Too Little Exercise and Too Much Sitting: Inactivity Physiology and the Need for New Recommendations on Sedentary Behavior

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Moderate- to vigorous-intensity physical activity has an established preventive role in cardiovascular disease, type 2 diabetes, obesity, and some cancers. However, recent epidemiologic evidence suggests that sitting time has deleterious cardiovascular and metabolic effects that are independent of whether adults meet physical activity guidelines. Evidence from "inactivity physiology" laboratory studies has identified unique mechanisms that are distinct from the biologic bases of exercising. Opportunities for sedentary behaviors are ubiquitous and are likely to increase with further innovations in technologies. We present a compelling selection of emerging evidence on the deleterious effects of sedentary behavior, as it is underpinned by the unique physiology of inactivity. It is time to consider excessive sitting a serious health hazard, with the potential for ultimately giving consideration to the inclusion of too much sitting (or too few breaks from sitting) in physical activity and health guidelines.

Introduction

There is now broad agreement among clinicians, exercise scientists, and public health experts that moderate- to vigorous-intensity physical activity has a key preventive role in cardiovascular disease, type 2 diabetes, obesity, and some cancers. However, when most experts and lay people think of physical activity, their focus tends to be on deliberate "exercising for health." Hence, specific prescriptive guidelines relating to the frequency, intensity, duration, and type of "purposeful" exercise necessary for health gain are a key feature of public health guidelines [1••,2,3]. The updated physical activity and health recommendations from the American College of Sports Medicine and the American Heart Association [1••,2] continue to emphasize participation in at least 30 minutes of moderate-intensity physical activity (which should be accumulated in bouts of at least 10 minutes) on 5 days per week or relatively more intense exercise for less time (20 minutes on 3 days per week).

However, a question that arises from consideration of the public health guidelines is, "What should the person who sleeps an average of 8 hours per day be doing for the remaining 15.5 hours of the day that they are not exercising?" [4••,5•]. Clearly not much of these 15.5 hours involves exercise, as recent population-based accelerometer studies indicate that, depending on the age of the adult, 1% to 5% of the waking day is spent in moderate to vigorous physical activity of any kind [6•,7•], and 0.5% to 1% of this is sustained for at least 10 minutes [6•].

In this regard, the updated recommendations [1••,2] have sought to clarify the role of the incidental activities of daily living by stating several times that the goal of moderate- to vigorous-intensity activity is intended to be in addition to routine activities, and examples like taking out the trash or walking from the car in the parking lot were not meant to be included in the prescriptive guidelines. Thus, what people do in their nonexercise time (Fig. 1) remains in the background of the physical activity and public health recommendations, with the focus being on the accumulation of 30 minutes of at least moderate-intensity physical activity each day.

However, this "background" may be equally important for health. In particular, there is new evidence on the importance of avoiding too much time in sedentary behav-

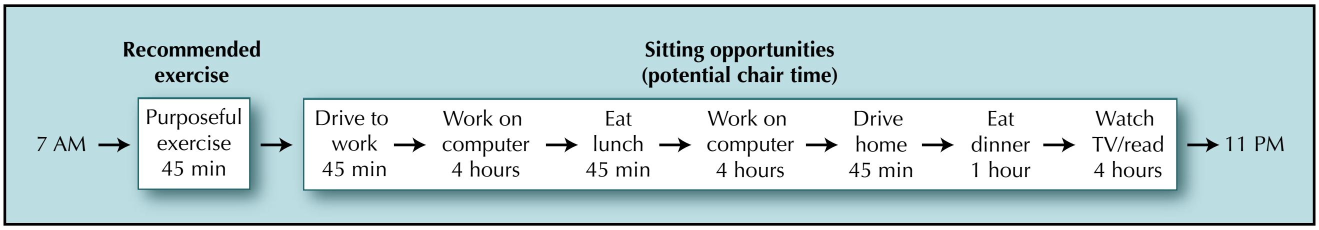

Figure 1. For an individual who sleeps 8 hours per day, the remaining 16 hours are typically filled with domestic and work duties. For this hypothetical "physically active" adult, a 45-minute exercise session of brisk walking prior to work ensures that the minimum level of purposeful exercise (30 minutes per day on 5 days per week) is achieved early in the day. However, this person then sits during the drive to work, at the computer before lunch, during lunch, at the computer after lunch, during the drive home, at dinner, and while watching TV. This hypothetical person may spend up to 95% of his waking hours sitting. However, because this person walked briskly for a sustained period of at least 30 minutes, current public health guidelines consider him "physically active." The term *active couch potato* or *exercising couch potato* is probably more appropriate.

iors (primarily sitting and other activities that involve low levels of metabolic energy expenditure) and the biologic mechanisms that underlie these associations [4••].

Sitting is the most common sedentary behavior of adults; people can sit for many hours at a time every day of the year. However, despite the ubiquitous nature of prolonged sitting in modern society, it is possible that we have not yet reached our full sitting potential nor realized the potential for dire future consequences [4••], given the rapidly evolving innovations in communications, transportation, and workplace technologies [8].

In this article, we consider "too much sitting" a distinct health hazard and describe recent findings from studies on the cardiometabolic consequences of prolonged sedentary time. We also consider provocative new findings from recent research on "inactivity physiology"—new perspectives that identify underlying biologic mechanisms that differ in distinct and important ways from the "physiology of exercising" [4••]. Collectively, these studies identify unique health consequences of "too much sitting" that are distinct from those of "too little exercise."

Epidemiologic Evidence Supporting an Increased Emphasis on Reducing Sitting Time

Epidemiologic observations from the middle of the 20th century showed that men whose jobs involved sitting for prolonged periods had a twofold increased risk of cardiovascular disease compared with men whose jobs required physical activity. Elevated rates of cardiovascular events were reported for occupationally sedentary English bus drivers and mail sorters relative to more active bus conductors and postal workers [9,10] and for occupationally sedentary versus physically active railroad industry workers in the United States [11].

New data on the prevalence of sedentary behaviors from a large population-based sample strengthen the case for seriously addressing the health implications apart from exercise guidelines. In 2003–2004, the National Health and Nutrition Examination Survey obtained objective measures of physical activity and sedentary time by having participants wear accelerometers for several days [12•]. Accelerometers are small electronic devices worn on the hip that collect movement data that are then downloaded for computer analysis. More than half of the waking day (55%) was spent sedentary [12•].

The Australian Diabetes, Obesity and Lifestyle Study (AusDiab) has provided a unique opportunity to examine the consequences of television viewing time on objectively measured indices of metabolic health and related biomarkers in a large, population-based sample of more than 11,000 Australian adults. In adults without known diabetes, a common surrogate for sitting time, self-reported television viewing time, was positively associated with undiagnosed abnormal glucose metabolism [13] and the metabolic syndrome [14]. When television time was considered as a continuous measure [15•], a detrimental, dose-response association was observed in women between television viewing time and 2-hour plasma glucose and fasting insulin. Importantly, all of these associations persisted after adjustment for sustained and moderate-intensity leisure-time physical activity and waist circumference.

Does Meeting Physical Activity Guidelines Obviate Concerns about Sedentary Behaviors?

A recent report from AusDiab [16•] examined the relationships of television viewing time with continuous metabolic risk in men and women who reported at least 150 minutes per week of moderate- to vigorous-intensity physical activity (which is the equivalent of the generally accepted public health guidelines for health-enhancing physical activity) [1••,2,3]. In this large group of healthy, physically active adults, significant detrimental dose-response associations of television viewing time were observed with waist circumference, systolic blood pressure, and 2-hour plasma glucose in men and in women as well as fasting plasma glucose, triglycerides, and high-density lipoprotein (HDL) cholesterol in women [16•]. This is an important observation because it allows the particular metabolic consequences of time spent being sedentary to be examined among those who would be considered by health care practitioners and public health experts to be sufficiently physically active for the prevention of cardiovascular disease. This finding reinforces our message about the deleterious health consequences of sitting time independent of the current physical activity (exercise) guidelines.

Recognizing the subjective nature of self-report data on television viewing time and the potential measurement error associated with such data acquisition, objectively measured (via accelerometers) sedentary time was assessed in a subsample of adults in the AusDiab study. Sedentary time was detrimentally associated with waist circumference, 2-hour plasma glucose, and triglycerides, but light-intensity activity was beneficially associated with waist circumference and 2-hour plasma glucose [17••,18]. Importantly, the significant associations of sedentary time and light-intensity activity with waist circumference and 2-hour plasma glucose remained after adjustment for time spent in objectively measured moderate- to vigorous-intensity activity [17••,18]. Sedentary time and light-intensity time were also highly negatively correlated (r = –0.96): the more time participants spent in light-intensity activity, the less time they spent being sedentary.

Light-intensity activity had a strong inverse relationship with sedentary time. This finding suggests that promoting light-intensity activity may be a feasible approach to ameliorating the deleterious health consequences of sedentary behavior. Additionally, epidemiologic evidence suggests that having a positive balance between light-intensity and sedentary time (eg, spending more time in light-intensity than sedentary time) is desirable because light-intensity activity has an inverse linear relationship with a number of cardiometabolic biomarkers [17••,18].

More recently, breaks in sedentary time (as distinct from the total volume of time spent being sedentary) were shown to have beneficial associations with metabolic biomarkers [19••]. Sedentary time was considered to be interrupted or broken if accelerometer counts rose up to or above 100 counts per minute [19••]. This can include activities as light in intensity as standing from a sitting position or walking a step. Independent of total sedentary time, moderate- to vigorous-intensity activity time, and mean intensity of activity, having a higher number of breaks in sedentary time was beneficially associated with waist circumference, body mass index, triglycerides, and 2-hour plasma glucose [19••]. These observational data indicate that there may be metabolic benefits to regularly interrupting sedentary time in addition to reducing overall sedentary time. However, further experimental and intervention studies are required to understand the mechanisms that may underlie these findings.

This set of findings from AusDiab shows important patterns of association with cardiometabolic health of adults' sedentary time, particularly television viewing time. In another review, we examined several new findings from studies in other countries that show similar patterns of association [4••].

The Emergence of the Inactivity Physiology Paradigm

The term *inactivity physiology* was first put forward in 2004 to describe the research on the potential causal role of sedentary behaviors in the development of cardiovascular and metabolic diseases [20]. The basic premise is that sitting too much is not the same as lack of exercise and, as such, has its own unique metabolic consequences. Our recent report comprehensively reviewed this and related topics in detail [4••].

The effects of postural allocation or sedentary behaviors on regulation of body weight provide a useful history in efforts to understand the significant and likely distinct effects of physical inactivity. An elegant investigation using the limited technologies existing in 1967 to measure standing time successfully attached a gravity-activated stopwatch to the leg of subjects to objectively quantify postural allocation [21]. Remarkably, this early study found that obese subjects stood about 3.5 hours per day less than lean subjects [21], a result recently confirmed and extended in a highly sophisticated study using modern inclinometers [22••]. A study in much larger numbers of subjects (1422) found that successful weight maintenance following weight loss was associated with avoidance of the most common sedentary behavior, watching television, and was independent of self-reported moderate to vigorous physical activity or other types of exercise [23•]. Despite these findings, remarkably few interventional studies have investigated mechanisms regulating substrate metabolism or energy balance during physical inactivity. Studies of bed rest by Bergouignan and Blanc [24] have provided much-needed insights. These perspicacious authors alluded to one pitfall possibly explaining why there is still so little scientific information explaining the cause of the current obesity problem in our society; perhaps too many scientists have assumed that the deleterious consequences of sedentary behaviors can be ignored in light of the benefits of exercise training. Taken together, these studies reveal the need for a proper appreciation of inactivity physiology so that the deleterious effects of too much sitting can be clearly identified.

Genetic association studies have suggested that different genomic regions are linked to different physical activity behavioral phenotypes [25,26]. Simonen et al. [26] speculated that "this may indicate that different domains of physical activity (eg, inactivity vs strenuous activity) are influenced by different mechanistic pathways and therefore different genes and genomic regions are detected for these traits." Dietz [27] concluded from his review of the literature in 1996 that "few analyses have been designed to examine whether inactivity and activity exert independent effects on health outcomes," with obesity as an exception. In this regard, our more recent studies of inactivity on global gene expression profiles or lipoprotein and triglyceride metabolism were entirely independent of differences in body weight because experiments were performed over a span of hours to 11 days, when weight was stable [28,29,30••].

The most definitive experimental evidence supporting the argument that simply not standing or performing very light-intensity movements has potent and unique metabolic effects deleterious for biochemical processes comes from studies in laboratory rats, in which all lifestyle and dietary factors are controlled absolutely [28,29,30••,31,32]. Rats housed in the research environment recruit specialized motor units for standing and low-intensity ambulation for about 8 or more hours per day [33], walk very little, and do not exercise unless they are provided with access to running wheels or treadmills. When rats were not exercised at all during their lives and were then prevented from standing or spontaneously walking (a low-intensity activity), there was a rapid and profound decrease in the concentration of plasma HDL cholesterol (22%) on the first day of inactivity that was sustained over many days [29].

Studies have used radioactive triglyceride tracers to examine metabolic effects of not standing on specialized leg muscles, such as the deep red quadriceps, that are designed for postural support (not all muscles have this same function). These muscles quickly lost more than 75% of their ability to siphon off the fat circulating in the lipoproteins from the bloodstream when incidental contractile activity was reduced [4••,28]. This was related to a 90% to 95% loss of lipoprotein lipase (LPL) activity locally in the most oxidative skeletal muscles in the legs, which are specialized for postural support. Whereas 4 hours of intermittent treadmill walking *in addition to* incidental activity had absolutely no effect on LPL, the physical inactivity caused by the reduction in the incidental activity had profound metabolic effects. In these muscles, the LPL enzyme activity was reduced without any decrease in the expression of the LPL gene, as revealed by a steady concentration in LPL mRNA not only for 1 day of inactivity but also for chronic and intermittent patterns of inactivity [28].

If physical inactivity is thought simply to be the mirror image of insufficient exercise, one might expect that the reverse of this effect on muscle LPL regulation would occur if the rats were exercise-trained. However, in heavily exercise-trained rats matched for diet, age, and genetic background, there was no change in LPL activity in the posturally specialized muscles such as the soleus or deep red quadriceps muscles [4••,32]. If the rats' training was sufficiently intense (a few hours per day of intense sprinting), it was possible to increase LPL activity somewhat in the glycolytic-rich muscles not typically recruited for standing or light movements, such as the superficial white quadriceps, but not in other muscle types [4••,32]. The increase also occurred via a different cellular mechanism involving significant increases in LPL mRNA expression, unlike the effect of inactivity [4••].

In summary, studies using sophisticated molecular biology and medical chemistry methodologies have found that exercise and physical inactivity change the body in different, unique ways. In these same studies, when rats were not simply standing in their cage, there was a rapid and dramatic loss of most of the enzyme residing in the blood vessels in the legs for capturing fat out of blood so it can be burned up by muscle. One parallel consequence of this was a remarkably rapid and clinically relevant decrease in HDL cholesterol. Hundreds of genes and molecular processes are impaired by physical inactivity (that is, reductions in standing or light ambulation time) [28] and by biologic mechanisms that are different from those that are activated by exercise. These findings are important, because they have begun to move beyond the correlational data obtained in epidemiologic observations and to provide much-needed experimental evidence. Clearly, the physical inactivity that is associated with the prevention of standing has some potent deleterious effects on biologic attributes (particularly lipoproteins) that are related to cardiovascular risk; thus, there are some specific benefits of routine low-intensity ambulation and standing in everyday life.

This perspective may have some radical implications for public health. If physical inactivity related to posture (sitting and lying down) exerts its own unique effects on one set of molecular processes while exercise sometimes exerts its effects through other pathways, the current public health guidelines emphasizing that people should exercise 30 minutes a day may be "undone" if the person spends the remaining 15.5 hours in sedentary time. Laboratory findings strongly corroborate with results of epidemiologic studies on the associations of sedentary behavior with metabolic biomarkers and health outcomes. A cornerstone of exercise physiology has been the "specificity principle," which states that the body responds to different physical activity patterns in specific and unique ways [4••]. This evidence points to an exciting new research agenda and to the need for a serious public health debate on how too much sitting might most appropriately be addressed as a significant hazard to health.

Research Directions: Understanding and Influencing Sedentary Behavior

While the evidence for the unique paradigm of inactivity physiology—and the epidemiologic evidence showing that too much sitting is a hazard to human health—is compelling, much remains to be understood scientifically [4••]. New data are needed on the relevant biologic mechanisms in adult humans, gathered through carefully conducted experimental studies, in much the same way that exercise physiology studies have enhanced our understanding of the importance of exercise [4••]. Such laboratory evidence on basic mechanisms, combined with data from prospective studies and controlled intervention trials, will help to strengthen the case for addressing too much sitting as a serious health problem [4••].

Laboratory studies with humans could be carried out with periods of sedentary and active time being experimentally manipulated, with the acute and chronic effects on the biomarkers of metabolic health being assessed. Prospective epidemiologic studies also are needed, ideally with objective measures of exposures (sedentary and physically active time) and outcomes (biomarkers and disease end points). Intervention trials are needed. With a clearer understanding of the unique determinants of sedentary behavior beginning to emerge and relevant conceptual models being developed, the field is now ready for behavioral intervention trials on the feasibility and health outcomes of changing sedentary behaviors [34–37].

Real-world experimental studies might be conducted with large groups of sedentary workers, with "no-treatment" controls who effectively would remain "normally" sedentary. Other studies could examine behavioral-change feasibility issues, including the practicalities of reducing total sedentary time across different domains in which sedentary behaviors are prevalent. For example, the domestic environment presents the opportunity to examine the feasibility of breaking up prolonged periods of watching television and using the computer.

New Directions for Future Guidelines and Public Policy

Given this new understanding of inactivity physiology and the health impacts of sedentary behavior, we would argue that there is now sufficient evidence for health practitioners and public health experts to expand their thinking beyond "purposeful exercise" and give serious consideration to officially recommending reductions in sedentary behaviors. Importantly, this new perspective on the deleterious health consequences of too much sitting should be seen as being additional to, and not as an alternative to, the well-recognized benefits of participation in health-enhancing moderate-intensity physical activity. At the very least, the potential consequences of the success of sedentary-behavior recommendations would be via beneficial increases in overall energy expenditure through higher volumes of light-intensity activity.

Communicating this new perspective to the public and to policy-makers will require some ingenuity and clear messages that it is neither one nor the other but both too little exercise *and* too much sitting (Fig. 1) that need emphasis. Many people will have a poor or limited understanding of what is meant by "sedentary time." Perhaps the most practical definition of sedentary time for the public could be based on postures such as sitting and lying down. People do not know their minute-by-minute energy expenditure or personal metabolic profile throughout the day, but they do know their posture. When people are sedentary and awake, they sometimes lie down but they usually sit. People sit at work. People sit to eat. People sit in social settings. Thus, public health recommendations about physical inactivity may be best placed if they use terminology related to posture: "Be aware of your posture throughout the day: sit less, stand more!"

Conclusions

Coming to grips with the new evidence that we have described will pose challenges. Innovations in public health policies will be needed. Reducing and breaking up the time that adults spend in sedentary behaviors must be seen as a possible public health priority. However, public health innovations tend to progress at a slow pace due to the conservative nature of consensus panels. Also, economic and political pressures can block progress on changes, especially when they involve most of the population, or may run counter to existing social or economic arrangements. As with other hazards such as too much sun exposure (and, we submit, too much sitting), the simple direct message is to warn against excessive exposure to the hazard. Could something as ordinary as sitting in chairs be plausibly grouped among other major health hazards? Are exercise scientists, medical professionals, and public policy-makers moving quickly enough on the basis of available evidence in making official recommendations on limiting sitting time? For the next update of physical activity and health guidelines, we should be asking what should be recommended regarding common physical *inactivity* behaviors such as too much sitting.

Because insidious health hazards are common and affect most of the population, people tend to think "surely it can't be bad for us." Most people now agree that secondhand smoke is to be avoided, but people had no such concerns until recently. Most thought the Marlboro Man was the picture of good health. We would suggest that, in the future, too much sitting might be considered in the same way as have other such insidious environmental and behavioral health hazards.

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Disclosures

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References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1.•• Haskell WL, Lee IM, Pate RR, et al.: **Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association.** *Circulation* 2007, **116:**1081–1093.

Updated physical activity for health guidelines recommend at least 30 minutes of moderate-intensity activity on at least 5 days per week or vigorous-intensity activity for 20 minutes on at least 3 days per week. This minimum recommended amount of activity is in addition to routine light-intensity activities of daily living, such as self-care, casual walking, grocery shopping, or tasks that take less than 10 minutes, such as walking to the parking lot or taking out the trash. Activities of daily life can only count toward the recommendation if the activities are moderate to vigorous and take at least 10 minutes.

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A comprehensive review discussing the several concepts forming the cornerstones for the inactivity physiology paradigm. One theme followed the reasons to believe that even though most people do not exercise regularly, there is still room for the average American "couch potato" to raise his or her risk for the common metabolic and cardiovascular diseases by sitting more.

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This review provides unique insights on sleep not considered elsewhere. It also focuses on the role that lifestyle plays in energy expenditure and health, with an emphasis on the importance of accounting for all components of energy expenditure and not just leisure-time physical activity.

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First population-based survey to objectively measure physical activity. Physical activity and inactivity were assessed with a uniaxial accelerometer in 1114 randomly recruited Swedish adults (age, 45 ± 15 years). Only 1% of Swedish adults accumulated 30 minutes of moderate to vigorous physical activity in at least 10-minute continuous bouts per day. Subjects wore the accelerometer for a mean of about 14 hours per day and spent 55.3% of this time in sedentary states (ie, < 100 counts per minute).

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This is the first objective measure of physical activity (accelerometer) in a representative sample of the US population (n = 6329). Physical activity declined with age (beginning at age 50) and from childhood to adolescence. Only 3.5% of 20- to 59-year-olds and 2.4% of those over 60 years attained the physical activity guidelines of at least 30 minutes of moderate- or greater-intensity activity on 5 of 7 days, accumulated in 10-minute bouts. These prevalence estimates are much lower than the previously reported adherence to recommended physical activity based on self-reports in national surveys (25%–46%).

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This population-based cross-sectional study reported that after adjustment for confounders and physical activity time, the time women spent watching television was positively associated with 2-hour plasma glucose, log fasting insulin, and log homeostasis model assessment of β-cell function (HOMA-%B) and inversely associated with log homeostasis model assessment of insulin sensitivity (HOMA-%S) ($P < 0.05$) but not with fasting plasma glucose. No significant associations were observed for men.

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This cross-sectional study showed that, even in adults who met the physical activity guidelines, significant, detrimental dose-response associations of television viewing time were observed with waist circumference, systolic blood pressure, and 2-hour plasma glucose in men and women and with fasting plasma glucose, triglycerides, and HDL cholesterol in women.

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In this cross-sectional study, sedentary time objectively measured via accelerometers was detrimentally associated with 2-hour plasma glucose, and light-intensity activity time was beneficially associated. These associations were independent of waist circumference and moderate- to vigorous-intensity activity.

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A prospective study of 1422 subjects determined that successful weight maintenance for at least 1 year and at least 13.6 kg of body weight loss was associated with a relatively minimal amount of TV watching. This finding was independent of dietary behaviors and physical activity, primarily based on self-reports of daily walking, stairs climbed, and exercise and recreational activities.

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