause of death worldwide.

Sedentary behaviour, too much sitting as distinct from too little exercise, is defined by low energy expenditure (ranging from 1.0 – 1.5 METs; metabolic equivalents or multiples of the basal metabolic rate) in a sitting or reclining position during waking hours [5]. Examples include sitting at work or home, watching television, or driving a car. Total time spent in sedentary behaviour (i.e. time accumulated across all sedentary behaviours) is starting to receive greater attention as a distinct behavioural entity and risk factor for a host of adverse health outcomes and cardiometabolic risk, which may be additional to the risks associated with lack of moderate-to-vigorous physical activity (MVPA) during leisure time [6-9].

Here, we focus on sedentary behaviours in a context of reducing cardiometabolic risk, highlighting:

- the high volumes of sedentary behaviour observed in adult populations
- the distinctions between physical inactivity and sedentary behaviour
- recent evidence from observational epidemiology studies on the associations of sedentary behaviour with cardiometabolic risk

- the potential cardiometabolic benefits of breaking up sedentary behaviour for the prevention and potential management of T2D and CVD risk
- newly emerging experimental evidence that aims to identify mechanisms and dose-response relationships
- the importance of a population-based approach
- future frontiers and opportunities in the sedentary research field.

HIGH VOLUMES OF SEDENTARY TIME IN ADULT POPULATIONS: OBJECTIVE MEASUREMENT FINDINGS

Sedentary behaviours are now a ubiquitous component of modern society (illustrated in **Fig. 1**). This was recently exemplified in a study showing a steady shift towards more sedentary occupations over the last 5 decades in the USA [10]. Time outside of work is also increasingly being taken up by sedentary behaviours, such as screen based activities and television watching [11, 12]. Recent population-based data from developed countries, using portable sensors (accelerometers) indicate that adults spend about 55-70% of their waking hours engaged in sedentary behaviours [13-16], with one study reporting ≥9 hours per day sitting on average [17]. This is illustrated in **Fig. 1,** which shows accelerometer-derived data on how adults in the USA typically allocate their time throughout the day. As the small and large arrows demonstrate, the potential to increase daily physical activity, and in turn, decrease sedentary time, may be of greater magnitude for light-intensity activity than it is for MVPA. To date, efforts to influence participation in MVPA at the population level, such as through large-scale campaigns to promote walking, and other initiatives to encourage people to exercise during their leisure time have achieved only modest success [18]. There may, however, be untapped preventive-health and clinical management potential through shifting the high volume of time spent sedentary to light-intensity activity.

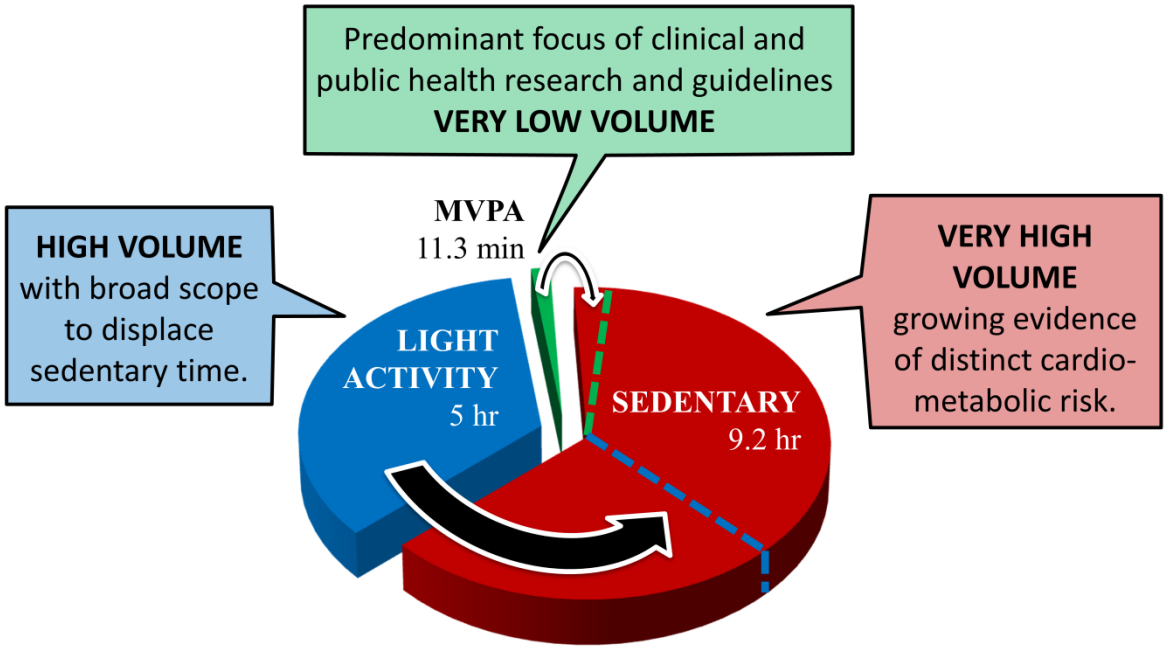

Fig. 1 Accelerometer data showing how 1367 older, overweight adults (mean age=70.5, mean BMI=29.7) from the U.S. National Health and Nutrition Examination Survey allocate their time throughout the day (using a <100 counts-per-minute cut-point); associated levels of light-intensity activity (100 to 1,951 cut-point); and moderate-to-vigorous intensity activity (1,952+ cut-point). The large and small arrows illustrate the potential scope for increasing light-intensity activity through displacing sedentary time and the very low volumes of MVPA typically observed.

The data shown in **Fig. 1** are sobering. Until recently, surveillance to identify the population prevalence of physically active and sedentary time has typically relied on self-reported MVPA during leisure time, or people's estimates of overall daily sitting or television/screen viewing time. However, activity monitoring using accelerometers (time, duration, frequency and intensity of movements) and inclinometers (sitting, standing and stepping) has more recently provided invaluable objective data [15, 19, 20]. With accelerometers, <100 counts per minute is typically classified as sedentary time [15], however the most accurate cut-point is yet to be universally agreed upon and may vary between different population groups.

Both objective and self-report measurement types have their strengths and limitations. Self-report is prone to recall and response bias, social desirability, or under- or over-reporting, while objective measurements are unable to differentiate between the different contexts of sedentary behaviours (i.e. the location and purpose of activities) and can be expensive in larger studies [21]. The increasing uptake of objective measurement in research

is now providing more definitive information on the relationship with cardiometabolic and health outcomes. Nevertheless, it is important to note that both self-report and objective methods are complementary in characterising sedentary behaviours and their relation to chronic disease biomarkers [22], thus both should continue to be utilised. For example, where interventions are concerned, it may be important to understand what types of sedentary behaviour are being undertaken, and often this can only be ascertained using self-report.

SEDENTARY BEHAVIOUR IS DISTINCT FROM NOT ENGAGING IN MODERATE-TO-VIGOROUS PHYSICAL ACTIVITY

The term 'sedentary' has sometimes been characterised as non-participation in moderate-to-vigorous activity (MVPA); in other words, sedentary behaviour has been characterised misleadingly as being the lower end of a physical activity continuum rather than 'sitting time'. However, with the rapidly proliferating body of evidence on sedentary behaviours within the research literature, using the term 'sedentary', (which originates from the latin term *sedere*, meaning 'to sit') to describe those who, technically, are 'physically inactive' is no longer appropriate [5, 23, 24]. Sedentary behaviours and light-intensity physical activity are strongly inversely related (see **Fig. 1**). Thus, conflating sedentary behaviour with lack of MVPA also takes the focus away from potentially distinct cardiometabolic effects of light-intensity physical activity and the significance of both physical activity and sedentary behaviour for health outcomes [14, 15].

In an adaptation of the graphic originally published by Swedish researchers [25], **Fig. 2** illustrates how MVPA, light-intensity activity and sedentary time are manifested in real life. The highest proportion of the adult populations from developed and developing countries can be found in the lower-left quadrant – not engaging in MVPA and spending much of their waking hours sitting. However, sedentary time and physical activity can coexist (the *Active Couch Potatoes* [15]) as is illustrated by the lower-right quadrant: a common example includes a desk-bound office worker who sits most of the day, but exercises in the morning before work.

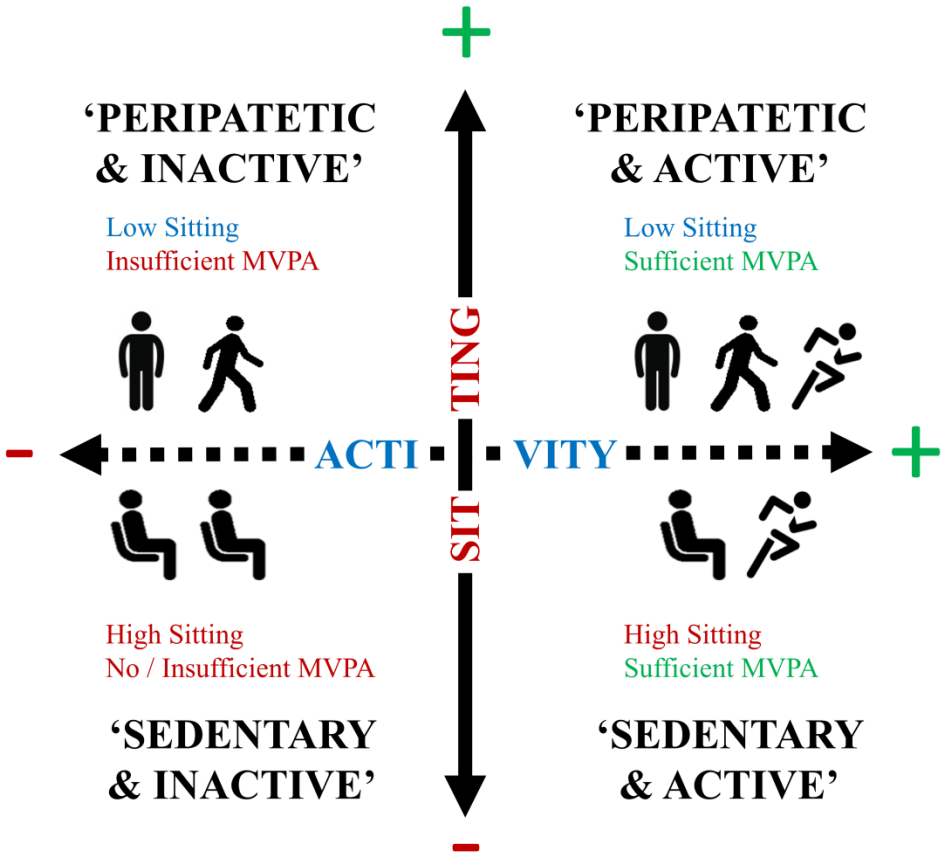

Fig. 2 Continuum of time spent sitting (vertical line) and in MVPA (horizontal line) as two distinct classes of behaviour. **Plus signs** = healthier behaviour pattern. **Minus signs** = riskier behaviour pattern (adapted from Ekblom-Bak, E, et al [25]). **Note:** Peripatetic = "to move around, and/or perambulate" and denotes not participating in MVPA, but sitting very little.

Another behaviour pattern (top left quadrant in **Fig. 2)**, but less common, can be characterised as *peripatetic* (derived from Greek Aristotle origins *peripatein*, "to move around, and/or perambulate"). In this context the individual is not participating in MVPA, but sitting very little. For optimal health outcomes, low levels of sitting time and participation in MVPA (the top right 'peripatetic & active' quadrant) would be what is considered to be the most desirable. However, with highly sedentary populations, it may be a more realistic strategy, at least initially, to encourage the adoption of the 'peripatetic and inactive' (top left) quadrant. Examples of simply being peripatetic include low intensity movements like standing and light walking, such as a shop keeper who may be 'on their feet' most of the day. The potential for increasing levels of such light-intensity physical activity, particularly as a corollary of reducing sedentary behaviour, as a public health strategy will be discussed later.

Both self-reported sedentary behaviours, such as television viewing time and objectively assessed sedentary time, are only weakly associated with the amount of time

spent in MVPA [26-28]; to reiterate the earlier point, being sedentary is not the same as being physically inactive. Moreover, a recent study in young healthy participants showed that increasing MVPA was not linked to lower sedentary time [29]. Research is also beginning to show that regardless of whether people are meeting public health physical activity recommendations (i.e. ≥150 minutes/week of MVPA), there are still adverse cardiometabolic consequences from exposure to prolonged bouts of sitting [7, 15, 30-33]. These findings have added further corroboration to the argument that sedentary behaviours are a separate cluster of behaviours that may impose distinct cardiometabolic risks to that of physical inactivity.

EFFECTS OF TOO MUCH SITTING ON CARDIOMETABOLIC RISK

Evidence from observational studies on sitting time and health outcomes

There is now a reasonably consistent base of epidemiological evidence reporting deleterious associations of sedentary behaviour with cardiometabolic health and mortality in adults. Grontved and Hu [6] published a meta-analysis of 8 prospective studies showing positive associations of television viewing time with T2D, CVD and all-cause mortality. This work was subsequently developed by Wilmot et al [32], who completed a more comprehensive systematic review and meta-analysis (16 prospective, 2 cross-sectional, 794,577 participants) that included all self-reported measures of sedentary behaviour (i.e. television/screen viewing time, sitting time, or both). These authors compared the highest sedentary group with the lowest and identified stronger and more consistent positive associations of high sedentary time with the relative risk of T2D (10 studies, RR 112%); however, significant positive associations were also shown for the risk of CVD (3 studies, RR 147%), and cardiovascular (7/8 studies, HR 90%) and all-cause (8/8 studies, HR 49%) mortality. Nonetheless, 6 of the included studies did not adjust for physical activity levels and the meta-analysis was unable to examine dose-response relationships.

Chau et al [34] reported the findings of a meta-analytic review (having identified six relevant studies) quantifying the prospective associations and dose-response relationships of total daily sitting time and all-cause mortality risk. After adjustment for MVPA, which had a moderate protective role (18% reduction in mortality risk), dose-response modelling estimated a 34% higher mortality risk for adults sitting 10 h/day versus 1 h/day. Every hour of daily sitting time was associated with a 2% increase in all-cause mortality risk. Notably, this incremental association increased to 5% for those sitting >7 h/day. An estimate of attributable fractions suggests 5.9% of deaths could be ascribed to daily sitting time, statistics

that are comparable to recent World Health Organisation [2] estimates for obesity (5%) and inactivity (6%).

Beneficial impacts of breaking up sedentary time: Using accelerometer measured sedentary time for 168 adults from the AusDiab study, Healy et al [35] observed that participants who had mostly uninterrupted sedentary time (i.e. sat for prolonged, unbroken periods of time) had a poorer cardiometabolic health profile (waist circumference, triglycerides, and blood glucose) compared to those who had more frequent breaks in their sedentary time. These findings were later confirmed in a large, representative, multi-ethnic, population-based sample (National Health and Nutrition Examination Survey), although only waist circumference and C-reactive protein showed consistent negative associations [20]. Importantly, both these studies adjusted for total sedentary time, suggesting not only the total amount of sedentary time, but also the manner in which it is accumulated, are important.

Evidence from experimental studies

A number of human experimental studies examining the impact of sedentary behaviour have now been reported. Saunders et al [36] recently conducted a systematic review of 29 human intervention studies, where acute (≤7 days only) sedentary behaviours (sitting, bed rest and leg immobilisation) were imposed. However, of the 29 studies, 6 applied a randomised design and only 3 of these [37-39] assessed markers of cardiometabolic risk for uninterrupted sitting lasting less than a day. Evidence was limited and of poor quality for changes in circulating glucose, insulin, and HDL and LDL cholesterol levels, and no studies examined whether the alterations in cardiometabolic risk biomarkers persisted once participants returned to normal life (i.e. cumulative effects). Nonetheless, consistent moderate quality evidence from the included studies suggests that uninterrupted sedentary behaviour results in deleterious changes in glucose tolerance, insulin sensitivity, and plasma triglyceride levels.

Since the 2012 systematic review by Saunders et al [36], several experimental studies have reported on the relationships between breaking up prolonged sitting and markers of cardiometabolic risk in adults [40-45]. Many of these have examined participants in a postprandial state, which is typical of, and highly relevant to, many modern-day human lifestyles. Transient excursions in glucose and lipids (postprandial dysmetabolism), as a result of high calorie meals rich in processed carbohydrates and saturated fat, promote oxidative stress that triggers a biochemical inflammatory cascade, endothelial dysfunction, and sympathetic hyperactivity. Repetitions of such postprandial ‘spikes’ throughout the day can create an environment conducive to the development of diabetic complications,

atherosclerosis and CVD [46, 47]. Thus, lifestyle modifications that can practically and effectively attenuate these exaggerated rises are likely to be of great importance.

Effects on postprandial glucose: In a large, randomised cross-over trial of 70 healthy, normal weight adults, Peddie et al [44] compared 9 hours prolonged sitting with two activity conditions (total duration matched): 1) a single 30 minute walking bout (60% of maximal capacity), followed by 8:15 hours prolonged sitting, and 2) 9 hours prolonged sitting interspersed with 84 second bouts (45% of maximum) of walking every 30 minutes. Significant attenuations in postprandial glucose (39%) and insulin (26%) levels, but no differences in triglyceride responses, were shown during the intermittent breaks condition only. These glucose and insulin attenuations, while of slightly greater magnitude, are consistent with those from a similarly designed trial involving inactive overweight/obese adults [37].

In a small well-controlled randomised cross-over trial using high-frequency blood sampling, Holmstrup et al [42] also observed that intermittent walking breaks (5 minute bouts every hour) over 12 hours enhanced postprandial glycaemic control in 11 obese participants with impaired glucose tolerance. Prolonged sitting was also compared to a duration and intensity matched treadmill walk (1 hour), which showed glucose attenuations, albeit of less magnitude. Of note, participants were required to consume liquid meals every 2 hours, which is arguably not very likely to be representative of 'normal daily life' feeding patterns.

Using continuous glucose measurements, Buckley et al [40] reported improvements in postprandial glycaemic control in a group of 10 (mostly female) office workers, with an afternoon of standing versus prolonged sitting. The study was, however, not randomised and likely underpowered through sample size, limiting its generalisability. More recently, however, Thorp et al [45] simulated a controlled office environment with 23 overweight/obese office workers, examining the 5-day (8 hours/day) effects of prolonged sitting (control) versus standing and sitting interchanges every 30 minutes using height-adjustable workstations. No temporal changes (Day 1 vs Day 5) between conditions were observed, possibly due to inadequate sample size, however a modest but significant reduction (11%) in postprandial glucose (though no attenuations in insulin or triglycerides) was observed with standing breaks.

Postprandial lipids: Miyashita and colleagues have utilised a laboratory model whereby postprandial lipaemia (triacylglycerol) is assessed the day following manipulations in physical activity. Collectively, they have demonstrated that accumulating daily activity in short (<10 minutes) bouts is sufficient, and as effective, as a single bout of continuous

exercise (30 minutes) for lowering postprandial lipaemia in young healthy and obese men [48-50]. Although relevant, their question in these studies has been more about the accumulation of activity (i.e. increasing energy expenditure) rather than the breaking up of sedentary behaviour per se. However, in their latest trial using a similar crossover design, the authors found that standing breaks (six 45 minutes bouts with 15 minutes sitting in-between) over 7.5 hours did not significantly reduce next-day postprandial lipaemia levels, compared to 7.5 hours prolonged sitting.

Changes observed among adults in free-living environments: Although controlled laboratory trials such as those described above offer insight into the physiological consequences of prolonged sitting, generalisability to free-living settings is complex and may be less certain. Thus, free-living interventions are ecologically relevant to ensure sedentary behaviours are accumulated in a manner that is applicable to real world settings. Duvivier et al [41] recently undertook a study using a cross-over design in 18 healthy young participants (mostly women). In a free-living environment, three conditions were compared, each lasting 4 days: 1) 14 hours/day of prolonged sitting, 2) sitting for 13 hours/day substituted with 1 hour of vigorous cycling (i.e. MVPA), and 3) sitting for 6 hours/day substituted with 6 hours sitting, 4 hours walking, and 2 hours standing (i.e. light-intensity physical activity). Importantly, the MVPA and light-intensity physical activity conditions had an equivalent energy expenditure (prolonged sitting was ~500 kcal lower). Fasting blood measurements (as part of an oral glucose tolerance test) were collected the morning after each condition. A significantly lower insulin response and improvements in triglycerides, non-HDL cholesterol, and Apo B were reported with the light-intensity physical activity condition, compared with both the sitting and MVPA conditions.

In summary, the evidence to date is generally suggestive of beneficial relationships between breaks in sedentary time and cardiometabolic risk biomarkers, with physiologically plausible candidate mechanisms at play. However, these relationships are not straightforward and further investigations are required.

Reducing and breaking up sedentary time as a potential management tool for patients with T2D

A cost-effective policy to combat chronic diseases is arguably through primary prevention. However, as the rates of non-communicable diseases continue to rise, it is important that the personal burden of symptoms is not marginalised. While most research has been conducted in healthy participants, the effects of reducing sedentary behaviour on symptom reduction and

overall quality of life is likely to be more apparent in clinical populations, including T2D patients, largely as a result of these individuals often being overweight/obese, deconditioned and highly sedentary [51, 52].

Unlike research in physical activity, studies have only recently begun to investigate the effect of sedentary behaviours, and their management, at the secondary and tertiary levels of prevention. In participants at greater risk of developing T2D, higher sedentary time has been shown to be predictive of elevated 2-h glucose, among other cardiometabolic risk factors, while breaks in sitting time are associated with lower 2-h glucose [53]. Detrimental associations of sedentary time on fasting insulin were recently shown in 528 patients with newly diagnosed T2D using objective sedentary measurement [54]; however, their 6 month follow-up analysis showed no beneficial changes with breaks in sedentary time. In a similar T2D cohort [55], higher sedentary time was positively associated with an elevated clustered metabolic risk (a sum of waist circumference, triacylglycerol, HbA1c, systolic blood pressure and HDL-cholesterol). Interestingly, MVPA time showed no beneficial associations on metabolic risk when sedentary time was accounted for in the group. Both of these studies in T2D patients showed that the detrimental effects of sedentary time were *independent* of MVPA. Additionally, a recent randomised cross-over study in 20 men with T2D reported that three 15 minute bouts of light-intensity walking compared to a day of prolonged sitting reduced postprandial glucose (17%) and insulin (11%), highlighting the potential of more regular activity bouts in T2D blood glucose management [56]. However, to date, no controlled experimental studies with T2D patients have investigated the impact of breaking up periods of prolonged sitting using brief and practical intermittent bouts of physical activity (less than 5 minutes).

There is now an empirical basis for advocating the reduction of overall sitting time as part of the treatment and management of T2D and CVD patients. While displacing sitting time with light activity breaks may be an effective management tool in itself, it is also plausible that such activity breaks could provide a further behavioural stepping stone towards participation in light and moderate-to-vigorous physical activity, which is already known to play an important role in both T2D and CVD populations. Nevertheless, more longitudinal and rigorously controlled experimental studies are required to determine causal relationships, and to assist with the translation of previous findings into the clinical landscape.

FUTURE OPPORTUNITIES FOR UNDERSTANDING SEDENTARY BEHAVIOUR AND DIABETES AND CARDIOVASCULAR RISK

Sedentary behaviour research is growing rapidly and is ripe with opportunity. Hereafter, we provide a perspective on some of the priority areas for future work, in light of the recent and thought provoking studies from the field.

Better understand the underlying mechanistic effects of sedentary behaviour and identify dose-response relationships

Sedentary behaviours, by definition, are characterised by relatively low energy expenditure, inferring a lack or absence of muscular contraction. Pioneering animal experimental work [57-59] has demonstrated that when compared to exercise training, prolonged periods of muscle unloading (sitting) reduce glucose uptake and elicit a greater and muscle-specific (mostly in oxidative fibres) lowering effect on lipoprotein lipase regulation (a key protein for controlling plasma triglyceride catabolism, HDL cholesterol, and other cardiometabolic risk factors). These initial findings stimulated the hypothesis that prolonged sedentary behaviours may engage molecular signalling pathways distinct from lack of MVPA, rather than the behaviours associated with them. As more experimental studies continue to emerge, it is becoming increasingly clear that there are likely to be multiple complex mechanisms and interacting pathways involved with cardiometabolic health. For instance, recent studies suggest that responses to sedentary behaviour may also be diet/energy intake related [39], or even linked to fibrinolytic factors [60] and skeletal muscle gene expression [61, 62].

Bed rest studies: Though less likely to be representative of daily living, experiments using enforced bed rest have provided further mechanistic insights, differentiating sedentary behaviour from physical inactivity [63]. For example, 5-10 days bed rest induced dysglycaemia and dramatic reductions in whole body, muscle and vascular insulin sensitivity in healthy participants [64-66]. Bed rest also induces changes in fat oxidation capacity and storage [65], muscle atrophy, and shifts toward more fast-twitch muscle fiber type – similar to pathways observed with metabolic dysregulation [63]. Interestingly, individuals with a specific genotype (T-allele of the *TCF7L2* gene – an important T2D susceptibility gene) were particularly at risk of metabolic abnormalities, with reduced insulin secretion in response to muscle inactivity induced insulin resistance [64]. Overall, these findings have illustrated the physiological effects and clinical importance of muscle inactivity, and the potential for varying inter-individual (gene) susceptibilities in response to a sedentary environment.

***Broadening the targeted 'physical activity' options*:** Collectively, observational and experimental findings seem to suggest that a certain minimal combination or criterion of mode (e.g. standing, activities involving resistance and/or sit-to-stand transitions), volume/intensity (e.g., light-intensity physical activity and/or MVPA) or patterning (e.g. activity bout and/or standing length/accumulation) of physical movement may be all that is required to practically and effectively attenuate the harmful cardiometabolic effects of too much sitting. Indeed, Dunstan et al [37] observed that irrespective of walking intensity, interruptions in sitting time with regular walking breaks significantly lowered glucose/insulin responses to a mixed meal, suggesting that the intensity of activity breaks may not be critical. Moreover, Duviver et al [41] provocatively concluded that 1 hour of daily physical exercise cannot compensate for the negative effects of inactivity on insulin sensitivity and plasma lipids if the rest of the day is spent sitting. Peddie et al [44] and Holmstrup et al [42] came to similar conclusions; that short brief activity breaks in sitting were as effective as a single continuous bout (30 and 60 minutes respectively) of exercise on glycaemic control. Although Miyashita et al [43] recently found that, compared to prolonged sitting, a single 30 minute exercise bout was more beneficial than standing breaks (6 x 45 minutes) in reducing postprandial triacylglycerol, they also noted that further research should assess whether variations in standing frequency and duration patterning (i.e. short and more regular sit-to-stand transitions) are of importance.

In summary, further high quality prospective, mechanistic and intervention studies are required to reveal the mechanisms by which prolonged sitting can influence T2D and CVD risk. Rigorously controlled and free-living study designs, utilising novel physical activity and sedentary intervention models and robust measurement of physiological/cardiometabolic risk outcomes within various population sub-groups, have the potential to add much needed specificity to sedentary behaviour guidelines to permit more explicit recommendations. However, until more specific, consistent and robust evidence is revealed, the general recommendation (currently embodied in the Australian [67] and UK [68] guidelines) is to reduce sedentary time where possible, supplementary to the well-established 'health enhancing' benefits of MVPA.

POPULATION-HEALTH CHALLENGES WILL REQUIRE ENVIRONMENTAL AND POLICY INITIATIVES

While observational and experimental studies will help identify specific methods and approaches that could be of benefit, there is the need to identify how new preventive

approaches might be most appropriately translated into policy and practice at the population level [69]. Evidence-based physical activity recommendations for reducing cardiometabolic risk are well established [70-72]; however, the wide-ranging potential health benefits of increasing physical activity levels remain largely unrealised [4, 18].

Two fundamental challenges persist at the population level. In the first, it is increasingly evident that a growing proportion of people are not meeting physical activity guidelines for various (inevitably complex) reasons [71, 73]. Despite large-scale physical activity intervention approaches and policy changes being put in place, physical activity continues to be rejected or ignored by large numbers [4, 18]. Second, growing numbers of people are spending disproportionate amounts of their time in prolonged and unbroken periods of sedentary behaviour [15, 33, 74], which appear to have deleterious health consequences even among those meeting physical activity recommendations [31, 32].

The prevailing *high-risk* approach to chronic disease prevention remains pertinent in those with or at increased risk of T2D and CVD, particularly given contemporary improvements in risk factor diagnosis and disease management [75, 76]. However, there is the need to consider what might be acceptable, cost-effective and implementable *population-wide* prevention strategies, in order to reduce T2D and CVD risk and burden. This is required to address a growing problem that is well beyond the capacities of clinically-based systems to address [69, 77-79].

An ecological perspective on changing sedentary behaviours

Sedentary behaviours are a new focus for research within the broader field of 'physical activity and health'. From a preventive health perspective, the potential of breaking up sitting time and increasing time spent in light-intensity physical activity has emerged as a compelling opportunity to make a practicable and meaningful impact on population activity levels [15, 80-82]. On average, MVPA occupies only a few minutes of many adults waking days, thus it has limited potential to displace sedentary time (see **Fig. 1**) [11, 83]. However, sedentary time and light-intensity physical activity (i.e. peripatetic) are strongly inversely associated (r=-0.96) [15]. Thus, there is greater potential to displace sedentary time with light-intensity physical activity and movement breaks (such as standing or light walking/activity). Pursuing more peripatetic behaviours (described in **Fig. 2**) by increasing light-intensity activity and breaking up sedentary time potentially may be more amenable to change than increasing MVPA. Future research studies are likely to shed more light on whether or not this is the case.

With the growing evidence on the benefits of reducing sedentary behaviour, there is now an impetus to conduct intervention trials that will inform health-care decisions in various contexts. Such trials can provide evidence on the feasibility, effectiveness, and benefits/harms of different prevention and management options [84]. As more detailed behavioural and objective data on the high volumes of sedentary behaviours emerge, there will be evidence to inform multi-level, ecological approaches to behavioural change strategies [82, 85].

Rather than focusing primarily on changing behaviour at the individual level – which is recognised to pose barriers and limitations beyond the individual's control – ecological approaches consider extrinsic influences on behaviour. The ultimate goal is to create environments and policies that make it safe, convenient, attractive, and economical to make health promoting choices, and then motivate and educate people to take up those healthy options [86]. A recent example of a purely environmental manipulation was in a workplace study whereby 24 sedentary workers were provided with sit-stand workstations for 4 weeks. There was a 66 minutes/day reduction in sitting time and various musculoskeletal and mood improvements; however, importantly, beneficial effects disappeared 2 weeks after the workstations were removed – suggesting that ongoing environmental support is required if such changes are to be sustained [87].

Ecological models have previously been employed with public health issues such as smoking and physical activity [86], and have recently been applied to sedentary behaviour [85, 88]. While the specifics of the multiple levels of influence identified by ecological models are covered elsewhere [86], in the context of sedentary behaviour, there would be four key domains to be addressed: *the home-environment setting*, particularly through addressing television viewing time and other screen time; *the commuting setting*, within which active transport options would reduce the time spent sitting in cars; *the occupational setting*, within which there are viable alternative work arrangements that do not have to involve sitting; and, *the neighbourhood and community setting*, within which walkable local destinations and outdoor recreational opportunities provide alternatives to time spent sitting in cars and spending leisure time primarily indoors.

Two recent workplace sitting interventions have included organisational (management consultation, workshop, and brainstorming), environmental (sit-stand workstations), and individual (one-to-one health coaching, self-regulation strategies, and motivational interviewing) elements. One trial reported successful reductions in sitting time by 125 minutes/day over 4 weeks [89], while two longer 12 week randomised controlled trials

reduced sitting time 94 minutes/day [90], and 58.7 minutes/day [91] respectively, with reductions in waist circumference compared to a control condition.

Multi-level ecological approaches applied to sedentary behaviour interventions have the potential to produce sustainable health behaviour change [82, 85, 86]. Thus, while multi-faceted approaches can be logistically challenging, the effort involved will be justified if further supportive evidence emerges from larger scale and longer duration studies, ideally with evidence of beneficial changes in indices of cardiometabolic risk.

CONCLUSIONS

Approaches to curbing modern day chronic disease epidemics have been the focus of much research and debate. Reducing time spent in sedentary behaviours is emerging as a novel and compelling public health strategy. While the sedentary behaviour research field is still in its infancy, a rapidly emerging and reasonably consistent body of evidence suggests that time spent in sedentary behaviours is a distinct risk factor for a host of health outcomes and cardiometabolic risk, independent of MVPA.

The potential to reduce time spent sitting during different settings over the day are abundant and it is possible that such opportunities may be more feasibly exploited than previous efforts to promote structured exercise programs and personal initiatives to engage in discretionary physical activity. Cross-talk between mechanistic, experimental/clinical, population and behavioural/environmental scientists will help further the scientific understanding of sedentary behaviour, identifying potential novel interventions and practical initiatives. Nonetheless, while explicit clinical recommendations regarding sedentary behaviours are yet to be refined, it seems prudent for clinicians and others – in the interest of 'doing no harm' – to advise *standing up more, sitting less, and taking every opportunity to move more, more often*!

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** of outstanding importance

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