The Health Risks Associated with Prolonged Sedentary Behaviour: A Systematic Review

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Contents

Abstract

Sedentary behaviour is associated with an increased risk of obesity, cardiovascular disease, type 2 diabetes mellitus, and a range of other adverse health outcomes. However, few systematic reviews or meta-analyses have synthesised the evidence of sedentary behaviour and adverse health outcomes in adults. This systematic review differed from other systematic reviews in that it included only prospective studies with clearly defined measurements of prolonged sedentary behaviour in otherwise healthy adults. A comprehensive search of major databases for studies measuring cardiovascular and metabolic outcomes identified 19 prospective studies, 16 of which were included after critical appraisal. The review revealed difficulties in identifying a consistent and unified definition of sedentary behaviour, and ambiguities in quantifying sedentary behaviour due to methodological limitations. Despite this, the results suggested that prolonged sedentary behaviour in adults, particularly sitting for more than three hours at a time, was consistently and strongly associated with an increased risk of cardiovascular disease, all-cause and cardiovascular disease mortality, and — to a lesser degree — type 2 diabetes mellitus; these associations appeared to be independent of a range of age, sex and lifestyle factors — and also, importantly, physical activity. No conclusions could be made for the risk of overweight or obesity, or for gallstones, due to conflicting results and methodological problems identified in the primary studies. Overall, high-quality systematic review and any meta-analysis of sedentary behaviour is constrained by the quality of the primary studies, including variation in the definition of sedentary behaviour and the methods used to measure it. These results strengthen the case for modifying physical activity guidelines to include recommendations on minimising sedentary behaviour, thereby making guidelines more relevant to contemporary lifestyles.

Declaration

I, Margaret Heaslop, certify that this work contains no material that has been accepted for the award of any other degree or diploma in any university or any other tertiary institution, and, to the best of my knowledge and belief, contains no material previously published or written by any other person, except where due reference has been made in the text.

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Margaret Jane Anne Heaslop
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Chapter 1 Introduction

1.1 Context of the review

Keeping sedentary behaviour to a minimum, while maintaining physical activity, is beneficial and necessary for maintaining good health. In 1953, a landmark study showed that incidence of heart attack was halved in London bus conductors who climbed the stairs of double-decker buses as part of their daily tasks, compared with bus drivers who spent most of the day sitting (Morris et al 1953). This study was one of the first scientific publications to link physical activity to a decreased risk of heart attack, and it challenged the then-held scepticism that physical activity or exercise could be protective against death from cardiovascular disease (Andrade and Ignaszewski 2007).

Since that time, years of observational and experimental research have confirmed the role of physical activity in preventing cardiovascular, metabolic, musculoskeletal and mental health-related morbidity and mortality (Bauman et al 2004). This is reflected in physical activity guidelines and consensus statements for children, adolescents and adults around the world, which recommend a minimum of 30 minutes of physical activity on most days of the week (see Appendix 7).

Today, however, an increasing number of studies show that there are also health risks associated with an overly sedentary lifestyle — whether it is for prolonged, uninterrupted periods, or for a significant proportion of total daily time. This has serious implications for Australians and for individuals across the developed world, because lifestyle for many is now characterised by a significant proportion of the day spent sitting down. For example, many of us, of all ages, are sedentary often by necessity during occupational and academic pursuits, during leisure time, and while commuting (Healy et al 2007). In the 2007–08 Australian National Health Survey of approximately 20 000 Australians, 73% reported sedentary behaviour or low exercise levels in the two weeks before the survey (ABS 2008). Occupational sedentary behaviour is particularly high for professional or office workers ('blue-collar' occupations were more active) (Mummery et al 2005). It also appears that the risks of sedentary behaviour may not attenuated by bouts of physical activity (Grøntved and Hu 2011, Proper et al 2011, Thorp et al 2011, van Uffelen et al 2010), although results from a recent prospective study (that 15-minute bouts of moderate–vigorous physical activity reduces mortality) suggest otherwise (Wen et al 2011).

National and international physical activity guidelines have not yet been updated to take into account the suspected risks associated with too much sitting or other sedentary behaviours. By failing to update physical activity recommendations to stipulate a minimum of sedentary behaviour, the recommendations may miss a large group of people who are at risk — that is, those who exercise for a certain number of hours each day, but spend the remainder of their leisure or work time sitting.

This gap between research and practice most likely reflects the gaps in, and limitations of, the primary research: although many intervention and observational studies have focused on sedentary behaviours in children, the corresponding research in adults is still lagging. Another cause of the gap are the methodological limitations associated with objectively measuring physical activity at a population level. There is also growing recognition that the research that has been done needs careful assessment, to reflect the fact that sedentary behaviour is different from a lack of physical activity, and must be measured in a way that reflects this difference.

This systematic review fills a gap in the secondary literature in that it provides a comprehensive analysis of the reported cardiovascular and metabolic health effects associated with prolonged sedentary behaviour (e.g. sitting for three or more hours at a time) that is based on a definition of true sedentary behaviour. The results from this systematic review are important for the future development of physical activity guidelines to include provisions on minimising sedentary behaviour.

Drawing on an overview of the broader literature, this chapter introduces the concept of sedentary behaviour and the difficulties of defining and measuring it, as well as the potential health effects of sedentary behaviour and why it should be investigated. The evolution of physical activity guidelines and the extent to which this reflects a growing understanding of sedentary behaviour is also discussed, and a brief overview of the existing review literature demonstrates how this review will build on current knowledge. Finally, the methodological basis for this systematic review is presented.

1.1.1 Defining sedentary behaviour

Sedentary behaviour is distinct from a simple lack of physical activity. Conceptually, it requires the act of sitting, generally for prolonged periods, coupled with immobility and minimal energy expenditure — that is, from 1 to 1.5 times the resting metabolic rate (Healy et al 2011, Pate et al 2008). True sedentary behaviours therefore exclusively include activities that involve sitting, such as while watching television, reading, talking on the telephone, while in transport (e.g. car, train), sitting at work (at a desk), or 'screen time' (using a computer, playing video or computer games).

Despite sedentary behaviour including this straightforward list of common activities, the way in which it is defined and measured in population-based studies is problematic. Until recently, sedentary behaviour has simply been regarded as a lack of physical activity, or a failure to meet a minimum level of physical activity (Pate et al 2008). Physical activity can be expressed using the metabolic equivalent (MET), which is the ratio of the metabolic rate of an activity and the resting metabolic rate. For adults, 1 MET is the equivalent of sitting quietly — which equals an oxygen consumption of 3.5 mL per kilogram per minute (Schofield et al 2009). Therefore, an activity that is 2 MET is twice the resting metabolic rate, which is similar to twice the energy expenditure of sitting quietly. The MET value of a range of activities has been measured, validated and published in a compendium of physical activity (Ainsworth et al 2011), which is referenced by many studies. The validity of the MET across differing body mass and body fat percentage has been questioned, particularly its tendency to overestimate resting energy expenditure by 14% in normal-weight adults, and 20% in obese adults (Byrne et al 2005). However, in large population-based studies, the MET remains the most objective and easily used indicator of level of physical activity at present.

There is emerging consensus that true sedentary behaviour has an energy score of 1.0–1.5 MET (Hamilton et al 2007, Healy et al 2008, Healy and Owen 2010, Owen et al 2010), with 1.5 MET being the cut-off for 'light' activity. Using this definition, sedentary behaviour includes activities such as lying or sitting down, for periods of approximately two hours or more; it does not include 'light activity' (e.g. standing, light household chores — activities of 1.6–2.6 MET), which have greater physiological requirements.

Healy and Owen (2010) summarise in depth the inherent problems of the primary studies looking at the associations between prolonged sedentary behaviour and health outcomes — namely, the tendency for people who do not meet a minimum of physical activity to be classed as 'sedentary'. 'Light' activities may play an important, but underestimated, role in maintaining health. Until recently, many studies have focused on higher intensity activities (e.g. sports, vigorous exercises — approximately $\geq$3 MET; fast running — approximately 8 MET), and have divided participants into groups of those who exercise (higher MET) and those who are 'sedentary' (i.e. do not exercise, but who may still spend a large portion of their day in the light activity category). Furthermore, some people may fall into both categories: they participate in high-energy activities (i.e. intense training for discrete periods of time) followed by periods of sedentary behaviour (e.g. office workers who run before work and then sit for most of the day; athletes who train vigorously and then recover for periods during the day).

Problems arise when studies simply define sedentary behaviour as a lack of physical activity and categorise participants as sedentary by default, rather than by directly measuring their participation in sedentary behaviours (Healy and Owen 2010). The implication is that activity is viewed as a dichotomous variable — active and inactive — yet there will be variability within both groups. As Pate et al (2008) observe, many studies therefore make claims about the effects of sedentary behaviour without actually measuring it. This point is the basis of most of the failings of the research studies in the field and has direct impact on any conclusions drawn from such research as a result. Similarly, any potential systematic review or meta-analysis that does not recognise the difference between sedentary behaviour and a lack of physical activity will further compound this problem.

1.1.2 Measuring sedentary behaviour in observational studies

Proxy or surrogate measures can be used to estimate prolonged sedentary behaviour, such as television viewing, time spent in transport, or time spent employed in sedentary jobs. These data are generally self-reported by study participants, which inherently involves recall and other biases. Instruments for measuring physical activity objectively, such as accelerometers (see, for example, Healy et al 2008, Kozakova et al 2010) or heart rate monitors (for example, Ekelund et al 2008, Helmerhorst et al 2009), are sometimes used. However, due to the relatively high costs and impracticalities of use with a large number of participants (compared with self-reported estimates), this is done in a minority of studies.

Studies of sedentary behaviours typically record behaviour in one of the following three domains (Healy et al 2011):

- estimates of total time spent sedentary across the day or week
- estimates of total time spent in sedentary behaviours during a specific time of day (e.g. work, leisure, transport)
- time spent in specific activities, used as surrogate markers of sedentary behaviours (e.g. television viewing, screen time).

Subjective measurements

Subjective measurements include self-reported behaviours over a specified timeframe. Participants are typically asked to estimate their time spent in sedentary or physical activities over a day, week or longer timeframe, either using a survey or a validated questionnaire (see below). These types of subjective measurements are less costly and easier to implement than other measurements. However, self-reported data (particularly when participants are asked to recall or estimate their activities over a long time period) are subject to recall bias and social desirability bias; they can also be time consuming to record and analyse (Steele et al 2003).

The accuracy of self-reported data can be improved through the use of standardised and validated questionnaires. The International Physical Activity Questionnaire (IPAQ) exists in long and short forms, and is a practical tool for measuring physical activity in large populations.[1] It is currently one of the most commonly used surveys (Schofield et al 2009) and includes measures of sedentary behaviour (sitting time). The test-retest reliability of the short and long forms of the IPAQ is good (Rosenberg et al 2008). However, the validity is only moderate (IPAQ-SF: r = 0.33; IPAQ-LF: r = 0.34), with self-reported estimates of sedentary behaviours typically lower than those measured by accelerometers (considered the gold standard) (Rosenberg et al 2008).

Kosakova et al (2010) cited the study by Ekelund et al (2006) to argue that self-reported physical activity or sedentary behaviour using physical activity questionnaires 'might introduce errors due to imprecise questions, misunderstanding of questions, and misclassification'. Ekelund et al (2006) ran a small (185 Swedish adults) trial of the validity of the short, seven-day, self-administered form of the IPAQ. The trial compared self-reported data from questionnaires with accelerometer readings collected for the same participants. Results indicated that the IPAQ had significant associations between self-reported activity levels and objectively measured physical activity in participants who met or exceeded minimum physical activity recommendations. However, the IPAQ had limited sensitivity to correctly identify inactive people (that is, it over-estimated physical activity for those who did not meet the minimum recommended daily activity levels). This discrepancy in measurement at the lower end of the physical activity scale has important implications for studies that use the IPAQ to assess sedentary behaviours; they may often be characteristic of cohorts at the lower end of the physical activity scale.

In summary, self-reported measures of sedentary behaviour and physical activity are often used, including to validate less structured self-reported estimates in subsamples of participants in large studies. They are useful for large population studies where time, budget and practicalities preclude the use of other, more objective measurements.

[1] https://sites.google.com/site/theipaq/, accessed 3 September 2011.

Objective measurements

The most commonly used objective measurements of sedentary behaviours — although still not used frequently overall — are heart rate monitors and accelerometers. Heart rate monitors are used to monitor changes in heart rate (and sometimes breathing rate), while accelerometers are motion sensors that detect body movement (acceleration) (Steele et al 2003). The use of both instruments, and their benefits and limitations, are well documented elsewhere (Esliger and Tremblay 2007).

In summary, the benefits of these objective measurements are that they are free from human biases that may plague self-reported data, they can be calibrated and tested for accuracy (although their accuracy depends on the quality of the model used), data can be recorded and analysed relatively quickly and with ease, and they can record frequency and intensity of activity (accelerometers) (Hills et al 2007, Steele et al 2003). Objective measures of sedentary behaviour can also be used to validate self-reported or other methods of measuring sedentary behaviour or physical activity (Pate et al 2008).

The drawbacks are that they are expensive (which may preclude their use in large studies enrolling thousands of participants), they can be impractical (e.g. intrusive or uncomfortable, not always waterproof), and they require other equipment (computers) to access the data.

Table 1.1 summarises the benefits and limitations of the most commonly used subjective and objective measures of sedentary behaviours. Currently, most of the studies of sedentary behaviour use self-reported measurements (in this systematic review, 14 of the 16 studies); very few (in this review, Helmerhorst et al 2009 and Kozakova et al 2010) use objective measurements to validate self-reported data. This is most likely due to the fact that the best study design to investigate risks associated with sedentary behaviours are large prospective cohort studies, for which using accelerometers or heart rate monitors would not be feasible.

Table 1.1 Advantages and disadvantages of the most commonly used subjective and objective measures of sedentary behaviours

<table>
<tr><th>Advantages</th><th>Disadvantages</th></tr>
<tr><td colspan="2">Self-reported methods</td></tr>
<tr><td colspan="2">Questionnaire</td></tr>
<tr><td>• Can use for large cohorts
• Relatively inexpensive
• Do not alter participants' behaviours</td><td>• Susceptible to systematic and random reporting bias (e.g. incorrect recall, social desirability)</td></tr>
<tr><td colspan="2">Short-term recall (e.g. 24 hours), diaries or behaviour logs</td></tr>
<tr><td>• Can use for large cohorts
• Relatively inexpensive
• Do not alter participants' behaviours</td><td>• Burden on participants (therefore affecting compliance)
• Susceptible to systematic reporting bias
• More expensive to implement than questionnaires</td></tr>
<tr><td colspan="2">The reliability and validity of self-reporting varies according to method; however, they are largely consistent with those for physical activity measures</td></tr>
<tr><td colspan="2">Objective measures</td></tr>
<tr><td colspan="2">Accelerometer</td></tr>
<tr><td>• Provide reliable, valid and stable data about sedentary behaviours
• Provide data about the way in which sedentary behaviours are accumulated</td><td>• Relatively expensive to implement
• Intrusive for participants, therefore affecting compliance and possibly changing behaviours</td></tr>
</table>

Source: based on Healy et al (2011)

1.1.3 Health effects of sedentary behaviour

For many people in developed countries (and increasingly, in developing countries), workplaces are sedentary, leisure-time activities are sedentary, and transport is automated; therefore, a large proportion of waking hours are spent sitting down (Anderson et al 2009).

As explained in this thesis, sedentary behaviour has been implicated in the development of many adverse health outcomes, particularly those relating to cardiovascular and metabolic health (obesity, cardiovascular disease, type 2 diabetes mellitus) (Grøntved and Hu 2011, Proper et al 2011, Thorp et al 2011), as well as cancer (van Uffelen et al 2010) and clinical depression (Teychenne et al 2010). This thesis is concerned with the associations for metabolic and cardiovascular outcomes, and the following sections summarise the significance of these outcomes in the context of the Australian population where possible. Due to the prevailing view, until recently, that sedentary behaviour and a lack of physical activity are equivalent, the information in these introductory sections also draws on research relating to physical activity or a lack thereof.

The physiological mechanism by which sedentary behaviour leads to cellular or metabolic changes is not yet understood. Animal studies indicate that sitting or lying down can prevent contraction of skeletal muscle fibres, which suppresses lipoprotein lipase activity (this enzyme regulates the update of triglycerides and fatty acids into muscle tissue, as well as the production of high-density lipoprotein cholesterol) (Thorp et al 2011). Enzymatic suppression does not appear to occur during standing or walking (that is, light activity). A comprehensive analysis of these physiological pathways is provided elsewhere (Hamilton et al 2007). Because evidence-based health care and systematic reviews are primarily concerned with clinical outcomes (Glasziou et al 2007), the physiological mechanisms of action are not discussed further in this thesis.

Overweight and obesity

Obesity and overweight are global health concerns in both the developed and developing world (Alberti and Zimmet 1998, Kelly et al 2008). In 2005, 33% of the global adult population (1.3 billion people) were overweight or obese, and this number is expected to reach 57.8% (3.3 billion people) by 2030 (Kelly et al 2008). The burden (in terms of morbidity and economy) for both developed and developing countries is potentially huge, with overweight and obesity leading to near epidemic rates of cardiovascular disease, type 2 diabetes mellitus, musculoskeletal problems and some cancers.

The most recent available Australian Government data on national obesity levels are from the 2007–08 National Health Survey (another national survey is currently in process) (ABS 2008). The National Health Survey showed that 61.4% of Australians were overweight or obese in 2007–08 (BMI >30), and this number is increasing (ABS 2008). In 2003, overweight and obesity were the cause of 7.5% of the total national burden of disease and injury (AIHW 2007), costing Australian society more than $21 billion in 2005 (ABS 2008).

The risk factors of overweight and obesity, and the relative contributions of these risk factors, are extensively debated and discussed in the literature (see Keith et al

2006 for a comprehensive review). Broadly, they include an imbalance between energy input and output, and genetic factors. As discussed throughout this thesis, there is growing concern that too much sedentary behaviour also makes a significant contribution (Westerterp 2001). Contemporary lifestyles are less active than ever before, and this inactivity appears to be at least as important a cause of overweight or obesity as diet (Prentice and Jebb 2004). This is also true for Australia, where the prevalence of overweight or obesity (that is, a body mass index [BMI] of $\geq$25) has more than doubled since the 1980s (Cameron et al 2003). A landmark Australian study — the 1999–2000 Australian Diabetes, Obesity and Lifestyle Study (AusDiab) — has confirmed a significant positive association between obesity and television-viewing time, and between obesity and reduced physical activity (Cameron et al 2003).

Many studies have been published on the impact of sedentary behaviours on children and adolescents. Cross-sectional and prospective studies indicate a strong positive association between measures of being sedentary, such as television viewing, computer or video game use, or other 'screen time' measures, and an array of negative health outcomes, including overweight or obesity, and reduced cardiorespiratory fitness (see reviews by Hills et al 2007, Reilly and McDowell 2003, Swinburn and Shelly 2008). The literature on adults is less extensive, but is growing as results from long-term prospective studies are published.

Cardiovascular disease

The International Classification of Diseases defines cardiovascular disease as all diseases and disorders of the heart and blood vessels (WHO 2007). In the 2007–08 National Health Survey (ABS 2008), there were more than three million cases of cardiovascular disease nationally, with most attributable to hypertension and coronary heart disease. Cardiovascular disease is one of the main causes of death in Australia, and the most costly health condition (costing 11% of the total health system expenditure in 2000–01; AIHW 2005).

It is widely accepted in the primary and secondary literature, and in clinical practice, that physical activity prevents atherosclerotic coronary artery disease, reduces atherosclerotic risk factors (e.g. hypertension, elevated triglyceride levels, glucose intolerance), and helps in the treatment of coronary artery disease, heart failure and claudication (Blair et al 2001, Powell et al 1987, Thompson et al 2003). Furthermore, exercise interventions are effective for cardiac rehabilitation after cardiovascular events (Heran et al 2011), and failure to meet minimum recommended levels physical activity (30 minutes of moderate-to-vigorous exercise on most days of the week) increases risk cardiovascular events (Pate et al 1995).

Type 2 diabetes mellitus

Type 2 diabetes mellitus is a metabolic disorder that has been described as a 'lifestyle disease', owing to the fact that its aetiology is associated with modifiable risk factors such as physical inactivity, poor diet and smoking (Zimmet et al 2001). The underlying causative mechanism is a disruption in insulin secretion or action, or both (Thomas et al 2006). This leads to raised plasma glucose levels and impaired carbohydrate, fat and protein metabolism, causing adverse ocular, neurological and cardiovascular effects.

Globally, prevalence of type 2 diabetes mellitus is now considered to be at epidemic levels (King et al 1998, Zimmet et al 2001). In Australia, type 2 diabetes mellitus was the sixth leading cause of death in 2009 (ABS 2011), with a national cost of $10.3 billion (Diabetes Australia 2011). Physical activity reduces blood sugar and lipid levels, and improves glucose tolerance, in people with type 2 diabetes mellitus (Orozco et al 2008). Conversely, it has been reported that both a lack of physical activity (Chipkin et al 2001, Sigal et al 2006), and too much sedentary behaviour (Helmerhorst et al 2009), increases the risk of type 2 diabetes mellitus.

1.1.4 The evolution of physical activity guidelines

In many countries, public health initiatives focus on promoting 'healthy eating' and physical activity through both dietary and physical activity guidelines and recommendations. Physical activity guidelines have traditionally recommended levels of physical activity that should be met to realise health benefits (that is, how much exercise to do) (Blair et al 2004). Globally, these recommendations have differed in terms of amount, intensity, frequency and type of recommended activity; they have also evolved over time.

The *Australian Physical Activity Guidelines for Adults* (Australian Government Department of Health and Ageing 2004) recommend a minimum of 30 minutes' physical activity on most days. These guidelines were based on the United States Centres for Disease Control and Prevention and the American College of Sports Medicine physical activity recommendations, first published in 1995 (Pate et al 1995).

In 2007, the *American Physical Activity Guidelines for Adults* (e.g. the American Heart Association and the American College of Sports Medicine) were updated to increase the intensity of recommended activity, and now also stipulate the inclusion of vigorous-intensity exercise, as well as exercises to increase muscle strength and bone health (Blair et al 2004). The World Health Organization is also currently updating their guidelines for adults to reflect the growing number of studies reporting increased physical activity and improved health. Despite these modifications, there is still no consensus on the recommended intensity or frequency of physical activity, or consistency in the way in which guidelines are presented at a regional and global level (Oja et al 2010). This problem is discussed in more detail in other reviews (Blair et al 2004, Lankenau et al 2004, Oja et al 2010).

Recognition of the impact of sedentary behaviour on metabolic health is beginning to influence physical activity guideline development, with a call for guidelines to change their focus from not only stating recommended levels of physical activity, but also recommending how much sedentary behaviour to avoid (Blair et al 2004). For example, the National Heart Foundation of Australia has published a factsheet — *Sitting less for adults* — to encourage adults in sedentary occupations to reduce their sitting time.[2] Despite this move to address the problem of sedentary behaviour and the publication of factsheets and consumer resources, none of the key national physical activity guidelines across the world yet recommend maximum amounts of sedentary behaviour.

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[2] See http://www.heartfoundation.org.au/SiteCollectionDocuments/HW-PA-SittingLess-Adults.pdf ; accessed 19 September 2011.

A summary of some key physical activity guidelines for adults across the world is provided in Appendix 7.

1.1.5 Why a systematic review is needed

As discussed above, few systematic reviews have been published on the effects of prolonged sedentary behaviour in adults, reflecting both the novelty and the difficulties of such research. However, this is changing rapidly, as an increasing number of primary studies on sedentary behaviours in adults are being published, almost matching the volume of research that has focused on these behaviours in children and adolescents. At the time of writing this thesis, other systematic reviews and a meta-analysis were published. The key systematic reviews focusing on sedentary behaviours in adults are summarised in Table 1.2 and discussed in further detail below. Comparisons with the findings of this systematic review are provided in Section 4.3.

Table 1.2 Systematic reviews of sedentary behaviours in adults

Reference	Study designs included	Results and comments
van Ufflen et al (2010)	Prospective cohort Cross-sectional Case–control	• Narrative synthesis of 43 studies of occupational sitting and BMI, cancer, cardiovascular disease, type 2 diabetes mellitus and mortality • No conclusions made because of heterogeneity of study design, measures and results • Studies published in Chinese, Dutch, English, French, German, Italian, Norwegian and Spanish; 9 studies excluded because not published in a language spoken by reviews
Grøntved and Hu (2011)	Prospective cohort	• Meta-analysis of 8 studies of television viewing and incidence of type 2 diabetes mellitus, cardiovascular disease and all-cause mortality • Statistically significant risk for all outcomes (linear for cardiovascular disease and type 2 diabetes mellitus; nonlinear for all-cause mortality: increasing with ≥3 hours television/day) • Studies published in English only
Proper et al (2011)	Prospective cohort	• 'Best-evidence synthesis' of 19 studies of sedentary behaviour (all domains) and body weight measures, cardiovascular disease risk, cancer, type 2 diabetes mellitus, mortality (all-cause and disease specific) • Moderate evidence for positive association with type 2 diabetes mellitus; strong evidence for all-cause and cardiovascular mortality; no evidence for cancer mortality; insufficient evidence for body weight measures, cardiovascular disease risk and endometrial cancer • Studies published in English only
Thorp et al (2011)	Prospective cohort (published since 1996)	• Narrative synthesis of 48 studies of sedentary behaviour (all domains) and all health-related outcomes • Significant positive association for mortality (all-cause and cardiovascular disease mortality, but not cancer-related mortality), as well as for weight gain from childhood to adulthood • Inconclusive evidence for disease incidence, weight gain (in adulthood), cardiometabolic risk, markers of insulin resistance • Studies published in English only

In their systematic review of occupational sitting and health, van Ufflen et al (2010) included cross-sectional, case–control and prospective studies. Half of the included cross-sectional and case–control studies showed positive association between occupational sitting and BMI, but the three included prospective studies had conflicting results and could not confirm the association. Two of the three prospective studies found a positive association between occupational sitting and type 2 diabetes mellitus (the third did not find an association), and of the six studies that examined mortality, four found a positive association for mortality, one found no association, and one found a decreased risk. The studies looking at cardiovascular disease all had conflicting results. Overall, the reviewers could not make any statistical or narrative conclusions due to the heterogeneity in study design (cross-sectional, case–control and prospective), measures and outcomes. Strengths of this review were the comprehensive search strategy, and clearly defined inclusion criteria and methods of critical appraisal.

Proper et al (2011) systematically reviewed the literature for prospective studies enrolling adults, and used a 'best-evidence synthesis' to assess study quality and synthesise the results. They included 19 studies of sedentary behaviour (14 high quality; 5 low quality); however, conflicting results meant that no conclusions could be reached for body mass index (BMI) gain, obesity (or other bodyweight measurements, including waist circumference) or the risk of cardiovascular disease. They did report a significant association between sitting time and type 2 diabetes mellitus, and 'moderate evidence' for an association for all-cause mortality and for cardiovascular disease mortality. This systematic review had several strengths: the reviewers used clearly defined inclusion criteria, including that the primary studies had to measure sedentary behaviour according to the definition by Pate et al (2008). Similarly, the methods of best-evidence synthesis were robust and objective.

In 2011, Thorp et al published a systematic review of prospective studies that examined the associations between total daily sedentary behaviour and health outcomes (mortality; disease incidence; overweight or obesity incidence, or weight gain; or any other health marker) in adults. They also included studies that followed participants from childhood or adolescence through to adulthood. This systematic review described itself as building on the findings of the systematic review by Proper et al (2011), by including studies published from 1996 to January 2011, and by including a greater number of studies than that former systematic review (by summarising the findings from all included studies, 'without prejudice of the methodologic quality of the studies' [Thorp et al 2011, p208], rather than using a more restrictive, best-evidence synthesis). As a result, 48 studies were included, with 45 using self-reported measurements of sedentary behaviour (including total sitting time, television-viewing time or other screen time). Only three studies used objective measurements of sedentary behaviour, or a combination of objective and subjective methods. The reviewers concluded that there was a significant positive association between sedentary behaviour and mortality (all-cause and cardiovascular disease mortality, but not cancer-related mortality), as well as for weight gain from childhood to adulthood. No conclusions could be reached for specific disease incidence (e.g. gallstones, type 2 diabetes mellitus), or for weight gain during adulthood or cardiometabolic risk, due to conflicting results of the primary studies. Overall, the reviewers cautioned against drawing firm conclusions because of the scarcity of the primary studies that met inclusion criteria. Although this systematic review was well constructed and comprehensive, most of the included studies used television viewing as a measure of sedentary behaviour, which inevitably tends to favour examination of leisure-time behaviours, rather than total daily sedentary behaviour.

The meta-analysis by Grøntved and Hu (2011) provides further robust data on associations between sedentary behaviour and adverse health outcomes. The study included prospective studies that measured sedentary behaviour in one domain (television viewing) only. Where studies only reported categorical variables, the reviewers used trend estimation methods to calculate continuous associations with television viewing. The researchers also obtained unpublished data from study authors to use in the meta-analysis. These unpublished data were not reproduced in the review paper, nor did the reviewers identify from which of their eight included studies they obtained unpublished data (the reviewers themselves were authors of two of the included papers). Outcomes were incidence of type 2 diabetes mellitus, cardiovascular disease and all-cause mortality. When data were pooled, there was a significantly increased risk associated with each outcome. Associations for cardiovascular disease and type 2 diabetes mellitus were linearly associated with increasing time spent sedentary; all-cause mortality risk was linear up to a threshold of three hours per day, at which point risk was markedly increased.

The meta-analysis by Grøntved and Hu (2011) was comprehensive, but at a risk of bias due to the use of unpublished data. It was published after this systematic review was registered, and the critical appraisal and data extraction phases complete. Results of the meta-analysis and this review are complementary, however, and together broaden our understanding of the effects of sedentary behaviours.

1.2 Methodological basis for the review

This systematic review followed Joanna Briggs Institute (JBI) methods for a quantitative systematic review.

The search strategy included prospective studies only, despite the great volume of cross-sectional studies that have been published on sedentary behaviour. Prospective cohort studies are useful for measuring diverse outcomes in large population groups over time (Mamdani et al 2005, Rochon et al 2005), and are situated higher in the evidence hierarchy than cross-sectional studies (Aromataris et al 2011). Compared with randomised controlled trials, prospective cohort studies are often less expensive and more practical to run, and also mean that diverse groups of people can be observed in a 'real-life' setting, while controlling for important confounders at the same time (Rochon et al 2005). Although prospective cohort studies cannot identify causal associations, they are still useful for gathering data regarding adverse effects and risks, which is particularly important for the study of sedentary behaviour and adverse health outcomes. Prospective studies can also be used when ethical reasons, such as deliberate exposure to known risks or causing harm by with-holding treatment, preclude randomised controlled trials (Aromataris et al 2011).

The literature includes a rapidly growing number of randomised controlled trials of interventions for reducing prolonged sedentary behaviours in children and adolescents (e.g. television-viewing time; Wahi et al 2011), and some in adults (De Cocker et al 2008) (see Section 4.7 for further discussion). Data from these trials will be useful at a later stage for identifying the most appropriate intervention; however, they have not been considered here due to the focus of this thesis on risks and associations of sedentary behaviours and adverse health outcomes. Furthermore, although randomised controlled trials are considered to be the gold standard for investigating the relationship between an intervention and an outcome, it is not practical to run a randomised controlled trial for the duration necessary to observe endpoints for chronic diseases such as cardiovascular disease mortality.

1.3 Review question and objectives

The purpose of this systematic review was to critically appraise, synthesise and present the best available evidence concerning the cardiovascular and metabolic risks associated with prolonged sedentary behaviour in otherwise healthy adults.

The specific review question was as follows:

- In adults who are not overweight, obese, or have any other existing metabolic or cardiovascular condition, does prolonged sedentary behaviour (activities of $\leq$1.5 MET, for two or more hours) increase the risk of obesity, type 2 diabetes mellitus, cardiovascular disease or other cardiometabolic health problems?

1.4 Inclusion criteria and key terms

Population

The review considered studies that included adults (approximately 18–65 years; i.e. not children or adolescents); males and females; and who did not have existing metabolic or cardiovascular health problems at baseline (e.g. obese, diabetic, cardiovascular disease, metabolic syndrome).

Exposure

Studies that evaluated sedentary behaviour, defined as prolonged sitting time, screen (television, computer) time, or any nonspecified sedentary behaviour (occupational or nonoccupational) were considered for inclusion. This inclusion criterion was defined to include specific measures of sedentary activity; for example, sedentary behaviour for more than three hours at a time, preferably accompanied by a MET value of $\leq$1.5, but not including standing. Therefore, for the purpose of this review, key terms are defined as follows:

- *Sedentary behaviour*: behaviours that have a low energy expenditure (e.g. $\leq$1.5 MET (Owen et al 2009, van Uffelen et al 2010) [metabolic equivalent — the ratio of the metabolic rate of an activity and the resting metabolic rate]). Sedentary behaviour does not include standing; rather, it can include:
  - *prolonged sitting*: sitting down for three or more hours at a time, without standing or walking breaks
  - *screen time*: time spent sitting in front of a computer, television, video game, etc (either at work or in leisure time)
  - *nonspecified sedentary behaviour*: any other behaviour that involves sitting or lying (e.g. driving, reading, listening to music, talking on the telephone).

Outcomes

This review considered studies that included the following primary outcome measures: incidence of obesity and obesity-related disease, including (but not limited to) type 2 (adult-onset) diabetes, cardiovascular incidents (e.g. stroke, myocardial infarction), cardiovascular disease (e.g. heart failure), metabolic syndrome (according to the World Health Organization definition), all-cause mortality/morbidity. Secondary outcomes included any cardiovascular or metabolic measures, such as insulin resistance or sensitivity, high blood pressure, BMI, lean body mass/body composition (including change in adiposity, lean body mass, weight, etc), abdominal obesity (waist circumference), percentage body fat.

For the purpose of this review, cardiovascular disease, coronary heart disease, ischaemic heart disease, atherosclerosis and myocardial infarction were considered under the umbrella term 'cardiovascular disease' — defined as any disease that affects the cardiovascular system (also known as heart disease).

Chapter 2 Review methods

Chapter 2 outlines the review methods, including a broad overview of the search methods, followed by a more detailed description of the critical appraisal, data extraction and data synthesis processes. Appendix 1 outlines the review protocol with inclusion and exclusion criteria; the detailed search strategies are provided in Appendix 2.

2.1 Search strategy

The search was not limited by earliest publication date; however, an end date of 13 March 2011 was used. Papers in languages other than English were excluded.

The search strategy aimed to find both published and unpublished studies. A three-step search strategy was used: an initial limited search of PubMed and CINAHL was undertaken, followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe relevant articles. A second search using all identified keywords and index terms was then undertaken across all included databases. Thirdly, the reference lists of all identified reports and articles were searched for additional studies.

Key words included those relating to the population and exposure (e.g. adult, sedentary lifestyle sedentary, sedentary behaviour, sitting, prolonged sitting, sitting time, sedentary time, television viewing, screen time, occupational sitting, physical inactivity), and outcomes (key words relating to obesity, cardiovascular disease, type 2 diabetes mellitus, stroke, etc). See Appendix 2 for the detailed search strategies for key databases.

2.2 Assessment of methodological quality

The methods of the review followed the standard methods prescribed by the Joanna Briggs Institute (JBI). A critical appraisal instrument was used, based on the standard JBI tool for cohort studies. Nine questions were used, relating to internal and external validity, with each question being scored as *adequate* (i.e. the paper provided a clear description of the characteristic, and met all the criteria), *inadequate* (i.e. the paper provided a clear description or explanation, but did not meet all the criteria) or *unclear* (i.e. the paper was unclear in its reporting or did not provide enough information to determine whether it met the criteria). Study quality, calculated from the scores of the nine-question critical appraisal form was determined as low (1–3), moderate (4–7) and high (8–9). See Appendix 3 for a copy of the critical appraisal form.

Consistency of interpretation and application of the appraisal instrument between the two reviewers was assessed and maintained by discussion and conferral following independent appraisal of six studies by the two reviewers. In particular, the question relating to the definition of sedentary behaviour (Question 2: do participants share similar sedentary behaviours?) was revised after this initial pilot appraisal of studies due to the physiological differences noted between true sedentary behaviour and light activity (see Section 1.1.1; Pate et al 2008). After discussion, the two reviewers agreed that they had assigned too much weight to Question 2 during the pilot critical appraisal process (the primary reviewer had included papers that scored 'inadequate' on this question, while the secondary reviewer had excluded them even if they scored well on other criteria). The review protocol (see Section 1.4 and Appendix 1) specified that studies must report some sort of measure of sedentary behaviours to be included (if they simply classified people as sedentary based on a lack of physical activity, they did not meet the inclusion criteria, regardless of whether the study was of high quality).

With this in mind, the reviewers agreed to revise the critical appraisal form in line with the objectives of the review and process as follows:

- If studies did not specifically report a measure of sedentary behaviour (e.g. $\leq$1.5 MET, hours spent sitting) they were excluded.
- If the studies did specifically report a measure of sedentary behaviour, they were included and were critically appraised.
- For these included studies, Question 2 then assessed how well defined the groups of participants were; for example, whether they were grouped according to a useful and narrow category of sedentary behaviour (e.g. 35–40 hours sitting/week, or a narrow MET range) versus too wide a classification (e.g. 20–40 hours/week). If they were grouped according to the latter, it indicated that the group potentially

contained participants who were not truly sedentary; therefore, dependent on full details, the question was likely to be marked unclear or inadequate.

- If the study seemed to include people who were sedentary for long periods of time but who also exercised vigorously at times (and were included in the sedentary group), then Question 2 would be scored as *unclear* or *inadequate*.

The critical appraisal form was amended to reflect this by deleting the following two criteria from the *inadequate* form in Question 2 of the original version: *Sedentary behaviour only defined indirectly as a lack of physical activity;* and *Sedentary behaviour only defined as accumulated time (e.g. over a day, week) interrupted by frequent breaks (i.e. not prolonged sedentary behaviour).* These changes were informed by the definition of sedentary as described by Pate et al (2008).

When assessing the studies, a total score for each study was calculated based on the number of questions that were scored as adequate. A cut-off score of five out of the total of nine was used for including or excluding studies. Studies that scored five or lower and that also had serious methodological issues were excluded.

Two reviewers independently assessed all the selected studies for methodological quality. Results were entered into the JBI-Meta Analysis of Statistics Assessment for Review Instrument (JBI-MAStARI), and any disagreements between the two reviewers were discussed and resolved (all disagreements were resolved without the need for a third reviewer).

The original review protocol included prospective and retrospective cohort studies, case–control studies and cross-sectional studies. However, after the initial searches, in line with the decisions made a priori in the review protocol (see Appendix 1), it was decided to limit the review to prospective cohort studies only, for the following reasons:

- there were many high-quality prospective studies available; therefore, it was superfluous to include study designs that were lower in the evidence hierarchy (i.e. retrospective cohort studies, cross-sectional and case–control studies), because prospective designs have greater internal validity and a lower risk of bias

- it became apparent that another systematic review (van Uffelen et al 2010) had recently been published on the cross-sectional studies relating to prolonged sedentary behaviour in adults (note that this was the only other published systematic review addressing this topic that was identified at the start of the project).

2.3 Data collection and extraction

A data extraction form for prospective studies was developed (see Appendix 4), and used to extract specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives. Data were extracted from the included papers by the primary reviewer only.

2.4 Data synthesis

Key characteristics of included studies were tabled and suitability for meta-analysis was assessed. However, at this stage, a meta-analysis of television viewing (as a proxy measure of sedentary behaviour) and health outcomes had been published, showing a clear association (Grøntved and Hu 2011).

In this systematic review, heterogeneity in all the exposure variables and the limited number of studies reporting on similar outcomes prevented a meta-analysis from being done. Instead, the results were combined in a narrative summary, and the risk of outcomes were analysed.

Chapter 3 Results

3.1 Search results

Figure 3.1 illustrates the number of citations identified by the database searching, the number of full text papers retrieved following scanning of titles and abstracts, and the numbers of papers selected for inclusion. Ultimately, following critical appraisal of 19 studies, 16 studies were included in the final analysis.

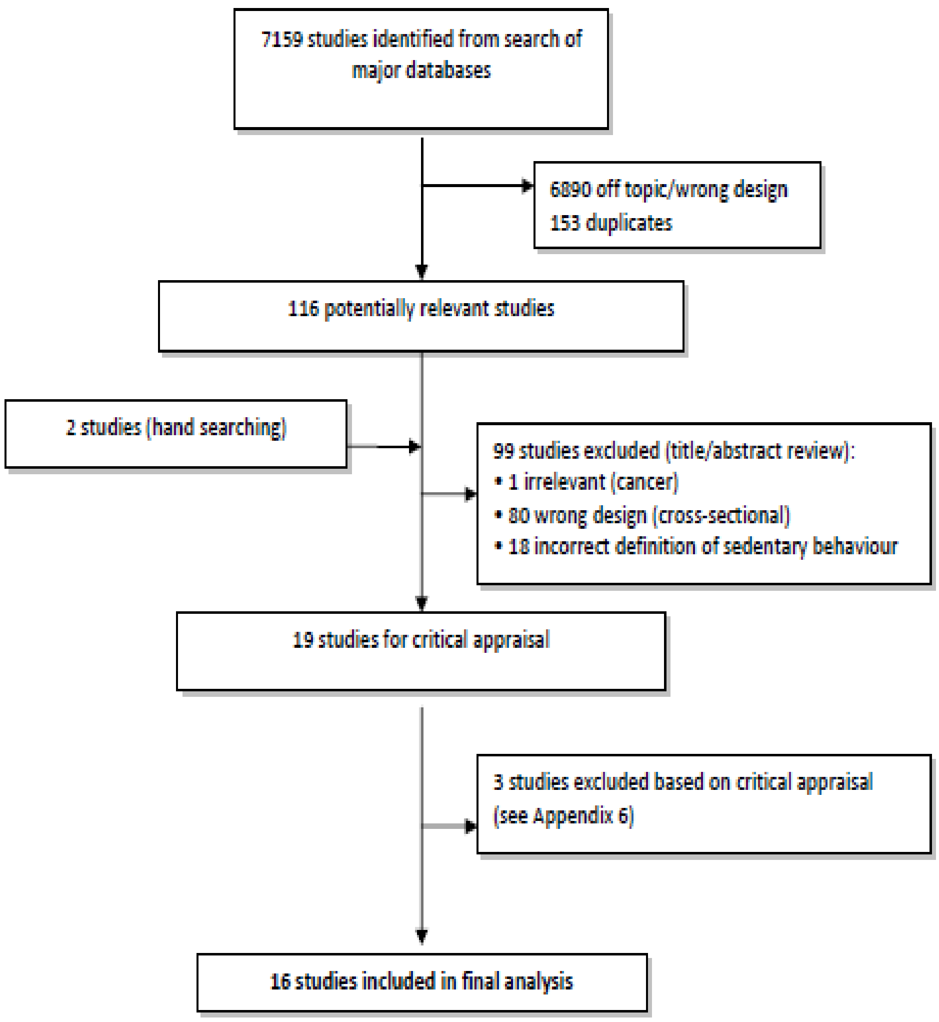

Figure 3.1 Search results

The full details of individual studies are shown in Table 3.1, and the key characteristics are described in more detail below.

3.2 Methodological quality

The included studies were of moderate quality, with most scoring 7–8 for the 9 questions on the critical appraisal form (see Appendix 2 for full details of study scores). Studies scored least well for their populations of interest (often poorly defined, or not representative of the whole population), data-collection methods (not objective), and outcome measures (not standardised or objective — i.e. few studies used standardised or validated tools). Studies that did not define or use a valid measure of sedentary behaviour (as defined in Section 1.4) were not selected for inclusion. Reviewer agreement was high and all discrepancies were resolved after discussion.

3.3 Association between sedentary behaviour and adverse outcomes

Overall, 11 studies reported an association between prolonged sedentary behaviour and an increased risk of adverse health effects (Arsenault et al 2010, Carlsson et al 2006, Helmerhorst et al 2009, Hu et al 2001, Hu et al 2003, Koh-Banerjee et al 2003, Kozakova et al 2010, Leitzmann et al 1999, Salonen et al 1988, Sjol et al 2003, Warren et al 2010); four found no association, or mixed results, with no association for some subgroups (women or men, various ages; see below) (Blanck et al 2007, Coakley et al 1998, De Cocker et al 2010, Katzmarzyk et al 2009); and one found an association between prolonged sedentary behaviour and a decreased risk of adverse health effects (Graff-Iversen et al 2007). Table 3.1 summarises the study characteristics and results.

Statistically significant dose-response relationships were reported between increasing time spent sitting and all-cause mortality (p for trend <0.0001, Katzmarzyk et al 2009); cardiovascular disease mortality (p for trend <0.0001, Katzmarzyk et al 2009) (p for trend <0.001, Warren et al 2010); incidence of type 2 diabetes mellitus (p for trend$=0.02$, Hu et al 2001); weight gain greater than 10 pounds (4.5 kg) (no trend data reported, Blanck et al 2007); and obesity ($p<0.001$, Hu et al 2003).

In the sections following Table 3.1, studies are addressed and analysed according to the outcome of interest. Any specific characteristics of the populations of interest, and the domain of sedentary behaviour (occupational only, leisure time only, total), are noted. For studies that recruited participants with a range of baseline characteristics (e.g. Blanck et al 2007, De Cocker et al 2010), only data relating to those who met the inclusion criteria (adults who were healthy and of a normal weight/BMI at baseline) are reported. Similarly, where studies reported on a range of outcomes; only those of interest to this systematic review, and identified a priori in the review protocol (see Appendix 1) are reported here. As detailed in Section 1.4, these adverse health outcomes are:

- obesity
  - abdominal obesity — measured by waist circumference
  - weight gain
  - overweight or obesity — indicated by BMI
- cardiovascular disease
  - incidence
  - atherosclerosis
- mortality
  - all-cause
  - cardiovascular disease mortality
- type 2 diabetes mellitus
- gallstones.

Table 3.1 Summary of included studies

Reference	Population, country, follow-up	Measure of sedentary behaviour	Outcome (measure)	Results and association with sedentary behaviour	Adjustments, limitations
Arsenault et al (2010)	21 729 adults (9564 men) 45–79 years United Kingdom 11.4 years	Physical activity Categorised according to activity in work and leisure. All 4 categories had the option of sedentary occupation (and no LTPA, etc according to category). Lowest activity category: sedentary job and no LTPA. However, no information given on how accumulated.	• Abdominal obesity (mean waist circumference) • Coronary heart disease (CHD) (only with obesity as a risk factor, not sedentary behaviour)	Positive association Physically inactive participants characterised by increased waist circumference. Mean waist circumference for normal-weight men (mean [SE]), age adjusted: • active: 86.4 (0.21) • moderately active: 87.0 (0.22) • moderately inactive: 87.4 (0.22) • inactive: 88.6 (0.22) *p* for trend <0.001 Mean waist circumference for normal-weight women (mean [SE]), age adjusted: • active: 73.7 (0.20) • moderately active: 73.9 (0.17) • moderately inactive: 74.7 (0.15) • inactive: 75.7 (0.20) *p* for trend <0.001	Adjusted for age, smoking, alcohol, family history CHD, hormone-replacement therapy use (women) Not adjusted for diet, despite obesity being an outcome Unclear description of sedentary behaviour

Blanck et al (2007)	18 583 women 40–69 years United States 7 years	Non-occupational sedentary time (average daily time sitting, excluding work); responses grouped into four: <3, 3–5, 6–8, >8 hours/day.	• Weight gain (self-report)	Positive association (>4.5 kg weight gain in non overweight only); no association (2.3–4-kgweight gain) OR (95%CI) weight gain: • 2.3–4 kg weight gain (nonoverweight women: BMI <25): – <3 hours/day: 1 – 3–5 hours/day: 1.07 (0.97, 1.18) – >5 hours/day: 1.06 (0.87, 1.30) • ≥4.5 kg weight gain (nonoverweight women, BMI <25) – <3 hours/day: 1 – 3–5 hours/day: 1.16 (1.04, 1.28) – >5 hours/day: 1.47 (1.21, 1.79)	Adjusted for age, hormone therapy use, BMI (<25 and ≥25), recreational physical activity, education, smoking, total energy Not clear how postmenopausal status established No adjustment for OPA. Despite being described as postmenopausal, not clear whether participants are retired (survey specifically asks participants to exclude any activity done at work)
Carlsson et al (2006)	27 374 women, recruited from general population (not clear how menopause status established) 51–85 years Scotland 5 years	Physical activity (self-reported), reported as total daily PA, PA at work, and reading/TV. Lowest activity group classed as ≤35 MET/hour/day.	• Mortality (population registries)	Positive association Authors concluded: *Women with low physical activity (35 MET*h/day) had a 3.22 times increased mortality (95%CI 2.35, 4.43) compared with the most active women (>50 MET*h/day).* Mortality RR (95%CI) • *Total daily PA (35.0 MET per day or less)* (adjusted for lifestyle and medical problems): 2.56 (1.85, 3.53) • *PA at work* (mostly sedentary (adjusted for lifestyle and medical problems): 1.81 (1.08, 3.05) • TV watching and reading (more than 6 h/day): 1.16 (0.8, 1.67)	Adjusted for diet, smoking, asthma, education, diabetes. However, does not seem to be corrected for cause of death or old age.

Coakley et al (1998)	19,478 male health professionals 40–75 years United States 4 years	TV/VCR viewing: self-reported average hours per week	• Weight gain (difference in pounds between baseline and follow up; self-reported, but well described)	Age-specific positive association Group 1 (45-54 years): ß (SEM) 0.02 (0.01), *p*<0.001 Not significant for other age groups	Adjusted for diet, quitting smoking, baseline weight, height, vigorous physical activity, high blood pressure, high cholesterol Not adjusted for hours spent sitting at work
De Cocker et al (2010)	5562 women 24.6–30.6 years Australia 6 years	Sitting time (self report) in both domains (work, leisure). However, only week-day results included in analysis (weekend results too unreliable)	• BMI (from self-reported weight gain)	No association (normal–underweight women) Sitting time in 2000 (predictor)→change in weight from 2000 to 2006 (outcome), ß (95%CI): • Underweight: 0.100, (−0.117, 0.317) • Normal weight: 0.030 (−0.051, 0.112) Change in sitting time from 2000 to 2003 (predictor)→change in weight from 2003 to 2006 (outcome), ß (95%CI): • Underweight: −0.055 (−0.182, 0.073) • Normal weight: −0.005 (−0.062, 0.052)	Adjusted for various things in the different models (weight or sitting time in 2000 only; additional adjustments for PA in 2000 and energy intake measured in 2003; additional adjustments for a range of population characteristics)

Graff-Iversen et al (2007)	47,405 adults (15,456 men) 35–49 years Norway 6 years	Physical activity Total PA (added dichotomous categories of LTPA and OPA); grouped into 4; lowest group = no occupational physical activity, no leisure-time physical activity Compared no PA versus any category of PA	• Overweight (BMI >27, objective measurements) • Mortality: CVD, CHD, sudden other cause (registries)	Negative association (women); no association (men) OR (95% CI) for overweight among men • Sedentary work: 1 • Light OPA: 0.91 (0.82, 1.00) • Moderate OPA: 0.95 (0.86, 1.05) • Heavy OPA: 0.97 (0.88, 1.97) OR (95% CI) for overweight among women: • Sedentary work: 1 • Light OPA: 1.18 (1.04, 1.34) • Moderate OPA: 1.51 (1.30, 1.74) • Heavy OPA: 1.67 (1.38, 2.03) RR (95% CI) for mortality • Sedentary work: 1 • Light OPA: 1.01 (0.92, 1.10) • Moderate OPA: 0.95 (0.87, 1.05) • Heavy OPA: 0.84 (0.76, 0.92) No association (for sedentary behaviour); negative association (physical activity) RR (95% CI) for mortality: • Sedentary work: 1 • Light OPA: 1.01 (0.92, 1.10) • Moderate OPA: 0.95 (0.87, 1.05) • Heavy OPA: 0.84 (0.76, 0.92)	Adjusted for age, smoking, leisure-time physical activity, income, BMI, education Use loosely defined categories of physical activity, but do distinguish between sedentary and light activity
Helmerhorst et al (2009)	376 adults (166 men) 49.4 $\pm$ 7.7 years United Kingdom (Caucasian) 5.6 years	Accelerometer-measured sedentary time: heart rate observations (minutes) below individually predetermined threshold (flex heart rate), expressed as % total time (waking hours) over 4 days	• Fasting insulin resistance using blood samples	Positive association Fasting insulin (log pmol/L) regression coefficients (ß) (95%CI) between objectively measured sedentary time and moderate–vigorous PA time at baseline, with fasting insulin Sedentary time (% time spent sedentary), ß (95% CI): ß =0.004 (0.0009, 0.006), *p*=0.009	Controlled for baseline age, sex, fat mass, fasting insulin, smoking status, physical activity and follow-up time

Hu et al (2001)	37,918 male health professionals 40–75 years United States 10 years	TV viewing time (average self-reported weekly time; biennial questionnaires) Categorised as 0-1, 2-10, 11-20, 21-40, and >40 hrs/week	• Type 2 diabetes mellitus (clinically diagnosed, based on self-reported symptoms)	Positive association Calculated incidence of DM (RR, 95%CI) per activity class, with 0.1 hours/week group as the reference group: • 0–1 hours/week: 1.0 • 2–10 hours/week: 1.49 (1.03, 2.15) • 11–20 hours/week: 1.39 (0.95, 2.05) • 21–40 hours/week: 1.77 (1.18, 2.64) • >40 hours/week: 2.23 (1.13, 4.39) *p* for trend=0.02	Controlled for age, smoking, alcohol, diet, BMI, family history of type 2 diabetes mellitus, cholesterol, blood pressure Population is health professionals (dentists, optometrists, pharmacists, podiatrists, osteopaths, and veterinarians); different occupational activity levels, which were not controlled for (asked about leisure-time physical activity only)
Hu et al (2003)	50 277 female nurses 46–71 years United States 6 years	Sitting time (average weekly time spent sitting at work, at home [i.e. TV], or away from home, or while driving); self-report Categories: • 0–1 hour • 2–5 hours • 6–20 hours • 21–40 hours • >40 hours	• Self-reported type 2 diabetes mellitus • Self-reported BMI (<30 or >30)	Positive association RR obesity (95%CI; with *p* for trend given), according to category of sedentary behaviours. More sitting associated with greater risk of BMI >30 compared with women who sat for 0–1 hours; RR (95% CI) = 1.25 (1.02, 1.54) for women who sat for >40 hours p<0.001 for trend across categories of sitting time	Controlled for age, hormone use, smoking, alcohol, physical activity, energy intake, fat intake, fibre intake, glycaemic load Recorded occupational sedentary behaviour at baseline but not follow-up.

Katzmarzyk et al (2009)	17 013 adults (7278 men) 18–90 years Canada ~12 years	Self-reported sitting time (over most days, in work, school, housework) Grouped into 5 groups: almost none of the time to almost all of the time, approximately one-quarter of the time, approximately half the time, approximately three-quarters of the time, or almost all of the time	• All-cause mortality • Cardiovascular disease mortality • Cancer mortality Canadian mortality database	Positive association for all cause, CVD and other mortality; no association for cancer mortality HR (95% CI) for all-cause mortality: • none of the time: 1.00 • 1/4 of the time: 1.00 (0.86, 1.18) • 1/2 of the time 1.11 (0.94, 1.30) • 3/4 of the time: 1.36 (1.14, 1.63) • almost all the time: 1.54 (1.25, 1.91) *p* for trend <0.0001 HR (95% CI) for CVD mortality: • none of the time: 1.00 • 1/4 of the time: 1.01 (0.77, 1.31) • 1/2 of the time 1.22 (0.94, 1.60) • 3/4 of the time: 1.47 (1.09, 1.96) • almost all the time: 1.54 (1.09, 2.17) *p* for trend=<0.0001 No significant results for cancer mortality HR (95% CI) for other mortality: • none of the time: 1.00 • 1/4 of the time: 1.06 (0.78, 1.41) • 1/2 of the time: 1.15 (0.84, 1.57) • 3/4 of the time: 1.65 (1.18, 2.31) • Almost all the time: 2.15 (1.47, 3.14) *p* for trend=<0.0001	Adjusted for age, leisure-time physical activity, smoking, alcohol, and physical activity readiness questionnaire. Certain groups of lower socioeconomic classes excluded (e.g. indigenous, institutionalised); study does not adjust for education or income otherwise.

Koh-Banerjee et al (2003)	16,587 male health professionals 40–75 years United States 6 years	Average weekly time spent watching TV (self-reported)	• Waist circumference (self-reported)	Positive association Increase in TV of 20 hours/week was significantly related to a 0.30 (0.12) cm waist gain, p=0.02	Adjusted for age, waist circumference at baseline and BMI, total calories, alcohol, physical activity, smoking Uses a health professional cohort, but does not adjust for occupational physical activity, although did record a range of leisure-time PA, and estimates total time spent watching TV (to check for an association with waist circumference increase over 6 years)
Kozakova et al (2010)	494 adults Mean age 44±8 years 3 years	Measured sedentary behaviour (time [mins] sedentary:light-intensity activity used as index of sedentary behaviour) using accelerometer and self-reports (IPAQ long-form questionnaire, mean+SD, median [interquartile range] and range)	• Carotid intima-media thickness (IMT) (used as a surrogate measure of atherosclerosis) using minimal luminal diameter of left common carotid artery (ultrasound imaging; µm) • 3-year IMT progression in different carotid segments	Positive association Regression coefficient for independent determinants of common carotid artery intima-media thickness (ß ± SE for the sedentary:light activity ratio): 0.14 ± 0.03 (*p* <0.0001//0	Adjusted for age, sex, weight, fat-free mass, fasting glucose

Leitzmann et al (1999)	60,290 female registered nurses 40–65 years at baseline United States 10 years	Physical activity (average time per week spent in specified activities; self report); leisure-time physical activity only. Categorised into quintiles of physical activity (MET hours/week): 0–1.6, 1.7–4.5, 4.6–10.5, 10.6–22.0, >22.0 However, also recorded weekly time spent inactive by estimating weekly time spent sitting at work or while driving (the 10 possible responses ranged from less than 1/2 hour to 90 or more hours per week). Also asked about time spent watching TV (Work and driving 6yrs. Watching TV 4 years) Lowest category = 0–1.6 MET/hr/wk, which is just over the cut-off for sedentary behaviour	• Gallstones (self-reported cholecystectomy; mostly confirmed by medical records)	Positive association Multivariate RR for women in the highest (cf. lowest) quintile of physical activity was 0.69 (95 percent confidence interval, 0.61 to 0.78) For sedentary behaviour: 41–60 hours per week sitting had a multivariate relative risk of 1.42 (95%CI, 1.06 to 1.89; cf. >6 hours per week sitting while at work or driving); and >60 hours per week sitting while at work or driving had a multivariate RR of 2.32 (95%CI, 1.26 to 4.26)	Adjusted for age; parity; use of oral contraceptives; use of postmenopausal hormones; history of type 2 diabetes mellitus; pack-years of smoking; use of cholesterol-lowering drugs; use of thiazide diuretics; use of nonsteroidal anti-inflammatory drugs; and intake of energy-adjusted dietary fibre, energy-adjusted carbohydrates, alcohol, and coffee, BMI

Salonen et al (1988)	15,088 adults 30–59 years Finland 6 years	Self-reported *activity* level (leisure time and occupational); lowest defined as 'mainly sitting'	Binary outcomes: • Ischaemic heart disease (IHD) (mortality) (*International Classification of Diseases*; no event/IHD death during the follow-up period) • BMI (<27 or >27 kg/m2); not stated how measured (only used as risk) • Other binary outcomes: leisure-time physical activity, occupational physical activity, BMI, sex, age, blood pressure, cholesterol, smoking	Positive association Tested the dependence of the association between physical activity and risk of death from IHD on a range of other factors. • Sedentary in leisure time: RR 1.3 (95%CI 1.1, 1.6) • Sedentary in work time: RR 1.3 (95%CI 1.1, 1.6) After adjusting for confounders, the risk for low leisure time PA was RR 1.2, 95%CI 1.0, 1.5; unchanged for work time The only statistically significant interactions including the variable IHD concerned leisure-time physical activity, occupational physical activity, BMI, and sex. The model was reduced to a saturated six-factor model that also included age	Adjusted for age, BMI, education, social network participation, cigarette consumption, serum cholesterol, blood pressure

Sjol et al (2003)	13,925 adults (50% female) 30–60 yrs Denmark 27 years	Physical activity (work and leisure) Self-reported occupational activity(from survey): • sedentary • moderately active • highly active • heavy manual Lowest group categorised as 'sedentary'	• Acute myocardial infarction, or death from acute myocardial infarction (death registries)	Positive association More occupational activity associated with lower risk of acute myocardial infarction: compared with 'sedentary'; RR (95% CI) = 0.61 (0.44, 0.84) for 'moderate and high' in 1964 and 1976	Adjusted for age, sex, smoking, education, BMI, cholesterol, blood pressure
Warren et al (2010)	7744 middle–upperclass men 20–89 yrs United States ~20 years	Sedentary behaviour (TV viewing and time spent in a car; self-reported weekly average); grouped in sedentary behaviour categories HR (95% CI) and CVD mortality rates (deaths per 10,000 person-years of follow-up) estimated by comparing each category of sedentary behaviour to the lowest category	• Cardiovascular disease (*International Classification of Diseases*) • Cardiovascular disease mortality (National Death Index plus death certificates)	Positive association CVD mortality increased across incremental quartiles of riding in a car (P_{trend} <0.0001) and combined sedentary behaviour (P_{trend} = 0.0002) but not TV (P_{trend} = 0.07) Direct association (car riding, combined sedentary behaviour and CVD mortality) was still significant in multivariate analysis, across time spent riding in a car (P_{trend} = 0.01) and combined sedentary behaviour (P_{trend} = 0.04)	Adjusted for age, physically inactive (yes or no), smoking, alcohol, BMI, hypertension, diabetes, cholesterol, family history CVD

BMI = body mass index; CHD = coronary heart disease; CI = confidence interval; CVD = cardiovascular disease; HR = hazard ratio; IHD = ischaemic heart disease; LTPA = leisure-time physical activity; MET = metabolic equivalent; OPA = occupational physical activity; OR = odds ratio; PA = physical activity; RR = risk ratio; TV = television; VCR = videocassette recorder.

3.3.1 Obesity

Description of studies

The risk of obesity associated with sedentary behaviour was reported in 7 of the 16 included studies. Three different indicators of obesity were used: abdominal obesity (two studies: Arsenault et al 2010, Koh-Banerjee et al 2003), weight gain (three studies: Blanck et al 2007, Coakley et al 1998, De Cocker et al 2010) and overall obesity (measured by BMI; two studies: Graff-Iversen et al 2007, Hu et al 2003). Length of follow-up varied from 4 years (Coakley et al 1998) to approximately 11 years (Arsenault et al 2010).

Dividing the studies into male and female subgroups allowed for narrative synthesis, but not meta-analysis. Four studies enrolled men: two investigated abdominal obesity (Arsenault et al 2010, Koh-Banerjee et al 2003), one examined weight gain (Coakley et al 1998) and one examined overweight or obesity (Graff-Iversen et al 2007). Overall, the results suggested that sedentary behaviour (or a lack of physical activity) was associated with increased risks for obesity in men (see Table 3.1); however, further information is needed to confirm the strength of the association.

Women's metabolic risks associated with sedentary behaviours were assessed in five studies. One used abdominal obesity as an outcome measure (Arsenault et al 2010), and two each used weight gain (Blanck et al 2007, De Cocker et al 2010) and overweight or obesity (Graff-Iversen et al 2007, Hu et al 2003). Overall, there were mixed results. Sedentary behaviour appeared to be associated with increased abdominal obesity, but it was not clear whether there was an association with the risk of weight gain or the risk of becoming overweight or obese (see Table 3.1).

Abdominal obesity

Two moderate-quality studies assessed the association between sedentary behaviour (Koh-Banerjee et al 2003) or physical inactivity (Arsenault et al 2010) and abdominal obesity, measured by changes in waist circumference (centimetres). Both reported a significant association between sedentary behaviour and increased abdominal obesity (see Table 3.2). However, the strength of the association and the intensity of sedentary behaviour that is needed to see the effect are not clear from the limited data available.

Arsenault et al (2010) used an indirect measure of sedentary behaviour (self-reported lack of physical activity) to investigate the risk of abdominal obesity and its subsequent association with coronary heart disease. The authors categorised a large cohort of middle-aged adults according to their self-reported levels of activity in work and leisure time over a decade. Participants were given options for describing themselves as sedentary in both domains (work, leisure), and the lowest activity group (i.e. the most sedentary) were those who reported a sedentary job and no leisure-time physical activity. The authors found that the inactive (sedentary) participants had an increased waist circumference at follow-up (men: 88.6 cm, women: 75.6 cm) compared with the active groups (men: 86.4 cm, women: 73.7 cm), irrespective of BMI ($p<0.001$; age-adjusted only; see Table 3.2). The study did not adjust for diet, despite obesity being the main outcome. (Note that baseline BMI was not adjusted for, because the study aimed to assess the risk of increased abdominal obesity irrespective of BMI.)

In contrast, Koh-Banerjee et al (2003) used a direct measure of sedentary behaviour (weekly television viewing) to investigate the risk of abdominal obesity. This moderate-quality study followed men over nine years, and found that an increase of 20 hours per week of television viewing (from any baseline amount) was significantly associated with a mean (+/-SD) gain in waist circumference of 0.30 (0.12) cm ($p=0.02$), after controlling for a range of lifestyle factors and BMI. Participants were male health professionals, which included people with a range of physical requirements (e.g. dentists, optometrists, veterinarians). However, occupational physical activity was not adjusted for in the analyses, although a range of leisure-time physical activities were recorded.

Table 3.2 Studies investigating sedentary behaviour and abdominal obesity

Study	Results
Arsenault et al (2010)	Mean waist circumference for normal-weight men (mean [SE]), age adjusted: • active: 86.4 (0.21) • moderately active: 87.0 (0.22) • moderately inactive: 87.4 (0.22) • inactive: 88.6 (0.22) *p* for trend <0.001 Mean waist circumference for normal-weight women (mean [SE]), age adjusted: • active: 73.7 (0.20) • moderately active: 73.9 (0.17)

	• moderately inactive: 74.7 (0.15) • inactive: 75.7 (0.20) *p* for trend <0.001
Koh-Banerjee et al (2003)	Increase in TV of 20 hours/week: • Age-adjusted analysis: waist change (cm): 0.45 $\pm$0.14 (*p*=0.00) • Multivariate analysis: waist change (cm): 0.30$\pm$0.12 (*p*=0.02)

Weight gain

Of the three studies that investigated the association between sedentary behaviour and weight gain, one enrolled men only (Coakley et al 1998) and two enrolled women only (Blanck et al 2007, De Cocker et al 2010). All three studies used direct measures of sedentary behaviour — two recording sitting during leisure time (Coakley et al 1998, Blanck et al 2007) and one measuring total daily sitting (De Cocker et al 2010). The three studies shared a similar follow-up time of four to seven years, which was sufficient duration for weight-specific outcomes to develop. Results are shown in Table 3.3.

Coakley et al (1998) used a direct measure of leisure-time sedentary behaviour (weekly hours spent watching television or videos — 'screen time') in middle-aged male health professionals. The difference in self-reported measures of weight at baseline and four-year follow-up was used to establish weight gain. Participants were categorised into three age groups. In the youngest group (45–54 years), there was a significant association between weekly screen-time hours and weight gain at four-year follow-up (ß [SEM] = 0.02 [0.01], *p*<0.001), but not in the other age groups (55–64 years, >65 years). In addition, an increase in weekly screen time to >14 hours was significantly associated with an average 1.2-kg weight gain at follow-up (95%CI 0.4, 2.0). Adjustments were made for a range of lifestyle factors (e.g. age, height, weight at baseline, smoking, vigorous physical activity). However, no adjustments were made for occupational physical activity, despite there being potential differences among occupations within the large health professional cohort that was enrolled (e.g. optometrists versus veterinarians; see also Koh-Banerjee et al 2003). The extent to which this affected the results was unclear, because the study focused on predictors of weight gain, rather than making specific claims about leisure-time physical activity.

Blanck et al (2007) similarly used a direct measure of sedentary behaviour (time spent sitting while watching television, reading or other nonoccupational activities) in postmenopausal women. Participants were categorised into one of four activity level groups, the most sedentary of whom reported ≥8 hours per day. Outcomes were dichotomised as a 2.3–4 kg weight gain and a ≥4.5 kg weight gain. Significant associations were only seen for ≥4.5 kg weight gain in normal-weight women: of the normal-weight women (BMI <25 kg/m^2 at baseline), the reported OR (95%CI) for those who watched ≥6 hours of television was 1.47 (1.21, 1.79), and 1.16 (1.04, 1.28) for those who watched 3–5 hours per day, compared with the reference group who watched fewer than 3 hours per day. There was no association in normal-weight women for 2.3–4 kg weight gain, nor was there a significant association for weight gain (any amount) in overweight women (BMI ≥25 kg/m^2). The associations remained after controlling for age and lifestyle variables, including nonoccupational sedentary behaviours (0–5.0, >5.0–17.0 and >17.0 MET hours per week).

De Cocker et al (2010) used self-reported weight gain to investigate the association with sedentary behaviour in a cohort of young Australian women. They also used change in sitting time (2000–03) as a predictor variable in a linear regression analysis of weight change (2003–06). There was no association between mean daily sitting time (and six-year change in weight for normal or underweight women (adjusting for physical activity and energy intake). Neither was there a significant prospective association between change in sitting time and change in weight (see Table 3.1).

Based on the results of these three studies, there appears to be a significant positive association between self-reported sitting time and weight gain; however, this association is true only for middle-aged (45–54 years) men of a higher socioeconomic class, and for a ≥4.5-kg weight gain in normal-weight, postmenopausal women. There appears to be no association for men of other ages, or for women of other weight categories or younger age.

Table 3.3 Studies investigating sedentary behaviour and weight gain

Study	Results
Blanck et al (2007)	OR (95%CI) of 2.3–4 kg weight gain (women with BMI <25): • <3 hours/day: 1 • 3–5 hours/day: 1.07 (0.97, 1.18) • >5 hours/day: 1.06 (0.87, 1.30) OR (95%CI) of >4.5 kg weight gain (women with BMI <25): • <3 hours/day: 1 • 3–5 hours/day: 1.16 (1.04, 1.28) • >5 hours/day: 1.47 (1.21, 1.79) OR (95%CI) of 2.3–4 kg weight gain (women with BMI ≥25): • <3 hours/day: 1 • 3–5 hours/day: 0.95 (0.83, 1.08) • >5 hours/day: 1.00 (0.80, 1.26) OR (95%CI) of >4.5 kg weight gain (women with BMI ≥25): • <3 hours/day: 1 • 3–5 hours/day: 1.05 (0.94, 1.18) • >5 hours/day: 0.98 (0.80, 1.21)
Coakley et al (1998)	Four-year weight gain • Group 1 (45-54 years): ß (SEM) 0.02 (0.01), *p*<0.001 • Group 2 (55-64 years): ß (SEM) 0.01 (0.01) *p* = not significant • Group 3 (>65 years): ß (SEM) 0.00 (0.01) *p* = not significant
De Cocker et al (2010)	Sitting time in 2000 (predictor)→change in weight from 2000 to 2006 (outcome), ß (95%CI): • Underweight: 0.100, (−0.117, 0.317) • Normal weight: 0.030 (−0.051, 0.112) Change in sitting time from 2000 to 2003 (predictor)→change in weight from 2003 to 2006 (outcome), ß (95%CI): • Underweight: −0.055 (−0.182, 0.073) • Normal weight: −0.005 (−0.062, 0.052)

Overweight or obesity

The two studies (Graff-Iversen et al 2007, Hu et al 2003) that assessed the risk of becoming overweight (BMI>27) or obese (BMI>30) were large (approximately 50 000 middle-aged participants in each) and were of sufficient duration to detect changes in body weight or composition (six years). Results were mixed (see Table 3.4), with an association between overweight and increasing levels of occupational activity in one (Graff-Iversen et al 2007), and an association between overweight and increasing levels of sedentary behaviour (weekly sitting time; women only) in the other (Hu et al 2003).

Graff-Iversen et al (2007) grouped participants (men and women) into one of four subgroups, with the most sedentary undertaking no physical activity at any time. The sedentary group was used as the baseline reference for determining the odds ratios

(95%CI) of the other, higher activity groups. The results suggested an increasing risk of overweight associated with increasing occupational activity in women only, with odds ratios (95%CI) of a BMI >27 of 1.18 (1.04, 1.34), 1.51 (1.30, 1.74) and 1.67 (1.38, 2.03) for light, moderate and heavy occupational physical activity, respectively. Strengths of this study included objective measures of outcomes (BMI measured by trained observers, use of death registries for mortality), and a correct separation of sedentary behaviour and light activity —although physical activity was used as the exposure (participants were categorised as 'sedentary' by default if they did not meet a minimum of physical activity at work). This was further reflected in the use of the sedentary group data as the baseline reference, reflecting the persisting, yet questionable, view that sedentary behaviour can be measured indirectly as a failure to meet a minimum level of physical activity. Adjustments were made for baseline BMI, education and income levels, and leisure-time physical activity (although the latter was estimated from single-item questionnaire asking for recall over the past year). Energy intake and diet were not adjusted for.

Hu et al (2003) found an association between sedentary behaviour and the risk of obesity in middle-aged female nurses by measuring sedentary activity directly as total weekly sitting time (television or video viewing, occupational, driving). Sedentary behaviour appears to have only been measured at baseline recruitment into the cohort, and not at the two, four or six-year follow-up. This may simply have been an error of the reporting, and the authors were contacted for clarification (29 August 2011). No reply was received. Physical activity levels (in pre-specified activities) were recorded at baseline and at two of the three follow-up points. Participants' transition to obesity (BMI >30) was recorded, based on self-reported height and weight data. The study found that greater weekly sitting times (>40 hours) were associated with an increased risk of obesity, compared with women who sat for only 0–1 hours: RR (95%CI) 1.25 (1.02, 1.54; $p<0.001$ for trend). The positive association remained after adjusting for a range of lifestyle factors (age, smoking, energy intake, physical activity, etc). The multivariate analyses controlled for a range of confounders, including energy intake, fat intake, fibre intake, glycaemic load and alcohol consumption.

Based on these two studies, it is unclear whether prolonged sedentary behaviour has an effect on the risk of becoming overweight or obese. Despite the large size of both studies, the significant differences in the study populations, exposures and outcomes make it difficult to combine or compare the results. Further studies using a direct measure of sedentary behaviour, and the same outcome measure (i.e. overweight — BMI $\geq$27 — or obese — BMI $\geq$30) would be useful.

Table 3.4 Studies investigating sedentary behaviour and overweight/obesity

Study	Results
Graff-Iversen et al (2007)	OR (95% CI) for overweight among men • Sedentary work: 1 • Light OPA: 0.91 (0.82, 1.00) • Moderate OPA: 0.95 (0.86, 1.05) • Heavy OPA: 0.97 (0.88, 1.97) *p* for trend =0.11 OR (95% CI) for overweight among women: • Sedentary work: 1 • Light OPA: 1.18 (1.04, 1.34) • Moderate OPA: 1.51 (1.30, 1.74) • Heavy OPA: 1.67 (1.38, 2.03) *p* for trend =<0.001
Hu et al (2003)	Multivariate RR (95%CI) obesity for sitting while watching TV (hours per week): • 0–1 h: 1.00 • 2–5 h: 1.22 (1.06, 1.42) • 6–20 h: 1.42 (1.24, 1.63) • 21–40 h: 1.65 (1.41, 1.93) • >40 h: 1.94 (1.51, 2.49) *p* for trend <0.001 Multivariate RR (95%CI) obesity for sitting at work, driving or away from home (h/week): • 0–1 h: 1.00 • 2–5 h: 1.02 (0.89, 1.18) • 6–20 h: 1.13 (0.98, 1.29) • 21–40 h: 0.96, 1.31) • >40 h: 1.25 (1.02, 1.54) *p* for trend=0.02 Multivariate RR (95%CI) obesity for all other sitting at home (h/week): • 0–1 h: 1.00 • 2–5 h: 0.99 (0.83, 1.18) • 6–20 h: 1.01 (0.85, 1.20) • 21–40 h: 0.90 (0.74, 1.10) • >40 h: 1.11 (0.85, 1.45) *p* for trend=0.52

3.3.2 Cardiovascular disease

Description of studies

Two studies investigating the association between sedentary behaviour and risk of cardiovascular disease reported different outcomes: carotid wall thickness (as an indicator of atherosclerosis; Kozakova et al 2010), and incidence of acute myocardial infarction (measured from autopsy or death registries; Sjol et al 2003). Four other studies that investigated the risk of mortality from cardiovascular disease or coronary heart disease, or ischaemic heart disease (Graff-Iversen et al 2007, Katzmarzyk et al 2009 and Warren et al 2010; and Salonen et al 1988, respectively) are presented under mortality, below.

One other study (Arsenault et al 2010) examined the risk of coronary heart disease and abdominal obesity in relation to sedentary behaviour; however, abdominal obesity was used as the indicator for incidence of coronary heart disease, rather than sedentary behaviour (see Section 3.3.1).

Atherosclerosis

Kozakova et al (2010) used a surrogate indicator of atherosclerosis — carotid wall thickness — to assess the risk associated with weekly sedentary time in a small group of healthy adults. Sedentary behaviour was measured using a single-axis accelerometer (i.e. measuring forward and backward movement only, not standing up or sitting down) and self-reported estimates.

At baseline, time spent sedentary was positively associated with intima media thickness (independent of age or other atherosclerotic risk factors). Over the three years, this risk was attenuated in people who participated in bouts of vigorous physical activity, compared with those who only did light-to-moderate physical activity: regression coefficient for independent determinants of common carotid artery intima media thickness ($ß \pm SE$ for the sedentary:light activity ratio) were 0.14 ± 0.03 (p <0.0001) (see Table 3.5). This study adjusted for important confounders (weight, fat-free mass and waist circumference), but did not adjust for education or income level. Furthermore, there was poor correlation between the uni-axis accelerometer-measured weekly sitting time and self-reported sitting time ($r = 0.19$; $p<0.0001$). Accelerometer-derived activity categories also differed from those classified by the

IPAQ (the IPAQ has been shown to have good inter-test reliability and moderate validity; Rosenberg et al 2008). Based on the reported accelerometry results, most (98.6+2.2%) of participants' time was spent sedentary or in light activity, which appeared to be high. Based on this single study (of only approximately 500 adults), there are inconclusive data to determine the effect of sedentary behaviour on atherosclerotic risk.

Table 3.5 Studies investigating sedentary behaviour and atherosclerosis

Study	Results
Kozakova et al (2010)	Regression coefficient (ß + SE — sedentary:light activity) for common carotid artery intima-media thickness: 0.14 + 0.03 (p <0.0001//0 3-year increase in intima-media thickness (µm): • Light activity: 22±51 µm • Moderate activity: 19±46 µm • Vigorous activity: 7±40 µm *p* for trend <0.05

Incidence of acute myocardial infarction

Sjol et al (2003) surveyed occupational and leisure-time physical activity over 27 years. Self-reported physical activity levels were compared with the incidence of acute myocardial infarction (measured using autopsy results or death registries; note that the study did not specifically look at cardiac mortality). Higher occupational activity was associated with a lower risk of death from acute myocardial infarction compared with the sedentary group (see Table 3.6).

The use of an indirect approach to investigating sedentary behaviour was reflected in the results and conclusions, which were framed from a physical activity perspective: the authors concluded that higher occupational *activity* was protective against acute myocardial infarction, compared with the sedentary group. Although the analyses took into account serum cholesterol levels, they did not adjust for diet or energy intake — poor diet is a risk factor for atherosclerosis (Hooper et al 2011). Neither was alcohol consumption recorded or adjusted for, because 'the measure changed from frequency of intake to amount' over the 27-year study duration (p 225). The study did, however, adjust for other important confounders (smoking, BMI, blood pressure, education level).

Table 3.6 Studies investigating sedentary behaviour and acute myocardial infarction

Study	Results
Sjol et al (2003)	Population-attributable risk (PAR) of acute myocardial infarction for men (1964–1991): • $RR_{moderate\ activity}$: 1.44 (*p*=0.53) • $RR_{sedentary}$: 1.95 (*p*=0.23) • PAR: 32.2% Population-attributable risk (PAR) of acute myocardial infarction for women (1964–1991): • $RR_{moderate\ activity}$: 1.00 (*p*=0.56) • $RR_{sedentary}$: 2.00 (*p*=0.31) • PAR: 23.4%

3.3.3 Mortality

Description of studies

Two studies investigated all-cause mortality (Carlsson et al 2006, Katzmarzyk et al 2009), and four studies investigated cardiovascular disease mortality (Graff-Iversen et al 2007, Katzmarzyk et al 2009, Salonen et al 1988, Warren et al 2010).

Three of the studies enrolled both men and women (Graff-Iversen et al 2007, Katzmarzyk et al 2009, Salonen et al 1988), one enrolled men only (Warren et al 2010) and one enrolled women only (Carlsson et al 2006). Only two used direct measures of sedentary behaviour (daily sitting time; Katzmarzyk et al 2009, Warren et al 2010), and all but one recorded behaviours in both domains of work and leisure (Warren et al 2010 measured sitting time in two specific activities only: watching televisions and riding in a car). Follow-up periods differed greatly (from 6 to 20 years); however, all were of sufficient duration for clinically important changes to occur. Participants' ages ranged from 18 to 90 years.

All-cause mortality

Carlsson et al (2006) estimated total daily activity levels (in MET hours per day) in postmenopausal women, and the risk of death from all causes. Activity levels were calculated using self-reported estimates of daily activity (household work, work, leisure time), and inactivity (sleeping during day, sitting at work or home). These data were converted to a MET value, and the least active of the five categories of participants were those who expended fewer than 35 MET per hour per day (which is only slightly more than sitting quietly for 24 hours [24 MET/hour/day]). This minimal level of physical activity indicated that the sedentary group was truly sedentary, despite the indirect measure of sedentary behaviour. Women in this group had a 3.22 times increased mortality (95%CI 2.35, 4.43) compared with the most active women (>50 MET per hour per day; see Table 3.7). The study was limited in the lack of adjustment for cause of death, or for old age, despite the cohort ranging from 51–85 years at baseline.

Similarly, Katzmarzyk et al (2009) measured the daily time spent sitting at work, school or during housework (using self-reported estimates) for a cohort of Canadian adults. Participants were categorised into quintiles of sitting time (ranging from none of the time to almost all the time). After adjusting for age and lifestyle confounders, they found that risk of all-cause mortality increased as sitting time increased from none of the time to almost all the time (*p* for trend <0.001; see Table 3.7).

Table 3.7 Studies investigating sedentary behaviour and all-cause mortality

Study	Results
Carlsson et al 2006	Mortality RR (95%CI) • *Total daily PA (35.0 MET per day or less)* (adjusted for lifestyle and medical problems): 2.56 (1.85, 3.53) • *PA at work* (mostly sedentary (adjusted for lifestyle and medical problems): 1.81 (1.08, 3.05) • TV watching and reading (more than 6 h/day): 1.16 (0.8, 1.67)
Katzmarzyk et al (2009)	HR (95% CI) for all-cause mortality: • none of the time: 1.00 • 1/4 of the time: 1.00 (0.86, 1.18) • 1/2 of the time 1.11 (0.94, 1.30) • 3/4 of the time: 1.36 (1.14, 1.63) • almost all the time: 1.54 (1.25, 1.91) *p* for trend <0.0001

Cardiovascular disease mortality

There were mixed results for the risk of cardiovascular disease mortality: three studies found that sedentary behaviour increased the risk, with a progressively higher risk across higher categories of sitting time (Katzmarzyk et al 2009, Warren et al 2010, Salonen et al 1988); the fourth found no association with sedentary behaviour (based on a sedentary occupation), although the authors did report evidence of a protective effect of physical activity (Graff-Iversen et al 2007).

Katzmarzyk et al (2009) measured the daily time spent sitting at work, school or during housework (using self-reported estimates) for a cohort of Canadian adults over approximately 12 years. Participants were categorised into quartiles of sitting time (almost none, one-quarter of the time, half of the time, three-quarters of the time). There was a progressively higher risk of cardiovascular disease mortality across higher levels of sitting time (HR: 1.00, 1.01, 1.22, 1.47, 1.54; p for trend <0.0001; see Table 3.8), independent of leisure-time physical activity (measured as MET hours per week).

In a large study, Graff-Iversen et al (2007) measured the association between physical activity and mortality from cardiovascular disease or coronary heart disease (among a range of other outcomes). As described above, the authors calculated risk for levels of physical activity levels in two domains (occupational, leisure time), as well as risks associated with total physical activity levels (the two domains combined). There was no significant association between 'sedentary' occupations (e.g. office work) and cardiovascular disease mortality. However, there was a significant association between heavy occupational physical activity and decreased risk of mortality (RR [95%CI] 0.84 [0.76, 0.92] for heavy occupational activity).

In a 20-year study, Warren et al (2010) used self-reported data to estimate the weekly hours that a cohort of men (middle-to-higher socioeconomic class) spent watching television and riding in a car (total time combined). Multivariate analysis was used to adjust for whether participants were physically active or inactive at other times (among other confounders). After adjusting for age and a range of lifestyle factors, there was a positive gradient of cardiovascular disease mortality across incrementals of total sedentary behaviour. Combined sedentary behaviour was associated with a 37% increased risk of cardiovascular disease mortality, compared with the referent group (<11 hrs/week).

Finally, Salonen et al (1988) recorded adults' leisure time and occupational physical activity over six years (note that they did not record sedentary behaviour). The lowest activity category was defined as 'mainly sitting'. Sedentary leisure and occupational time were both associated with an increased risk of death from ischaemic heart disease (sedentary in leisure time: RR 1.3 [95%CI 1.1, 1.6]; sedentary in work time: RR 1.3 [95%CI 1.1, 1.6]). After adjusting for confounders, the risk for low leisure-time physical activity was RR 1.2 (95% CI 1.0, 1.5), but unchanged for work time.

Table 3.8 Studies investigating sedentary behaviour and cardiovascular disease mortality

Study	Results
Graff-Iversen et al (2007)	RR (95% CI) for cardiovascular disease mortality: • Sedentary work: 1 • Light OPA: 1.01 (0.92, 1.10) • Moderate OPA: 0.95 (0.87, 1.05) • Heavy OPA: 0.84 (0.76, 0.92)
Katzmarzyk et al (2009)	HR (95% CI) for cardiovascular disease mortality: • none of the time: 1.00 • 1/4 of the time: 1.01 (0.77, 1.31) • 1/2 of the time 1.22 (0.94, 1.60) • 3/4 of the time: 1.47 (1.09, 1.96) • almost all the time: 1.54 (1.09, 2.17) *p* for trend=<0.0001
Salonen et al (1988)	RR(95%CI) for death from ischaemic heart disease: • Sedentary in leisure time: RR 1.3 (95%CI 1.1, 1.6) • Sedentary in work time: RR 1.3 (95%CI 1.1, 1.6) After adjusting for confounders, the risk for low leisure time PA was RR 1.2, 95%CI 1.0, 1.5, but unchanged for work time
Warren et al (2010)	• Cardiovascular disease mortality increased across incremental quartiles of riding in a car (P_{trend} <0.0001) and combined sedentary behaviour (P_{trend} = 0.0002) but not television (P_{trend} = 0.07) • Direct association (car riding, combined sedentary behaviour and cardiovascular disease mortality) was still significant in multivariate analysis, across time spent riding in a car (P_{trend} = 0.01) and combined sedentary behaviour (P_{trend} = 0.04)

3.3.4 Type 2 diabetes mellitus

Description of studies

Type 2 diabetes mellitus is classed as a lifestyle disease due to its strong association with poor diet, lack of physical activity, high blood pressure and overweight or obesity (Zimmet et al 1997). Three included studies measured risk or incidence of type 2 diabetes mellitus, or markers thereof (e.g. insulin resistance), and all reported significant associations. However, only one of the studies controlled for physical activity in nonsedentary times (Helmerhorst et al 2009); the other two studies did not adjust for occupational physical activity (Hu et al 2001, Hu et al 2003).

Type 2 diabetes mellitus

Hu et al (2001) found a significant association between average weekly television viewing time (self-reported on biennial questionnaires) and type 2 diabetes mellitus in middle-aged male health professionals: the relative risk (95%CI) of type 2 diabetes mellitus incidence for men who watched more than 40 hours of television per week was 2.23 (1.13, 4.39), while for those who watched 2–10 hours per week, although relative risk was reduced in comparison, it still appeared significant: 1.49 (1.03, 2.15) (p for trend = 0.02; the least sedentary group, who watched less than one hour each week, was used as the reference category; see Table 3.9). Diabetes status was clinically diagnosed based on self-reported symptoms from a questionnaire, rather than a direct, in-person diagnosis.

Two years later, Hu et al (2003) assessed similar relationships between sedentary behaviours (self-reported time watching television, sitting at work or home, time spent driving) and incidence of type 2 diabetes mellitus (and obesity; see Section 3.3.1) — this time in a cohort of middle-aged female registered nurses. There was a significant positive association between television-viewing time and risk of type 2 diabetes mellitus: each two-hour per day increment in television viewing was associated with a 7% (95%CI 0%, 16%) increase in type 2 diabetes mellitus. Standing or walking for two hours per day, however, reduced the risk of type 2 diabetes mellitus by 12% (95%CI 7%, 16%).

In one of the few studies that used an objective measurement of sedentary behaviour, Helmerhorst et al (2009) used measured minute-by-minute heart rates and 'free-living' sedentary time to investigate the effect of sedentary behaviour on insulin resistance in a small cohort of middle-aged adults. Specifically, they were interested in whether the effect of sedentary behaviour on insulin resistance was independent of moderate–vigorous physical activity. In a multivariate model that accounted for baseline age, sex, fat mass, fasting insulin, smoking, follow-up time, and moderate–vigorous physical activity, time spent sedentary at baseline was significantly associated with increased fasting insulin levels (from observer-issued blood tests) at follow-up (ß = 0.004, 95% CI 0.0009, 0.006, p = 0.009). No adjustments were made for diet, education or income (participants were middle-aged Caucasian adults of a higher socioeconomic status — enrolled from Cambridge, United Kingdom).

Table 3.9 Studies investigating sedentary behaviour and type 2 diabetes mellitus

Study	Results
Hu et al (2001)	Type 2 diabetes mellitus incidence (RR, 95%CI) per category of weekly television-viewing time: • 0–1 hours/week: 1.0 • 2–10 hours/week: 1.49 (1.03, 2.15) • 11–20 hours/week: 1.39 (0.95, 2.05) • 21–40 hours/week: 1.77 (1.18, 2.64) • >40 hours/week: 2.23 (1.13, 4.39) *p* for trend=0.02
Hu et al (2003)	Multivariate RR (95%CI) type 2 diabetes mellitus for sitting while watching TV (hours per week): • 0–1 h: 1.00 • 2–5 h: 1.09 (0.85, 1.39) • 6–20 h: 1.30 (1.03, 1.63) • 21–40 h: 1.44 (1.21, 1.85) • >40 h: 1.70 (1.20, 2.43) *p* for trend <0.001 Multivariate RR (95%CI) type 2 diabetes mellitus for sitting at work, driving or away from home (h/week): • 0–1 h: 1.00 • 2–5 h: 0.99 (0.81, 1.20) • 6–20 h: 1.10 (0.91, 1.33) • 21–40 h: 1.12 (0.89, 1.33) • >40 h: 1.48 (1.10, 2.01) *p* for trend=0.005 Multivariate RR (95%CI) type 2 diabetes mellitus for all other sitting at home (h/week): • 0–1 h: 1.00 • 2–5 h: 0.87 (0.67, 1.13) • 6–20 h: 0.98 (0.76, 1.26) • 21–40 h: 0.94 (0.70, 1.24) • >40 h: 1.54 (1.10, 2.18) *p* for trend=0.004
Helmerhorst et al (2009)	Fully adjusted model: sedentary time plus moderate–vigorous physical activity (MPVA) and fasting insulin (log pmol/L). Sedentary (%): • ß (95%CI) 0.004 (0.0009, 0.006) • p=0.009 • R^2=0.441 MPVA (%): • ß (95%CI) 0.009 (–0.007, 0.02) • p=0.290 • R^2=0.441

3.3.5 Gallstones

A common type of gallstone is the cholesterol type, formed from increased secretion of cholesterol from the bile duct — a condition that is exacerbated by obesity

(Leitzmann et al 1999). Indeed, obesity, poor diet and a lack of exercise are all thought to be risk factors for cholesterol-type gallstones (Johnston and Kaplan 1993).

Leitzmann et al (1999) investigated the association between leisure-time physical activity and the risk of cholecystectomy in a large cohort of female registered nurses. Although the study recorded participants' weekly self-reported physical activity levels (converted to MET hours per week), data were also collected of weekly self-reported sitting time (i.e. television-viewing time) at four time points during the 10-year follow-up. Participants were grouped into quintiles of physical activity, with the lowest category reaching 0–1.6 MET per hour per week — a value that just exceeds the threshold between sedentary behaviour and light activity (Hamilton et al 2007, Pate et al 2008). Physical activity appeared to protect against cholecystectomy, while there was a gradient of increased risk as weekly sitting time increased: for women who sat for more than 60 hours per week, the RR was 2.32 (95%CI 1.26, 4.26) compared with 1.42 (95%CI 1.06, 1.89) for women who sat for 41–60 hours each week (sitting for 0–5 hours per week was used as the reference value; see Table 3.10). Associations remained even after adjusting for confounders (smoking, diet, alcohol and baseline BMI). Importantly, the mediating effect of body weight on risk of gallstone disease was accounted for in the multivariate analyses to assess the effects of sedentary behaviour or physical activity, independent of BMI. No significant attenuation of associations was found.

Table 3.10 Studies investigating sedentary behaviour and gallstones

Study	Results
Leitzmann et al (1999)	RR (95%CI) cholecystectomy (multivariate model) per category of physical activity (MET/h/week): • 0–1.6 MET/h/week: 1.0 • 1.7–4.5 MET/h/week: 0.95 (0.86, 1.06) • 4.6–10.5 MET/h/week: 0.92 (0.83, 1.03) • 10.6–22.0 MET/h/week: 0.83 (0.74, 0.93) • >22.1 MET/h/week: 0.79 (0.71, 0.89) *p* for trend <0.001

Chapter 4 Discussion

This chapter analyses each disease outcome in detail before discussing the overall characteristics (quality and limitations) of the included studies, and placing the conclusions in the context of the broader systematic review literature. A more detailed discussion of the limitations of the included studies then follows, including problems with populations, size and duration, and exposure and outcome measures. The strengths and limitations of this systematic review are also examined. Finally, implications for future research and for clinical practice are discussed.

4.1 General discussion

The results suggest that prolonged sedentary behaviour — in particular, excessive sitting — is consistently associated with an increased risk of cardiovascular disease, all-cause and cardiovascular disease mortality, and type 2 diabetes mellitus. Furthermore, these associations appear to be independent of a range of age, sex and lifestyle confounders — most importantly, physical activity.

Conversely, data for the variety of outcome measures indicative of increased body weight, including increased BMI, becoming overweight or obese, and increased waist circumference, were conflicting. Variations and numerous methodological disparities in the included studies precluded any conclusions from being made. It was also unclear from the single study included whether prolonged sedentary behaviour had an effect on the risk of gallstones.

Studies that reported dose-response associations showed that risk of mortality (cardiovascular and all-cause), type 2 diabetes mellitus and >4.5 kg weight gain increased as sitting time increased (Katzmarzyk et al 2009, Warren et al 2010, Hu et al 2001, Hu et al 2003, Blanck et al 2007). Each two-hour increase in sedentary time (television watching) appeared to convey a 7% increase in type 2 diabetes mellitus risk (Hu et al 2003). Hu et al (2003) recommended keeping television viewing to fewer than 10 hours per week, and walking briskly for a minimum of 30 minutes each day to reduce the risk of type 2 diabetes mellitus. When considering these dose–response data together, it was difficult to identify a cut-off for the number of hours of sitting per day or per week at which risk became apparent, due to the differences in what the primary studies measured and reported (e.g. categories of sitting time, statistical analyses, outcome measures). However, a dose-response association for sedentary behaviour is physiologically plausible based on the consistent categorical associations between sedentary behaviour and the outcomes reported in the primary studies. This has since been confirmed in a recent separate meta-analysis (Grøntved and Hu 2011), which reported dose-response associations for all-cause and cardiovascular mortality, and type 2 diabetes mellitus, but not for weight gain or obesity. In this meta-analysis, which used published and unpublished data, three or more hours of sitting a day (specifically, watching television) increased the risk of all-cause mortality, while dose-response associations for type 2 diabetes mellitus and cardiovascular disease increased in a linear fashion across two-hour increments. Other systematic reviews (Thorp et al 2011, van Uffelen et al 2010) could not investigate dose-response associations, due to the limited number of included studies reporting this information in adults (as published data).

Overall, the results (whether they were indicative of positive, negative or no significant association) may have been influenced by shortcomings of study design. Measuring and interpreting sedentary behaviours (as well as physical activities) in a 'real-life' context is difficult and subject to many largely unavoidable biases and constraints that arise from the financial and practical difficulties of running large population-based studies, as well as those due to residual confounding. Some of the included studies also had reporting ambiguities (e.g. time points of follow-up, recruitment and maintenance of cohort groups, descriptions of methods) that made interpretation of the data presented difficult.

Despite some methodological limitations of the included studies, specific measures of daily or weekly sedentary behaviour (either at work, home, or in specific activities such as television viewing or transport) were used. This is an encouraging sign that sedentary behaviour is being increasingly recognised as having specific effects that warrant careful investigation, rather than being extrapolated from a deficit of physical activity. Furthermore, the number of large, prospective studies of sedentary behaviour is growing and possibly also reflects this same trend in the research.

4.2 Sedentary behaviour and health risks

The following sections briefly discuss risk attributable to sedentary behaviour by adverse health outcome reported. A more detailed discussion of these associations in light of the studies' strengths and limitations, and the findings of the wider review literature, follows.

4.2.1 Obesity and weight gain

The literature included a high proportion of studies focused on obesity or weight gain (i.e. body weight or composition outcomes), either as an undesirable health outcome in its own right, or as a risk factor for the many well-documented obesity-related diseases. However, heterogeneity of outcomes, populations, exposures and measures of the seven studies included here (Arsenault et al 2010, Blanck et al 2007, Coakley et al 1998, De Cocker et al 2010, Graff-Iversen et al 2007, Hu et al 2003, Koh-Banerjee et al 2003) made it difficult to draw useful conclusions about the association between prolonged sedentary behaviour and the risk of body weight or composition outcomes for all adults.

Overall, the results suggested that sedentary behaviour (or a lack of physical activity) may be associated with increased risks for obesity in men, but only those aged 45–54 years. There were mixed results for women: sedentary behaviour appeared to be associated with increased abdominal obesity, but it was not clear whether there was an association with the risk of BMI change or weight gain (apart from a ≥4.5 kg weight gain in normal-weight, postmenopausal women), or the risk of becoming overweight or obese.

Failure to adjust for relevant confounders was a common problem. For example, Arsenault et al (2010) did not adjust for diet or energy intake, despite obesity (abdominal obesity) being the primary outcome (see Section 4.4.4 for further discussion of the role of obesity as an intermediary for other health outcomes). Three of the studies (Arsenault et al 2010, Coakley et al 1998, Hu et al 2003) did not adjust for the education or income level of participants. Lower socioeconomic status is associated with a higher risk of becoming overweight or obese (Reidpath et al 2002). Therefore, populations with a higher socioeconomic level and educational status, such as the health professional cohorts enrolled by Coakley et al (1998), Hu et al (2003) and Koh-Banerjee et al (2003) are more likely to have a greater awareness of healthy behaviours.

4.2.2 Cardiovascular disease

Apart from cardiovascular disease mortality (which is discussed in Section 4.2.3, under mortality), results for cardiovascular disease outcomes were conflicting. This may have been due to the use of different outcome measures, poor methodology and insufficient data across the included studies. The single small (approximately 500 adults) study investigating atherosclerotic risk (Kozakova et al 2010) was insufficient to determine any associations with sedentary behaviour, particularly given the methodological concerns (see Section 4.4). Nor could conclusions be made about the association between sedentary behaviour and the incidence of acute myocardial infarction, based on data from another single study (Sjol et al 2003). At best, it can be concluded that prolonged sedentary behaviour does not improve atherosclerotic outcomes or lower the risk of acute myocardial infarction.

Three of the included studies (Graff-Iversen et al 2007, Salonen et al 1998, Sjol et al 2003) did not adjust for important confounders, particularly those relating to energy intake, diet or and alcohol consumption. Saturated fat has been implicated in development of cardiovascular disease (Hooper et al 2011), while alcohol appears to lower the risk (Rimm et al 1999).

4.2.3 Mortality

Sedentary behaviour appears to be associated with an increased risk of all-cause mortality. The two studies (Carlsson et al 2006, Katzmarzyk et al 2003) that measured the risk of all-cause mortality both reported that risk increased as sedentary time or physical inactivity increased. Both studies were large (approximately 27 000 and 17 000 participants) and used relatively well-defined categories of sedentary behaviour or physical inactivity. The results were derived from specific subgroups (postmenopausal women and middle-class Canadian adults); however, the findings are in line with those of other systematic reviews (Grøntved and Hu 2011, Proper et al 2011, Thorp et al 2011; see Section 4.3), which drew on wider populations.

Of all the outcomes of interest in this systematic review, mortality from cardiovascular disease showed the strongest association with sedentary behaviour. Two studies reported a risk for men and women that increased across progressively higher categories of sitting time. Data from two papers that were sufficiently similar (Katzmaryk et al 2009, Warren et al 2010) were extracted for a meta-analysis, but because the association was already clear — and supported by the results of the meta-analysis by Grovnted et al (2011) (see Section 4.3) — meta-analysis was not considered necessary.

Study quality was moderate to good, although Katzmaryk et al (2009) did not adjust for socioeconomic status, energy intake or diet. Warren et al (2010) adjusted for diagnosed hypercholesterolemia, but did not adjust for slightly lower (but still elevated) cholesterol levels, or for energy intake or diet. As mentioned previously, saturated fat intake has been linked to the development of cardiovascular disease (Hooper et al 2011).

4.2.4 Type 2 diabetes mellitus

The three included studies that measured risk of type 2 diabetes mellitus or insulin resistance all reported significant positive associations. Risk of type 2 diabetes mellitus appeared associated with even ‘light’ sedentary behaviours of 2–10 hours per week and increased further as sedentary time increased in adults. Similar trends were reported in both men and women (Hu et al 2001; 2003). The single, small (N=376) study of fasting insulin resistance (Helmerhorst et al 2009) was insufficient on its own to determine any associations; however, the results from all three studies investigating diabetes risk combined suggest that there is likely to be an association with sedentary behaviour.

Some methodological issues need to be taken into account when interpreting these results. Subjectivity of outcome measures (type 2 diabetes mellitus diagnosis based on self-reported symptoms; Hu et al 2001) may have led to misdiagnosis and subsequently impacted the validity of the findings. Lack of adjustment for physical activity, particularly in health professional cohorts, with differing physical requirements in their daily occupational tasks (Hu et al 2001, Hu et al 2003), may also have influenced the results reported. The non-representative populations of the studies may limit the extent to which the results can be generalised to the wider adult population (as they were based on male and female health professional cohorts, with potentially greater awareness of healthy behaviours than the general population; Hu et al 2001, Hu et al 2003; and middle-aged Caucasian adults of a higher socioeconomic status; Helmerhorst et al 2009).

4.2.5 Gallstones

The single, large (*N*=>60 000) study found that risk of cholecystectomy (gallstone removal) increased as weekly sitting time increased (Leitzmann et al 1999). However, the study was limited by the cut-off point for the sedentary group, which — at 0–1.6 MET/hour/week — just exceeded the commonly agreed threshold between sedentary behaviour and light activity (Hamilton et al 2007, Pate et al 2008). Furthermore, the cohort was limited to female registered nurses in the United States, and adjustments did not include social or economic status.

Despite these limitations, the study was of a moderate quality and was sufficiently large to see meaningful results. However, additional studies are needed to confirm the suggested association between sedentary behaviour and the risk of gallstones in middle-aged, middle-class women, as well as to determine whether there is a similar risk in other groups of people.

4.3 Findings from the wider review literature

The results discussed above are largely supported by the three other published systematic reviews (Proper et al 2011, Thorp et al 2011, van Ufflen et al 2010) and the meta-analysis of prolonged sedentary behaviour (Grøntved and Hu 2011). The strongest associations appeared to be for all-cause and cardiovascular disease mortality, with Grøntved and Hu (2011), Proper et al (2011) and Thorp et al (2011) all finding significant positive associations (sitting and all-cause or cardiovascular disease mortality), similar to this review. In their meta-analysis, Grøntved and Hu (2011) found a nonlinear association for time spent watching television and all-cause mortality — the risk increased when participants watched more than three hours of television per day. van Uffelen and colleagues (2010) reported mixed results for mortality (four studies with an association, one without, and one with a decreased risk). They cautioned against drawing conclusions for any outcomes, due to the heterogeneity in study designs, measures and outcomes. This seems to be an overly cautious approach, in light of the consistent results reported in both the primary studies and the other systematic reviews showing a significant positive association between sedentary behaviour and all-cause and cardiovascular disease mortality (even if the strength of the association is not yet clear). The meta-analysis by Grøntved and Hu (2011) provides the strongest indication yet of the risks associated with sedentary behaviours, and these data — combined with the data reported from this review — indicate that there is indeed an association between leisure-time sedentary behaviour and mortality.

The other systematic reviews reported differing conclusions for incidence of cardiovascular disease (excluding cardiovascular disease mortality), with three (Proper et al 2011, Thorp et al 2011, van Uffelen et al 2010) concluding that there were not enough data to determine the effect of prolonged sitting. Cardiovascular disease encompasses a range of conditions (and surrogate markers), and the multitude of outcome measures used in the primary studies may have led to the variety of findings. These collective results matched the conclusions of this systematic review, on the basis of the four included studies, which had methodological problems. Grøntved and Hu (2011) reported a significant positive association between television viewing and risk of cardiovascular disease in their systematic review and meta-analysis, although this analysis was based on both published and unpublished data (as discussed in Section 1.1.5). However, the meta-analysis supported the findings of the individual papers, and the findings of the meta-analysis is likely to be more informative than the overly cautious conclusions of the other systematic reviews — including this one. Based on experimental (Bey and Hamilton 2003) and cross-sectional (see, for example, Kronenberg et al 2000, Sidney et al 1996, Thorp et al 2010) studies, and the fact that there is a clear association between sedentary behaviour and cardiovascular disease mortality, as discussed above, it is physiologically plausible that sedentary behaviour leads to poorer cardiovascular health — whether directly, or through an intermediary step of weight gain or obesity.

Weaker associations have been reported for the risk of type 2 diabetes mellitus in the systematic review literature: this review identified an association, as did Grøntved and Hu (2011), Proper et al (2011) (two studies) and van Uffelen (2010) (two studies).

Thorp et al (2011) reported that there were not enough data to determine any specific disease incidence, including type 2 diabetes mellitus. However, cross-sectional data reported from other large population-based studies, such as the Australian Diabetes, Obesity and Lifestyle Study (AusDiab), add weight to the positive association, with television viewing time linked to markers of cardiometabolic risk (impaired glucose metabolism and metabolic syndrome) in Australian adults who participated in moderate-to-vigorous physical leisure-time activity. A cross-sectional report published from the AusDiab data revealed that, for each one-hour increase in daily television viewing, there was a 12% (95% CI –0.01–27%; p=0.07) and 26% (95% CI 14–46%; p=0.0001) increase in prevalence of metabolic syndrome in men and women respectively, irrespective of physical activity (Dunstan et al 2005). In another cross-sectional study, Healy et al (2008) described the 'active couch potato' phenomenon after finding that adults who spent of their waking hours in sedentary behaviour, yet still met physical activity recommendations (150 minutes per week of moderate-to-vigorous activity), did not counteract their risk of increased waist circumference, systolic blood pressure, two-hour or fasting plasma glucose levels, triglycerides or high-density lipoprotein cholesterol.

Despite the large number of prospective and cross-sectional studies that have investigated obesity, all four systematic reviews that included body weight outcomes (weight gain, BMI gain, waist circumference, risk of becoming overweight or obese) reported conflicting results, methodological problems with the primary studies, and insufficient data to make conclusions. These conclusions reflected the findings of this review. Grøntved and Hu (2010) did not include body weight outcomes in their systematic review and meta-analysis. Furthermore, three randomised controlled trials of interventions to reduce television-viewing time have been published: two enrolling children showed that reducing viewing time slowed the rate of BMI increase and reduced the number of meals eaten in front of the television (Robinson et al 1999), and reduced BMI and energy intake (Epstein et al 2008); neither showed any affect on self-reported levels of physical activity. The third randomised controlled trial enrolled 36 overweight and obese adults; there were no significant effects on BMI or energy intake after halving viewing time over a three-week period, although there was a significant increase in reported physical activity levels (Otten et al 2009). This trial was most likely underpowered and of too short a duration (three weeks) for clinically important changes. However, these randomised controlled trials do indicate that there are benefits (rather than any harms, or no effects) in reducing sedentary time. Cross-sectional studies have also found an association between sedentary behaviour and obesity or weight gain (Brown et al 2005, Jakes et al 2003, Martinez-Gonzalez 1999, Sugiyama et al 2008), metabolic syndrome (Bertrais et al 2005), glucose metabolism and insulin levels (Dunstan et al 2004, Ford et al 2010) and cardiovascular disease (Jakes et al 2003). Furthermore, Chang et al (2008) reported that watching more than 20 hours per week of television was significantly associated with an increased risk of metabolic syndrome in Asian men and women (independent of physical activity). Bowman (2006) reported that men and women who watched more than two hours of television per day had a significantly increased risk of higher BMI, overweight or obesity. Of these cross-sectional studies, only Bertrais et al (2005) and Jakes et al (2003) were included in the systematic review by van Uffelen et al (2010).

A limited number of studies of any design have been published on sedentary behaviour and the risk of gallstones (at the time of writing, only that by Leitzmann et al 1999 had been published). There are also very few studies of physical activity as a mediator of gallstone risk: two cross-sectional studies (Sarin et al 1986, Williams and Johnston 1980) and three case–control studies (Linos et al 1989, Misciagna et al 1999, Ortega et al 1997) reported an inverse association between physical activity and gallstones, although methodological problems such as lack of adjustment for confounders other than age may limit the validity of the results (see Leitzmann et al 1999 for further discussion).

4.4 Study quality

Study quality had a significant effect on the conclusions of this systematic review. While some included studies in this systematic review met some criteria for high quality (e.g. participants representative of the wider population, standardised definition of sedentary behaviour, objective and validated outcome measures, adjustment for all important confounders), none met all the criteria.

4.4.1 Size and duration

The size and duration of the included studies varied considerably, as did the time-points of measurement. This review attempted to control for this somewhat in the inclusion criteria (by only including studies that had a minimum follow-up time to allow for long-term changes to manifest — i.e. three years). Data from large longitudinal studies that began decades ago are being published; two (Sjol et al 2003, Warren et al 2010) were included in this systematic review and had follow-up periods of 30 and approximately 20 years, respectively (the average duration of the remainder of the included studies was seven years). Such long time periods are valuable for observing the development of chronic diseases, such as type 2 diabetes mellitus, cardiovascular disease and cancer (rather than measuring prognostic indicators or 'early warning signs' of the disease or other surrogate outcomes). However, long-term prospective studies that were initiated in the 1970s and 1980s will reflect the understanding of that time, focusing on physical inactivity (rather than the adverse effects of sedentary behaviour), and using imperfect definitions and measurements of sedentary behaviours (Graff-Iversen et al 2007). This must be taken into account as an unavoidable limitation of this relatively new field of research.

4.4.2 Study populations

Many of the studies were part of larger, long-term cohort studies, and at times, these sorts of study populations were selective, rather than representative of the general population. For example, Coakley et al (1998), Hu et al (2001), Hu et al (2003), Koh-Banerjee et al (2003) and Leitzmann et al (1999) all recruited health professionals (nurses, doctors, optometrists, pharmacists, veterinarians, etc). The use of these cohorts may influence the results, and may also limit the extent to which findings can be extrapolated to the general population: these groups may have a greater awareness of healthy behaviours; other research has suggested a link between higher socioeconomic and educational status and better health profiles (Phillips and Klein 2010).

Of the studies that measured obesity outcomes, Koh-Banerjee et al (2003) and Coakley et al (1998) did not adjust for their health professional cohorts' physical activity in work or other domains, despite the fact that the definition of health professional included, for example, dentists, optometrists and veterinarians — all of whom have differing occupational physical activity requirements. Accounting for these differences in physical activity may be important, considering the cut-off between sedentary behaviour ($\leq$1.5 MET) and light activity ($\geq$1.6 MET) is slight.

Other nonrepresentative cohorts were those enrolled by Helmerhorst et al (2009) (Caucasian men); Katzmarzyk et al (2009) (certain groups of lower socioeconomic status excluded — e.g. indigenous, institutionalised — and no adjustments made for education or income); and Warren et al (2010) (middle–upper-class American men). Overall, the results of the included studies are relevant for middle-aged adults — 14 of the 16 studies enrolled participants aged 30+ years (with 10 of these studies enrolling people aged 40+ years). Only two studies (De Cocker et al 2010, Katzmarzyk et al 2009) enrolled younger participants (24–30 years, and 18–90 years, respectively). In general, these limitations do not mean that the results of the individual studies are not useful. Rather, it means that they must be interpreted and applied with caution, recognising that they may only be valid for subgroups of specific age, sex or socioeconomic status (Mamdani et al 2005).

Finally, some participants may have been predisposed to sedentary behaviours if they had undetected preclinical stages of cardiovascular and metabolic diseases at baseline. Controlling for this selection bias is difficult for chronic conditions that have an insidious onset and long latency periods.

4.4.3 Measurements

Exposure measures

A limitation of the primary studies became obvious during the study selection and critical appraisal stages of the review project. Among the papers reviewed during the searching process, most had poorly defined categories of participants; for example, grouping them into 'active' and 'sedentary' groups, despite the latter including people who did light-to-moderate physical activity (based on an estimated MET value of $\geq$1.6 MET). These studies were excluded during the study selection process. The cut-off of $\leq$1.5 MET was used, because activities that expend a higher MET value have greater physiological requirements (Pate et al 2008). Many studies therefore make claims about the effects of sedentary behaviour without actually measuring it. This is the basis of most of the problems with the primary studies when considering the exposure of interest and its impacts, particularly on any claims made about the effects of sedentary behaviour (Pate et al 2008). The problem is carried over into the review literature, if synthesis of the primary studies fails to distinguish between study groups who are truly sedentary and those who are not. Schofield et al (2009) note that one important problem with some of the review literature is the inference that time spent in sedentary behaviours is directly related to time spent being physically active (i.e. because people are categorised as sedentary by default if they do not meet a specific level of physical activity).

Many studies did not attempt to measure the duration of sedentary behaviour (i.e. in unbroken blocks of time), but used an estimate of total 'sedentary' time averaged for the preceding week, month or year. The pattern of sedentary behaviour may be just as important for health outcomes as the total accumulated amount (people can be physically active according to guideline recommendations but still classed as sedentary). Reporting an average number of hours spent sedentary will not distinguish between prolonged or interrupted sedentary time, ruling out analysis of the potentially beneficial effects of regular breaks from sitting (Pate et al 2008).

Objective measurements of sedentary behaviour (e.g. using multi-axis accelerometers) have been shown to correlate with self-reported data collected in physical activity questionnaires (Ekelund et al 2006, Kurtze et al 2008). However, using a single-axis accelerometer that detects horizontal and not vertical movement (e.g. standing from being seated and vice versa) could reduce the accuracy of measurement. Kozakova et al (2010) classified almost all (approximately 98%) of their healthy participants as sedentary using this method, but also reported weak correlation with self-reported and IPAQ-assessed measurements (under which 'low physical activity' is defined as not reaching at least 600 MET-minute/week; IPAQ Research Committee 2005). The results from Kozakova et al (2010) are unlikely to be accurate if extrapolated to the wider population.

Outcome measures

A significant limitation of the primary studies was the use of subjective outcome measurements. This was especially problematic for the studies of weight gain or obesity: only two (Arsenault et al 2010, Graff-Iversen et al (2007) of the seven studies used objective measurements (i.e. biometric measurements taken by trained observers). The others (Blanck et al 2007, Coakley et al 1998, De Cocker et al 2010, Hu et al 2003, Koh-Banerjee et al 2003) used self-reported estimates of height, weight, weight gain and waist circumference. Self-reported data are always subjective, particularly those relating to weight and height (Nyholm et al 2007).

Recall over long periods of time (e.g. a month, a year) is also subject to high recall bias (White et al 1998).

Furthermore, the use of BMI as an indication of body fat is problematic. At the individual level, using self-reported height and weight to calculate BMI is problematic due to people's tendency to under-report their weight and over-report their height (ABS 2008). This is less problematic at a population level, where BMI can be a useful and practical tool for measuring body mass and patterns of changes in large groups of people — as long as large enough groups are enrolled (ABS 2008). In some populations, however, BMI is inappropriate, because it does not give a true indication of body fat (ABS 2008, Jebb and Moore 1999). Populations undertaking heavy physical activity (e.g. see Graff-Iversen et al 2007) may have a high BMI due to a higher percentage of muscle mass (rather than body fat), thereby skewing measures. Skinfold tests or hip or waist circumference would be a more accurate measure (ABS 2008).

4.4.4 Adjustments

There was great variation in the confounders that were measured and adjusted for in the primary studies. This — in addition to the heterogeneity in populations, outcomes and measurements — made it difficult to pool data for a meta-analysis. Failure to adjust for important confounders, such as physical activity, or diet or energy intake, further limited the results from the studies.

Residual confounding was apparent in some of the included studies, making it difficult to establish direct associations between sedentary behaviour and the outcomes of interest. Residual confounding, which is caused by factors that are direct, intermediate steps on a causal pathway between exposures and outcomes, is problematic, and sometimes unavoidable in observational research (McNamee 2003). One of the best-known examples of residual confounding is the relationship between smoking and cancer: assessing the risk of lung cancer from any other cause will be confounded by exposure to tobacco (whether directly or indirectly) (Tardon et al 2005).

Several residual confounders were pertinent to the results of this review. Diet (how much people eat, as well as what they eat — the proportion of saturated fat, triglycerides, carbohydrates, etc), in particular, is a confounder for all the outcomes investigated in this systematic review, but is difficult to adjust for completely, particularly in large and long-term prospective studies. Compounding the problem is the risk of social desirability or recall biases in self-reported diet information (Hebert et al 1995). There is a well-recognised tendency for people to increase their dietary intake through snacking (especially on kilojoule-dense food) while watching television (Bowman 2006, Owen et al 2010). Adjusting for energy intake, as well as socioeconomic status, alcohol intake and smoking status, could help to minimise self-selection bias (whereby people with certain health characteristics may be more likely to occupy sedentary jobs) (van Uffelen et al 2010).

Failure to adjust for baseline BMI or body weight measures was also apparent in two of the included studies (Hu et al 2003, Katzmarzyk et al 2009). Obesity (abdominal obesity, weight gain, and overweight and obesity) is an intermediate risk factor for the other health outcomes measured in this systematic review, and might arise from sedentary behaviour. For example, obesity increases the risk of cardiovascular disease (including atherosclerosis), mortality and insulin resistance through leptin, adiponectin, interleukin-6, tumour necrosis factor-α and other bioactive mediators released by adipose tissue (Van Gaal et al 2006). Obesity is also a risk factor for cholesterol-type gallstones, although the exact mechanism is not yet understood (Grundy 2004). Studies must therefore adjust for obesity to prevent any true associations between sedentary behaviour and these outcomes from being masked. Indeed, Thorp et al (2011) noted that many of the associations for disease incidence (type 2 diabetes mellitus, and site-specific cancer incidence) reported in the primary studies were attenuated in multivariate analyses, when further adjustments were made for BMI, strengthening the case for overweight and obesity as risk factors in their own right.

Grøntved and Hu (2011) explored the role of obesity and as diet as possible mediators between sedentary behaviour and other health outcomes by including multivariate models that did and did not adjust for BMI, obesity or diet. In their meta-analyses, using the multivariable-adjusted estimates that adjusted for dietary variables attenuated the risk of type 2 diabetes mellitus with television-viewing time compared with models that did not adjust (pooled RR, 1.18 [95%CI 1.12, 1.25] per two hours of television viewing; P<0.01; compared with pooled RR, 1.20 [95%CI 1.14, 1.27] per two hours of television viewing; P<0/001). Further adjusting for BMI or obesity, the association was attenuated further, but still statistically significant: pooled RR, 1.13 (95%CI 1.08, 1.18) per two hours of television viewing (P<0.001). This effect was not seen for cardiovascular disease or all-cause mortality.

Finally, of the 16 studies that measured sedentary behaviour during a particular domain (e.g. occupational, leisure time), only 6 adjusted for physical activity at other times. Failing to measure and adjust for occupational activity and sedentary behaviour, when claiming to assess the effects of leisure time sedentary behaviour (and vice versa) (e.g. Patel et al 2010, Leitzmann et al 1999; compare with Graff-Iversen et al 2007), must surely be as significant a consideration as adjusting for age, smoking status or other important confounders (Owen et al 2010).

4.5 Discussion of methods

This systematic review had several strengths. Inclusion and exclusion criteria were clearly defined in the systematic review protocol. The review also used a rigorous definition of sedentary behaviour (based on Pate et al 2008) in an attempt to exclude studies that grouped sedentary behaviour and light activity together. Study quality was also critically appraised using predetermined criteria. Assessment of these criteria in selected studies resulted in 16 studies being included. The systematic review by Proper et al (2011) included a similar number of studies (19 — including studies with cancer as an outcome), but fewer than the systematic review by Thorp et al (2011; 48 studies), which included prospective studies spanning the transition from childhood and adolescence to adulthood, as well as 'all studies without prejudice of the methodologic quality of the studies' (p208).

Restricting this systematic review to prospective studies conveyed certain intrinsic benefits and limitations. Prospective studies are ideal for investigating risk factors and predicting specific outcomes by allowing longitudinal observation of risk factors and disease manifestation over time, and they are not plagued by many of the limitations of other non-experimental study designs (Aromataris et al 2011, NHMRC 2009). For example, cross-sectional studies only show associations at a particular point in time, which is often not useful for investigating chronic disease or long-term physiological and anatomical changes. Currently, there is a larger proportion of cross-sectional than prospective studies in the sedentary behaviour literature, most likely reflecting the fact that the field is relatively new.

However, prospective studies do have limitations, and this was apparent in the quality of the studies included in this systematic review. Prospective studies can be more expensive to run in large populations than cross-sectional studies; attrition rates can be high (particularly in long-term studies over decades); and diagnostic criteria, measures and methods can change over the duration of the study. This may have been the case with some of the studies included in this review, which spanned a time in which our understanding of what constitutes true sedentary behaviour changed.

Finally, although prospective studies can establish an association and help to clarify causal relationships, they cannot be used to establish causality on their own (Aromataris et al 2011). For the latter, randomised controlled trials are needed. In the context of sedentary behaviour, randomised controlled trials of interventions to minimise sitting time, and that carefully exclude — or adjust for — such factors that cause residual confounding, would be invaluable for our understanding of the effects of sedentary behaviours. Randomised controlled trials investigating risk (i.e. by imposing sedentary behaviour, rather than encouraging interventions to minimise it) are unethical and not likely to be approved by ethics committees. As the field of sedentary behaviour research is relatively new, and prospective observational studies have served their purpose in helping to establish that the associations exist, before meaningful investigation of interventions can occur. As such, this systematic review was justified in its focus on prospective studies. Future synthesis of the primary literature would benefit from including any randomised controlled trials as they are published.

This systematic review had several limitations. First, the protocol was registered in 2010, and was conducted over 18 months. At the time of registration, few other systematic reviews on sedentary behaviours had been published (those that were looked at specific domains of sedentary time, rather than total daily time). Therefore, this systematic review topic was novel at the time of inception. Over the course of its development, other systematic reviews have been published, reflecting the increase in the numbers of primary studies, and interest in the topic.

Second, the review methodology only included papers published in English, which may have led to publication bias and excluded some important studies. One of the other published systematic reviews (van Uffelen et al 2010) used a search strategy that included prospective and cross-sectional studies published in languages other than English — according to the review methods, nine papers were excluded because they were written in languages not spoken by the authors, leaving only one of the 43 included studies published in a language other than English. The other published synthesises of existing literature (Grøntved and Hu 2011, Proper et al 2011, Thorp et al 2011) limited searches to studies published in English. Limiting searches in this way may reduce the extent to which the results can be extrapolated to other populations or cultural groups.

Third, the review methods were also impaired by the study selection process, which was made difficult due to the lack of a clear and agreed definition of sedentary behaviour in the primary literature (the definition of Pate et al 2008 is robust, but not necessarily followed by all researchers — many still define sedentary behaviour as the lack of moderate-to-vigorous physical activity). During the study selection stage, it became clear that many papers reviewed during the initial title and abstract review had poorly defined categories of participants; for example, grouping them into 'active' and 'sedentary' groups, despite the latter including people who did light-to-moderate physical activity (based on an estimated MET value of $\geq$1.6 MET). These studies were excluded; however, other studies that appeared to include some other measure of inactivity or sedentary behaviour in addition to a described lack of physical activity (e.g. a sedentary job, television-viewing time) were retained for closer analysis. Subsequently, during the study selection stage, some of these studies were excluded because their groups of 'sedentary' participants did not meet the inclusion criteria on closer inspection (i.e. they included some people who participated in light activity and therefore were not truly sedentary).

This was a limitation of the study selection process, which ideally should have detected these studies during the initial title and abstracts review, rather requiring full-text retrieval. However, it is not unexpected for a systematic reviewer to develop a more comprehensive understanding of the literature as a review progresses. Despite the fact that critical appraisal was done by two people, this systematic review was limited by the use of only one data extractor. The extracted data were discussed (by the two critical appraisers), but the subsequent interpretation would have benefited from dual data extraction to further remove the possibility of error or bias. All decisions to include or exclude studies, and the underlying reasons and numbers, were recorded transparently.

Fourth, as discussed in Section 4.4.4, observational studies of exposures and risks are influenced by residual confounding from other risk factors such as obesity and diet. The fact that residual confounding influenced the conclusions that could be drawn from the primary studies was another limitation of this systematic review. In addition, the role of obesity, in particular, as an intermediary for other outcomes could have been investigated further by comparing those studies that checked for attenuating effects with those that did not.

Finally, although the outcomes of interest included all major cardiovascular and metabolic conditions, it would also have been useful to include cancer (from all causes). Primary studies have reported an association between sedentary behaviour and breast cancer (e.g. George et al 2010, Levi et al 1999a), ovarian cancer (e.g. Pan et al 2005, Zhang et al 2004) and colorectal cancer (e.g. Gerhardsson et al 1988, Levi et al 1999b). This association has not been confirmed in the systematic reviews that included cancer as an outcome (Proper et al 2011, van Uffelen et al 2010), which suggested an association from analysis of cross-sectional studies but not prospective studies. With an aging global population and corresponding increasing incidence of cancer (AIHW 2008), any elucidation of risk factors would be beneficial.

4.6 Implications for research

Many implications for future research — particularly better design of primary studies — became apparent during this systematic review. These limitations need to be addressed for changes in practice to occur. Ideally, primary studies investigating the effects of prolonged sedentary behaviours would:

- use a prospective study design with large study and control groups (to ensure adequate power); randomised controlled trials would be useful for testing interventions once the size of the association between true sedentary behaviour and health outcomes is determined

- use a standardised definition of sedentary behaviour that stipulates activities with an energy cost of less than 1.5 MET for three or more hours' duration
- measures sedentary behaviour and its duration using an objective and validated method (e.g. multi-axis accelerometer), or self-reported measures that follow a standardised format (e.g. IPAQ questionnaire) and that are validated in appropriate subpopulation numbers
- use standardised and validated measures for all outcomes
- take into account the possible mediating effects of outcomes such as obesity on other pertinent outcomes (e.g. mortality, cardiovascular disease, type 2 diabetes mellitus)
- adjust for important confounders: age, smoking status, alcohol consumption, and — importantly — physical activity and sedentary behaviour at *all* times outside the time of interest intended by the stated aims of the study.

Scarcity of meta-analyses is most likely an extension of the differing conceptual view of what constitutes sedentary behaviour, and availability of similar enough data to combine statistically, as described earlier. In studies that measure and report sedentary behaviour as a mark of physical inactivity, this 'low' activity level of the 'sedentary' group is used to establish baseline risk; as physical activity increases incrementally, the risk of various adverse health outcomes reportedly decreases. Meta-analysis of such 'trend' data (Graff-Iversen et al 2007, Bekkering et al 2008) will therefore not inform as to the risks associated with true sedentary behaviour. Clearly reported data derived from prospective studies that measure true sedentary behaviour directly, and that have been identified by the rigorous process of systematic review, are needed for pooling in a meta-analysis to provide robust evidence of the associated health risks of such behaviour. Such an undertaking will also help to identify gaps in the current understanding of the risks associated with true sedentary behaviour.

Further investigation of the dose-response relationship would be useful to see whether there is a plausible gradient across different amounts of time spent in sedentary behaviour. Intervention studies would be useful to determine whether there is a cut-off for 'safe' versus 'harmful' levels of sedentary behaviour — and if so, what this cut-off is. Primary studies and systematic reviews report different cut-off points for sedentary behaviour, from two hours (Bowman 2006, Hu et al 2003) and three hours (Grøntved and Hu 2011) per day to 20 hours per week (Chang et al 2008). Identifying a more specific 'danger' range would be more likely to influence behavioural changes to reduce people's sedentary time, and to include recommendations of maximum safe amounts of sedentary behaviours in revised physical activity guidelines.

Similarly, the way in which sedentary behaviour is accumulated needs to be investigated further, particularly whether it can be ameliorated by physical activity. That is, does breaking up sedentary behaviour (i.e. changing from sitting to standing, walking, or bursts of physical activity) decrease the risk of adverse health outcomes? If so, how frequent do the interruptions need to be, and what do the interruptions need to entail (should they increase heart rate, or is standing quietly adequate)? Studies have indicated that interrupted sitting time is linked to smaller waist circumference, lower BMI, and lower levels of triglycerides and two-hour plasma glucose (Healy et al 2008). Some randomised controlled trials (Wen et al 2011) have indicated that 15-minute bursts of physical activity are also beneficial; further investigation would be helpful.

At the physiological level, we still do not have a clear understanding of the cellular responses to sedentary behaviour; for example, how the physiological effects of excessive physical inactivity differ from those of excessive sitting, and whether they are directly reversed by bursts of moderate-to-vigorous activity. This has been investigated to some extent in studies of bed rest and weightlessness (Hamilton et al 2007), and studies documenting withdrawal of exercise (and imposed sedentary behaviour) from athletes (Rogers et al 1990), which confirm the deleterious effects of sedentary behaviours on a range of health outcomes (Pate et al 2008). However, it is important to remember that these studies do not reflect a free-living context, and as Pate et al (2008) point out, no studies to date have 'systematically withdrawn typical forms of moderate-to-vigorous physical activity from the lifestyles of normally active persons and observed the health-related physiologic effects of such a treatment' [p174]. It would also be useful to know the extent to which the adverse health effects are caused by sedentary activity in its own right (i.e. the physiological mechanisms), or by the displacement of time that would otherwise be spent in light-to-moderate physical activity.

4.7 Implications for practice

The results of this systematic review strengthen the case for broadening the scope of physical activity guidelines to include recommendations for minimising sedentary behaviour. Changing behaviour, however, is a major undertaking that relies on robust evidence from six separate stages of research (Owen et al 2010):

- identifying associations between exposures and outcomes
- measuring exposures correctly
- identifying patterns of exposures (e.g. behaviours) in specific populations (cultural groups, age groups, men versus women, different comorbidities)
- identifying determinants of these behaviours
- testing interventions to minimise behaviours (through randomised controlled trials)
- changing public health guidelines and policy using evidence-based methods.

Currently, there is a reasonable body of evidence for the first stage, but less information for the remainder (Owen et al 2010). As data from more long-term prospective studies become available, and interventions for reducing sedentary behaviour in adults are identified and tested in randomised controlled trials, there will be capacity to focus public health guidelines and information campaigns to re-educate people about the benefits of reducing sitting time in all domains (occupation, leisure, transport), as well as the concurrent benefits of maintaining physical activity levels. Behavioural changes to reduce daily sedentary time may be more effective if supported by technologies (e.g. standing desks or workstations) or regulation (e.g. requirements for regular breaks during working or school days) to be effective (Owen et al 2010). However, very few intervention studies have been published for reducing sedentary behaviour in adults, although there are some for increasing physical activity levels (e.g. see De Cocker et al 2008 for a pedometer-based community intervention to increase physical activity).

Due to scarcity of high-quality data on interventions for reducing adults' sedentary behaviours, we may have to look to studies of interventions to reduce sedentary behaviour in children or adolescents — although there is great variation in the types of interventions and mode of delivery (and no consensus as to what is optimal) (DeMattia et al 2007). A recent systematic review and meta-analysis showed that interventions were not effective for reducing BMI or overall screen time in children (approximately 4–11.5 years), although there was a significant effect in preschool children ($\leq$6 years) (Wahi et al 2011).

Obviously, further research is needed to identify effective interventions that are tailored to adults. In the meantime, public health organisations such as the National Heart Foundation are bridging the gap by promoting active lifestyles and minimal sedentary behaviour via factsheets that draw on cross-sectional and prospective studies (see for example *Sitting less for adults*, National Heart Foundation 2011).[3] Any evidence-based changes in practice should be accompanied by regular review to measure their effectiveness (Grimshaw et al 2004).

Revising health messages at a population scale is costly but not impossible. For example, Cancer Council Victoria's 1981 'Slip! Slop! Slap!' campaign to reduce sun exposure was extended in 2007 to encourage other behaviours (seek shade and wear sunglasses: 'Slip, Slop, Slap, Seek, Slide'), to further reduce the risk of skin cancer.[4] Perhaps the most significant behavioural changes in response to public health campaigns in Australia has been the anti-tobacco campaign, which began in the 1970–80s (Scollo and Winstanley 2008) and is still in progress (with recent introduction of the Australian Government's Tobacco Plain Packaging Bill 2011). Smoking prevalence has decreased by from 34% of the total Australian adult population in 1980 to 19% in 2007. Based on these previous examples, changing work, leisure and transport behaviours to minimise sedentary time may be possible. Currently, *Australia's Physical Activity Guidelines for 5–12 Year Olds* (Australian Government Department of Health and Ageing 2004) recommend limiting screen time (television or computer games) to less than two hours per day. Until we have a better evidence base for the effects of sedentary behaviours in adults, it might be useful to use this as a basis for revising the general physical activity guidelines.

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[3] See http://www.heartfoundation.org.au/SiteCollectionDocuments/HW-PA-SittingLess-Adults.pdf (accessed 28 October 2011).

[4] See http://www.cancer.org.au/cancersmartlifestyle/SunSmart/Campaignsandevents/SlipSlopSlapSeekSlide.htm (accessed 9 October 2011).

Chapter 5 Conclusions

This systematic review shows that sedentary behaviour — particularly sitting for periods of three or more hours — increases the risk of cardiovascular disease, all-cause and cardiovascular mortality, and type 2 diabetes mellitus, irrespective of age, sex or physical activity levels. More research is needed to determine whether there are true associations for overweight or obesity, or for gallstones. The extent to which obesity and other intermediate outcomes influence cardiovascular and metabolic outcomes, and the residual confounding effects of diet, also need further investigation.

Overall, the results of this systematic review strengthen the case for expanding physical activity guidelines to include recommendations for minimising sedentary behaviour, to reflect our increasingly sedentary contemporary lifestyles. These implications for practice are significant. Changing sedentary behaviours at the population level will have far-reaching implications for the future burden of disease in Australia, in light of the growing national (and international) incidence of obesity, cardiovascular disease and type 2 diabetes mellitus.

Appendix 1 The review protocol

Criteria for considering studies in this review

Types of studies

This review was limited to prospective cohort studies only. The original systematic review protocol specified that all types of studies (randomised controlled trials — if any, prospective and retrospective cohort studies, case–control studies and cross-sectional studies) would be included. However, after some initial searches, the review was limited to prospective cohort studies only, for the reasons discussed in Section 2.2.

The search was limited to papers published in English, before 13 March 2011.

Types of participants

The review considered studies that included adults (approximately 18–65 years; i.e. not children or adolescents); males and females; and who did not have existing metabolic or cardiovascular health problems at baseline (e.g. obese, diabetic, cardiovascular disease, metabolic syndrome).

Types of interventions

The review considered studies that evaluated sedentary behaviour, defined as prolonged sitting time, screen (television, computer) time, or any nonspecified sedentary behaviour (occupational or nonoccupational). This inclusion criterion was defined to include specific measures of sedentary activity; for example, sedentary behaviour for more than three hours at a time, preferably accompanied by a MET value of ≤ 1.5, but not including standing. However, in the initial screening process, it was clear that this criterion was too specific, and not appropriate to the types of behaviours that were able to be measured in many of the studies. Therefore, a different criterion was needed — specifically, that studies must have defined sedentary behaviour, and measured it in a defined way.

Therefore, for the purposes of the review, these key terms are defined as follows:

- *sedentary behaviour*: behaviours that have a low energy expenditure (e.g. $\leq$1.5 MET (Owen et al 2009, van Uffelen et al 2010) [metabolic equivalent — the ratio of the metabolic rate of an activity and the resting metabolic rate]). Sedentary behaviour does not include standing; rather, it can include:
  - *prolonged sitting*: sitting down for several hours at a time, without standing or walking breaks
  - *screen time*: time spent sitting in front of a computer, television, video game, etc (either at work or in leisure time)
  - *nonspecified sedentary behaviour*: any other behaviour that involves sitting or lying (e.g. driving, reading, listening to music, talking on the telephone).

Types of outcome measures

This review considers studies that include the following primary outcome measures: incidence of obesity and obesity-related disease, including (but not limited to) type 2 (adult-onset) diabetes, cardiovascular incidents (e.g. stroke, myocardial infarction), cardiovascular disease (e.g. heart failure), metabolic syndrome (according to the World Health Organization definition), all-cause mortality/morbidity. Secondary outcomes will include any cardiovascular or metabolic measures, such as insulin resistance or sensitivity, high blood pressure, body mass index (BMI), lean body mass/body composition (including change in adiposity, lean body mass, weight, etc), abdominal obesity (waist circumference), percentage body fat.

Search strategy

The search strategy was used or adapted for the following databases:

- PubMed
- EMBASE
- CINAHL
- Cochrane Library
- PEDro
- PsychINFO
- SPORTDiscus
- Web of Knowledge
- Web of Science
- Google Scholar
- Centre for Reviews and Dissemination (DARE).

A second search for unpublished studies included the Australasian Digital Theses Program (ADT), Proquest, MEDNAR, the US National Institutes of Health international clinical trials registry (www.clinicaltrials.gov), and direct contact with principal investigators of relevant studies, where appropriate and possible.

Appendix 2 Detailed search strategies for key databases

Pubmed

#1 Sedentary Lifestyle[mh] OR sedentary life*[tiab] OR sedentary behav*[tiab] OR physical inactivity[tiab] OR sitting time[tiab] OR prolonged sitting[tiab] OR sedentary time[tiab] OR television viewing[tiab] OR "screen time"[tiab] OR occupational sitting[tiab]

#2 Cardiovascular Diseases[mh:noexp] OR Cardiovascular Diseases/epidemiology*[mh:noexp] OR Cardiovascular Diseases/mortality[mh:noexp] OR Cardiovascular Diseases/prevention & control[mh:noexp] OR cardiovascular disease[tw] OR heart disease[tw] OR vascular disease[tw]

#3 Myocardial infarction[mh] OR Myocardial infarction/epidemiology[mh:noexp] OR Myocardial infarction/etiology[mh:noexp] OR Myocardial infarction/prevention & control[mh:noexp] OR myocardial infarction[tw] OR heart attack[tw]

#4 Hypertension[mh:noexp] OR Hypertension/epidemiology[mh:noexp] OR Hypertension/etiology[mh:noexp] OR Hypertension/prevention and control[mh:noexp] OR hypertension[tw] OR blood pressure[tiab]

#5 Coronary disease[mh] OR Coronary disease/epidemiology[mh:noexp] OR Coronary disease/etiology[mh:noexp] OR Coronary disease/prevention& control[mh:noexp] OR coronary disease[tw]

#6 Arteriosclerosis[mh] OR Arteriosclerosis/epidemiology[mh:noexp] OR Arteriosclerosis/etiology[mh:noexp] OR Arteriosclerosis/prevention & control[mh:noexp] OR arteriosclerosis[tw]

#7 #2 OR #3 OR #4 OR #5 OR #6

#8 Overweight[mh] OR Overweight[tw] OR Obese[tw] OR Obesity[tw]

#9 Weight gain[mh] OR Weight gain*[tw] OR Adiposity[tw] OR Abdominal fat[mh] OR Abdominal fat*[tw]

#10 Body weight[mh:noexp] OR Body weight[tw] OR Body weight changes[mh:noexp] OR Body mass index[mh] OR Body mass index[tw] OR Bmi[tw]

#11 Waist-hip ratio[mh] OR Waist hip ratio*[tw] OR Waist to hip ratio*[tw] OR Skinfold thickness[mh] OR Skinfold thickness*[tw]

#12 Metabolic syndrome[tw] OR Metabolic syndrome X[mh]

#13 #8 OR #9 OR #10 OR #11 OR #12

#14 Diabetes Mellitus, Type 2[mh] OR Diabetes Mellitus, Type 2/epidemiology[mh:noexp] OR Diabetes Mellitus, Type 2/etiology[mh:noexp] OR Diabetes Mellitus, Type 2/prevention & control[mh:noexp]

#15 Insulin resistance[mh] OR insulin resistance[tw] OR "impaired glucose tolerance"[tw] OR glucose intoler*[tw] OR non*insulin dependent[tw] OR non*insulin treated[tw]

#16 type 2 DM[tw] OR type II DM[tw] OR type II diabetes[tw] OR type 2 diabetes[tw] OR diabetes mellitus type 2[tw] OR diabetes mellitus type II[tw] OR adult diabetes[tw] OR maturity onset diabetes[tw] OR late onset diabetes[tw] OR stable diabetes[tw] OR adult diabetic[tw] OR maturity onset diabetics[tw] OR late onset diabetics[tw]

#17 #14 OR #15 OR #16

#18 Stroke[mh] OR Stroke/epidemiology[mh:noexp] OR Stroke/etiology[mh:noexp] OR Stroke/prevention & control[mh:noexp] OR stroke[tw] OR carotid artery thrombosis[tw] OR cerebrovascular accident[tw] OR cerebral infarction[tw] OR cerebral hemorrhage[tw]

#19 #7 OR #13 OR #17 OR #18

#20 #1 AND #19

Limits: Humans, all adults (19+)

CINAHL

#1 TX "sedentary lifestyle" or TI "sedentary life*" or AB "sedentary life*" or TI "sedentary behav*" or AB "sedentary behav*" or TI "sedentary time" or AB "sedentary time" OR TX "life style" OR TX sedentary OR TX television OR TI "physical inactivity" or AB "physical inactivity" or TI "sitting time" or AB "sitting time" or TI "prolonged sitting" or AB "prolonged sitting" or AB "occupational sitting" or TI "occupational sitting" OR TI "television viewing" or AB "television viewing" or TI "screen time" or AB "screen time"

#2 (MH "Cardiovascular Diseases+/EP/ET/PC/PR/RF") OR TX "cardiovascular disease" or TX "heart disease" or TX "vascular disease" OR (MH "Hypertension+/EP/ET/PC/RF/PR") OR TX "blood pressure" OR (MH "Coronary Disease/ET/EP/PR/PC/RF") OR TX "coronary disease" OR (MH "Arteriosclerosis/EP/ET/PC/PR/RF") OR TX arteriosclerosis

#3 TX overweight OR TX obesity OR TX obes* OR TX "weight gain" OR TX "body weight" OR TX "body weight changes" OR "body mass index" OR (MH "Body Weight+") OR (MH "Body Mass Index") OR (MH "Arm Circumference") OR (MH "Waist-Hip Ratio") OR (MH "Abdominal Fat") OR TX "abdominal fat" OR TX "skinfold thickness"

#4 (MH "Glucose Metabolism Disorders+/EP/ET/PC/PR/RF") OR (MH "Insulin Resistance+/EP/ET/PR/PC/RF") OR (MH "Diabetes Mellitus, Insulin-Dependent/EP/ET/PC/PR/RF") OR TX "type 2 diabetes" OR TX "type II diabetes" OR TX "adult diabetes" OR TX "late onset diabetes" OR TX "metabolic syndrome X"

#5 (MH "Cerebrovascular Disorders+/EP/ET/PC/PR/RF") OR TX stroke

#6 #2 OR #3 OR #4 OR #5

#7 #1 AND #6

Limits: All adults (18-44), middle aged (45-64), Aged 65+, humans, English

EMBASE

#1 ('Sedentary Lifestyle' or 'sedentary life*' or 'sedentary behav*' or 'physical inactivity' or 'sitting time' or 'prolonged sitting' or 'sedentary time' or 'television viewing' or 'screen time' or 'occupational sitting').ti,sh,hw,ab,kw

#2 ('Cardiovascular Diseas*' or 'heart disease' or 'vascular disease').sh,hw,ab,kw.

#3 ('Myocardial infarction' or 'heart attack').sh,hw,ab,kw.

#4 ('Hypertension' or 'blood pressure').sh,hw,ab,kw.

#5 ('Coronary disease' or 'Arteriosclerosis').sh,hw,ab,kw.

#6 ('Overweight or 'Obese' or'Obesity' or 'Weight gain' or 'Weight gain*' or 'Adiposity' or 'Abdominal fat*' or 'Body weight' or 'body mass index' or Bmi').sh,hw,ab,kw.

#7 ('Waist-hip ratio' or 'Waist to hip ratio*' or 'skinfold thickness').sh,hw,ab,kw.

#8 ('Metabolic syndrome' or 'Metabolic syndrome X').sh,hw,ab,kw.

#9 ('Diabetes Mellitus, Type 2' or 'Diabetes Mellitus' or 'Insulin resistance' or 'impaired glucose tolerance' or 'glucose intoler*' or 'non*insulin dependent').sh,hw,ab,kw.

#10 ('Stroke' or 'carotid artery thrombosis' or 'cerebrovascular accident' or 'cerebral infarction' or 'cerebral hemorrhage').sh,hw,ab,kw.

#11 #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

#12 #1 AND #11

Limits: human and english language and (clinical trial or randomized controlled trial or controlled clinical trial or multicenter study) and ("diagnosis (sensitivity)" or "diagnosis (specificity)" or "prognosis (sensitivity)" or "prognosis (specificity)" or "prognosis (optimized)" or "causation-etiology (sensitivity)" or "causation-etiology (specificity)" or "causation-etiology (optimized)") and english and (conference abstract or conference paper or journal or proceeding or report or "review" or short survey) and (adult <18 to 64 years> or aged <65+ years>)

Web of Science

"Sedentary Lifestyle" OR "sedentary behaviour" OR "physical inactivity" OR "sitting time" OR "prolonged sitting" OR "sedentary time" OR "television viewing" OR "screen time" OR "occupational sitting"

AND cardiovascular disease OR heart disease OR heart attack OR vascular disease OR myocardial infarction OR hypertension OR blood pressure OR atherosclerosis OR arteriosclerosis

OR overweight OR obesity OR weight gain OR weight OR body weight OR body mass index OR BMI OR obes* OR metabolic syndrome OR waist-hip ratio OR skinfold thickness OR abdominal obesity OR diabetes mellitus OR type two diabetes OR type 2 diabetes OR adult diabetes OR diabetes OR glucose intolerance OR glucose sensitivity OR non insulin dependent

OR stroke OR carotid artery thrombosis OR cerebrovascular accident OR cerebral infarction OR cerebral hemorrhage

Limits: Subject Areas=(cardiac & cardiovascular systems or endocrinology & metabolism or peripheral vascular disease or health policy & services or medicine, general & internal or multidisciplinary sciences or nutrition & dietetics or public, environmental & occupational health or medicine, research & experimental or health care sciences & services or respiratory system) and document type=(article or proceedings paper)

Cochrane Library

#1 MeSH descriptor Sedentary Lifestyle, this term only OR (sedentary life* OR sedentary behav* OR physical inactivity OR sitting time OR prolonged sitting time OR sedentart time OR television viewing OR "screen time" OR occupational sitting)

#2 (MeSH descriptor Cardiovascular Diseases, this term only) OR (MeSH descriptor Cardiovascular Diseases, this term only with qualifiers: EP,ET,MO,PC) OR (MeSH descriptor Myocardial infarction) OR (MeSH descriptor Myocardial infarction, this term only with qualifiers: EP, ET, MO, PC) OR (cardiovascular disease OR heart disease OR vascular disease OR myocardial infarction OR heart attack)

#3 (MeSH descriptor Hypertension, this term only) OR (MeSH descriptor Hypertension, this term only with qualifiers: EP,ET,MO,PC) OR (hypertension OR blood pressure)

#4 (MeSH descriptor Coronary disease) OR (MeSH descriptor Coronary disease, this term only with qualifiers: EP,ET,MO,PC) OR (coronary disease)

#6 (MeSH descriptor Arteriosclerosis) OR (MeSH descriptor Arteriosclerosis, this term only with qualifiers: EP,ET,MO,PC) OR arteriosclerosis

#7 #2 OR #3 OR #4 OR #5

#8 (MeSH descriptor Overweight) OR (overweight or obese or obesity) OR (MeSH descriptor Weight gain) OR (weight gain* or adiposity or abdominal fat or abdominal fat*)

#9 (MeSH descriptor Body weight, this term only) OR (MeSH descriptor Body weight changes, this term only) OR (MeSH descriptor body mass index) OR (body weight or body mass index or BMI)

#10 (MeSH descriptor Waist-hip ratio) OR (MeSH descriptor Skinfold thickness) OR (waist hip ratio* or skinfold thickness*)

#11 (MeSH descriptor Metabolic syndrome X) OR (Metabolic NEXT syndrome)

#12 #7 OR #8 OR #9 OR #10

#13 #6 OR #11

#14 #1 AND #12

Note: none of the 8 Cochrane reviews were relevant. A quick analysis of the other review, and of the clinical trials, showed that they were not relevant either (as expected). Other, more appropriate (for the question) databases searched instead.

Appendix 3 Critical appraisal tool (cohort studies)

1. Is the sample representative of patients in the population as a whole?

Adequate	• Authors describe the target population that they want to look at • Authors mention or describe how population was selected/recruited, and whether it was representative of the whole population. • Inclusion and exclusion criteria are defined. • At a minimum, the following baseline demographics of the participants are given: – age, sex – baseline measurements of whatever outcomes will be investigated (e.g. weight, BMI, waist circumference, etc) – baseline degree of exposure (sedentary behaviour) as a specific measure of sedentary behaviour/prolonged sitting (categorical or continuous; self-report or objective), or as defined by MET value • Additional information can include: – socioeconomic status/employment status – geographical location (e.g. developing world/developed world), PA levels.
Inadequate	• No mention of how target population selected/recruited, or whether representative of the whole population. • Inclusion/exclusion criteria not defined. • Age or sex described only
Unclear	• Unclear descriptions of any/all the above.

Note: descriptions should include both study and control groups, and an explanation of how comparable they are.

Response

2. Do the participants share similar sedentary behaviours?

Adequate	• *Sedentary behaviour* defined using METs, estimation of energy expenditure, or other measure of total unbroken time for activity of interest: – prolonged sitting, screen time, other • *Prolonged* sedentary behaviour defined as: – >3 hours/day of sedentary time (unbroken, or largely unbroken) (preferably reported with an accompanying MET value - <1.5 MET) – a minimum of 21 hours of sedentary behaviour (as above) per week, total MET value <1.5 MET – occupational or other sitting/sedentary behaviour.
Inadequate	• Sedentary behaviour not defined at all, or not defined in specific terms; or • Sedentary behaviour only defined by proxy as a total proportion of day/week spent inactive (no details given on whether time sedentary is prolonged, or broken up)
Unclear	• Unclear description of sedentary behaviour (no details given on whether time sedentary is prolonged, or broken up)

Response

3. Has bias been minimised in relation to selection of cases and controls?

Adequate	• Description of how the study and control groups were selected (e.g. by predefined cohort with clear follow-up period and clear points of measurement) • Sample sizes given. • The numbers of participants at each stage of the study are reported.
Inadequate	• No description of how groups were selected
Unclear	• Details of all the above are unclear.

Response

4. Are confounding factors identified and strategies to deal with them stated?

Adequate	• Key confounders (e.g. smoking status, existing CV/metabolic disease, excessive alcohol use) are recognised and participants excluded if present. • Physical activity (note: not *in*activity) reported at baseline and throughout. • Any remaining confounders (e.g. socioeconomic status, occupation, location) are described and adjusted for, if possible, in the analyses. • Diet can be adjusted for or not (irrelevant for my review).
Inadequate	• No mention of confounders, or no attempt to take into account. • Participants included despite presence of key confounders (smoking, existing CV/metabolic disease, excessive alcohol use).
Unclear	• Participants excluded on the basis of some, but not all, key confounders. • Explanation unclear.

Response

5. Are the outcomes assessed using objective criteria?

Adequate	• Description of how data were collected. • Description of how each outcome was measured (existing definitions or diagnostic criteria; validated tools) • Clear definition of key terms used for each outcome and measurement (e.g. weight gain, presence of metabolic/CV disease markers — either primary or surrogate outcome)
Inadequate	• No or poor description of outcomes and measurements • Key terms not defined or quantified (self-reported data,)
Unclear	• Descriptions of outcomes and measurements unclear

Response

6. Was the follow-up carried out over a sufficient time period?

Adequate	• Study duration and follow-up defined clearly (including times at which measurements were taken) • Follow-up time adequate for each outcome to manifest (e.g. a minimum of 3 years). • Alternatively, follow-up time adequate for surrogate outcomes to manifest (e.g. minimum of approximately 6 months).
Inadequate	• Follow-up time too short for surrogate outcomes to manifest (if used or reported).
Unclear	• Follow-up time too short for primary outcomes to manifest, but not clear whether surrogate outcomes measured.

Response

7. Were the outcomes of people who withdrew described and included in the analysis?

Adequate	• Participants analysed in the groups to which they were assigned at baseline • All participants included in final calculations, regardless of whether their outcomes were measured. • Losses to follow-up described clearly and outliers accounted for.
Inadequate	• Participants not analysed in the groups to which they were assigned at baseline. • No explanation of loss to follow up, or loss to follow-up significant.
Unclear	• Loss to follow-up described but unclear, incomplete, or numbers in text do not match figures.

Response

8. Were the outcomes measured in a reliable way?

Adequate	• All outcomes measured using standard methods or instruments. • Authors mention the reliability and/or validity of the measurements they use (including trained data collectors).
Inadequate	• Estimates only, or incorrect methods, or standardised definitions/methods/instruments not used. • No mention of reliability or validity of the measures used.
Unclear	• Not enough information to determine how outcomes measured • Reliability or validity not clear.

Response

9. Was appropriate statistical analysis used?

Adequate	• Appropriate statistical methods used and described, and methods for addressing confounders included. • Numbers of participants with missing data reported, and appropriate statistical methods used if data missing for more than 20%.
Inadequate	• Statistical methods not described, or inappropriate methods used. • Missing data not mentioned or accounted for.
Unclear	• Statistical methods unclear.

Response

Overall appraisal

Include	Exclude	Seek further information
Comments (including reasons for exclusion		

Appendix 4 Data extraction tool (cohort studies)

Reviewer Meg Heaslop Author Journal	Date Year Record no

Study method	RCT	Quasi-RCT	Longitudinal (prospective)
	Retrospective	Observational	Other

Participants

Setting	
Population	
Sample size	

Interventions or exposures [i.e. types of sedentary behaviours]

Exposure 1	
Exposure 2	
Exposure 3	

Clinical outcome measures [specify whether primary or secondary]

Outcome description	Scale/measure

Study results

Dichotomous data

Outcome description	Intervention ( ) number / total number	Intervention ( ) number / total number

Continuous data

Outcome description	Intervention ( ) number / total number	Intervention ( ) number / total number

Authors' conclusions

Comments

Appendix 5 Critical appraisal scores

Note: Scores shown for both reviewers. Scores calculated on total number of 'adequate' scores.

Reference	Q1 Sample	Q2 Exposure	Q3 Selection	Q4 Confounders	Q5 Outcome	Q6 Follow-up	Q7 Maintenance	Q8 Reliability	Q9 Statistics	TOTAL
Arsenault et al (2010)	A	U	U	A	A	A	U	A	A	6
	A	U	A	U	A	A	A	A	A	7
Benuza et al (2007)	I	U	I	A	I	A	I	U	A	3
	U	A	U	U	U	U	A	A	A	4
Blanck et al (2007)	A	A	A	A	I	A	A	I	A	7
	A	A	A	A	I	A	A	U	A	7
Carlsson et al (2006)	A	A	A	A	I	A	A	I	A	7
	A	A	A	U	A	A	A	U	A	7
Coakley et al (1998)	A	U	A	A	A	A	A	I	A	7
	A	U	A	A	A	A	A	A	A	8
De Cocker et al (2010)	A	I	A	A	I	A	U	U	A	5
	A	A	A	A	I	A	A	A	A	8
Graff-Iversen et al (2007)	A	A	A	U	A	A	I	I	A	6
	A	A	A	A	A	A	A	A	A	9
Hancox et al (2004)	A	I	U	U	A	A	A	I	U	4
	A	U	A	U	I	A	A	U	U	4
Helmerhorst et al (2009)	A	A	A	A	A	A	U	A	A	8
	A	U	A	A	A	A	U	A	A	7
Hu et al (2001	A	A	A	A	A	A	A	A	A	9
	U	I	A	A	A	A	U	A	A	6
Hu et al (2003)	A	A	A	A	I	A	A	U	A	7
	U	A	A	A	U	U	A	A	A	6
Johansson et	A	U	A	I	A	A	I	I	A	5

al (1988)	U	A	A	I	A	A	I	I	U	4
Katzmarzyk et al (2009)	I	U	A	A	U	A	A	U	A	5
	A	A	A	A	U	A	U	A	A	7
Koh-Banerjee et al (2003)	A	U	A	A	A	A	A	I	A	7
	A	A	A	U	A	A	A	U	A	7
Kozakova et al (2010)	A	A	A	A	A	A	A	A	A	9
	A	A	A	U	A	A	I	A	A	7
Leitzmann et al (1999)	A	A	A	A	U	A	U	I	A	6
	A	A	A	U	A	A	A	A	A	8
Salonen et al (1988)	A	A	U	A	A	A	A	U	A	7
	A	U	A	U	A	A	A	A	A	7
Sjol et al (2003)	A	A	A	A	A	A	A	U	A	8
	A	A	A	A	A	A	A	A	A	9
Warren et al (2010)	A	A	A	A	I	A	A	I	A	7
	A	U	A	A	A	A	A	U	A	7

A = adequate; I = inadequate; U = unclear.

Appendix 6 Excluded studies

Reference	Reason for exclusion
Beunza JJ et al (2007). Sedentary behaviors and the risk of incident hypertension — the SUN cohort. *American Journal of Hypertension* 20(11):1156–1162.	Dynamic cohort recruitment (inadequate follow-up for outcomes); poorly measured and reported; definition of sedentary behaviour inadequate
Hancox RJ et al (2004). Association between child and adolescent television viewing and adult health: a longitudinal birth cohort study. *Lancet* 364(9430):257–262.	Inadequate definition of sedentary behaviour, combined with poorly defined, collected and reported data (self-reported, no information given on whether standardised forms/data collection given, methods not validated, incorrect statistical interpretation)
Johansson S et al (1988). Physical inactivity as a risk factor for primary and secondary coronary events in Goteborg, Sweden. *Eur Heart J* 9(Suppl L):8–19.	Study quality too low (poor score on Q4, 7, 8), half of study population do not meet criteria (disease at baseline)

Appendix 7 Summary of physical activity guidelines

Guideline	Recommendations
Physical Activity Guidelines for Adults (Australian Government)	Minimum of 30 minutes of moderate-intensity physical activity on most, preferably all, days (this can be done all at once, or by combining bursts of 10–15 minutes each over the day) Think of movement as an opportunity, not an inconvenience; be active in as many ways as you can; do regular, vigorous activity for extra health and fitness (this does not replace the other recommendations, but is an additional recommendation for those who are able, and wish, to achieve greater health and fitness benefits)
The National Guidelines on Physical Activity for Ireland (Department of Health and Children)	At least 30 minutes of moderate activity a day, five days a week (or 150 minutes a week) (for all adults, 18–64 years)
Physical Activity Guidelines for Americans (US Department of Health and Human Services)	2 hours and 30 minutes per week of moderate-intensity, or 1 hour and 15 minutes (75 minutes) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate and vigorous-intensity aerobic physical activity Aerobic activity should be performed in episodes of at least 10 minutes, preferably spread throughout the week Additional health benefits are provided by increasing to 5 hours (300 minutes) a week of moderate-intensity aerobic physical activity, or 2 hours and 30 minutes a week of vigorous-intensity physical activity, or an equivalent combination of both Adults should also do muscle-strengthening activities that involve all major muscle groups performed on 2 or more days per week (all adults, 18–64 years)
Canada's Physical Activity Guide to Healthy Living (Public Health Agency of Canada)	Does not stipulate an amount, but encourages people to 'build physical activity into your daily life'; for example, moderate activity can consist of 30 minutes, 4 days a week The guidelines are currently being reviewed
Choosing Activity: A Physical Activity Action Plan (UK Department of Health)	For general health benefit, adults should achieve a total of at least 30 minutes a day of at least moderate intensity physical activity on 5 or more days of the week
Global Recommendations on Physical Activity for Health (WHO)	At least 150 minutes of moderate-intensity aerobic physical activity per week or at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week or an equivalent combination of moderate- and vigorous-intensity activity Aerobic activity should be performed in bouts of at least 10 minutes duration
New Zealand Ministry of Health physical activity guidelines	View movement as an opportunity, not an inconvenience Be active every day in as many ways as possible Put together at least 30 minutes of moderate intensity physical

	activity on most if not all days of the week If possible, add some vigorous exercise for extra health benefits and fitness
Exercise and Physical Activity Reference for Health Promotion 2006 (EPAR2006): Physical Activity, Exercise and Physical Fitness (Ministry of Health, Labour and Welfare of Japan, 2006)	Either a daily walk of 8000–10 000 steps; or 35 minutes of jogging or tennis, or one hour of brisk walking, per week

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