Time spent being sedentary:

an emerging risk factor for poor health

SEDENTARY TIME IS AN INDEPENDENT RISK FACTOR FOR DISEASE

Sedentary time (ST), or time being physically inactive, is an important risk factor for all-cause mortality and a range of diseases including cardiovascular disease and cancer.¹ It has a global impact on mortality comparable with tobacco use and obesity.² Moreover, high volumes of intensive activity only attenuate, and do not reduce, the risk posed by ST.³ Replacing ST with light physical activity (PA) leads to improvements in insulin sensitivity and plasma lipid profiles that are not replicated by simply adding bouts of moderate or vigorous physical activity to a sedentary lifestyle,⁴ indicating that being sedentary may trigger a distinct disease process.

The UK has high rates of physical inactivity and performs poorly when compared internationally. Approximately 25% of adults achieve <30 minutes of PA a week, and 80% of children under 15 years are not meeting current PA recommendations in the UK.⁵ The causes are multifactorial, including societal and political drivers. ST is a disease of public health and primary care importance, and primary care clinicians have a key role in educating and guiding individuals at both primary and secondary prevention levels. Unfortunately, recent evidence suggests that there is poor awareness of the availability and use of physical activity guidance in primary care.⁶

Additionally, there is little current understanding as to what constitutes 'being sedentary' and of the mechanisms by which physical activity or inactivity impact on health and disease.

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UNDERSTANDING SEDENTARY TIME

Increasing our understanding of these processes is important for several reasons. First, developing knowledge of how physical inactivity or activity contribute to health and disease teaches us about how the human body interacts with the modern world at a cellular level. PA affects homeostatic regulation in almost all systems of the body. Understanding how this translates into health benefits involves investigating how cellular and organ responses to PA and ST are co-ordinated, communicated, and regulated, and how they converge into adaptations at an organ or system level. Indeed, the US National Institute of Health in 2014 identified that uncovering these mechanisms was of crucial importance and discovery potential for human health.⁷

Second, deciphering the molecular and cellular drivers of ST or PA-induced effects potentially opens the door to personalised exercise medicine in primary care, including biomarkers of activity and targeted, individualised, exercise prescriptions. Finally, a better understanding of the mechanistic biology of ST is crucial to drive informed and structural public health interventions to tackle sedentary behaviours, and to

increase awareness of how sedentary-induced biological processes affect different groups. If sedentary time poses as much of a risk to human health as we think it might, implementing effective interventions will require changes to the way we live and work as a society.

WHAT CONSTITUTES SEDENTARY TIME IS ONLY NOW BECOMING CLEAR

Part of the difficulty in investigating the adverse effects of sedentary time is the heterogeneity of terms used to define it. The term 'sedentary' is used interchangeably with 'physically inactive', 'sitting time', and 'screen or TV time'. Meta-analyses, which included studies measuring inactivity, television-viewing time, and total sitting time, show that ST increases the risk of cardiovascular disease, cardiovascular mortality, and all-cause mortality.¹ A more sensitive approach is characterised by the recent Sedentary Behaviour Research Network (SBRN) consensus, which defines sedentary time as 'any waking behaviour characterised by an energy expenditure ≤ 1.5 metabolic equivalents (METs), while in a sitting, reclining or lying posture'.⁸ Use of consensus definitions and measurements such as this one in research studies will help to consolidate future research into the effects of being sedentary. Moreover, as the adverse consequences of being sedentary are only partially abrogated by even high levels of PA,³ 24-hour activity profiles, consisting of varying degrees of energy expenditure along with sleep and sedentary time, will develop our understanding of this complex concept further.

WHAT DRIVES ST-INDUCED DISEASE?

ST is increasingly seen as an inflammatory condition. Prolonged ST is associated with endothelial cell dysfunction, which may be related to decreased shear stresses on lower limb vasculature.⁹ In a recent study, four days of moderate to vigorous exercise

Box 1. Resources available to guide consultations regarding PA and ST, and to guide people regarding increasing their own PA

Title	Web address	Description
Prescribing Movement	https://www.movingmedicine.ac.uk	Structured guidance on conversations with patients about physical activity
There's Only One You	https://www.nhs.uk/oneyou	Evidence-based guidance and information for the public regarding health improvement
Couch to 5K: week by week	https://www.nhs.uk/live-well/exercise/couch-to-5k-week-by-week	A weekly running programme, including podcasts, aimed at gentle and incremental progress
Start active, stay active: infographics on physical activity	https://www.gov.uk/government/publications/start-active-stay-active-infographics-on-physical-activity	Infographics explaining the guidelines and benefits of physical activity across age ranges and in pregnancy

PA = physical activity; ST = sedentary time.

regimens significantly lowered biomarkers of endothelial dysfunction when compared to prolonged ST alone, but reduction of ST itself did not.⁴ This suggests that the adverse effects of ST cannot be explained by dysfunction of the endothelium alone.

However, reducing ST did have a positive effect on metabolic markers of insulin sensitivity and lipids when compared to the vigorous exercise or sedentary group. Indeed, exercise has both short- and long-term effects on plasma metabolic and gut microbiome profiles when compared to sedentary individuals, and established athletes have a more diverse functional gut microbiome than that observed in low or high BMI sedentary controls.¹⁰

Finally, ST and PA have implications on immune regulation and function. Toll-like receptor-mediated immune cell activation in response to pathogens is increased in active individuals when compared to sedentary controls,¹¹ suggesting that sedentary behaviour weakens the response to pathogenic insults. In contrast, PA is associated with reductions in systemic inflammation, with muscle-derived cytokines (myokines) providing a potential link between exercise-induced muscle activity and immunological and anti-inflammatory function.¹²

FUTURE DIRECTIONS

The biological responses to the spectrum of physical inactivity to activity are integrative and likely encompass vascular, metabolic, and immunological systems. The propensity of our current society to sedentary lifestyles means that uncovering these biological mechanisms is important to drive understanding of how modern lifestyles affect health, and of what measures might reverse this. Moreover, research in this field, particularly with developing metabolomics and proteomics technology, can potentially open the door to personalised exercise recommendations and biomarkers of progress. The impact of this public health problem with profound biological implications provides an avenue for research and solutions which primary care and public health professionals are well-placed to deliver.

PRACTICAL CONSIDERATIONS

Although much is yet unknown regarding the harmful effects of ST, physical activity promotion in primary care can improve uptake,⁶ and there are some key messages that primary health care professionals can use to guide patients. First, prolonged sitting is harmful, but we are not yet at the stage

to issue guideline quantities or thresholds. Advice to break up sitting time and to increase physical activity can only be positive, such as encouraging people to incorporate cycling or walking into a commute, take regular short breaks from their desk, or hold 'walking meetings' while at work. Public Health England infographics⁵ and the Moving Medicine (Prescribing Movement) resource are freely available to guide structured discussion and motivational interviewing, and campaigns, such as There's Only One You and Couch to 5K, can be helpful to guide increases in PA levels (Box 1).

Second, where prolonged ST is unavoidable, the associated increases in mortality can be attenuated by increasing daily physical activity.³

Finally, as primary care practitioners we can lead through example. Simply getting up from our chairs to call our patients from the waiting room is an example of how sitting time can be broken, and of how small interventions can be slotted into busy schedules.

David Salman,

Academic Clinical Fellow in Primary Care, Department of Primary Care & Public Health; MSK Laboratory, Department of Surgery & Cancer, Imperial College London, London, UK.

ADDRESS FOR CORRESPONDENCE

David Salman

Department of Primary Care & Public Health; MSK Laboratory, Department of Surgery and Cancer, Imperial College London, UK

Email: d.salman11@imperial.ac.uk

Mustafa Farooqi,

Academic Foundation Doctor, Department of Primary Care & Public Health, Imperial College London, London.

Alison McGregor,

Professor of Musculoskeletal Biodynamics, MSK Laboratory, Department of Surgery & Cancer, Imperial College London, London.

Azeem Majeed,

Professor of Primary Care, Department of Primary Care & Public Health, Imperial College London, London.

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