



UNIVERSIDADE DE LISBOA
FACULDADE DE MOTRICIDADE
HUMANA



**PATTERNS OF SEDENTARY BEHAVIOR:
INSIGHTS FROM OBSERVATIONAL AND EXPERIMENTAL STUDIES
ON BODY COMPOSITION AND ENERGY EXPENDITURE**

Tese elaborada com vista à obtenção do Grau de Doutor em
Motricidade Humana na especialidade de Atividade Física e Saúde

Tese por compilação de artigos, realizada ao abrigo da alínea a) do nº2 do art.º 31º do
Decreto-Lei nº 230/2009

Orientador: Doutora Analiza Mónica Lopes de Almeida Silva

Júri:

Presidente

Doutor Francisco José Bessone Ferreira Alves

Vogais

Doutor Jorge Augusto Pinto Silva Mota

Doutor Manuel João Cerdeira Coelho e Silva

Doutor Luís Fernando Cordeiro Bettencourt Sardinha

Doutor Sebastien François Martin Chastin

Doutora Maria Isabel Caldas Januário Fragoso

Doutora Analiza Mónica Lopes de Almeida Silva

PEDRO ALEXANDRE BARRACHA DA GUERRA JÚDICE

Maio de 2016

FCT

Fundação para a Ciência e a Tecnologia

MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

The work presented in this dissertation was supported by the Portuguese Foundation for Science and Technology (Grant: SFRH/BD/81403/2011).

Acknowledgements/Agradecimentos

Uma tese de doutoramento é, a meu ver, o culminar de um longo processo de aprendizagem e formação. Mas apesar do seu carácter individual espelha colaborações, trabalho de equipa e espírito de entre-ajuda entre pessoas, sem as quais não teria sido possível. Por tudo isto, gostaria de agradecer em primeiro lugar à minha orientadora, Professora Doutora Analiza Mónica Silva por ter sido sempre um exemplo a seguir enquanto cientista. Também pelo convite inicial para ingressar com ela num programa de doutoramento após a iniciação à investigação aquando do mestrado e, por em momentos difíceis da sua vida pessoal, ter estado sempre presente.

O desenvolvimento deste trabalho não teria sido possível sem o Professor Doutor Luís Bettencourt Sardinha. A sua trajetória científica permite que hoje tenhamos à nossa disposição um dos melhores laboratórios de composição corporal e dispêndio energético do mundo. Também, um agradecimento muito especial às minhas antigas colegas de doutoramento, agora já doutoradas e “mães”, Diana Santos e Catarina Matias, por me terem facultado alguns dos seus ensinamentos e, acima de tudo, à Diana pelo espírito crítico que sempre cultivou. A todos os Professores e colegas do *Exercício e Saúde*, que sempre me acolheram neste núcleo e me transmitiram o gosto pela investigação e acima de tudo, pelo trabalho de equipa.

À Professora Doutora Isabel Fragoso e ao Professor Doutor Pedro Teixeira, por me inspirarem, quando foram meus professores, mas também por pertencerem à minha Comissão de Acompanhamento de Tese e, por isso, terem acompanhado e controlado mais de perto aquilo que foi o meu percurso enquanto aluno de doutoramento.

Um agradecimento muito especial aos meus colegas e amigos João Magalhães e Luís Teixeira, o João que partilhou comigo muitas das madrugadas de avaliações, as viagens a congressos, etc. Ao Luís, por ser a pessoa mais generosa que conheço, e por todas as horas “perdidas” a desenvolver código, aplicações ou a resolver qualquer outro tipo de problema informático.

O trabalho aqui desenvolvido não teria sido possível, sem a colaboração de todos os participantes, que disponibilizaram horas, dias e alguns semanas do seu tempo para estarem connosco. A todos vós o meu agradecimento profundo.

Um agradecimento especial ao meu tio, Professor Doutor Miguel Gaspar, por toda a amizade e ajuda (especialmente na escrita em Inglês) que foi um incentivo. Relativamente ao Inglês, não queria deixar de agradecer também aos meus colegas, aquando da minha estadia na Austrália, pelas longas conversas (umas científicas outras não), que melhoraram em muito o meu Inglês.

À minha mãe, ao meu pai, à minha irmã e à minha namorada. Todo o amor, conforto e incentivo que me deram durante esta fase é insubstituível mas claro, um agradecimento por desde sempre me terem educado e ensinado a ser cada vez melhor e por acreditarem sempre em mim. Sem dúvida que, a honestidade, a simplicidade aliada à procura da excelência, valores que me transmitiram, moldaram todos os momentos e foram um impulso para chegar com sucesso ao fim desta etapa.

A todos muito OBRIGADO!

Abstract

It is recognized that sedentary behavior (SB) has deleterious effects on numerous health outcomes and it appears that physiological mechanisms underlying these harms are distinct from the ones explaining moderate-to-vigorous physical activity (MVPA) benefits. Sedentary behavior represents a large portion of human's life and is increasing with technological development. A new current of opinion supports the idea that the manner SB is accumulated plays an important role. This dissertation presents six research studies conducted under the scope of SB. In the methodological area, the first study highlighted the magnitude of potential errors in estimating SB and its patterns from common alternative methods (accelerometer and heart rate monitor) compared to ActivPAL. This study presented the accelerometer as a valid method at a group level. Two studies (2 and 5) were performed in older adults (the most sedentary group in the population) to test the associations for SB patterns with abdominal obesity using accelerometry. The findings showed positive graded associations for prolonged sedentary bouts with abdominal obesity and showed that those who interrupted SB more frequently were less likely to present abdominal obesity. Therefore, public health recommendations regarding breaking up SB more often are expected to be relevant. The associations between sedentary patterns and abdominal obesity were independent of MVPA in older adults. However, the low MVPA in this group makes it unclear whether this independent relationship still exists if highly active persons are analysed. Study 3 inovates by examining the association of SB with body fatness in highly trained athletes and found SB to predict total fat mass and trunk fat mass, independently of age and weekly training time. Study 4 also brings novelty to this research field by quantifying the metabolic and energetic cost of the transition from sitting to standing and then sitting back down (a break), informing about the modest energetic costs ($0.32 \text{ kcal}\cdot\text{min}^{-1}$). Finally, from a successful multicomponent pilot intervention to reduce and break up SB (study 6), an important behavioral resistance to make more sit/stand transitions despite successfully reducing sitting time ($\sim 1.85 \text{ hours}\cdot\text{day}^{-1}$) was found, which may be relevant to inform future behavioral modification programs. The present work provides observational and experimental evidence on the relation for SB patterns with body composition outcomes and energy regulation that may be relevant for public health interventions.

Key-words: *sedentary behavior; breaks; body composition; energy expenditure; intervention.*

Resumo

É reconhecido, que o comportamento sedentário (CS) tem efeitos nefastos em enúmeros parâmetros de saúde, sendo que os mecanismos fisiológicos subjacentes a esses malefícios são distintos daqueles que explicam os benefícios da actividade física moderada a vigorosa (AFMV). O comportamento sedentário representa uma grande parte da vida do ser humano e está a aumentar a par do desenvolvimento tecnológico. Uma nova corrente de opinião defende a ideia de que a forma como o CS é acumulado poderá ter um papel importante. A presente dissertação inclui seis artigos realizados no âmbito do estudo do CS. Na área metodológica, o primeiro estudo destaca a magnitude dos potenciais erros na estimativa do CS e interrupções deste comportamento através de métodos objectivos de avaliação da AF (acelerómetro e monitor de frequência cardíaca) em comparação com o ActivPAL. Este estudo apresenta o acelerómetro como um método válido ao nível de grupo. Foram realizados dois estudos (2 e 5) em idosos (o grupo mais sedentário da população) para testar as associações dos padrões de acumulação do CS com a obesidade abdominal utilizando acelerometria. Os resultados mostraram associações positivas para períodos contínuos e prolongados em CS com a obesidade abdominal, sendo que quem interrompe o CS com maior frequência está menos propenso a apresentar obesidade abdominal. Portanto, as recomendações de saúde pública para que se interrompa o CS mais frequentemente são esperadas relevantes. As associações encontradas entre os padrões de acumulação do comportamento sedentário e a obesidade abdominal foram independentes da APMV em idosos. No entanto, a baixa APMV neste grupo faz com que não seja claro se essa relação de independência ainda existe, em pessoas altamente treinadas. Assim, o estudo 3 trouxe inovação, ao examinar a associação do CS com a gordura corporal em atletas de alto rendimento. O CS apresentou-se como um preditor da massa gorda total e massa gorda do tronco, independentemente da idade ou do tempo de treino semanal. O estudo 4 também inova este campo de pesquisa por ter, pela primeira vez, quantificado o custo metabólico e energético de uma transição entre o estar sentado para o estar de pé e retorno à posição sentada (um “break”), informando dos custos energéticos modestos ($0.32 \text{ kcal} \cdot \text{min}^{-1}$). Finalmente, de uma intervenção piloto bem sucedida que objetivou a redução e interrupção do CS (estudo 6), encontrou-se uma resistência comportamental para aumentar o número de “breaks” no CS, apesar de uma redução significativa no tempo passado sentado ($1.85 \text{ horas} \cdot \text{dia}^{-1}$), informando assim futuros programas de modificação comportamental. O presente trabalho fornece evidência observacional e experimental sobre a relação entre os padrões de CS com variáveis de

composição corporal e regulação energética que podem ser relevantes para intervenções de saúde pública.

***Palavras chave:** comportamento sedentário; intervalos; composição corporal; dispêndio energético; intervenção.*

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Abbreviations

ADL	activities of daily living
AEE	activity energy expenditure
BMI	body mass index
CCC	concordance correlation coefficient
CONSORT	Consolidated Standards of Reporting Trials
CPM	counts per minute
CV	coefficient of variation
CVD	cardiovascular disease
DIT	diet-induced thermogenesis
DLW	doubly labelled water
DXA	dual energy X-ray absorptiometry
EE	energy expenditure
EMG	electromyography
EI	energy intake
FFM	fat-free mass
FM	fat mass
HDL	high density lipoprotein
HOMA	homeostatic model assessment
HR	heart rate
ICC	intraclass correlation coefficient
IMT	intima-media thickness
IPAQ	international physical activity questionnaire

IS	insulin sensitivity
LIPA	low intensity physical activity
LPL	lipoprotein lipase
MVPA	moderate-to-vigorous physical activity
NEAT	non-exercise activity thermogenesis
NIH	National Institute of Health
NHANES	National Health and Nutrition Examination Survey
OR	odds ratio
PA	physical activity
REE	resting energy expenditure
RER	respiratory exchange ratio
ROI	region of interest
RR	relative risk
SB	sedentary behavior
TBW	total body water
TEE	total energy expenditure
TV	television
WC	waist circumference
WHO	World Health Organization
UK	United Kingdom
USA	United States of America
VO_{2max}	Maximal oxygen consumption

CHAPTER 1

Introduction to the dissertation

It has recently emerged that sedentary behavior – time spent sitting or reclining during waking hours – is independent of a lack of physical activity (PA) as individuals can be sufficiently active, based on the recommended PA guidelines, but also spend the majority of their waking day engaging in sedentary behavior. The culprits of sedentary behavior in both developed and developing nations have included: reduced frequent periods of active human transport (walking, cycling), increased sedentary leisure pursuits at home (television (TV) viewing and computer-based activities) and less manual occupations with increased amounts of seated technical work.

In the past 5 years, an accelerated amount of evidence has been published on the links between sedentary behavior and the leading causes of mortality (cardiovascular disease (CVD), diabetes and some cancers). Much of the evidence has been from cross-sectional and/or prospective observational studies, however, a number of recent interventions have highlighted potential mechanisms in an attempt to demonstrate causality (Buckley et al., 2015). Moreover, a large portion of the investigation on sedentary behavior's associations with health have been relying on subjective methods to estimate sedentary time, therefore obtaining valid and reliable measurements of sedentary behavior remains a research priority because self-reports are prone to recall bias, and sedentary habits do not appear to be well represented by measures of individual behaviors such as TV viewing.

Thus, the first study on this thesis aimed to highlight the magnitude of potential errors in estimating sedentary time and breaks in sedentary time from the common alternative objective methods and a less popular method in the framework of sedentary behavior, but that has proved to be valid for higher PA intensities and that combines accelerometry and heart-rate (HR) information. Because misclassification errors from the commonly used surrogates are potentially large, this raises concerns that alternative methods used in many epidemiological observations may have underestimated the true effects caused by too much sitting (Celis-Morales, Perez-Bravo, Ibañez, Salas, Bailey & Gill, 2012). Additionally, no previous study has examined the validity for this combined method to estimate sedentary behavior and breaks from sedentary time, which explains this study.

A recent 16-year follow-up study (Pulsford, Stamatakis, Britton, Brunner, & Hillsdon, 2015) examined the associations between all-cause mortality and five separate sitting time indicators. The results suggest that mortality risk was not associated with sitting time in this cohort, and that these findings may be due in part to a protective effect of an higher than average energy expenditure (EE) from the habitual active transport associated with London-based employees but also because they relied on self-report measures of sitting (Pulsford et al., 2015). Another explanation is that this longitudinal study only considered the total sitting time and recent evidence suggests that it is prolonged, uninterrupted sitting that may be the most harmful, rather than total sedentary time (Brug & Chinapaw, 2015). In fact, further research is needed to address the uncertainties regarding the true nature of the exposure and the biological mechanisms that underpin previously observed associations between sedentary time and health outcomes.

Evidence that too much sitting is detrimental to health in youth is less convincing and inconsistent (Chinapaw, Proper, Brug, van Mechelen, & Singh, 2011; Tremblay et al., 2011) and this may be due to a lack of quality studies and/or the fact that such effects will emerge only later in life. Worldwide, older adult population has increased substantially and it is estimated to reach approximately 22% of the world's population by 2050 (Scully, 2012). The elderly are the most obese group in the population and conflicting findings have been presented regarding the relation for sedentary behavior with obesity (Foong et al., 2014; Healy, Matthews, Dunstan, Winkler, & Owen, 2011; Larsen et al., 2014; McGuire & Ross, 2012; Saunders et al., 2013; Scheers, Philippaerts, & Lefevre, 2012). Therefore, this thesis add to the scientific knowledge by examining the cross-sectional associations of different sedentary bouts' durations with abdominal obesity risk in older adults (study 2), which are the age group that spends more time in sedentary behavior and less time in moderate-to-vigorous PA (MVPA) (Brug & Chinapaw, 2015).

An animal model-based physiological and mechanistic framework for sedentary behavior introduced the idea that the cardiometabolic risks of prolonged sitting may not be mitigated by frequent muscle contractions throughout the day reinforcing the role of sedentary behavior as a health risk factor, independent of PA (Hamilton, Hamilton, &

Zderic, 2004). However, the idea of independency between sedentary behavior and PA comes from studies including non-athletic populations where MVPA levels may not be as high to significantly neutralize the deleterious effects of spending extended time in sedentary behavior. Therefore, the present thesis presents a novelty since it includes a study (study 3) that aimed to understand if the independent relationship between sedentary behavior and MVPA with adiposity measures is still present, when much higher levels of PA exist (athletes).

Recent evidence from adult studies suggest that patterns of sedentary behavior (i.e., breaks in sedentary time), may be the cornerstone in this sedentary behavior-health pathway but the mechanisms underlying these associations and how body composition and EE are affected by reducing sedentary time or changing its patterns are not well understood. Study 4 aimed to determine the differences in metabolic and energy cost of sitting, standing per se, and the action of get up and return to a seated position (sit/stand transition·min⁻¹) in a laboratorial randomized experiment. By including this methodological approach, it was possible to estimate the additional contribution of performing a sit/stand transition that was needed in the literature, and to understand the energetics of the very common act of transitioning between sitting and standing that takes place about an average of 40-60 times each day (Craft et al., 2012; Smith et al., 2015).

The findings from study 4 showed that, from an energetic point of view, there was a significant gain with the simple act of breaking sedentary time. In line with this, a number of countries have recently issued specific recommendations to reduce the amount of time spent in sedentary behavior by introducing “breaks” as part of their PA guidelines (Buckley et al., 2015). Therefore, study 5 aimed to examine the cross-sectional associations for the number of breaks from sedentary time (assessed with accelerometry) with abdominal obesity in a representative sample of portuguese older adults.

Finally, observational studies do not allow assurance about the direction of the associations or how sedentary time manipulation may benefit human health. Few interventions focused exclusively on reducing sedentary behavior of adults, examining its own effectiveness. Thus, the last study of this thesis (study 6), adds relevant

information on the effectiveness of a short-term multicomponent intervention to reduce and break up sitting time in sedentary overweight/obese adult office workers.

1.1. Dissertation structure

The present dissertation incorporates a compilation of six research articles already published, in peer-review journals with an established ISI Impact Factor. To clarify the framework of these studies this dissertation is organized as follows:

Chapter 2 includes a literature review of the topic, highlighting how the study of sedentary behavior has been built, particularly by looking in detail to the prevalence and temporal trends of these behaviors, including lifespan changes. Secondly, the main (observational and experimental) findings on the relationships between sedentary behavior and its patterns with mortality and morbidity outcomes, along with the main gaps that currently exist regarding the study of body composition and EE were presented. In addition, based on this organization, the current literature regarding the effectiveness of sedentary behavior-related interventions was reviewed. Finally, this section includes a methodological approach to the sedentary behavior research area, by summarizing the widely used methods to measure and estimate sedentary variables and finishes by highlighting the main research goals of the dissertation.

A detailed review of the methodology used in the present dissertation is showed in **Chapter 3**. Apart from the fact that in the six studies a methods section was included, it was found relevant the inclusion of a methodology chapter. In this chapter a more detailed explanation of the methods used through the studies will be provided, specifically if a general description was provided.

Chapters 4 to 9 correspond to the six studies that were conducted to answer the research goals that are stated in Chapter 2.

Chapter 10 corresponds to a general discussion that provides a summary and integrated discussion of the main findings obtained within the six studies of this dissertation. Practical applications, taking in consideration the main findings were also pointed out in the end of this section.

The bibliographic references were presented by the end of each section adopting the American Psychological Association style (APA).

1.2. List of articles and conference abstracts as first author

The investigation carried out as part of the present doctoral research program resulted in the following publications, and communications (oral/poster) as first author:

1.2.1. PEER-REVIEWED ARTICLES PUBLISHED THAT ARE RELATED TO THE DISSERTATION:

- Júdice, P. B., Santos, D. A., Hamilton, M. T., Sardinha, L. B., & Silva, A. M. (2015). Validity of GT3X and Actiheart to estimate sedentary time and breaks using ActivPAL as the reference in free-living conditions. *Gait Posture*, 41(4), 917-922. doi: 10.1016/j.gaitpost.2015.03.326
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CHAPTER 2

Literature Review

2.1. Overview

The human body, with approximately 640 muscles and 206 bones, is made to move. However, hi-tech advances in civilized societies within the last 50 years have created an environment that encourages sedentary behavior. Human intelligence and concurrent development created a scenario where the majority of the waking day is spent sitting in a chair watching TV, working at a desk, playing video games, ordering take-out and delivery, reading, shopping, banking, eating a meal at a table, or navigating the stock market (Owen, Salmon, Koohsari, Turrell, & Giles-Corti, 2014). Technology's sedentary seduction is still growing and the pinnacle for sedentary behavior may have not been reached (Owen, 2012).

Some of the first findings of the harmful effects of too much sitting actually had early research roots in the 1950s, when scientists showed that men in physically active jobs had less coronary artery disease during middle-age than men in physically inactive jobs (Morris & Crawford, 1950). Regular PA positively influences most physiological processes in the human body. Inversely, physical inactivity has been associated with obesity (Vandelanotte, Sugiyama, Gardiner, & Owen, 2009), metabolic disorders (Healy, Dunstan, et al., 2008; Hu, Li, Colditz, Willett, & Manson, 2003), and all-cause mortality (Patel et al., 2010; van der Ploeg, Chey, Korda, Banks, & Bauman, 2012).

There is now rapidly emerging evidence on the adverse associations for sedentary behavior with biomarkers of health and health outcomes (Henson, Yates, Biddle, et al., 2013; Loprinzi, 2013). These biomarkers and health outcomes include waist circumference (WC), body mass index (BMI), high-density lipoprotein cholesterol (HDL), C-reactive protein, triacylglycerols, and insulin (Henson, Yates, Biddle, et al., 2013; Loprinzi, 2013). A sedentary lifestyle also has a direct effect on inactivity-induced factors including deep venous thrombosis and poor lipid metabolism (Hamilton, Hamilton, & Zderic, 2007). Thus, sedentary behavior has emerged as a new risk factor for health (Katzmarzyk, 2010; Owen, 2012) with several systematic reviews on the relationship between sedentary behavior and health conditions been published, showing a key role on diseases such as CVD, type 2 diabetes, cancer, obesity, metabolic syndrome (Grontved & Hu, 2011; Lynch, 2010; Rhodes, Mark, & Temmel, 2012;

Thorp, Owen, Neuhaus, & Dunstan, 2011; Wilmot et al., 2012), mental disorders, and musculoskeletal diseases (Rezende, Rey-López, Matsudo, & Luiz, 2014).

Sedentary behavior's epidemiological research is accumulating in the last decade and includes all the studies that examined the relationships for overall sedentary time and specific sedentary behaviors (e.g., screen-time, sitting time) with health parameters, diseases, and mortality rates. However, information have been building mostly from observational cross-sectional studies, some longitudinal findings, but few experimental investigations (Buckley et al., 2015). Therefore, more experimental studies that manipulate sedentary behavior and its specific forms, to examine the correspondent effects on health indicators and disease's incidence are needed to explore the direction of causality and the feasibility of these interventions' strategies in real life settings (Buckley et al., 2015).

A secondary research area relates to the sedentary behavior's assessment and methodological issues related to the research and validation of new subjective and objective methods for the assessment of overall sedentary time and its patterns, as well as specific domains or behaviors such as sitting time or screen time (Atkin & Gorely, 2012). These research domains will be the basis for this chapter: first, sedentary behavior's prevalence and temporal trends. Secondly, the most important observational and experimental findings in sedentary behavior research area and its application nuances will be gathered. Finally, the most commonly used methods for sedentary behavior's assessment and its limitations will be presented.

2.2. Sedentary behavior

2.2.1. DEFINITION

The word sedentary comes from the original Latin meaning of *sedere* (sit). Sedentary behaviors are those pursuits undertaken while awake that involve sitting or reclining and that result in little or no PA energy expenditure (PAEE) – typically 1 to 1.5 times the resting metabolic rate. Common sedentary behaviors include watching TV, using a computer, or driving (Sedentary Behavior Research Network, 2012).

Not surprisingly, in recent years there has been a growing body of opinion that sedentary behavior should be considered a distinct construct from low intensity PA (LIPA) and MVPA due to independent health associations. So as not to be confused with physical inactivity, (lack of MVPA) (Sedentary Behaviour Research, 2012). The time adults spend sedentary is relatively independent from their time spent in MVPA. For example, an individual may frequently participate in MVPA but still spend substantial amounts of their time in sedentary behavior (Craft et al., 2012). Studies of temporal patterning of sedentary behavior demonstrate that MVPA and sedentary behaviors compete for time at limited periods during the day, and show that over 24 hours, there is time for both (Biddle, Marshall, Gorely, & Cameron, 2009). In contrast, sedentary behavior is strongly and inversely associated with time spent in LIPA, such as standing and light ambulation (Healy, Wijndaele, et al., 2008). Therefore strategies to reduce sedentary behavior must be centered on replacing these behaviors with LIPA activities.

2.2.2. THE INACTIVITY PHYSIOLOGY PARADIGM AND POTENTIAL PHYSIOLOGICAL MECHANISMS

There is still some confusion in the literature regarding the concept of physical inactivity. It is commonly used to either describe those who are performing insufficient amounts of MVPA and by the other hand the time spent in sedentary activities, which are two distinct concepts. The word sedentary has been more frequently applied to mean lack of exercise instead of the original meaning of (sit). Hamilton and colleagues have moved toward using the word “inactivity” and have coined the term inactivity physiology to minimize confusion and emphasize the distinctive characteristics between sitting too much or exercising too little (Hamilton, Hamilton, & Zderic, 2004).

This research has given rise to the “inactivity physiology paradigm,” or that “sitting too much is not the same as lack of exercise, and as such, has its own unique metabolic consequences” such as decreased lipoprotein lipase (LPL) activity in skeletal muscles in the legs (Hamilton et al., 2007) and the expression of various genes linked to inflammatory responses (Latouche et al., 2013). In fact, Hamilton et al. (2007) stated that “some of the specific cellular and molecular processes explaining the responses

during inactivity physiology versus exercise physiology are qualitatively different from each other” and that “signals harming the human body during too much inactivity are not always the same signals boosting health above normal with a bolus of exercise several times per week”.

These authors showed that one day of inactivity had a several-fold greater change in LPL activity than the exercise training response (Hamilton et al., 2007). Also, the effects of inactivity on LPL suppression were greatest in the most red oxidative muscle regions while in contrast, exercise by running the same type of rats increased LPL gene expression and LPL activity in the most white glycolytic skeletal muscles and not in oxidative muscles (Hamilton et al., 2007). Furthermore, the magnitude of LPL suppression during inactivity after reducing standing/low-intensity ambulation was much greater than the increase after adding exercise on top of normal non-exercise physical activity. This investigation support the specificity principle because the cellular responses to inactivity and exercise are qualitatively different (Hamilton et al., 2007).

Although not without controversy regarding the mechanisms, many studies in humans and animals have documented a strong and positive relationship between LPL and plasma triglyceride uptake (Bey & Hamilton, 2003; Herd, Kiens, Boobis, & Hardman, 2001) and HDL levels (Ahmadzadeh & Azizi, 2014; Bey & Hamilton, 2003). Compelling evidence has shown that the loss of LPL activity at the vascular endothelium impairs optimal tissue-specific uptake of lipoprotein-derived fatty acids and may contribute to the risks frequently observed during metabolic diseases such as obesity, metabolic syndrome, type 2 diabetes, and coronary heart disease (Hamilton et al., 2004). LPL may also have some positive effects on hypertension (Stump, Hamilton, & Sowers, 2006), preventing diet-induced adiposity, and insulin resistance have also been reported but not in all models (Hamilton et al., 2004; Jensen et al., 1997).

Even small reductions in LPL activity have been reported to increase five times the odds ratio for death and greater coronary heart disease in human studies over healthy controls (Wittrup, Tybjaerg-Hansen, & Nordestgaard, 1999) and studies experimentally raising LPL activity provide evidence for less diet-induced atherosclerosis in transgenic rabbits (Fan et al., 2001), less diabetic hyperlipidemia

(Myers et al., 2002), and less dietary-induced adiposity in transgenic mice overexpressing muscle-specific LPL activity (Jensen et al., 1997).

Along with LPL, pathway analysis indicated that the main biological functions affected by sitting time were related to small-molecule biochemistry, cellular development, growth and proliferation, and carbohydrate metabolism (Latouche et al., 2013). Interestingly, relative to prolonged sitting, activity bouts (seated with 2-min bouts of light or moderate intensity treadmill walking every 20 min) increased expression of nicotamide N-methyltransferase, which modulates anti-inflammatory and anti-oxidative pathways and triglyceride metabolism (Latouche et al., 2013). Activity bouts also altered expression of 10 genes involved in carbohydrate metabolism, including increased expression of dynein light chain, which may regulate translocation of the GLUT-4 glucose transporter and facilitate glucose's entrance to the cells (Latouche et al., 2013). Finally, these are some of the mechanisms that may explain sedentary behaviors' associations with several health indicators and chronic conditions, justifying the importance of considering sedentary behavior as an independent health risk factor from MVPA.

2.2.3. THE IMPORTANCE OF STUDYING SEDENTARY BEHAVIOR

Current PA guidelines for adults are focused on increasing MVPA levels but data from the United States of America (USA) and Portugal indicate that only about 5% of adults meet these recommendations (Baptista et al., 2012; Troiano et al., 2008). Therefore, it is clear that there are some natural barriers that difficult the accomplishment of actual MVPA recommendations. Sedentary behavior is becoming an important component of the exercise and health equation, and non-exercise activity thermogenesis (NEAT) a widespread concept on recent investigation (Levine, Vander Weg, Hill, & Klesges, 2006). NEAT is the EE for everything except sleeping, eating or sports-like exercise activities (Levine et al., 2006). Two people with the same weight can have markedly variable activity levels, it is not surprising that NEAT varies substantially between people by up to 2000 kcal-day⁻¹ and there is a high inverse relation between NEAT and time spent in sedentary behaviors (Levine, 2007).

In terms of energy balance it is well known that walking for 30 min·day⁻¹ spends a significant amount of energy and is associated with better health but if a person reduces sedentary time by 2 hours·day⁻¹ by shifting it for LIPA, the same amount of energy could be expended as they would during a 30 min walk. So it is important to find out if health benefits start to add up along with this type of activities that contribute to NEAT. One of the most striking findings from a well executed cohort study (Matthews et al., 2012) with an 8.5 years follow up was that those who reported participating in more than 7 h·week⁻¹ of MVPA during leisure time but who also watched TV \geq 7 hours·day⁻¹ had 50% greater risk of death from all causes and twice the risk of death from CVD relative to those who undertook the same amount of MVPA but watched TV < 1 hour·day⁻¹ (Matthews et al., 2012).

Therefore, high levels of MVPA seemed not to fully mitigate health risk associated with prolonged sedentary behavior (Matthews et al., 2012). Regardless, this idea of independency between sedentary behavior and MVPA is still inconclusive (Bakrania et al., 2016; Kwon, Burns, Levy, & Janz, 2013) and has been based on research including children, adults, and older adults with typical levels of exercise. Thus, extending these findings to a highly trained population that performs significantly greater levels of MVPA would be fundamental.

Additionally, based on the evidence that prolonged sedentary behavior is detrimental to health, a new question started to rise. Is it only important to reduce total sedentary time or does the number of interruptions in sedentary time play an important role? Intriguingly, adults whose sedentary time is mostly uninterrupted (prolonged unbroken sitting) have a poorer cardiometabolic health profile compared to those who interrupt or had more frequent breaks (Healy, Dunstan, et al., 2008; Henson et al., 2015). However, human studies focusing on the acute effects of breaking up sedentary time are scarce and have not focused on the energetic implications with possible repercussions on energy regulation and concurrent body composition changes. Therefore, stronger evidence is needed to inform specific recommendations on sitting within future global public health PA guidelines (Thomas et al., 2012).

Since people spend the majority of their waking day in sedentary pursuits (more than 50%), the above question is two-fold important once it displays that, on one hand it

might be difficult for people to reduce the great amounts of sedentary behavior they perform during the day, but on the other hand, it might be easier to introduce active breaks in their real life routines, which could be a more ecological approach to this problem. Regardless, more evidence on the relationship between sedentary time and its patterns with risk biomarkers and health conditions is required, specially in the elderly, the age group that consistently presents the highest percentage of time in sedentary behavior and concomitantly an understudied group in this issue of sedentary patterns.

Additionally, specific and clear findings on the effectiveness to reduce and interrupt the great amount of these deleterious behaviors in free-living conditions and considering different domains (e.g., leisure time, work) have been poorly explored. To be able to inform specific recommendations and public health guidelines it is of great importance to comprehend in what extent people are able to change their sedentary habits. Thus, more interventional studies that focus on reducing and breaking up sedentary time are desired.

2.2.4. PREVALENCE OF SEDENTARY BEHAVIORS AND TEMPORAL TRENDS

Sedentary behavior is by far the most prevalent behavior in human's waking day and it is common for people to spend at least one half of their waking day in sedentary behavior (Baptista et al., 2012; Clark, Healy, et al., 2011). According to the National Health and Nutrition Examination Survey (NHANES) data, USA adults are sedentary approximately 57–58% of the day (Church et al., 2011). Similarly, a study performed in Europe, objectively measured sedentary time among 140 adult women and found that time spent in sedentary pursuits was 530 min·day⁻¹, which also corresponded to 55% of the day (Curry & Thompson, 2014). In Portugal, the amount of time adults spent in sedentary behavior is similar to the former studies, with older adults attaining 70% (9 to 10 h·day⁻¹) of their waking hours in sedentary time (Baptista et al., 2012).

Over the last 50 years daily occupation-related EE has decreased by more than 100 calories with total sedentary private jobs (< 2 METs) increasing approximately 10% from 1960 to 2010 (Church et al., 2011). For the non-occupational domain, a population representative data from Australia (Chau, Merom, et al., 2012), involving respondents aged 20 years and over, N=5851 (1992), N=6419 (1997) and N=5505 (2006) found the

same trend, with total non-occupational sedentary time being slightly lower in 1997 than in 2006 (Chau, Merom, et al., 2012). Compared with 1997, adults spent more time in sedentary transport (6.7 min) and sedentary education (6.3 min) in 2006 while household and leisure sedentary time remained stable (Chau, Merom, et al., 2012). The time engaged in different types of leisure sedentary activities changed between 1997 and 2006: leisure time computer use increased, while other leisure time sedentary behaviors (e.g., reading, listening to music, hobbies and crafts) showed small concurrent reductions (Chau, Merom, et al., 2012). In 1992, leisure screen time was lower than in 2006: TV-viewing (-24.2 min) and computer use (-35.3 min) (Chau, Merom, et al., 2012).

Sitting time, more specifically TV viewing in particular is one of the most prevalent sedentary behaviors occupying 40% of daily leisure time in some European countries and about 50% in Australia and in the USA (Craft et al., 2012). A longitudinal study (van der Ploeg et al., 2013) aimed to determine the modification in non-occupational sedentary behavior in Dutch adult population between 1975 and 2005 and found that most non-occupational sedentary behavior was during leisure time, and the proportion of sedentary leisure time that comes from screen time increased from 26% in 1975 to 43% in 2005, and sedentary transport increased by 2 hours·week⁻¹ within the same period of time (van der Ploeg et al., 2013).

In summary, these findings suggest that sedentary behavior occupies more than half of a person's waking day and it has been increasing alongside the technological development (van der Ploeg et al., 2013). From these studies, it can also be concluded that not only the work related sedentary behavior has been increasing but also the leisure time sedentary time attributed to screen time and inactive transport (van der Ploeg et al., 2013). Thus, these findings reinforce the idea that leisure time must be considered when targeting sedentary behavior reductions and efforts must be on decreasing screen-time (Craft et al., 2012; van der Ploeg et al., 2013).

However, most of these longitudinal studies used subjective measures of sedentary behavior and few preferred more valid methods such as objective measures of sedentary time. There is evidence that subjective measures underestimate sedentary behavior (Matton et al., 2007; Healy et al., 2011). In fact, in one of the larger studies to

date using inclinometry (ActivPAL device in 91 adult women), the average weekly sitting time was 64 hours and the average weekly standing time (non-stepping) was 27 hours (Craft et al., 2012), meaning that the time spent in sedentary behavior is more than twice the time spent in LIPA activities, which shows that the lower amounts of sedentary time found in previous studies, using subjective methods, may have weakened the real associations with health outcomes.

Most of these findings come from the USA or Australia and this must be addressed as a limitation. In fact, a recent study that examined the trends in adult sitting time, between 2002 and 2013 across 27 European countries (Milton, Gale, Stamatakis, & Bauman, 2015) found that time spent in sedentary behavior may not be increasing in the European region, and prolonged sitting may, in fact be decreasing (Milton et al., 2015). This study considered three categories; 'low' (0 to 4h30 min), 'middle' (4h31 min to 7h30 min), and 'high' levels of sitting (>7h30 min) and found that the prevalence of 'high sitting' decreased steadily from 23.1% (95% CI=22.2-24.1) in 2002 to 21.8% (95% CI=20.8-22.8) in 2005, and 17.8% (95% CI=16.9-18.7) in 2013 (Milton et al., 2015). Although important, these findings result from a survey and therefore rely on subjective measures of sedentary behavior which may explain the contradicting results (Milton et al., 2015).

Nonetheless of the positive trend found for the European countries, there is still a great percentage (18%) of people who sit more than 7h30 min per day underscoring the importance of future interventions to reduce and break up sitting time (Milton et al., 2015). In fact, a recent study performed in France (Saidj et al., 2015) included 35,444 working adults and found that on workdays, adults spent a mean (SD) of 4.17 (3.07) h/day in work sitting, 1.10 (1.69) h/day in transport sitting, 2.19 (1.62) h/day in leisure time sitting, 1.53 (1.24) h/day viewing TV/DVDs, 2.19 (2.62) h/day on other screen time, and 0.97 (1.49) on non-screen time. On non-workdays, this was 0.85 (1.53) h/day in transport sitting, 3.19 (2.05) h/day in leisure time sitting, 2.24 (1.76) h/day viewing TV/DVDs, 1.85 (1.74) h/day on other screen time, and 1.30 (1.35) on non-screen time (Saidj et al., 2015).

2.2.5. LIFESPAN TRENDS

Childhood-adolescence & adolescence-adulthood

During childhood, learning means spending lots of time at school where children are indebted to be seated during the entire classes. An investigation found that 97% of traditional classes' time is spent sitting (Cardon, De Clercq, De Bourdeaudhuij, & Breithecker, 2004) which represents approximately 5 hours of sitting. In Portugal, 9-11 years-old children spent $\sim 510 \text{ min}\cdot\text{day}^{-1}$ of objectively measured sedentary time developing along adolescence (Baptista et al., 2012). This means that approximately 8.5 hours of the awaking day is spent sitting or reclining (Baptista et al., 2012).

Adolescence is a period involving dramatic physiological and psychological changes; however, the transition to adulthood implies for many people to leave their family homes and important lifestyle changes might also occur. To the authors' best knowledge, the European Youth Heart Study (EYHS) was one of the first cohorts using accelerometry at population level to objectively measure sedentary time in children and adolescents (Ortega et al., 2013). Participants from the original cohort participated in a second examination 6 to 10 years later. This cohort study found that MVPA decreased from childhood to adolescence and from adolescence to young adulthood; whereas sedentary time increased only from childhood to adolescence, with no substantial change from adolescence to young adulthood (Ortega et al., 2013). Nonetheless, the average daily sedentary time for the late adolescence early adulthood was about 9 hours $\cdot\text{day}^{-1}$. In addition, the decline in MVPA and increase in sedentary time is significantly greater in boys than girls (Ortega et al., 2013).

Finally, these longitudinal findings highlighted that the magnitude of change observed in sedentary time was 3–6 times larger than the change observed in MVPA (Ortega et al., 2013). Accordingly, another longitudinal study including British children from 12 to 16 years of age reported an increase in objectively measured sedentary time from childhood to adolescence and added that sedentary behavior increased with age, at the expense of LIPA (Mitchell et al., 2012). This is important, once it emphasizes that sedentary behavior increases independently of MVPA reductions and therefore these two domains must be perceived separately, with specific strategies for each one.

Furthermore, it seems that the increase in sedentary behavior lasting ≥ 30 min in duration contributed greatly to the increase in total sedentary behavior (Mitchell et al., 2012), which makes this trend even more perturbing, as it is prolonged sedentary behavior that seems to be more associated with reduced health (Mitchell et al., 2012).

Adulthood-elderly

It was previously presented that sedentary behavior increases from childhood to adolescence remaining relatively constant from adolescence to young adulthood (Ortega et al., 2013). However, among adulthood, there is evidence of an increase in the amount of time spent sedentary (Hagstromer, Kwak, Oja, & Sjostrom, 2014). A prospective study in a representative sample of Swedish adults investigated changes in sedentary time assessed with accelerometry over six years and found a significant increase of $26 \text{ min}\cdot\text{day}^{-1}$ (Hagstromer et al., 2014).

Accordingly, two population-based surveys of 25-79-year-old inhabitants were conducted in Denmark in 2007 (N=69.800, response rate 52.3%) and 2010 (N=77.517, response rate 54.8%), and information on sedentary behavior was obtained from self-report questionnaire (Aadahl et al., 2013). The main conclusions were that in 2007, the entire survey population reported a mean daily sleeping duration of 7.4 hours, leisure sitting time of $3.4 \text{ hours}\cdot\text{day}^{-1}$, occupational sitting of $4.4 \text{ hours}\cdot\text{day}^{-1}$ and in 2010, duration of sleep was unaltered, sedentary leisure time and sedentary work time had increased by 12.6 min and $13.2 \text{ min}\cdot\text{day}^{-1}$, respectively, which represents a $26 \text{ min}\cdot\text{day}^{-1}$ increase in sedentary pursuits in only 3 years (Aadahl et al., 2013).

Generally, sedentary behavior increases across lifespan and older adults are the most sedentary segment of society – spending about 70% (9 to 10 $\text{hours}\cdot\text{day}^{-1}$) of their waking hours in sedentary time (Baptista et al., 2012; Evenson, Buchner, & Morland, 2012; Healy, Clark, et al., 2011) or even more (Harvey, Chastin, & Skelton, 2013) and the least amount of time in MVPA (Baptista et al., 2012). In addition, it has been reported that adults older than 60 years can reach approximately 80% of their awake time in sedentary activities which represents 8 to 12 hours per day (Davis et al., 2011; Matthews et al., 2012). Findings from the USA and Europe reported that objectively measured sedentary time was higher in those who were older than 50 years (Matthews

et al., 2012) and 65 years (Davis et al., 2011), respectively. Similarly, (Hallal et al., 2012) conducted a global assessment in more than 60 countries and found that the elderly had the highest prevalence of reporting a minimum of 4 hours of daily sitting time, which according to a population-based study can be due to the transition to retirement (Barnett, van Sluijs, Ogilvie, & Wareham, 2014).

The elderly population

Worldwide, older adult population has increased substantially, and it is estimated to reach approximately 22% of the world's population by 2050 (Scully, 2012). The risk of non-communicable diseases increases with age, and the World Health Organization (WHO) has created many recommendations for behavior change to reduce the burden of non-communicable diseases and disabilities among the elderly. It is well established that PA plays a key role in the prevention of diseases such as CVD, cancer, type 2 diabetes, accidental falls, obesity, metabolic syndrome (Edwardson et al., 2012; Gennuso, Gangnon, Thraen-Borowski, & Colbert, 2015; Kim, Tanabe, Yokoyama, Zempo, & Kuno, 2013; Saleh & Janssen, 2014; Uemura et al., 2013; Wagner et al., 2012), mental disorders, and musculoskeletal diseases (Rezende et al., 2014). However, in the last decade sedentary behavior has emerged as a new risk factor for health (Katzmarzyk, 2010; Owen, 2012).

Older adults who are less sedentary tend to age more successfully and report better quality of life (Balboa-Castillo, Leon-Munoz, Graciani, Rodriguez-Artalejo, & Guallar-Castillon, 2011; Dogra & Stathokostas, 2012). Also, there has been shown to be an association between older adults' self-reported sedentary behavior and negative health outcomes such as BMI, WC, fat mass, cholesterol ratio, metabolic syndrome, diabetes (Larsen, Allison, et al., 2014; Rezende et al., 2014; Stamatakis, Davis, Stathi, & Hamer, 2012), an increased risk of sarcopenia (Gianoudis, Bailey, & Daly, 2015), and increased risk of all-cause mortality (Rezende et al., 2014). Additionally, similar associations were observed for TV time while non-TV self-reported sedentary behavior showed associations only with diabetes (Stamatakis, Davis, et al., 2012). In fact, time watching TV, is the predominant sedentary behavior and has been the specific type of sedentary behavior that presents the most consistent associations with health

parameters, independent of meeting PA guidelines (Inoue et al., 2012; Rezende et al., 2014; Stamatakis, Davis, et al., 2012).

However, most of the findings within sedentary behavior research area in older adults result from studies using subjective measures of sedentary behavior with few studies considering objective measures of sedentary behavior. Though, contradicting findings exist regarding the associations for objectively measured sedentary behavior with health parameters (Bann et al., 2015; Foong et al., 2014; Stamatakis, Davis, et al., 2012). In opposition to what was verified for the self-reported sedentary behavior, accelerometry derived sedentary time was only associated with WC, and no associations for BMI, cholesterol ratio, metabolic syndrome or diabetes were found in older adults (Stamatakis, Davis, et al., 2012). Similarly, another study using accelerometry-derived sedentary behavior found no associations with adiposity after adjusting for time spent at other PA, in older adults (Foong et al., 2014).

In contrast, a more recent study considering a large sample of older adults found that greater time spent in LIPA and lower sedentary time assessed by accelerometry were associated with lower BMI (Bann et al., 2015). Therefore, these findings are consistent with the hypothesis that replacing sedentary activities with LIPA could lead to lower BMI levels and obesity prevalence among the population of older adults (Bann et al., 2015). However, longitudinal and experimental studies are needed to strengthen causal inferences (Bann et al., 2015). Also, these contradicting findings indicate that more evidence for the associations between objectively measured sedentary behavior with health outcomes, specifically obesity measures, are needed in older adults (Bann et al., 2015).

The determinants that explain why older people are the most sedentary group in the population were investigated in a recent study (Chastin, Fitzpatrick, Andrews, & DiCroce, 2014) and older women expressed that their sedentary behavior is mostly determined by pain which acts as an incentive to sit (Chastin et al., 2014). Lack of energy in the afternoon, pressure from direct social circle to sit and rest, societal and environmental typecasting that older adult are meant to sit, and lack of environmental facilities to allow activity pacing were some other highlighted factors that older adults consider determinants of their sedentary behavior (Chastin et al., 2014). Some are

identical to those affecting PA (self-efficacy, functional limitations, ageist stereotyping) but some appear specific to sedentary behavior (locus of control, pain) and should be further investigated in future interventions (Chastin et al., 2014).

Although population-based cross-sectional studies have reported interesting information about sedentary levels in different age groups, only longitudinal studies using objective methods are able to accurately describe changes in PA and sedentary time across lifespan periods, but these type of studies are lacking. Furthermore, the higher prevalence of sedentary behavior in the elderly justifies more research on this population group. Specially, examining older adults' sedentary patterns in more detail is a research priority.

Only recently, studies have investigated the associations for sedentary patterns with health outcomes in older adults (Chen et al., 2015; Davis et al., 2014; Gennuso, Thraen-Borowski, Gangnon, & Colbert, 2015; Gianoudis et al., 2015; Sardinha, Ekelund, et al., 2015; Sardinha, Santos, Silva, Baptista, & Owen, 2015). The majority of these studies found interruptions in sedentary time to improve physical function (Chen et al., 2015; Davis et al., 2014; Gennuso, Thraen-Borowski, et al., 2015; Gianoudis et al., 2015; Sardinha, Ekelund, et al., 2015; Sardinha, Santos, et al., 2015) and metabolic syndrome (Bankoski et al., 2011) of older adults.

However, older adults are the age group that has the highest prevalence of obesity (Sardinha et al., 2012) and to the authors knowledge, only one study examined the associations for sedentary patterns with obesity measures in older adults (Chastin, Ferriolli, Stephens, Fearon, & Greig, 2012), suggesting an association for a more fragmented sedentary behavior with lower total body fat (Chastin et al., 2012). Though, more investigation is needed and sedentary patterns analysis must go beyond the simple breaking pattern (number of breaks from sedentary time) and examine how long sedentary time must be interrupted before it exacerbates obesity (e.g., studying sedentary bouts of distinct durations). Also, it is important to consider specific measures of obesity (e.g., abdominal obesity) that could be more suggestive of poor health in older adults (Sardinha et al., 2012).

2.2.6. PATTERNS OF SEDENTARY TIME

The FITT principle that comes from the exercise physiology area, allows to prescribe a certain dose of PA based on frequency, intensity, time, and type. Tremblay and colleagues in 2010 suggested that this principle can be transposed to the sedentary behavior research area, as SITT. **S**edentary frequency would be the number of bouts in sedentary time; **I**nterruptions as the breaks in sedentary time; **T**ime, as the total duration of bouts and time spent in these bouts; and finally the **T**ype of sitting behavior that people engage (watching TV, working on the computer) (Tremblay et al., 2010).

Sedentary patterns reflect the manner as sedentary behavior is broken or accumulated and is generally represented by breaks in sedentary time considered in terms of how frequently sedentary time is interrupted with LIPA or MVPA activity bouts (Lord et al., 2011). For example, two adults may exhibit the same total amount of sedentary time but have different accumulation or breaking patterns during the day (Lord et al., 2011). Sedentary patterns may also include the analysis of specific sedentary periods of different durations (eg., non-prolonged or prolonged bouts).

Increasing attention is paid to the potential health effects of people's sedentary bouts and breaks, rather than total sedentary time (Diaz et al., 2015). Therefore, it is important to understand the patterns of accumulation and interruption of sedentary time and also if there is any weekly-trend in real-life settings in order to be more assertive when planning interventions and strategies to reduce sedentary time.

The longitudinal Iowa Bone Development study collected accelerometry data at approximately 5, 8, 11, 13, and 15 years of age and aimed to describe the change in the frequency of sedentary breaks during a 10-year period (Kwon, Burns, Levy, & Janz, 2012). The frequency of sedentary breaks decreased by more than 200 times per day and both boys and girls showed significantly fewer breaks on weekdays from morning to 3:00 p.m. than on weekends for the same period (Kwon et al., 2012). The frequency of sedentary breaks was slightly higher among boys than among girls (Kwon et al., 2012). Therefore, breaks in sedentary time notably decreased during childhood and adolescence. During school hours, boys and girls have fewer breaks in sedentary time

than during any other period of weekday or weekend day, leading to more prolonged sedentary behavior (Kwon et al., 2012).

A recent investigation (Diaz et al., 2015) studied 8096 participants from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study and aimed to examine the patterns of objectively measured sedentary behavior in a national cohort of middle-aged and older adults (Diaz et al., 2015). This study concluded that the number of sedentary bouts ≥ 20 , ≥ 30 , ≥ 60 , and ≥ 90 min were 8.8 ± 2.3 , 5.5 ± 1.9 , 1.9 ± 1.1 , and 0.8 ± 0.7 bouts \cdot day $^{-1}$, respectively and that accounted for 60%, 48%, 26%, and 14.2% of total sedentary time, respectively (Diaz et al., 2015). These findings are important once they showed that a large proportion of total sedentary time was accumulated in prolonged uninterrupted bouts of sedentary time. In fact, almost one half of total sedentary time was accumulated in sedentary bouts longer than 30 min (Diaz et al., 2015).

A study including office workers (Parry & Straker, 2013) found that sustained sedentary time (bouts > 30 min) was proportionally greater on work days compared to non-work days, and also during work hours compared to non-work hours (Parry & Straker, 2013). Weekly work time sustained sedentary time (bouts > 30 min) was 18.2 hours \cdot week $^{-1}$ making work time account for 56.7% of total weekly sustained sedentary time (32.1 hours \cdot week $^{-1}$). Prolonged sustained sedentary bouts (sedentary bouts > 60 min) accounted for 12.7 hours over a whole week (Parry & Straker, 2013). Also, brief periods of LIPA were proportionally less on work days compared to non-work days, and also during work hours compared to non-work hours (Parry & Straker, 2013).

Extending these findings, a group of 197 overweight/obese adult women spent 64.1% of the day in sedentary pursuits, engaging in 10.5 daily bouts of sedentary behavior per hour of sedentary time, and each bout lasted approximately 6.4 min (Baruth, Sharpe, Hutto, Wilcox, & Warren, 2013). All women engaged in ≥ 1 daily bout of sedentary behavior ≥ 10 and ≥ 30 min, and most (83%) engaged in ≥ 1 bout ≥ 60 min. Participants were slightly more sedentary during the evening (6 pm–midnight) and on weekdays (Baruth et al., 2013). On average, participants took 90.9 breaks \cdot day $^{-1}$ from sedentary behavior and each break lasted 3.3 min (Baruth et al., 2013). These findings

make it clear that week days, specifically working days must be target by interventions and programs aiming to reduce and break up sedentary time, however non-working hours and leisure time ought not be discarded (Baruth et al., 2013).

Although office work has traditionally been considered a ‘low risk’ occupation in terms of chronic health outcomes, it may in fact increase the risk of mortality and cardiometabolic disorders due to overall accumulated sedentary time and especially sustained sedentary time at work (Parry & Straker, 2013). Given the evidence for a health impact of sedentary time, work based activity interventions should therefore target reducing total sedentary time and also emphasise the importance of interrupting sedentary time and provide an opportunity to participate in LIPA (Baruth et al., 2013).

A more recent study described the patterns of accelerometer determined sedentary time among adults using a nationally representative sample from the USA (Evenson, Wen, Metzger, & Herring, 2015). Using 2003-2006 NHANES data, 7931 adults wore an ActiGraph accelerometer for one week. For weighted percentage of sedentary time out of total wearing time, 5 classes were identified from most to least sedentary: 6.3% of population (weighted mean 660.2 min·day⁻¹), 25.1% (546.8 min·day⁻¹), 37.7% (453.9 min·day⁻¹), 24.0% (354.8 min·day⁻¹), and 7.0% (256.3 min·day⁻¹). Four of the classes showed generally similar results across every day of the week. In contrast, the least sedentary class showed a marked rise in percent of time spent in sedentary behavior on the weekend (weighted mean 336.7-346.5 min·day⁻¹) compared to weekdays (weighted mean 255.2-292.4 min·day⁻¹). This is important, once it showed that the least sedentary class during work days (more active jobs) appeared to compensate on the non-working days by being more sedentary (Evenson et al., 2015).

A cross-sectional study (Jefferis et al., 2014) found that older men from UK spent on average 618 min, or 72% of their day in sedentary behaviors (<100 counts·min⁻¹) and that on average, men accumulated 72 bouts of sedentary time per day, with 7 breaks in each sedentary hour (Jefferis et al., 2014). Men had on average 5.1 sedentary bouts of ≥ 30 min, which accounted for 43% of sedentary time, and 1.4 bouts of ≥ 60 min, which accounted for 19% of daily sedentary time (Jefferis et al., 2014). Additionally, men who were over 80 years old, obese, depressed, and had multiple

chronic conditions accumulated more sedentary time and spent more time in longer sedentary bouts (Jefferis et al., 2014).

These findings highlight that prolonged sedentary time tend to increase during life and the number of spontaneous interruptions presented an inverse trend, with less breaks from sedentary time in older adults compared to adults. Also, these findings showed that school (for children) and work (for adults) are the contexts where sedentary behavior is mainly promoted, but leisure time also needs to be targeted. In fact, older adults (retired from work) presented the highest levels of sedentary behavior in the population, but more important, the longest bouts in sedentary behavior (Jefferis et al., 2014). Therefore, not only the work-settings promote sedentary behavior, but other social features guide people to be sedentary in their leisure time.

Finally, the time of the day when people are more sedentary varies with age and sedentary patterns are also specific for each age group. For example, older adults seem to increase sedentary behavior through the course of the day to peak in the evening (Sartini et al., 2015), while children are more sedentary in the mornings (Kwon et al., 2012). Thus, interventions to encourage people to reduce and break up sedentary time need to take account of current specific sedentary behavior patterns.

2.3. Observational findings for sedentary behavior with health

2.3.1. *ALL-CAUSE AND NON-COMMUNICABLE DISEASES' MORTALITY*

Four non-communicable diseases; CVD, chronic respiratory disease, diabetes mellitus, and cancer-account for over 60% of all deaths globally (Dugani & Gaziano, 2016). In recognition of this significant epidemic, the United Nations set forth a target of reducing the four major non-communicable diseases by 25% by 2025 (Dugani & Gaziano, 2016). CVD alone represents half of these deaths and is the leading cause of death globally, representing as much as 60% of all deaths in regions such as Eastern Europe (Dugani & Gaziano, 2016). Therefore, as an independent risk factor, it is important to comprehend the associations for sedentary behavior with all-cause and non-communicable diseases' mortality.

The results from a meta-analysis of prospective cohort studies (Grøntved & Hu, 2011) suggest that TV viewing (the most prevalent sedentary behavior) is consistently associated with higher risk of fatal CVD, and all-cause mortality. They observed that the pooled relative risk per 2 hours of TV viewing per day were 1.15 (95% CI, 1.06-1.23) for fatal CVD, and 1.13 (95% CI, 1.07-1.18) for all-cause mortality (Grøntved & Hu, 2011). Therefore, each 2 hours per day of TV viewing were associated with a 13% increase in all-cause mortality (Grøntved & Hu, 2011). Based on incidence rates in the USA, the estimated absolute risk difference (cases per 100 000 individuals/year) per 2 hours of TV viewing·day⁻¹ were 38 for fatal CVD, and 104 for all-cause mortality.

A large scale study that included 61 395 men and 73 201 women aged 45-75 years among five racial/ethnic groups confirmed that leisure sitting time, particularly watching TV, may increase CVD mortality (Kim, Wilkens, et al., 2013). Total daily sitting was not associated with mortality in men, whereas in women the longest sitting duration (≥ 10 hours·day⁻¹ vs < 5 hours·day⁻¹) was associated with 19% increased CVD mortality (Kim, Wilkens, et al., 2013). Regardless, TV viewing does not represent the total amount of sedentary time that people spend during the day, and only characterizes a portion of total sedentary behavior (Craft et al., 2012). In fact, people may sit for long periods of time while at work (e.g., using computer) and not present any TV viewing time or vice versa. Thus, studies examining the associations between total sedentary time or total sitting time with health parameters are more informative.

Sitting is a more general sedentary behavior than TV viewing and has also been linked to CVD and all-cause mortality and to decreased life expectancy with 3 hours per day of sitting leading to a life expectancy decrease of 2 years (Katzmarzyk & Lee, 2012; Owen et al., 2014). In (Ford & Caspersen, 2012), for each 2 hours of additional sitting time there was a 5% increase in CVD mortality (HR 1.05; 95% CI 1.01–1.09). Four recent prospective cohort studies investigated the relationship between sedentary behavior and mortality (all-cause, CVD, colorectal cancer, and other causes). The first study showed that individuals who spent less than 8 hours sitting·day⁻¹ had a lower risk of all-cause mortality (hazard ratio (HR)=0.70, 95% CI: 0.60 to 0.82) when compared with their sedentary peers (Martinez-Gomez, Guallar-Castillon, Leon-Munoz, Lopez-Garcia, & Rodriguez-Artalejo, 2013).

In a second study (Leon-Munoz et al., 2013), individuals were classified as consistently sedentary (> median in 2001 and 2003), newly sedentary (< median in 2001 and > median in 2003), formerly sedentary (> median in 2001 and < median in 2003), and consistently nonsedentary (< median in 2001 and 2003). They found that when compared with the consistently sedentary group, there was a trend for the newly sedentary individuals (HR 0.91; 95% CI 0.76 - 1.10) and formerly sedentary individuals (0.86; 95% CI 0.70 - 1.05) to be protected against all-cause mortality but only the consistently non-sedentary group was significantly protected in relation to the consistently sedentary group (0.75; 95% CI 0.62 - 0.90) (Leon-Munoz et al., 2013). These findings reinforce the idea that sedentary behavior must be reduced as early in life as possible and that people must concern during their whole life.

A third study examining a colorectal cancer survivor population (Campbell, Patel, Newton, Jacobs, & Gapstur, 2013) identified that more than 6 hours per day of pre-diagnosis leisure sitting time was associated with a higher risk of all-cause mortality (RR, 1.36; 95% CI, 1.10 to 1.68) and mortality from all other causes (not CVD and colorectal cancer) (RR, 1.48; 95% CI 1.05-2.08) when compared with fewer than 3 hours per day in leisure sitting time (Campbell et al., 2013). Similarly, a dose-response relationship between sitting time and all-cause mortality was found in a recent study (Pavey, Peeters, & Brown, 2015). Compared with participants who sat < 4 h·day⁻¹, those who sat 8-11 h·day⁻¹ had a 1.45 times higher risk of death and those who sat ≥ 11 h·day⁻¹ had a 1.65 times higher risk of death (Pavey et al., 2015). For each extra hour·day⁻¹ spent sitting, there was an increase of 3% in the risk of all-cause mortality (Pavey et al., 2015).

Finally, a recent systematic review and meta-analysis (Biswas et al., 2015) between sedentary behavior and outcomes for CVD and diabetes (14 studies), cancer (14 studies), and all-cause mortality (13 studies) was published. Prospective cohort designs were used in all but 3 studies and significant HR associations were found between sedentary behavior and all-cause mortality (HR, 1.240 [95% CI, 1.090 to 1.410]), CVD mortality (HR, 1.179 [CI, 1.106 to 1.257]) and cancer mortality (HR, 1.173 [CI, 1.108 to 1.242]). Also, greater amounts of sedentary time were associated with a 49% increased risk for premature mortality (Wilmot et al., 2012), and

interestingly, it has been suggested that sedentary behavior per se is associated with shorter leukocyte telomere length, a known marker of premature mortality (Loprinzi, 2015).

In conclusion, the findings on the associations for sedentary behavior with mortality rates support the idea that sedentary behavior must be considered an independent health risk factor with significant deleterious effects on the main non-communicable diseases and premature mortality. Although sedentary behavior, sleeping and PA are thought to be independently associated with health outcomes, it is unclear whether these associations are due to the direct physiological effects of each behavior or because, across a finite 24 hour day, engagement in one behavior requires displacement of another (Stamatakis et al., 2015).

A recent study (Stamatakis et al., 2015) examined the replacement effects of sedentary behavior (total sitting, television/computer screen time combined), sleeping, standing, walking, and MVPA on all-cause mortality using isotemporal substitution modeling (Stamatakis et al., 2015). This investigation concluded that although replacing sedentary behavior with walking and MVPA are associated with the lowest mortality risk, replacements with equal amounts of standing and sleeping are also linked to substantial mortality risk reductions (Stamatakis et al., 2015). These findings are important as they justify that replacing sedentary time with LIPA, which is more reasonable and feasible in real life settings, can thus represent a viable alternative to reduce the risk of disease and increase people's quality of life.

Associations for sedentary behavior with non-fatal CVD

Cardiovascular disease is the leading cause of death globally except in Africa (Dugani & Gaziano, 2016). The underlying mechanisms vary depending on the disease in question and may be caused by high blood pressure, smoking, diabetes, lack of exercise, obesity, high blood cholesterol, poor diet, excessive alcohol, and also the time spent in sedentary behavior.

In fact, sedentary is not only associated with CVD mortality as it seems to be responsible for an higher incidence of this disease. Recently, higher levels of sedentary behavior have been related to higher cardiovascular events (Ford & Caspersen, 2012;

Grøntved & Hu, 2011; Thorp et al., 2011; van Uffelen et al., 2010; Wilmot et al., 2012) and five systematic reviews investigated the association between sedentary behavior and CVD in adults (Ford & Caspersen, 2012; Grøntved & Hu, 2011; Thorp et al., 2011; van Uffelen et al., 2010; Wilmot et al., 2012).

Two of these reviews indicated conflicting associations for sedentary behavior (occupational and general), with cardiovascular outcomes, underscoring the fact that there have been few studies addressing this topic (Thorp et al., 2011; van Uffelen et al., 2010). In opposition, two recent systematic reviews including meta-analysis concluded that the results are consistent and showed a significant positive association between sedentary behavior (≥ 2 television hours·day⁻¹; screen-time and sitting time) and CVD, regardless of PA levels, with summary measures of 1.15 (95% CI, 1.06–1.23) and 2.47 (95% CI, 1.44–4.24), respectively (Grøntved & Hu, 2011; Wilmot et al., 2012).

Another review of prospective studies (Ford & Caspersen, 2012) showed that greater sedentary behavior was associated with an increased risk of fatal and non-fatal CVD events and found that 2 hours·day⁻¹ of screen-time and sitting time were associated with an increase of 5% (HR 1.05; 95% CI 1.01–1.09) and 17% (HR 1.17; 95% CI 1.13–1.20) in cardiovascular events, respectively. Compared with the lowest levels of sedentary time, risk estimates ranged up to 1.68 for the highest level of sitting time and 2.25 for the highest level of screen time after adjustment for several covariates, including measures of PA (Ford & Caspersen, 2012). In accordance, recent findings (Borodulin, Karki, Laatikainen, Peltonen, & Luoto, 2014) from a follow-up study of 8.6 years continue to suggest that the total amount of daily sitting is a risk factor for incident CVD, but more research is needed to understand the etiology of sedentary behavior and CVD, specifically how different sedentary patterns may associate with CVD.

In line with this, a cross-sectional study developed in Spain (Garcia-Hermoso et al., 2015) included 263 healthy adults (59.3% women), carotid intima-media thickness (IMT) was measured by carotid ultrasonography, and sedentary behavior was objectively measured over 7 days using ActiGraph accelerometers. Total sedentary time and sedentary time in bouts ≥ 10 min were higher in participants with a larger mean carotid IMT ($> P75$) (Garcia-Hermoso et al., 2015). Regardless of the cross-sectional

data, these findings support the idea that reducing sedentary time by increasing the number of breaks in sedentary time might represent a useful additional strategy in the CVD prevention (Garcia-Hermoso et al., 2015). However, more research on the relationships between sedentary patterns and CVD risk markers are necessary.

Associations for sedentary behavior with non-fatal cancer

Sedentary behavior has also been suggested to be associated with incident cancer (Lynch, 2010; Thorp et al., 2011; van Uffelen et al., 2010). Several systematic reviews investigated the association between sedentary behavior and cancer in adults (Lynch, 2010; Thorp et al., 2011; van Uffelen et al., 2010). These reviews showed that sedentary behavior (overall sitting time, sitting outside of work, and TV viewing) are associated with an increase in the risk of colorectal, breast, endometrial, ovary, and prostate cancer (Lynch, 2010; Thorp et al., 2011; van Uffelen et al., 2010). However, conclusions are still based on a limited number of studies, some of which did not consider confounding factors such as BMI and PA.

A recent meta-analysis (Cong et al., 2014) included 23 studies (27 231 colon cancer cases and 13 813 rectal cancer cases) and found that sedentary behavior was associated with colon cancer RR was 1.30 (95% CI: 1.22-1.39) but did not have a significant association with rectal cancer (RR 1.05, 95% CI, 0.98-1.13). Subgroup analyses suggested that the odds ratio (OR) of colon cancer was 1.46 (95% CI: 1.22-1.68) in the case-control studies, and the RR was 1.27 (95% CI: 1.18-1.36) in the cohort studies, the OR of rectal cancer was non-significant in the case-control studies 1.06 (95% CI: 0.85-1.33), and the RR was 1.06 (95% CI, 1.01-1.12) in the cohort studies (Cong et al., 2014).

Another meta-analysis that included 17 prospective studies (Shen et al., 2014), with a total of 857,581 participants suggested that sedentary behavior increases the risk of cancer (RR=1.20, 95% CI=1.12–1.28), with no evidence of heterogeneity between studies (Shen et al., 2014). Subgroup analyses demonstrated associations between sedentary behavior and some types of cancer (endometrial cancer: RR=1.28, 95% CI=1.08–1.53; colorectal cancer: RR=1.30, 95% CI=1.12–1.49; breast cancer: RR=1.17, 95% CI=1.03–1.33; and lung cancer: RR=1.27, 95% CI=1.06–1.52).

However, there was no association for sedentary behavior with ovarian cancer (RR=1.26, 95% CI=0.87–1.82). This meta-analysis reinforced previous findings and added that these associations were independent of traditional confounders including BMI, PA and EI (Shen et al., 2014).

Finally, irrespective of the consistent findings regarding the associations for sedentary behavior with cancer found in previous studies, more investigation is needed and future studies must examine how sedentary patterns may affect cancer incidence.

2.3.2. MORBIDITY

Morbidity refers to the unhealthy state of an individual, while mortality refers to the state of being mortal. Mortality rate is the rate of death in a population and a morbidity rate looks at the incidence of a disease across a population and/or geographic location during a single year. Both concepts can be applied at the individual level or across a population. The two are often used together to calculate the prevalence of a disease (Desai, Zhang, & Hennessy, 1999). As survival improves with modernization and populations age, mortality measures do not give an adequate picture of a population's health status. Indicators of morbidity such as the prevalence of chronic diseases and disabilities become more important (Desai et al., 1999).

There is rapidly emerging evidence on the associations for sedentary behavior (adverse) and LIPA (beneficial) with biomarkers of health and chronic diseases (Henson, Yates, Biddle, et al., 2013; Loprinzi, 2013). These biomarkers include WC, BMI, HDL, C-reactive protein, triacylglycerols, and insulin. Chronic conditions include obesity, metabolic syndrome, and type 2 diabetes (Grøntved & Hu, 2011; Henson, Yates, Biddle, et al., 2013; Loprinzi, 2013; Lynch, 2010; Rhodes et al., 2012; Thorp et al., 2011; Wilmot et al., 2012).

In fact, several systematic reviews gathering the information for sedentary behavior with health outcomes among adults have been published in the past years (Grøntved & Hu, 2011; Lynch, 2010; Rhodes et al., 2012; Thorp et al., 2011; Wilmot et al., 2012). Grøntved and colleagues suggested that TV viewing is consistently

associated with higher risk of type 2 diabetes (Grøntved & Hu, 2011). They observed RRs of 1.20 for type 2 diabetes per every 2 hour increase in TV viewing per day but they relied on cross-sectional data only.

Thorp et al., (2011) systematically review and provide an informative synthesis of findings from longitudinal studies published since 1996 reporting on relationships between sedentary behavior and health related outcomes in adults (Thorp et al., 2011). Findings indicate a consistent relationship of self-reported sedentary behavior with weight gain from childhood to the adult years. However, findings were mixed for associations with disease incidence, weight gain during adulthood, and cardiometabolic risk (Thorp et al., 2011). Of the two studies that used device-based measures of sedentary time, one showed that markers of obesity predicted sedentary time, whereas inconclusive findings have been observed for markers of insulin resistance (Thorp et al., 2011).

From the 48 studies included in Thorp's systematic review, 46 incorporated self-reported measures including total sitting time; TV viewing time only; TV viewing time and other screen-time behaviors, with only two studies using objective measures of sedentary behavior (Thorp et al., 2011). Moreover, most studies to date have focused solely upon the health outcomes associated with TV viewing and used subjective measures for total sedentary time while the health outcomes of other forms of sedentary behavior, for example, occupational sitting or 'total' objectively measured sedentary time, are less clear (Thorp et al., 2011). Therefore, using objective accelerometer data from the 2003–2006 NHANES, Healy and colleagues suggested that reductions of 1–2 h of sedentary time could equate to substantial reductions in the risk for non-fatal CVD (Healy, Matthews, Dunstan, Winkler, & Owen, 2011) and a sedentary lifestyle also has a direct effect on inactivity-induced factors including deep venous thrombosis and poor lipid metabolism (Hamilton et al., 2007).

Regardless of the quality of sedentary behavior assessment, it has been found to be an independent risk factor for numerous diseases. Specific information on the associations for sedentary behavior with each of the main chronic diseases will be presented below. These conditions include; obesity, metabolic syndrome, and type 2

diabetes. Additionally, specific information on the studies that examined the associations for sedentary patterns with these health conditions will be presented in subchapters.

Moreover, given that obesity and adiposity-related measures are the main outcomes from this thesis, a separate chapter will be considered where the literature on the associations for sedentary behavior with whole body markers of obesity will constitute a subchapter, and the associations for sedentary behavior with molecular level of body adiposity (and an overview of the energetics regulation) another subchapter.

Sedentary behavior and metabolic syndrome

Metabolic syndrome is a constellation of risk factors for CVD and type 2 diabetes, abnormal plasma triglycerides and HDL as markers of impaired lipid metabolism, elevated plasma glucose, blood pressure, and WC. Approximately a quarter of the USA adult population has metabolic syndrome (Hamilton, Hamilton, & Zderic, 2014) and a meta-analysis found that people who spend higher amounts of time in sedentary behaviors have greater odds of having metabolic syndrome (Edwardson et al., 2012).

Studies have shown that the classification of people with metabolic syndrome have all been directly related to sitting time (Bertrais et al., 2005; Dunstan et al., 2005; Ford & Caspersen, 2012). Estimations from prolonged TV viewing and computer time led to the conclusion that too much sitting can more than double the risk for metabolic syndrome (Bertrais et al., 2005; Dunstan et al., 2005; Ford & Caspersen, 2012). Accordingly, Dunstan et al. (2005) found that for each 1h increase of TV viewing per day, there was a 26% increase in the prevalence of metabolic syndrome in women. Furthermore, the magnitude of this negative association for 1 h of sedentary TV time was about the same as the positive association for 30 min of extra PA aimed at boosting health (Dunstan et al., 2005).

These findings are confirmed in a recent investigation (Gennuso, Gangnon, et al., 2015), where the relationship between daily sedentary time and metabolic syndrome was linear and characterised by an OR of 1.09 (95% CI 1.01, 1.18) for each hour of sedentary behavior (Gennuso, Gangnon, et al., 2015; Scheers, Philippaerts, & Lefevre, 2013). Total sedentary time was associated with the following components: high

triacylglycerol, low HDL-cholesterol and high fasting glucose (Gennuso, Gangnon, et al., 2015). It is important to point out that those detriments in metabolic risk factors and disease outcomes due to sedentary behavior are often independent of BMI or other markers for excess adiposity (Bertrais et al., 2005; Dunstan et al., 2005; Ford & Caspersen, 2012). This latter point is suggestive that specific effects of sitting may be caused by inactivity per se and are not a reflex of chronic changes in body composition.

Compared with people without metabolic syndrome, people with metabolic syndrome spent a greater percentage of time as sedentary (67.3 vs. 62.2%), had longer average sedentary bouts (17.7 vs. 16.7 min), and had fewer sedentary breaks (82.3 vs. 86.7), adjusted for age, sex, ethnicity, education, alcohol consumption, smoking, BMI, diabetes, heart disease, and PA (Bankoski et al., 2011). Accordingly, a cross-sectional study that included 483 middle-aged Japanese adults found that LIPA and sedentary behavior were significantly and contrarily associated with the risk of metabolic syndrome, independent of MVPA (Kim, Tanabe, et al., 2013). The findings included sedentary behavior's associations with triglycerides ($\beta = 5.815$; 95% CI: 1.791 to 9.838), HDL-C ($\beta = -1.491$; 95% CI: -2.262 to -0.720), and a total Z-score for metabolic syndrome ($\beta = 0.329$; 95% CI: 0.164 to 0.494), but no associations for sedentary behavior with other biomarkers of risk, such as blood pressure (Kim, Tanabe, et al., 2013).

Using data from the 2003–2006 NHANES, Sisson et al., (2009) found that leisure time sedentary behavior ≥ 4 hours \cdot day $^{-1}$ was associated with odds of having metabolic syndrome of 1.94 (95% CI, 1.24, 3.03) in men compared to ≤ 1 hour \cdot day $^{-1}$ (Sisson et al., 2009). Leisure time sedentary behavior ≥ 4 hour \cdot day $^{-1}$ was also associated with higher odds of elevated WC (1.88, CI, 1.03, 3.41), low HDL-C (1.84, CI, 1.35, 2.51), and high blood pressure (1.55, CI, 1.07, 2.24) in men (Sisson et al., 2009). In women, odds of metabolic syndrome were 1.54 (CI, 1.00, 2.37) with ≥ 4 hours \cdot day $^{-1}$ of leisure time sedentary behavior and no associations with risk of individual risk factors were found (Sisson et al., 2009).

Interestingly, using data from the 2005–2006 NHANES, Buman et al., (2014) showed that for every 30 min of sedentary behavior that were reallocated to MVPA there was a 2–25% improvement in biomarkers of risk (e.g., WC, HDL, triglycerides,

insulin). This study also identified that for every 30 min of sedentary behavior that were reallocated to LIPA, there was a 2–4% improvement in biomarkers (e.g., triglycerides, insulin, β -cell function). This is important as it identifies that the reductions seen in the sedentary behavior + PA interventions (~30 min) are clinically meaningful regardless of whether sedentary behaviors are reallocated to LIPA or MVPA (Buman et al., 2014).

Regardless of the cross-sectional findings on the deleterious associations for sedentary behavior with metabolic syndrome, contradicting results still exist. Furthermore, longitudinal investigation is needed to assess causality. In line with this, a longitudinal study aimed to determine whether sedentary behavior was associated with increased accumulation of visceral fat and other deleterious changes in cardiometabolic risk over a 6-year follow-up period among adult participants in the Quebec Family Study (Saunders, Tremblay, Després, et al., 2013). This study found that neither baseline sedentary behavior nor changes in sedentary behavior were associated with longitudinal changes in visceral adiposity in adult men or women.

With the exception of WC, the present study found no evidence for a relationship between sedentary behavior and any marker of cardiometabolic risk (Saunders, Tremblay, Després, et al., 2013). Although longitudinal, this study used subjective measures of sedentary behavior, which is a limitation that may explain the opposing findings. Thus, more longitudinal research using objective methods for sedentary behavior assessment, and experimental evidence on the effects of sedentary time manipulation with metabolic health are needed.

Sedentary patterns and metabolic syndrome

Healy and colleagues' study was the first to find associations for breaks in objectively measured sedentary time with biological markers of metabolic risk (Healy, Dunstan, et al., 2008). Independent of total sedentary time and MVPA, increased breaks in sedentary time were beneficially associated with WC (standardized beta = -0.16, 95% CI -0.31 to -0.02, P = 0.026), BMI (beta = -0.19, -0.35 to -0.02, P = 0.026), triglycerides (beta = -0.18, -0.34 to -0.02, P = 0.029), and 2-h plasma glucose (beta = -0.18, -0.34 to -0.02, P = 0.025). A more recent study found that adults' breaks in sedentary time were inversely associated with abdominal obesity (OR = 0.71, 95% CI = 0.55-0.91) and

hypertriglyceridemia (OR = 0.79, 95% CI 0.63-0.99) (Scheers et al., 2013). However, in opposition to Healy's study, these associations were no longer significant after adjustment for MVPA and total sedentary time (Scheers et al., 2013).

Confirming the findings from Healy's investigation, a study from the Canadian Health Measures Survey (Carson et al., 2014) based on a 4935 group of adults and older adults aged 20-79 years old, examined how total sedentary time, patterns of sedentary time (≥ 20 min prolonged sedentary bouts, number of sedentary breaks), and MVPA were associated with WC, systolic and diastolic blood pressure, HDL, triglycerides, low-density lipoprotein cholesterol, insulin, and glucose (Carson et al., 2014). The results from this study showed that total sedentary time and time in ≥ 20 min prolonged sedentary bouts were associated with higher insulin, and lower diastolic blood pressure levels (Carson et al., 2014). Furthermore, each additional 10 breaks \cdot day⁻¹ were associated with 0.32 (0.02, 0.62) mmHg lower systolic blood pressure, 0.01 (0.00, 0.02) mmol/l higher HDL, 3.72 (1.34, 6.13) % lower triglycerides, 0.57 (0.23, 0.92) % lower glucose, and 4.19 (1.80, 6.63) % lower insulin (Carson et al., 2014).

These findings indicate that breaking up sedentary time may be particularly important for metabolic health (Carson et al., 2014) but contradicting findings have also been found (Gennuso, Gangnon, et al., 2015; Henson, Yates, Biddle, et al., 2013). A study from the UK comprised 878 participants and objectively assessed total sedentary time and its patterns with ActiGraph GT3X accelerometers. Detrimental associations for total sedentary time with 2 h plasma glucose, triacylglycerol and HDL were found, but no associations for the breaks in sedentary time (Henson, Yates, Biddle, et al., 2013). In accordance, two recent studies found no relationship between breaks in sedentary time and metabolic syndrome (Alkahtani, Elkilany, & Alhariri, 2015; Gennuso, Gangnon, et al., 2015). Therefore, more experimental research is needed to confirm these cross-sectional findings, and conclude about the causality in the relationship between sedentary patterns and metabolic syndrome.

Sedentary behavior and type 2 diabetes

Diabetes mellitus, commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. Type 2

diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses a lack of insulin may also develop. According to the International Diabetes Federation as of 2014, an estimated 387 million people have diabetes worldwide, with type 2 diabetes making up about 90% of the cases (Shi & Hu, 2014).

A longitudinal study published in *JAMA* (Hu et al., 2003) documented 1515 newly diagnosed cases of type 2 diabetes during the 6 years of follow-up. After adjustment for age, the time spent watching TV was significantly associated with increased risk of type 2 diabetes (Hu et al., 2003). The RRs across categories of average hours spent watching TV per week were 1.10, 1.30, 1.53, and 1.98 (P for trend, < 0.001) (Hu et al., 2003). Thus, while it is certainly plausible that excess body fat may contribute in part to the reason why TV time or other sedentary behaviors are related to diabetes risk, these epidemiological data are also alluding to the need to consider additional and more distinct mechanisms beyond BMI and body fat (Hamilton et al., 2014).

Furthermore, the metabolic processes are constantly reflecting altered states of contractile activity and are not on the same time scale wherein changes in body composition would occur (Hamilton et al., 2014). In fact, fasting and 2-h postload plasma glucose, and fasting insulin were measured in 2,761 women and 2,103 men (mean age 54 years) without clinically diagnosed diabetes from the 2004-2005 Australian Diabetes, Obesity and Lifestyle (AusDiab) study (Thorp et al., 2010). This study found that sitting time was detrimentally associated with 2-h postload plasma glucose and fasting insulin, but only fasting insulin and glucose (men only) remained deleteriously associated with TV viewing time after adjustment for WC (Thorp et al., 2010).

Additionally, a recent study that included 541 individuals (average age=65 years, female=33%) found both sedentary behavior and MVPA to be strongly associated with insulin sensitivity after adjustment for age, sex, ethnicity, medication, smoking status and accelerometer wear time (Yates, Davies, et al., 2015). In this study, sedentary and MVPA time were objectively measured using accelerometers. Fasting and 2-hour post-challenge insulin and glucose were assessed, and insulin sensitivity was calculated

(Yates, Davies, et al., 2015). The findings from this study showed that every 30 minute difference in sedentary time was inversely associated with a 4% difference in insulin sensitivity, whereas every 30 minutes in MVPA was positively associated with a 13% difference in insulin sensitivity (Yates, Davies, et al., 2015).

Therefore, regardless of the lower association found for sedentary behavior compared with MVPA, this study showed a significant and inverse association for objectively measured sedentary behavior with insulin sensitivity, independently of MVPA (Yates, Davies, et al., 2015), and emphasize the need for the development of individualized interventions aiming at decrease the amount of time spent in hyperglycemia by reducing sedentary time (Fritschi et al., 2015; Yates, Davies, et al., 2015). Moreover, preliminary findings reveal that time spent in sedentary behavior can be reallocated into LIPA or MVPA with differences in insulin sensitivity, but stronger and more consistent associations were seen for MVPA (Yates, Henson, et al., 2015).

Regardless, the assumption that sedentary behavior must be replaced by MVPA instead of LIPA in order to enhance metabolic health is far from absolute certainty. Another recent study considered 279 adults with type 2 diabetes, and using isotemporal substitution models, found that LIPA was significantly associated with lower fasting plasma glucose (relative rate: 0.98, 95% CI: 0.97, 0.99; $p < 0.05$) but no biomarker was significantly associated with non-prolonged sedentary time (<30 min) or MVPA (Healy, Winkler, Brakenridge, Reeves, & Eakin, 2015). Additionally, lower mean prolonged sedentary time ($-30 \text{ min} \cdot \text{day}^{-1}$) with higher mean LIPA time ($+30 \text{ min} \cdot \text{day}^{-1}$) was significantly associated with lower WC ($\beta = -0.77$, 95% CI: -1.33, -0.22 cm) (Healy et al., 2015). Lower mean prolonged sedentary time ($-30 \text{ min} \cdot \text{day}^{-1}$) with either 30 min/day higher mean non-prolonged sedentary time ($\beta = -0.35$, 95% CI: -0.70, -0.01 kg/m^2) or LIPA time ($\beta = -0.36$, -0.61, -0.11 kg/m^2) was associated with significantly lower mean BMI (Healy et al., 2015).

Therefore, it seems that the mechanisms explaining the metabolic impairments associated with sedentary behavior may go beyond the correspondent increase in body fatness and be explained by the acute contractions of skeletal muscle improvements in insulin action and local factors in skeletal muscle linking lipid metabolism to metabolic control (Hamilton et al., 2014). In addition, one study examined the potential

associations for sedentary behavior with markers of chronic low-grade inflammation and adiposity in a population at a high risk of type 2 diabetes mellitus (Henson, Yates, Edwardson, et al., 2013).

This study concluded that sedentary behavior was detrimentally associated with C-reactive protein, IL-6, and leptin (Henson, Yates, Edwardson, et al., 2013) but these associations were attenuated after adjustment for MVPA with only IL-6 remaining significant (Henson, Yates, Edwardson, et al., 2013). This result was unaffected after further adjustment for BMI and glycosylated haemoglobin (Henson, Yates, Edwardson, et al., 2013), suggesting that sedentary behavior may influence some markers of adiposity associated inflammation, independent of MVPA, glycaemia and anthropometric measures attributable to central adiposity (Henson, Yates, Edwardson, et al., 2013). These findings support that the deleterious effects of sedentary behavior may be particularly pertinent for those individuals who do not undertake sufficient amounts of MVPA.

Sitting at work and sitting at home have been both associated with significantly increased risk of diabetes. A prospective study (Helmerhorst, Wijndaele, Brage, Wareham, & Ekelund, 2009) showed that physiologically measured sedentary behavior was associated with hyperinsulinemia measured 5.6 years later in 376 healthy middle-aged Caucasian participants (166 men; 210 women). Furthermore, this association was independent of baseline confounders including age, sex, fat mass, fasting insulin, smoking status, follow-up time, and MVPA. In this study, sedentary time was objectively measured by individually calibrated min-by-min heart rate (HR) monitoring at both baseline and follow-up. These findings encompass previous cross-sectional findings using objective measurements of sedentary time suggesting that this behavior is associated with 2 h blood glucose (Healy et al., 2007) and metabolic syndrome features (Healy, Wijndaele, et al., 2008).

In an analysis of data from the European RISC study (Lahjibi et al., 2013), sedentary time and MVPA were assessed by accelerometry at baseline in 313 men and 414 women, aged 30-60 years. Three years later, anthropometry, glucose, and insulin were available for 549 participants. In longitudinal analyses, higher baseline sedentary time was associated with 3 year increases in fasting glucose, fasting insulin and the

homeostatic model assessment (HOMA) insulin resistance index score for the 50% of the study population who increased their BMI by at least 0.3 kg/m². These relationships remained significant after adjusting for time spent in MVPA (Lahjibi et al., 2013).

Similar to the long-term associations found for sedentary behavior with diabetes (Helmerhorst et al., 2009; Hu et al., 2003; Lahjibi et al., 2013), a short-term longitudinal descriptive study (3-5 days) showed this same trend (Fritschi et al., 2015). Involving 86 patients with type 2 diabetes this study found a relationship between time spent in sedentary behavior and hyperglycemia, as identified through the use of objective, continuous data collection methods for both sedentary behavior and glucose levels across multiple days (Fritschi et al., 2015). Therefore, it seems that the metabolic harms associated with sedentary behavior are apparent from a chronic manner but also manifest in an acute way (Fritschi et al., 2015).

Sedentary patterns and type 2 diabetes

In addition to the effects of total sedentary time, the manner in which it is accumulated may also be important. Healy et al., (2008) examined the association of breaks in objectively measured sedentary time with biological markers of metabolic risk in 168 adults (Healy, Wijndaele, et al., 2008). The main findings showed that independent of total sedentary time and MVPA, increased breaks in sedentary time were beneficially associated with triglycerides (beta=-0.18, -0.34 to -0.02, P=0.029), and 2-h plasma glucose (beta=-0.18, -0.34 to -0.02, P=0.025) (Healy, Wijndaele, et al., 2008).

This was one of the first studies that provided evidence on the importance of avoiding prolonged uninterrupted periods of sedentary behavior (Healy, Wijndaele, et al., 2008). Emerging evidence on the potential benefits of regularly interrupting sedentary time (i.e., reducing prolonged, unbroken sedentary time) on glucose clearance and insulin sensitivity have been found (Healy, Matthews, et al., 2011; Henson, Yates, Biddle, et al., 2013), but observational studies present contradicting findings on the associations for sedentary patterns with metabolic indicators (Falconer, Page, Andrews, & Cooper, 2015; Healy, Matthews, et al., 2011; Henson, Yates, Biddle, et al., 2013).

Henson et al., (2013) considered a sample of 878 people with known risk factors for type 2 diabetes mellitus and found detrimental linear associations for sedentary time

with 2 h plasma glucose ($\beta=0.220$, $p<0.001$), triacylglycerol ($\beta=0.206$, $p=0.001$), and HDL-cholesterol ($\beta=-0.123$, $p=0.029$), but no associations for the breaks in sedentary time with any cardiometabolic variables after adjustment for sedentary time and BMI (Henson, Yates, Biddle, et al., 2013). Regardless, this study found breaks in sedentary time to be inversely associated with measures of adiposity (Henson, Yates, Biddle, et al., 2013). Similarly, Falconer et al., (2015) found that reallocation of 30 min of prolonged bout sedentary time with 30 min of short bout sedentary time was associated with lower BMI and WC in people with type 2 diabetes (Falconer et al., 2015) but no differences for insulin sensitivity or glucose (Falconer et al., 2015).

Observational studies have demonstrated strong associations between sedentary patterns and body composition rather than metabolic parameters (Falconer et al., 2015; Healy, Matthews, et al., 2011; Henson, Yates, Biddle, et al., 2013) but these contradicting findings may be explained by the cross-sectional nature of these data, not allowing to translate the potential acute effects of breaking up sedentary time. In fact, one study found associations for objectively measured breaks in sedentary time with markers of chronic low-grade inflammation and adiposity in a population at a high risk of type 2 diabetes mellitus (Henson, Yates, Edwardson, et al., 2013), with breaks in sedentary time inversely associated with IL-6 and leptin (Henson, Yates, Edwardson, et al., 2013).

Though observational data generate hypothesis that sedentary behavior may affect health in different ways, contradicting findings have been found. Causality within these associations must be tested, therefore sedentary behavior research area must turn its attention to experimental studies, in which more consistent evidence have been found. Below, the main experimental findings for sedentary behavior and its patterns with health parameters will be presented.

2.3.3. BODY COMPOSITION AND ENERGY BALANCE REGULATION

Associations for sedentary behavior with whole body obesity markers

Obesity has become a worldwide epidemic. According to the WHO (2009) overweight and obesity are among the leading risk factors for mortality in the World

and are responsible for 5% of deaths globally, corresponding to nearly 3 million deaths every year worldwide (Finucane et al., 2011). In adults, associations have been found for overall sedentary time with increased BMI (Bell, Kivimaki, Batty, & Hamer, 2014; Nicklas et al., 2014; Stamatakis, Hirani, & Rennie, 2009) and WC (Stamatakis et al., 2009; Swartz, Tarima, et al., 2011). Furthermore, these associations seem to be independent of MVPA levels (Gennuso, Gangnon, Matthews, Thraen-Borowski, & Colbert, 2013; Inoue et al., 2012; Swartz et al., 2012).

Another study included 0.5 million Chinese adults and found that each 1.5 hours·day⁻¹ greater leisure sedentary time was associated with a 0.19 unit higher BMI, and a 0.57 cm larger WC, for any given PA level (Du et al., 2013). Regardless, the findings concerning the role of sedentary behavior in obesity are inconclusive and inconsistent and disparities in associations have also been observed, with studies reporting an association for sedentary time with the presence of abdominal obesity in older women, but not in older men (Healy, Matthews, et al., 2011; Scheers, Philippaerts, & Lefevre, 2012).

As an indicator of sedentary behavior, TV viewing is the most commonly reported daily activity during leisure time (Grøntved & Hu, 2011). Several studies have reported that prolonged TV viewing is associated with increased BMI in adults and older adults (Hu et al., 2003; Inoue et al., 2012; Qi et al., 2012; Xu, Li, Ware, & Owen, 2008). In fact, a longitudinal study published in *JAMA* (Hu et al., 2003) found that during 6 years of follow-up, 3757 women who were not obese (BMI < 30) at baseline (7.5%) became obese, and the time spent watching TV was positively associated with the risk of obesity (Hu et al., 2003). The age-adjusted RRs across categories of TV watching (2-5, 6-20, 21-40, > 40 h·week⁻¹) compared to the reference (≤ 1 h·week⁻¹) were 1.23, 1.42, 1.68, and 2.00, respectively (P for trend, < 0.001). Further adjustment for exercise levels and other covariates did not appreciably alter the RRs (Hu et al., 2003). Sitting at work or away from home or driving were also significantly associated with elevated risk of obesity (Hu et al., 2003). In contrast, time spent standing or walking around at home was associated with a lower risk of obesity (Hu et al., 2003).

Inoue and colleagues confirmed these findings and considering older adults found that, as compared with the reference category (high TV/insufficient MVPA), the

ORs (95% CI) for overweight/obesity were 0.93 (0.65, 1.34) for high TV/sufficient MVPA, 0.67 (0.47, 0.97) for low TV/sufficient MVPA, and 0.58 (0.37, 0.90) for low TV/insufficient MVPA. These findings are important as they indicate that older adults who perform sufficient MVPA but still had high amounts of TV time did not significantly present lower odds for overweight/obesity (Inoue et al., 2012) compared to the reference group. Moreover, older adults presenting sufficient MVPA and low TV time presented higher odds for overweight/obesity compared to the insufficient MVPA and low TV time. Thus, regardless of the cross-sectional data, this investigation suggests that TV time may play a more important role than MVPA levels on the risk for high BMI (Inoue et al., 2012).

Interactions between TV watching, leisure time PA and genetic predisposition in relation to BMI in 7740 women and 4564 men from 2 prospective cohorts were examined in a study published in *Circulation* (Qi et al., 2012). Data on PA and TV watching were collected 2 years before assessment of BMI. In both women and men, the genetic associations with BMI strengthened with increased hours of TV watching. An increment of 10 points in the weighted genetic risk score was associated with 0.8, 0.8, 1.4, 1.5, and 3.4 kg/m² higher BMI across the 5 categories of TV watching (0-1, 2-5, 6-20, 21-40, and >40 h/wk). In contrast, the genetic association with BMI weakened with increased levels of PA (Qi et al., 2012). Most importantly, the interactions of TV watching and PA with genetic predisposition in relation to BMI were independent of each other (Qi et al., 2012).

Despite the associations for sedentary behavior with obesity markers being widely studied, the relationship among sedentary behavior, weight gain, weight loss and weight regain are understudied and yet unproven (Taylor, Kimbro, Evans-Hudnall, Haughton McNeill, & Barnes, 2015). A recent cross-sectional survey (Taylor et al., 2015) was administered to 1110 African Americans who had intentionally lost 10% of their body weight. Those who lost weight and maintained at least 10% weight loss for a year were classified as weight loss maintainers; all others were classified as weight loss re-gainers.

The findings from this study were that each additional daily hour of sedentary time was associated with an increase in BMI and poorer weight loss maintenance,

therefore high levels of sedentary behavior were associated with poorer weight-loss maintenance even for those with high levels of PA (Taylor et al., 2015). Regardless of the cross-sectional data, the implications for this study are that PA and sedentary behavior, independently and combined, are associated with weight loss maintenance (Taylor et al., 2015). However, more experimental research is required to either support or refute an association between sedentary behavior and weight status and to establish causality. Additionally, there are some studies on the relationship between sedentary patterns and obesity outcomes but more investigation using objective measures of sedentary assessment is needed.

Sedentary patterns and whole body obesity markers

The concept of "breaks" in sedentary behavior has emerged as a potential modifier of detrimental effects on adiposity caused by sedentary behavior (Ayabe et al., 2013; Chastin et al., 2012; Healy, Matthews, et al., 2011; Oliver et al., 2012). The recommendations to "break" sedentary time stems from the seminal study by Healy et al. (2011) that found the number of accelerometry identified interruptions of sedentary behavior to be associated with markers of obesity and cardiometabolic health, specifically BMI, WC, triglycerides, and 2-h plasma glucose (Healy, Dunstan, et al., 2008).

In fact, years later, the first population-representative findings on the deleterious associations of prolonged sedentary time with cardio-metabolic and inflammatory biomarkers was published by these authors (Healy, Matthews, et al., 2011). They found that independent of potential confounders and total sedentary time, people's breaks in sedentary time were beneficially associated with WC (Healy, Matthews, et al., 2011). Another study including adults at high risk of type 2 diabetes also found breaks in sedentary time to be inversely associated with WC (Henson, Yates, Biddle, et al., 2013) and a study including older adults (Bankoski et al., 2011) found that those presenting a large WC had a higher percentage of sedentary time, a longer average sedentary bout, and fewer breaks in sedentary time (Bankoski et al., 2011).

More recently, a cross-sectional study using a general sample of adults confirm the findings from Healy's investigation, and found that more breaks in sedentary time

were associated with lower WC, independently of MVPA levels and total sedentary time (Oliver et al., 2013) which is in accordance with a more recent meta-analysis (Chastin, Egerton, Leask, & Stamatakis, 2015) that systematically reviewed the existing research investigating the relationship for breaks in sedentary behavior with whole body obesity markers in adults (Chastin et al., 2015).

Based on 10 observational studies, this meta-analysis showed an association for breaks from sedentary time with BMI and WC, independent of total sedentary time (Chastin et al., 2015). The results are suggestive of an association with BMI with some certainty (Chastin et al., 2015) and the results are less homogeneous and the uncertainty is higher for WC (Chastin et al., 2015). However, when significant associations were found, the strength of the relationships were consistent across studies: $-0.05 \text{ kg/m}^2/\text{break}$ for BMI and -0.17 cm/break for WC (Chastin et al., 2015).

In conclusion, the theory that lower sedentary behavior levels with higher interruptions or breaks in sedentary time are associated with obesity was supported by the evidence (Chastin et al., 2015). However, these studies considered whole body measures of obesity (BMI and WC) and do not inform about the associations for sedentary patterns with more specific adiposity measures such as fat mass (FM) or visceral adipose tissue. Therefore, research considering the molecular level of body composition analysis when examining the associations with sedentary behavior is still limited and further investigations are necessary to confirm this preliminary evidence.

Associations for sedentary behavior with body composition

Associations for sedentary behavior with whole body obesity markers (e.g., BMI) have been found (Bakrania et al., 2016; Carson et al., 2014; Du et al., 2013; Healy, Matthews, et al., 2011; Oliver et al., 2013). The rationale for these associations is basically based upon energetic arguments and the hypothesis are that, spending more time in sedentary pursuits will minimize the EE while in these behaviors, which would cause an energetic imbalance that favors fat deposition. However, there is some work suggesting that PA may alter body composition without concomitant changes in BMI, by preferentially reducing visceral and/or subcutaneous fat (Thomas et al., 2000; Tremblay et al., 1990).

Little is known about sedentary behavior and regional body composition, but the field of body composition has developed and current techniques allow the assessment of regional and more specific adiposity measures. Although expensive and less achievable, methods such as dual-energy X-ray absorptiometry (DXA), computed tomography, or magnetic resonance, estimate body composition components at the molecular and cellular levels of analysis. Thus, regardless the lack of studies, evidence on the associations for sedentary behavior and its patterns with this level of body composition analysis will be presented below.

Associations for sedentary behavior with body fat mass have been found (Chastin et al., 2012; Larsen et al., 2013; Swartz, Tarima, et al., 2011). A study that included 0.5 million Chinese adults found that each 1.5 hours·day⁻¹ greater leisure sedentary time was associated with 0.44 percentage points more body fat, for any given PA level (Du et al., 2013). Also by using DXA measurements, Swartz and colleagues found that accelerometer-related sedentary time was positively associated with measures of body fatness in older adults (Swartz et al., 2012). Furthermore, Chastin and colleagues extended these findings by considering an ActivPAL inclinometer, which is more accurate method for sedentary behavior assessment, and by additionally analyzing the associations for sedentary patterns (Chastin et al., 2012).

This study presented a direct relationship between sedentary behavior and adiposity in older men and also found that the pattern of accumulation seems to be important, with less fragmented sedentary time associated with higher total body and lower limb adiposity for both men and women. Thus, showing that individuals who break up their sedentary time had lower body fat compared with those who engaged in more prolonged periods of sedentary time (Chastin et al., 2012).

Another study explored the associations of self-reported leisure PA and sitting time with regional fat depositions among community-dwelling older adults (Larsen, Allison, et al., 2014). Using computed tomography to assess pericardial, intrathoracic, subcutaneous, visceral, and intermuscular fat, this study found that greater sedentary time was associated with greater pericardial and intrathoracic fat (Larsen, Allison, et al., 2014). They also found that each hour of weekly PA was associated with 1.85 cm² less visceral fat, but was not associated with other fat depositions. Conversely, each hour of

daily sitting was associated with 2.39 cm more pericardial fat but was not associated with any other fat depositions, which leads to the conclusion that sitting and PA have distinct associations with regional fat deposition in older adults (Larsen, Allison, et al., 2014).

Regardless, the findings concerning the role of sedentary behavior in adiposity measures are inconclusive and inconsistent, with some studies reporting no relation between adults' overall sedentary time and total FM (Foong et al., 2014) or abdominal FM (McGuire & Ross, 2012; Saunders, Tremblay, Despres, et al., 2013). Using computed tomography, Saunders and colleagues longitudinal investigation found that neither baseline sedentary behavior nor changes in sedentary behavior were associated with changes in visceral adiposity in adult men and women (Saunders, Tremblay, Després, et al., 2013). Regardless of the contradicting findings, this study considered self-reported measures of sedentary behavior and did not examine how the patterns of accumulation could impact adiposity, which is a major limitation to this study.

More recently, cross-sectional studies using general samples of adults confirm the findings from Healy's investigation, and found that more breaks in sedentary time are associated with lower adiposity, independently of MVPA levels and total sedentary time (Ayabe et al., 2013; Chastin et al., 2012; Oliver et al., 2012). Ayabe and colleagues assessed the relationship between bouts of very short daily PA lasting less than 10 min with abnormal fat distributions in female adults (Ayabe et al., 2013). Using computed tomography to evaluate the area of visceral adipose tissue and subcutaneous adipose tissue, this study concluded that a smaller area of visceral adipose tissue was associated with a higher frequency of LIPA and MVPA bouts lasting 1-5 min (Ayabe et al., 2013).

In line with this, Chastin et al. (2012) found an inverse relationship for breaks in sedentary time with overall FM among older adults (Chastin et al., 2012). This study is two-fold important, once it confirmed previous findings from adult populations and showed the same trend for the elderly, and additionally they used more accurate methods for both sedentary patterns and obesity assessment (Chastin et al., 2012).

Using DXA to estimate fat mass and ActivPAL (an inclinometer) to measure breaks from sedentary time, this study found strong and negative correlations for

sedentary time fragmentation (breaks) with FM percentage ($r=-0.847$; $P=0.002$) and lower limb FM ($r=-0.806$; $P=0.005$) (Chastin et al., 2012). Regardless, few studies have explored the associations for sedentary patterns with adiposity measures, and future research should also seek to move beyond the crude concept of breaks and endeavor to understand the pattern of accumulation of sedentary behavior in more detail. Likewise, observational and experimental studies using more accurate methods for the sedentary behavior assessment (e.g., ActivPAL) combined with molecular level of body composition measures are relevant to understand how different sedentary patterns may affect regional FM deposition.

Sedentary behavior and energy balance regulation

The foundation for the associations between sedentary behavior and its patterns of accumulation and total/regional obesity markers is basically based upon energetic arguments. Therefore, a summary of the experimental findings on the EE associated with sedentary behavior's alterations are presented below.

It is ironic that despite sitting being a ubiquitous behavior in all people, there are relatively few well-controlled studies actually assessing the EE of sitting (Kanade, Gokhale, & Rao, 2001; Lanningham-Foster et al., 2009; Lante, Reece, & Walkley, 2010; Levine, Schleusner, & Jensen, 2000; Rao, Gokhale, & Kanade, 2008; Swartz, Squires, & Strath, 2011). Sitting (as one watches TV, reads, and types on a computer) alone may account for more than 9–10 hours of many individuals' waking days and thus, accurate assessment of the metabolic rate during sitting is essential in order to minimize errors in estimates of sedentary behavior (Matthews et al., 2012).

Most of the studies that have assessed the EE of sitting behaviors (Kanade et al., 2001; Lanningham-Foster et al., 2009; Lante et al., 2010; Levine et al., 2000; Rao et al., 2008; Swartz, Squires, et al., 2011) were focused on comparing basal metabolic rates to the energy cost of LIPA or MVPA and included one or two sedentary behaviors. TV viewing has been frequently assessed in these studies, whereas other common sedentary activities, such as typing and reading, are less well studied (Matthews et al., 2012).

However, one study quantified the total EE of three different durations of PA within a 30-minute sedentary period and examined the potential benefits of

interrupting sedentary behavior with PA for weight control (Swartz, Squires, et al., 2011). Bout one contained no walking interruptions. Bout two contained a 1-minute walking period. Bout three contained a 2-minute walking period and bout four contained a 5-minute walking period.

This study showed that more energy was expended during each 30 minutes sedentary bout with a walking break than in the 30 minute sedentary bout (Swartz, Squires, et al., 2011). On average, participants expended an additional 3.0, 7.4, and 16.5 additional net kilocalories during bouts 2, 3, and 4, respectively compared with bout 1. When extrapolated for a full eight-hour working day, this data shows that an individual would theoretically expend an additional 24, 59 or 132 kilocalories per day, if they stood up and walked at a normal, self selected pace for one, two or five minutes every hour, respectively, compared with sitting for the 8-hour period (Swartz, Squires, et al., 2011).

Results from quantifying the metabolic and energy cost (MEC) associated with "sitting" and "standing" have produced equivocal results (Torbeyns, Bailey, Bos, & Meeusen, 2014) with large variation between the mean values for the MEC of standing versus sitting (Reiff, Marlatt, & Dengel, 2012; Schuna et al., 2014). The public is being sent confusing messages about the energetics of changing posture. Mainstream media are now awash with reports that suggest "simply standing burns considerably more calories than sitting", and how this is justification for why standing desks are becoming "de rigueur" for socially-conscious employers (Schuna et al., 2014). However, supporting research often compares sitting to a variety of non-sitting behaviors (Elmer & Martin, 2014; Schuna et al., 2014) instead of defining the MEC of the type of standing that characterizes standing still when a person might for example be typing at a standing desk or standing in a meeting.

Increasing daily EE is a valid way to improve overall health and wellbeing (Levine et al., 2006). While the workplace has been identified as an environment to promote changes in sedentary behavior, leisure time also represents a good alternative for reducing sedentary time. Programs that focus on employee-initiated voluntary PA achieved modest increases in employees' EE. An intervention found that reducing TV viewing produced a statistically significant increase in EE in overweight/obese adults

but no apparent change in energy intake (EI) after 3 weeks of intervention (Otten, Jones, Littenberg, & Harvey-Berino, 2009). The findings from this study are important once they highlighted that reducing TV viewing time increased EE and did not alter EI, which would promote a healthier energy balance that could help people to control weight gain or even lose weight (Otten et al., 2009).

Another 13-week intervention study (Pedersen, Cooley, & Mainsbridge, 2014) including desk-based employees aimed to increase workday EE by interrupting prolonged occupational sitting time and introducing short-bursts of PA to employees' daily work habits. The intervention consisted of regular (every 45 min) passive prompts delivered through desktop computer that required employees to stand up and engage in a short-burst of PA whereas the control group continued with their normal work routine (Pedersen et al., 2014). This study found that the intervention group increased the calories expended during the workday from pre-test ($M=866.29 \pm 151.40$ Kcal) to post-test ($M=1054.10 \pm 393.24$ Kcal), while the control group decreased calories expended during the workday from pre-test ($M=982.55 \pm 315.66$ Kcal) to post-test ($M=892.21 \pm 255.36$ Kcal). Therefore, reducing sedentary time by breaking up with PA bursts seems to be effective for increasing employee work-related EE (Pedersen et al., 2014).

It is increasingly recognized that standing represents a solution to extended periods of sitting but a recent longitudinal study in adults (Chaput et al., 2015), that aimed to examine the association between workplace standing time and the incidence of overweight/obesity and impaired glucose tolerance/type 2 diabetes found that greater occupational standing time was not sufficient to prevent the development of overweight/obesity and impaired glucose tolerance/type 2 diabetes in adults (Chaput et al., 2015). Therefore, more information on the energetics of sitting, standing, and specially the transitions between these two behaviors (breaks) are needed.

In fact, much scientific interest has been emerging about the possible metabolic benefits of interrupting sitting time by introducing LIPA breaks (standing and walking activities) throughout the workday (Healy, Matthews, et al., 2011; Henson, Yates, Biddle, et al., 2013; Peddie et al., 2013). However, future efforts are needed to better understand the potential benefits of higher amounts of standing time on the prevention of chronic diseases and although seemingly straightforward to quantify, there is a need

for research to carefully quantify these behaviors' EE, while accounting for body composition.

2.4. Experimental findings for sedentary behavior

Evidence has emerged identifying sedentary behavior (prolonged sitting) as a novel risk factor for several diseases and all-cause mortality, independent of time spent in MVPA. As this evidence is primarily observational in nature, further experimental research investigating potential mechanisms and dose-response relationships are necessary (Owen, Sparling, Healy Gè, Dunstan, & Matthews, 2010).

2.4.1. EFFECTS OF CHANGES IN TOTAL SEDENTARY TIME

There is some controverting findings regarding the effects of changes in sedentary behavior with health parameters. For example a 12-week intervention showed that reducing sedentary time, without exercise training, by an average of 50 min per day was not sufficient to elicit benefits on risk factors for type 2 diabetes and CVD (Kozey Keadle et al., 2014). In opposition, a 6-week trial (Adams, Davis, & Gill, 2013) of a combined face-to-face and online intervention to reduce sedentary behavior in overweight/obese women found that participants increased self-reported PA and reduced self-reported sedentary behavior as compared to the control group, and experienced the additional health benefit of reduced WC (Adams et al., 2013). In addition, twenty-nine of the 40 participants experienced reductions in WC, and the mean decrease was 2.25 (SD = 2.84) cm, showing that interventions to reduce sedentary behavior may provide a non-exercise alternative for potentially reduce WC, a risk factor for type 2 diabetes (Adams et al., 2013).

More examples of studies showing opposing findings for the effects of sedentary behavior changes on health-related outcomes exist (Andersen, Ekelund, & Anderssen, 2015; Manini et al., 2015; Saunders, Tremblay, Després, et al., 2013). But there are limited data about the minimal amount of sedentary behavior change required to produce meaningful health benefits (Manini et al., 2015). Additionally, sedentary behavior interventions would benefit from having more knowledge regarding the timing of expression of the metabolic and physiological outcomes. Potentially longer

interventions to reduce sedentary behavior might have erroneously considered the timing for examining outcomes and consequently fail such point, due to the sometimes short window of opportunity, thus concluding no significant effects for sedentary behavior changes in those variables. Moreover, the fact that the long term findings demonstrate changes in adiposity can be explained by the more chronic nature of this type of variables.

Therefore, studies comparing a single day of sitting to controlled amounts of LIPA are only starting to emerge and are insightful because the time is short enough to identify some of the more potent responses that are independent of changes in body composition (Dunstan et al., 2012; Duvivier et al., 2013; Manohar et al., 2012; Stephens, Granados, Zderic, Hamilton, & Braun, 2011). Stephens et al., (2011) observed a 39% reduction in insulin stimulated glucose uptake after a day of sitting compared to a trial with LIPA activities (Stephens et al., 2011).

The activities were diverse and mimic many of the typical activities of daily living, such as dishwashing, folding clothes, and putting away groceries, with an additional EE of $\sim 44 \text{ kcal}\cdot\text{hour}^{-1}$, in the active trial compared to the sedentary control trial (Stephens et al., 2011). The main contribution from this study was that although the intensity was below the range described as “health promoting”, insulin action was impacted and the effect was still evident in the next morning after a night of rest (Stephens et al., 2011), highlighting that replacing sitting time with LIPA activities during a day, results in acute improvements in the glucose metabolism with concurrent medium-term benefits (Stephens et al., 2011).

Another experimental study (Duvivier et al., 2013) considered three protocols; 1) Participants were instructed to sit $14 \text{ hr}\cdot\text{day}^{-1}$ (sitting regime); 2) to sit $13 \text{ hr}\cdot\text{day}^{-1}$ and to substitute 1 hr of sitting with vigorous exercise (exercise regime); 3) to substitute 6 hrs sitting with 4 hr of walking and 2 hr of standing (minimal intensity PA regime) (Duvivier et al., 2013). This study concluded that one hour of daily physical exercise cannot compensate the negative effects of inactivity on insulin level and plasma lipids, if the rest of the day is spent sitting. Thus, replacing sedentary time with a large amount of non-exercise PA (walking/standing) is more effective than one hour of physical exercise in reducing plasma triglyceride, non-HDL cholesterol, and postprandial insulin

(Duvivier et al., 2013). This study is important because experimentally confirmed the findings from observational studies that performing MVPA does not compensate for the deleterious effects of being seated all day and furthermore, replacing sedentary behavior with LIPA activities may be a good alternative (Duvivier et al., 2013).

Similarly, a recent randomized controlled intervention (Andersen et al., 2015) that aimed to increase PA level and not to specifically reduce sedentary time per se, in a group of sedentary men (N=150), found that the reduction in objectively measured sedentary time was beneficially associated with changes in postprandial log-transformed plasma insulin ($\beta=0.002$; 95% CI, 0.001-0.003), C-peptide ($\beta=3.7$; 95% CI, 1.5-6.0), and glucose concentration ($\beta=0.006$; 95% CI, 0.002-0.1), independent of changes in MVPA, WC, and other confounders (Andersen et al., 2015).

Furthermore, a study including male patients with type 2 diabetes investigated the impact of activities of daily living (ADL) versus MVPA on 24 h glycemic control (van Dijk et al., 2013). This was a randomized crossover trial consisting of three experimental periods. Participants were studied under sedentary control conditions, and under conditions in which prolonged sedentary time was reduced either by three 15-min bouts of ADL or by a single 45-min bout of MVPA (van Dijk et al., 2013). Blood glucose concentrations were assessed by continuous glucose monitoring, and plasma insulin concentrations were determined in frequently sampled venous blood samples (van Dijk et al., 2013).

The results from this study showed that hyperglycemia (glucose >10 mmol/L) was experienced for 6 h 51 min per day during the sedentary control condition and was significantly reduced by exercise (4 h 47 min; $P < 0.001$), but not by ADL (6 h 2 min; $P=0.67$). The cumulative glucose incremental areas under the curve (AUCs) of breakfast lunch, and dinner were 35% ($P < 0.001$) and 17% ($P < 0.05$) lower during the exercise and ADL conditions, respectively compared with the sedentary condition (van Dijk et al., 2013). The insulin incremental AUCs were, respectively, 33% ($P < 0.001$) and 17% ($P < 0.05$) lower during the exercise and ADL conditions compared with the sedentary condition. Thus, when matched for total duration, MVPA seems to be a more effective strategy to improve daily blood glucose homeostasis than repeated bouts of ADL. Nevertheless, the introduction of repeated bouts of ADL during prolonged sedentary

behavior forms a valuable strategy to improve postprandial glucose handling in patients with type 2 diabetes (van Dijk et al., 2013).

In summary, there are apparent evidence that reducing sedentary behavior improves metabolic health, specifically for the glucose metabolism, but there is still doubt regarding the type of activity that must replace sitting behaviors so that the benefits are empowered. The findings on the importance of activities' intensity are still inconsistent and the ideal patterns of sedentary behavior's interruptions are yet to be discovered.

2.4.2. EFFECTS OF PROLONGED AND UNINTERRUPTED SEDENTARY TIME

In addition to the harms of total sedentary behavior, observational findings on the metabolic benefits associated with breaking up sedentary time more often are building. However, these findings do not allow causality and therefore experimental evidence is needed in order to test the hypothesis generated in the observational studies.

Dunstan et al., (2012) using a three-treatment acute crossover trial: 1) uninterrupted sitting; 2) seated with 2-min bouts of light-intensity walking every 20 min; and 3) seated with 2-min bouts of moderate-intensity walking every 20 min was the first to experimentally conclude that interrupting sitting time with short bouts of light or moderate intensity walking lowered postprandial glucose and insulin levels in overweight/obese adults (Dunstan et al., 2012).

Regardless of the higher magnitude of change for the MVPA breaks condition, this study found LIPA breaks to also significantly reduced postprandial glucose and insulin levels (Dunstan et al., 2012). Therefore, this treadmill walking study highlighted the need for more studies to focus on even lighter activities as it would not be practical for people to alter the workplace or other domains to replace many hours of sedentary time with MVPA (Dunstan et al., 2012). This study suggested that introducing LIPA breaks in sedentary behavior may promote healthier metabolic status in an acute way (Dunstan et al., 2012).

Furthermore, there is still uncertainty if these positive effects may gather with time and recently, Larsen and colleagues compared the cumulative (3-day) effect of

prolonged sitting on metabolic responses during a mixed meal tolerance test, with sitting that is regularly interrupted with brief bouts of light-intensity walking (seated with 2-min bouts of light-intensity walking every 20 min) (Larsen et al., 2015). These authors found that the glucose iAUC was higher in sit condition compared with the breaks condition on days 1 and 3 respectively. Also, the insulin iAUC was higher on both days (Larsen et al., 2015). Thus, this study added to the research field that breaking up sitting over 3 days sustains, but does not enhance, the lowering of postprandial glucose and insulin (Larsen et al., 2015).

In opposition, a randomized crossover trial (Altenburg, Rotteveel, Dunstan, Salmon, & Chinapaw, 2013) tested the hypothesis that the acute metabolic effects of prolonged sitting can be compensated by hourly interruptions to sitting using hourly 8 min MVPA cycling exercise bouts. However, only the postprandial levels of C-peptide were lower with no change in glucose, triglycerides, or cholesterol levels compared to 8 h of prolonged sitting (Altenburg et al., 2013). Therefore, even by considering interruptions in sitting time requiring a muscle activity of seven to eight times the resting value, this study did not find any significant changes in cardiometabolic indicators except for C-peptide (Altenburg et al., 2013). Considering previous studies, the findings from this study may suggest that the frequency of breaks (hourly breaks) was not sufficient to enhance metabolic pathways (Altenburg et al., 2013).

Furthermore, a study with a similar protocol to Dunstan's trial (Bailey & Locke, 2015) examined if performing two distinct LIPA breaks (standing and walking slowly) would impact postprandial glucose differently. This study consisted in three trials: (1) uninterrupted sitting; (2) seated with 2 min bouts of standing every 20 min; and (3) seated with 2 min bouts of LIPA walking every 20 min (Bailey & Locke, 2015). Plasma glucose area under the curve was lower in the activity-break condition compared to the uninterrupted sitting and standing-break conditions: mean area under the curve 18.5, 22.0, and 22.2 mmol L/5 h, respectively, ($p < 0.001$) (Bailey & Locke, 2015). This study found no difference between uninterrupted sitting and standing-break conditions and therefore suggests that interrupting sitting time with frequent brief bouts of LIPA, but not standing, imparts beneficial postprandial responses that may enhance cardiometabolic health (Bailey & Locke, 2015).

In contrast, Thorp and colleagues examined whether reductions in sitting time through alternating 30 min bouts of sitting and standing would reduce postprandial glucose, insulin, and triglyceride responses in overweight/obese sedentary office workers and found differences for plasma glucose ($P=0.007$) but not for serum insulin (Thorp, Kingwell, Sethi, et al., 2014). Adjusted mean glucose incremental area under the curve was lowered by 11% after the intervention condition compared to control. Therefore, alternating sitting with standing in 30-min bouts resulted in modest beneficial effects on postprandial glucose responses in overweight/obese office workers (Thorp, Kingwell, Sethi, et al., 2014).

Findings from this study showed that participants' fatigue was higher during the sit condition (mean 67.8 (95% CI 58.8 to 76.7)) compared with the stand/sit condition (52.7 (43.8 to 61.5); $P<0.001$) and that the lower back musculoskeletal discomfort was reduced during the stand/sit condition (31.8% reduction). Despite concentration/focus being significantly higher during the sit condition ($P=0.006$), there was a trend towards improved overall work productivity in favour of the stand-sit condition ($P=0.053$) (Thorp, Kingwell, Owen, & Dunstan, 2014). Thus, transitioning from a seated to a standing work posture every 30 min across the workday, relative to seated work, not only improved metabolic markers (Thorp, Kingwell, Sethi, et al., 2014), as led to significant reductions in fatigue levels and lower back discomfort in overweight/obese office workers, while maintaining work productivity (Thorp, Kingwell, Owen, et al., 2014).

The findings for the benefits of standing are therefore inconsistent (Bailey & Locke, 2015; Dunstan et al., 2012; Thorp, Kingwell, Sethi, et al., 2014), and it seems that investigation have turn their attention to walking and other non-standing activities while performing breaks. In line with this, 70 adults participated in a randomized crossover trial with 3 arms (Peddie et al., 2013). The prolonged sitting intervention involved sitting for 9 h, the PA intervention involved walking for 30 min and then sitting, and the regular-activity-break intervention involved walking for 1 min and 40 s every 30 min (Peddie et al., 2013). This study found a 37% reduction in plasma glucose iAUC and 18% reduction in plasma insulin iAUC observed when regular activity breaks were performed (Peddie et al., 2013), suggesting that regularly breaking prolonged

sitting with short (1 min 40 s) bouts of walking activity is more effective than a single continuous (30 min) bout of PA at lowering postprandial glucose and insulin concentrations in healthy, normal-weight adults (Peddie et al., 2013).

These results confirm and exacerbate previous findings (Bailey & Locke, 2015; Dunstan et al., 2012), by showing that very short breaks can stimulate metabolic pathways and reduce overall postprandial glucose and insulin levels compared to a single longer bout of PA (Peddie et al., 2013). In addition to the opposing findings for the standing condition, this study highlighted that the key factor is based on transitioning from one behavior to another and the specific metabolic alterations that may result from these transitions.

However, from these experimental studies it may be concluded with some certainty that breaking up sedentary behavior improves metabolic health such as postprandial glycaemia and insulinemia. However, the mechanisms underlying these effects are unclear. Nonetheless, one of the possible mechanisms underlying the improvement in metabolism, by interrupting prolonged sitting may be the reduction of oxidative stress (Johnson, Padilla, Harris, & Wallace, 2011). In fact, metabolic disorders, including hyperglycemia and hyperinsulinemia are caused by the endothelial dysfunction through elevation of oxidative stress (Wallace, Johnson, Padilla, & Mather, 2010).

Accordingly, one study examined if breaking sitting by standing and acute exercise reduced postprandial oxidative stress (Takahashi, Miyashita, Park, Sakamoto, & Suzuki, 2015). This study considered 3 trials (sitting, standing, and exercise), each lasting 2 days, in a randomised order. On day one of sitting trial, participants sat in a chair. For the standing trial, the participants stood 6 times, for a 45-minute period each time. For the exercise trial, the participants walked or ran for 30 minutes (Takahashi et al., 2015). On day two of each trial, participants rested and consumed the standardised breakfast and lunch. Blood samples were collected fasting and at 2, 4, and 6 hours postprandially (Takahashi et al., 2015).

This study found that concentrations of serum derivatives of reactive oxygen metabolites measured at 4 hours and 6 hours were similar than that in the fasting state in

the sitting trial, but were significantly reduced for the standing and exercise trials. Therefore, these results indicate that breaking sitting time may be relevant for improving postprandial oxidative stress, regardless of the intensity of activity performed within breaks (Takahashi et al., 2015).

Besides these glucose/insulin related benefits, evidence is emerging to suggest that patterns of accumulation of sedentary time (breaks in and bouts of sedentary time) may also be important to CVD health. One study found that interrupting sitting time with either LIPA or MVPA bouts of walking, significantly lowered systolic blood pressure by 2–3 mmHg and diastolic blood pressure by 2 mmHg, relative to uninterrupted sitting (Larsen, Kingwell, et al., 2014). Additionally, the blood pressure decrease was not dose-related to the intensity level of the breaks, providing support to earlier findings that breaks in sedentary time per se are beneficially associated with cardiometabolic risk biomarkers regardless of the intensity of the activity performed during the breaks (Healy, Dunstan, et al., 2008).

Finally, from the same randomized controlled trial performed by Dunstan et al., (2012) at Baker IDI in Australia, Howard and colleagues found that prolonged sitting increases fibrinogen and reduces plasma volume, with associated increases in hemoglobin and hematocrit (Howard et al., 2013). This investigation found that activity breaks attenuated these responses, indicative of an ameliorating influence on the procoagulant effects of uninterrupted sitting (Howard et al., 2013).

In conclusion, more experimental studies work toward the goal of successfully reducing sedentary time to amounts consistent with meaningful disease prevention but more research is needed to inform about the ideal type of activity that must replace sedentary behavior and also the best frequency to interrupt sedentary time. Because the proportion of the population that is most in need for sedentary behavior interventions has the greatest health concerns, it would be unrealistic for research that does not pay close attention to non-fatiguing and safe types of PA. Given these issues, one of the most high impact questions that is still almost totally unresolved is what behaviors will be most effective and practical. Therefore, the main findings on the effectiveness of previous interventions to reduce and break up sedentary behavior will be presented below.

2.5. Effectiveness of interventions to reduce and interrupt sedentary behavior

2.5.1. *NON-SEDENTARY BEHAVIOR SPECIFIC INTERVENTIONS*

A meta-analysis systematically reviewed the literature and compared the effectiveness of controlled interventions with focus on PA and/or sedentary behaviors for reducing sedentary behavior in adults (Prince, Saunders, Gresty, & Reid, 2014). This meta-analysis provides consistent evidence that large and clinically meaningful reductions in sedentary time can be expected from interventions with focus on reducing sedentary behaviors while PA and PA/sedentary behavior's interventions do not generate meaningful reductions in sedentary time (Prince et al., 2014).

With only 14 studies reporting greater reduction in sedentary behavior compared to the control group, and 29 studies reporting no difference between the intervention and control groups, this meta-analysis identified that overall PA interventions resulted in approximately 19 min·day⁻¹ reduction in sedentary behavior (Prince et al., 2014). Considering the combined PA/sedentary behavior interventions, seven studies reported that the intervention group had a significantly greater reduction in time spent being sedentary than the control group (Prince et al., 2014), while seven studies reported no significant difference between the intervention and control groups (Prince et al., 2014). Regardless of the better results when introducing sedentary behavior's specific strategies, the overall mean reduction attributed to the PA/sedentary behavior interventions was about 35 min·day⁻¹ (Prince et al., 2014).

In fact, the majority of PA interventions showed no significant differences between the intervention and control groups for sedentary time (Prince et al., 2014). While there was variability among the populations and the actual PA interventions, it is worth noting that only two PA interventions involving older adults (≥ 60 years) reported significant differences in sedentary time (Burke et al., 2013; Mutrie et al., 2012). Burke et al. (2013) reported a significant intervention effect with a mean difference of 57 min·day⁻¹ of self-reported sitting time, while Mutrie and colleagues reported that sedentary time in the intervention group was 67.5 min·day⁻¹ lower compared to the

control group (Mutrie et al., 2012). Therefore, these two studies may suggest that PA interventions may exclusively reduce sedentary behavior when older adults are considered.

A more recent systematic review and meta-analysis of 34 studies also aimed to evaluate the effect of interventions which included sedentary behavior as an outcome measure in adults (Martin et al., 2015). They found an average reduction of 22 min·day⁻¹ in sedentary behavior in the intervention groups (N=5868). Furthermore, this meta-analysis concluded that lifestyle interventions (combined PA/sedentary behavior interventions with a dietary/nutrition component) reduced sedentary behavior by 24 min·day⁻¹ (N=3981, moderate quality), while interventions focusing on sedentary behavior reduction only presented a mean reduction of 42 min·day⁻¹ (N=62, low quality) (Martin et al., 2015). Also, this meta-analysis reinforced previous findings, that there is no evidence of an effect of PA and combined PA/sedentary behavior interventions on reducing sedentary time in adults (Martin et al., 2015).

Martin's meta-analysis gathered all the randomized controlled trials that directly or indirectly interfere with sedentary behavior. In summary, types of intervention varied substantially between studies (Martin et al., 2015). Nine studies aimed at increase PA levels, 3 studies combined both approaches of reducing sedentary behavior and increase PA levels, one study assessed the effect of a dietary intervention on sedentary behavior, and 20 studies applied a multicomponent lifestyle intervention (Martin et al., 2015). Only two studies employed an intervention that specifically aimed to reduce sedentary behavior (Evans et al., 2012; Pedersen et al., 2014) and they had "low quality" suggesting that "further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate". Thus, the lack of specific quality interventions to reduce sedentary behavior justify future interventions to consider strategies to reduce and break up sedentary behavior (Martin et al., 2015).

2.5.2. SEDENTARY BEHAVIOR-ONLY INTERVENTIONS

Prince and colleagues' meta-analysis included more sedentary behavior-only interventions compared to the one from Martin et al., (2015) since their criteria were less demanding (Prince et al., 2014). In this meta-analysis, seven studies (Alkhajah et al., 2012; Carr, Karvinen, Peavler, Smith, & Cangelosi, 2013; Healy et al., 2013; Kozey Keadle et al., 2014; Neuhaus, Healy, Dunstan, Owen, & Eakin, 2014; Otten et al., 2009; Pronk, Katz, Lowry, & Payfer, 2012) reported that the intervention group had a significantly greater reduction in time spent being sedentary than the control group, while only one study reported no significant difference between the intervention and control groups (Prince et al., 2014).

In opposition to the non-specific sedentary behavior interventions, the effectiveness of these sedentary behavior specific interventions was much higher and consistent, corresponding to a reduction in sedentary time of approximately 91 min·day⁻¹ (Prince et al., 2014). A study that was not included in these meta-analysis, due to its publication date, examined the feasibility of reducing sitting behavior and increase sit-to-stand transitions, in overweight/obese older adults that completed an 8-week theory-based intervention (Rosenberg et al., 2015).

Using an inclinometer (ActivPAL) to measure sedentary behavior and its patterns, this intervention resulted in a decrease of 27 min·day⁻¹ in sitting time, and sit-to-stand transitions remained constant, while standing time increased by 25 min·day⁻¹ (Rosenberg et al., 2015). A conclusion from this study was that reducing sitting time is feasible, and this intervention showed preliminary evidence of effectiveness among older adults with overweight and obesity to significantly reduce sitting time. However, there seems to be a natural resistance for increasing the number of breaks in sedentary time, an issue that must be considered in future interventions (Rosenberg et al., 2015).

Interventions to reduce sedentary behavior at work

Data from the WHO stated that workers represent approximately half the global population and most of the population spends an average of one third of adult life at work. Therefore, workplace must be a fertile setting in which to introduce strategies to reduce sitting time and break up periods of prolonged sitting to improve health. In

particular, office-based workers are highly sedentary, making them a key target group for intervention. For many office workers, the bulk of their daily sitting time occurs at work (Brown, Miller, & Miller, 2003). Thus, the office is a key setting to reduce prolonged sitting (van Uffelen et al., 2010; Wong, Gilson, van Uffelen, & Brown, 2012), and this is an important consideration in the context of the duty of care obligations of employers to ensure, so far as it is reasonably practicable, the provision and maintenance of a work environment for employees without risks to health and safety (van Uffelen et al., 2010; Wong et al., 2012).

Encouraging breaks from sedentary behavior while working may be a direction worth exploring in future research on occupational sitting, especially given the evidence on the metabolic health risks associated with extended periods of sitting (Bailey & Locke, 2015; Carson et al., 2014; Chastin et al., 2015; Dunstan et al., 2012; Healy, Dunstan, et al., 2008). However, it is not clear whether workplace interventions to reduce sitting time would simply aim to decrease the total volume of sitting time or to interrupt prolonged periods of sitting, in order to positively affect health (Shrestha, Ijaz, Kukkonen-Harjula, Kumar, & Nwankwo, 2015).

Interventions for reducing sedentary behavior at work can involve various types of PA of light or moderate intensity. Workers can be encouraged to be more physically active through changes in the workplace environment. For example, an ordinary office desk can be replaced with a sit-to-stand desk, which is height adjustable and allows the person to alternate posture between sitting and standing (Alkhajah et al., 2012; Karol & Robertson, 2015; Mansoubi, Pearson, Biddle, & Clemes, 2015; Neuhaus, Healy, et al., 2014). Another alternative is a vertical workstation that allows the use of a personal computer while walking on a treadmill at a self-selected velocity (Levine & Miller, 2007; MacEwen, MacDonald, & Burr, 2015; Schuna et al., 2014) or a stepping/pedaling device placed under the desk that allows the user to pedal while being seated at work (McAlpine, Manohar, McCrady, Hensrud, & Levine, 2007; Shrestha et al., 2015; Torbeyns et al., 2014).

Sedentary behavior can also be decreased by changing the design of workplaces, for example placing printers further away from desks, by promoting walking or other exercise groups like dance or gym groups during work time, by encouraging employees

to walk around office buildings during breaks or to take a walk to communicate with fellow employees instead of using the telephone or email (Thogersen-Ntoumani, Loughren, Duda, Fox, & Kinnafick, 2010). Another strategy is to change workplace's policy to introduce frequent breaks within the organisational schedule for short bouts of activity in workplace settings or for conducting walking or standing meetings. Meeting rooms can be equipped with sit-to-stand workstations, so that employees can choose to stand during meetings if they wish (Thogersen-Ntoumani et al., 2010).

These are some of the strategies that have the potential of providing an opportunity to a large number of people, who mostly sit at work, to reduce their sitting time (Shrestha et al., 2015). For this reason, there is a greater number of interventions to reduce sedentary behavior at work and few have focused on leisure time.

In line with this, a 12-week randomised controlled trial (Parry, Straker, Gilson, & Smith, 2013) was conducted including workers (n=62, aged 25-59 years) in Perth, Australia. Three groups developed interventions with a participatory approach: 1) 'Active office' (n=19), which consisted of an electronically height adjustable desk with integrated treadmill or a treadmill plus a stationary cycle ergometer; 2) 'Traditional PA' (n=14), pedometer challenge to increase activity between productive work time and; 3) 'Office ergonomics' (n=29), "active" sitting (moving whilst in the chair) and breaking up computer tasks (Parry et al., 2013).

The findings showed a reduction in sedentary time on work days of -1.6% and -1.7% during work hours and a significant increase in the number of breaks/sedentary hour on work days and during work hours (Parry et al., 2013). This study explored novel ways to modify work practices to reduce occupational sedentary behavior and concluded that participatory workplace interventions can reduce sedentary time, increase the frequency of breaks, and improve LIPA and MVPA of office workers by using a variety of interventions (Parry et al., 2013).

However, a recent systematic review concluded that at present, there is very low quality evidence that sit-to-stand desks can reduce sitting time at work and the effects of policy changes and information and counselling are inconsistent (Shrestha et al., 2015). Shrestha and colleagues found very low quality evidence that sit-stand desks with or

without additional counselling reduced sitting time at work, at one week follow-up (one study) and at three months' follow-up (two studies) compared to no intervention. Regardless, sitting time during the whole day decreased with sit-to-stand desks compared to no intervention (one study) as did sitting bouts lasting 30 minutes or more (two studies) (Shrestha et al., 2015).

Sit-stand desks did not have a considerable effect on work performance and had an inconsistent effect on musculoskeletal symptoms and sick leave (Shrestha et al., 2015). Also, this review concluded that walking strategies had no considerable effect on sitting at work (one study, 179 participants, low quality evidence) and guideline-based counselling seemed to reduce sitting time at work (one study, 396 participants, low quality evidence). Furthermore, inconsistent effects of computer prompting on sitting time at work were found, with one study showing no considerable effect on sitting at work at 10 days' follow-up, while another study reported a significant reduction in sitting at work at 13 weeks' follow-up (Shrestha et al., 2015). Finally, computer prompting software also led to a non-significant increase in EE at work at 13 weeks' follow-up (Shrestha et al., 2015).

A recent review systematically summarized the evidence for activity-permissive workstations on sedentary behavior and concluded that the pooled effect size from the meta-analysis was -77 min of sedentary time/8 h workday (Neuhaus, Eakin, et al., 2014). Regardless of the small sample size of some studies included in this meta-analysis, these findings suggest that activity-permissive workstations can be effective to reduce occupational sedentary time, without compromising work performance (Neuhaus, Eakin, et al., 2014).

Reinforcing these findings a recent controlled intervention examined the effects of an environmental change on occupational sedentary time, musculoskeletal comfort and work ability, and the usability of sit-stand workstations in office work via a self-reported questionnaire (Gao, Nevala, Cronin, & Finni, 2015). In this study, the intervention group (n = 24) used sit-stand workstations during 6 months and the control group (n = 21) used traditional sitting workstations. The findings showed that working at sit-stand workstations can reduce sitting time compared to control workstations (-6.7% vs. 5.0%, p=0.019), which was reallocated mostly to standing (r=-0.719,

$p < 0.001$). Furthermore, sit-stand workstations improved perceived musculoskeletal comfort in the neck and shoulders, as well as work ability (Gao et al., 2015). This study also stated that while the environmental change alone was effective, it is likely that promoting the daily use of sit-stand workstations with counselling would lead to even more substantial positive effects.

Finally, a recent comprehensive review suggests that some amount of standing during an 8-hour workday could be beneficial without compromising worker's comfort or productivity, however stated that there is very little data on the efficacy of treadmill and bicycle workstations (Karol & Robertson, 2015). Thus, several strategies have been employed to reduce and break up workplace sedentary behavior, but opposing findings have been found for their effectiveness. Moreover, multicomponent interventions have been tested and they seem more effective as they gather different strategies.

In the literature, multicomponent interventions are characterized by focusing in more than one domain (e.g., changing both workplace and leisure time), but also the ones considering more than one strategy for reducing sedentary behavior in one domain-only (e.g., introducing both sit-stand workstations and step goals). Regardless of the lack of multicomponent interventions that exist, they will be presented as follows.

Multicomponent interventions to reduce sedentary behavior

Healy and colleagues investigated the short-term efficacy of a multicomponent intervention to reduce office workers' sitting time (Healy et al., 2013). The 4-week intervention emphasized three key messages: "Stand Up, Sit Less, Move More" and comprised organizational, environmental, and individual strategies to reduce and break up sedentary time. Changes in the time spent sitting, in prolonged sitting (≥ 30 min), standing, and moving were objectively measured by ActivPAL (Healy et al., 2013).

The findings from this intervention showed that the intervention group significantly reduced workplace sitting time (mean change [95%CI]: -125 [-161, -89] min/8-h workday), with changes primarily driven by a reduction in prolonged sitting (-73 [-108, -40] min/8-h workday). Also, it was found that workplace sitting was almost exclusively replaced by standing (+127 [+92, +162] min/8-h workday) with non-significant changes to stepping time (-2 [-7, +4] min/8-h workday) (Healy et al., 2013),

thus suggesting that a multicomponent workplace intervention can substantially reduce sitting time in an office setting.

Healy's intervention considered different strategies to reduce sedentary behavior but it only targeted the workplace domain. Therefore, another multicomponent intervention including university employees consisted of a theory-based, internet-delivered programme, a portable pedal machine to reduce sedentary behavior at work and a pedometer for the leisure time during 12 weeks (Carr et al., 2013). The intervention group reduced daily sedentary time by $-58.7 \text{ min}\cdot\text{day}^{-1}$ and participants logged on to the website 71.3%, used the pedal machine 37.7%, and pedalled an average of $31.1 \text{ min}\cdot\text{day}^{-1}$ in all working intervention days. This study suggested compliance to the intervention with significant reductions in daily sedentary time among full-time sedentary employees (Carr et al., 2013). Regardless of using several strategies that also include changes in the leisure time, these interventions yet emphasized the workplace settings.

In opposition, a randomized controlled trial evaluated the effectiveness of a mindfulness-based multi-component intervention on leisure time and work-based sedentary behavior, fruit intake and determinants of these behaviors (van Berkel, Boot, Proper, Bongers, & van der Beek, 2014). The control group received information on existing lifestyle behavior-related facilities that were already available at the worksite, while 129 workers received a mindfulness training, followed by e-coaching, lunch walking routes and fruit (van Berkel et al., 2014). Outcome measures were assessed at baseline and after 12 months using questionnaires. However, after 12 months, there were no differences in sedentary behavior between the intervention and control groups. Thus, this mindfulness-based multi-component intervention was not effective in reducing sedentary behavior (van Berkel et al., 2014).

Barwais and colleagues assessed the effectiveness of a 4-week intervention in which an online personal activity monitor (Gruve-Technologies™) was used to reduce overall sedentary behavior among sedentary adults (Barwais & Cuddihy, 2015), and found that the amount of time spent in sedentary activities decreased and LIPA increased, within three domains (work, transportation and leisure time) (Barwais & Cuddihy, 2015). Interestingly, the large effect sizes were associated with leisure time

domain, suggesting that when participants had to reduce overall sedentary behavior, leisure time was the preferred domain in which people changed their sedentary behavior (Barwais & Cuddihy, 2015).

In summary, while reducing sedentary behavior is emerging as a new workplace health priority with interventions being planned for the recent years (Bergman, Boraxbekk, Wennberg, Sorlin, & Olsson, 2015; Hall, Mansfield, Kay, & McConnell, 2015), there is still a lack of evidence that these interventions are effective (Wong et al., 2012). Additionally, an important question started to rise “Is There a Compensation Effect?” or in other words; what is expected to observe in the leisure time when people reduce their time spent sitting at work or vice-versa. This topic is of great importance and needs to be addressed in future investigations. Therefore, more well designed multicomponent and leisure time-only interventions are needed.

Interventions to interrupt sedentary behavior

Moreover, there is still uncertainty regarding the effectiveness of interventions to reduce sitting time and simultaneously increase the daily number of sit/stand transitions, and the interaction between these two domains. A recent study assessed whether it was feasible for working and non-working older adults to reduce these two different behavioral targets and concluded that both groups changed the targeted behavior exclusively without changing the other behavior (Kerr et al., 2016).

Another intervention found that participants significantly reduced duration of average sitting bouts (16%) and the number of sitting bouts of ≥ 60 minutes (54%) (Swartz et al., 2012). Also total sitting time was reduced by 6.6% and duration of the longest sitting bout by 29%. Therefore these authors concluded that interventions that focus on disrupting sitting time only in the workplace may result in less sitting (Swartz et al., 2012). A pilot study demonstrated that when employees were exposed to a passive prompt, as opposed to an active prompt, they were five times more likely to fully adhere to completing a movement break every hour of the workday.

Regardless of the few interventions that specifically targeted the number of transitions, they suggest that people are willing to participate in coercive workplace e-health interventions but there is a need for further investigation.

Interventions to reduce leisure time sedentary time

Regardless of workplace, people spend great amounts of sedentary behavior in their leisure time, while watching TV, using a computer, or reading (Aadahl et al., 2013; Balboa-Castillo et al., 2011; Chau, Merom, et al., 2012; van der Ploeg et al., 2013). A recent study (Bennie et al., 2015) showed that medians for work, leisure time and transport-related sitting time were ~56%, ~32% and ~11% of total daily sitting time, among a sample of Australian office-based employees (Bennie et al., 2015). This study concluded that given the high contribution of occupational sitting to total daily sitting time among desk-based employees interventions must focus on the work setting (Bennie et al., 2015).

However, different sitting time domain's classifications exist, and if we would consider transport-related sitting time as non-work settings, and therefore be included in leisure sitting time, we would have approximately 44% of daily leisure sitting time. Thus, 44% of a day is a significant amount of time to be neglected, and future interventions must focus on reducing leisure sitting time. Compared to the high number of interventions to reduce and break up sedentary behavior while at work, interventions to specifically reduce leisure time sedentary behavior are scarce.

One study (Lakerveld, Bot, van der Ploeg, & Nijpels, 2013) assessed the short and long-term (6 and 24 months) effects of a primary care-based lifestyle intervention on different domains of leisure time sedentary behaviors in Dutch adults. However, the findings showed that primary care-based general lifestyle intervention was not more effective in reducing leisure time sedentary behaviors than providing brochures in adults at risk for chronic diseases (Lakerveld et al., 2013), probably because physical, and environmental alterations are necessary for reducing leisure time in sedentary pursuits.

Studies on intergenerational transmission of PA and sedentary behavior have shown that parents play a critical role in their children's PA and sedentary behavior (Jago, Sebire, Edwards, & Thompson, 2013; Xu, Wen, & Rissel, 2015). Therefore, interventions focusing on reducing adults' sedentary behavior while at home may additionally help to reduce children's sedentary behavior which is of great importance, once early childhood is a good time to promote healthful lifestyle habits. In fact, with a

multimedia approach, a pilot study aimed to evaluate the feasibility of a large randomized controlled trial examining the effects of a video-based program on mothers' and children's sedentary behavior (Tuominen, Husu, Raitanen, & Luoto, 2016).

This study introduced a combination of music, exercise, and a potentially motivating movement-to-music video program in the home environment and found that less sedentary behavior was revealed in week 2 than in week 1 among both intervention group mothers (56.6 vs. 53.3 %) and for intervention group children (49.5 vs. 46.0 %) (Tuominen et al., 2016). With approximately 4% reduction in leisure sedentary time this intervention found that the use of music and video content together may yield added benefits in efforts to reduce sedentary behavior and increase PA among mothers and their children in the home environment (Tuominen et al., 2016).

While not described by the authors as specific intervention to target leisure sitting time, a pilot intervention explored an individualised strategy aimed at reducing sedentary behaviors in older Scottish adults (Fitzsimons et al., 2013). Whereas this group of people was already in retirement it might be considered a specific intervention to reduce leisure sitting time. Furthermore, participants received an individualised consultation targeting sedentary behavior incorporating feedback from an activPAL activity monitor (Fitzsimons et al., 2013).

Interestingly, objectively measured total time spent sitting/lying was reduced by 24 min/day ($p=0.042$), a reduction of 2.2% (Fitzsimons et al., 2013). Regardless of the distinct strategies used to reduce leisure sedentary behavior, the overall reduction (2.2%) found in this study is in accordance with the one found for the Tuominen and colleagues' intervention (3.3%), therefore suggesting that in leisure time it may be expected a reduction of this magnitude.

Another four-week intervention aim to reduce sedentary behavior and increase PA levels in daily living for sedentary adults (Barwais, Cuddihy, & Tomson, 2013). While not specifically targeting leisure time, the strategy used in this intervention end up interfering more with this domain than any other. Participants in the intervention group interacted with an online personal activity monitor (Grube Solution™ MUVE,

Inc., USA). The device was designed to motivate a reduction in sedentary behavior and increase PA in the activities of daily living (Barwais et al., 2013).

The Gruve Solution is an activity-based approach built around the concept of NEAT. The monitor is a tri-axial accelerometer system that tracks time spent on daily sedentary, light, moderate, and vigorous intensity PA via a wearable device and an accompanying online service. It monitors a participant's daily PA at 20 Hz and stores the minute data on the device for later uploading to the interactive online software through a Universal Serial Bus (USB) port (Barwais et al., 2013).

These data subsequently provide the user with an easy-to-understand visualization of daily activity patterns. Goal-setting features are activated alongside simple graphs and charts to enhance the self-monitoring of EE (Barwais et al., 2013). The findings from this study showed that this self-control based strategy was able to decrease participants sedentary time by 21% (2.3 hours/day) and increased their LIPA by 36.7% (2.5 hours/day). However, despite leisure time being contemplated in this intervention we want to reinforce that this was not a leisure time specific intervention (Barwais et al., 2013).

In conclusion, there is a lack of specific interventions that targeted leisure time sedentary behavior reductions in adults, with only two studies that specifically aimed to reduce sedentary behavior in the leisure time (Lakerveld et al., 2013; Tuominen et al., 2016). The closest we found in the literature were lifestyle interventions that additionally to strategies for increasing PA levels, also examined sedentary behavior reductions, and few interventions aimed to specifically and exclusively reduce sedentary behavior in the leisure time. Also, leisure time specific interventions have not included environmental/physical changes (as found for the work settings) but instead appealed to self-control strategies with monitors feedback, or educational sessions for clarification regarding the deleterious effects of sedentary behavior. Thus, considering the limitations found for this domain, more interventions to reduce leisure sitting time, including specific and relevant strategies for behavioral alterations are needed.

Compensatory mechanisms

In addition, another reason for interventions to target leisure time is due to the hypothesis that compensatory mechanisms may exist, and when people reduce work-related sedentary behavior, they may compensate by being more sedentary during non-work settings. In fact, King et al., (2007) suggested that individuals may compensate for higher EE during exercise training by increasing sedentary behavior and/or decreasing non-exercise PA during the rest of the day (King et al., 2007), but data on compensatory behavior in response to exercise training are equivocal (Blaak, Westerterp, Bar-Or, Wouters, & Saris, 1992; Hollowell et al., 2009; Kempen, Saris, & Westerterp, 1995; Kozey-Keadle et al., 2014; Turner, Markovitch, Betts, & Thompson, 2010; Willis et al., 2014).

Large individual differences in changes in non-exercise PA within studies have been found and one study showed that half of the women who started an exercise training program actually decreased total daily EE (Di Blasio et al., 2012). These authors concluded that additional intervention would be necessary to ensure that a decrease in non-exercise PA and consequent increase in sedentary behavior does not occur (Di Blasio et al., 2012). Likewise, compensatory mechanisms may exist when people are driven to reduce sedentary behavior in one domain, with potential alterations in the other domains. However, the findings on the behavioral responses to sedentary behavior reduction interventions are limited, and equivocal findings have also been found (Chau, van der Ploeg, Merom, Chey, & Bauman, 2012; Mansoubi et al., 2015; Tigbe, Lean, & Granat, 2011).

Tigbe et al., (2011) found that having a more active occupation was not associated with more inactivity during non-work hours, thus suggesting no compensatory mechanisms for sedentary behavior (Tigbe et al., 2011). In opposition, another study found that workers with sitting jobs were significantly more likely to be sufficiently active during leisure time than workers with mostly standing, walking or heavy labor jobs (Chau, van der Ploeg, et al., 2012). Furthermore, workers with leisure time sitting of less than 4 hours per day had significantly lower obesity risk than workers with 4 or more hours per day of leisure time sitting independent of PA and

occupational activity, proposing that leisure sitting time may have a stronger association with obesity risk than occupational sitting (Chau, van der Ploeg, et al., 2012).

To the authors knowledge, only one experimental study (Mansoubi et al., 2015) examined whether the introduction of a sit-to-stand workstation among office workers led to reductions in sitting during working hours, and whether office workers compensate for any reduction in sitting at work by increasing sedentary time and decreasing PA outside work. Compared to baseline, the proportion of time spent sitting after 3 months significantly decreased and time spent standing and in LIPA increased during working hours (Mansoubi et al., 2015).

Interestingly, compared to baseline the proportion of time spent sitting significantly increased and LIPA significantly decreased during non-working hours across the follow-up measurements, and no differences were seen in MVPA during non-working hours throughout the study (Mansoubi et al., 2015). Thus, these findings suggested that introducing a sit-to-stand workstation significantly reduce sedentary behavior during working hours, but these changes were compensated for by reducing activity and increasing sitting outside of work (Mansoubi et al., 2015). Similar to what happened for the exercise interventions, a sedentary behavior reduction intervention that focus on working settings must be accompanied by an intervention outside of working hours to limit behavior compensation (Mansoubi et al., 2015).

2.6. Sedentary behavior assessment

The accurate assessment of sedentary behavior is important for monitoring prevalence and trends in different population groups including compliance with guidelines, determining dose-response associations with health indicators, identifying specific aspects of sedentary behavior that are associated with health, and informing intervention strategy design and effectiveness.

It is unclear how the choice of sedentary behavior indicator may influence these associations. For example, objective determinations of sedentary time are expected to be more accurate than subjective measures such as questionnaires, once this information is not dependent of people's view and memory. However, one study (Stamatakis, Hamer,

Tilling, & Lawlor, 2012) examined the associations between sedentary behavior and a set of cardiometabolic risk factors (WC, BMI, systolic and diastolic blood pressure, total and HDL, glycated haemoglobin), and analysed whether these associations differed depending upon self-report or objectively sedentary behavior assessment (Stamatakis, Hamer, et al., 2012). In this particular study, sedentary behavior was consistently associated with cardiometabolic risk only when it was measured by self-report (Stamatakis, Hamer, et al., 2012). The accelerometry derived sedentary time was only associated with total cholesterol. Thus, choosing the correct method is not as straight and more discussion on this issue is needed (Celis-Morales et al., 2012).

A range of subjective and objective methods have been used in sedentary behavior research to quantify sedentary time and describe what people are doing when they are sedentary (i.e., what behaviors they engage in). This section refers to instruments that attempt to measure the domains of sedentary behavior (mode, context, duration and patterns) through subjective and objective methods. Questionnaires are the most commonly reported method of capturing sedentary behavior (Clark et al., 2009; Clark, Thorp, et al., 2011; Cleland et al., 2014; Clemes, David, Zhao, Han, & Brown, 2012) and the majority of which are self-administered, although in-person and telephone interview formats have also been used (Matton et al., 2007).

Questionnaires, have focused predominantly on TV viewing or other screen-based behaviors. Typically, such measures demonstrate moderate reliability but slight to moderate validity (Atkin & Gorely, 2012). Other self-report methods, such as diaries, although less used in epidemiological studies to date, are also considered. Accelerometry is increasingly being used for sedentary behavior assessments; this approach overcomes some of the limitations of subjective methods, but detection of specific postures and postural changes by this method is somewhat limited (Atkin & Gorely, 2012; Kozey-Keadle, Libertine, Lyden, Staudenmayer, & Freedson, 2011). Instruments developed specifically for the assessment of body posture (e.g., ActivPAL) have demonstrated good reliability and validity in the limited research conducted to date (Atkin & Gorely, 2012).

An overview of the methods available to measure sedentary behavior and the main strengths/limitations associated with each method will be described below. The

choice of which method(s) to use is determined by the nature of the research question and the relative accuracy and feasibility of measurement methods.

2.6.1. SUBJECTIVE METHODS

Self-report questionnaires

To date, the majority of studies using self-report measures have centred on capturing daily TV-viewing time as a proxy marker of overall sedentary behavior (Clark et al., 2009). Many of the questionnaires used to capture TV-viewing time have not reported reliability and validity data. In those that provided psychometric data in adults, reliability coefficients were generally fair to high (test–retest $r=0.32-0.93$), but concurrent validity was highly variable ($r=-0.19-0.80$) (Clark et al., 2009). In fact, the measurement of TV-viewing time as an indicator of total sedentary time is problematic, as this behavior does not appear to be representative of overall sedentary behavior (Sugiyama, Healy, Dunstan, Salmon, & Owen, 2008).

Studies drawing inferences about the impact of overall sedentary behavior from assessments of TV viewing should be interpreted with caution (Atkin & Gorely, 2012). One study examined validity and reported that TV-viewing time was significantly less, when measured by self-report compared with an objective measure (Matton et al., 2007). Other self-report questionnaires have focused more on global measures of sedentary behavior, such as total daily sitting time, but similarly, the measurement properties of many such instruments have not been adequately demonstrated (Marshall, Miller, Burton, & Brown, 2010).

The International Physical Activity Questionnaire (IPAQ) was designed to provide an internationally standardized method of measuring PA and sedentary behavior in surveillance studies (Craig et al., 2003). The sedentary item in the IPAQ has generally been shown to have moderate reliability (Spearman $\rho > 0.7$ for test–retest data) but moderate to poor convergent validity (Spearman $\rho < 0.5$) when compared with objectively measured sedentary behavior by accelerometry (Craig et al., 2003).

Recent work has attempted to develop more refined measurement tools that assess multiple sedentary behaviors (e.g., TV viewing, reading, socializing) and/or

domain-specific behaviors (e.g., sitting at work or at home and motorized travel) (Clark, Thorp, et al., 2011; Marshall et al., 2010). These show promise, but further development and validation work is required. One recent study reported that when compared with accelerometer' sedentary time, a single-item question significantly underestimated sedentary behavior, whereas a domain-specific questionnaire, with multiple items, more accurately assessed average sitting time (Clemes et al., 2012).

However, the single-item questionnaire had preferential limits of agreement, demonstrating smaller measurement error (both random and systematic), possibly because of fewer responses being required (Clemes et al., 2012). This may suggest that more detailed questionnaires will be needed for sedentary behavior prevalence and surveillance studies, whereas single-item questionnaires may be more appropriate for health-related epidemiological research, where ease of use and the ability to rank behaviors of interest are the dominant requirements.

The qualitative attributes (e.g., recall period and question/response format) and mode of administration (e.g., interviewer-/self-administered) of existing self-report instruments are extremely varied. Comparison of test–retest results in adults does not clearly demonstrate that one recall period or administration format is superior to another (Clark et al., 2009). There is some evidence that concurrent validity may be better in adults when participants recall a typical day compared with a 7-day or 12-month recall period (Clark et al., 2009). However, these observations derive from studies in different populations and use different reference measures (Clark et al., 2009). In addition, adults and children appear to better recall sedentary behavior for weekdays than weekends, perhaps because of greater variability in behavior patterns at weekends (Clemes et al., 2012; Marshall et al., 2010).

The strengths of self-report questionnaires are the cost-effectiveness, readily accessible to the majority of the population and the relatively low participant burden. Self-report tools can also be used to identify the type of behavior and the context in which it occurs, information that may be used to inform intervention design (Atkin & Gorely, 2012). Limitations of self-report measures are the consistent poor validity, the vulnerability to be influenced by cultural norms and the perceived social desirability. Achieving linguistic and conceptual equivalence in the translation of self-report tools is

also challenging, limiting the comparability of data collected in different populations (Atkin & Gorely, 2012).

Diaries

Sedentary behavior is multi-faceted and, as such, sometimes requires more detailed assessment than can be obtained by markers of overall sitting time. Retrospective self-reports collected at research or clinic visits are limited by recall bias and are not well suited to address how behavior changes over time and across contexts. Moreover, certain types of behavior, particularly those that are sporadic or intermittent in nature, may be difficult to recall accurately for a time frame of greater than a few hours (Atkin & Gorely, 2012; Shiffman, Stone, & Hufford, 2008).

Ecological momentary assessment (EMA) involves repeated sampling of subjects' current behaviors and experiences in real time, in subjects' natural environments. EMA aims to minimize recall bias, maximize ecological validity, and allow study of microprocesses that influence behavior in real-world contexts. EMA studies assess particular events in subjects' lives or assess subjects at periodic intervals, often by random time sampling, using technologies ranging from written diaries and telephones to electronic diaries and physiological sensors (Atkin & Gorely, 2012; Shiffman et al., 2008).

To overcome some of the problems associated with behavioural recall, diaries and EMA methods have been developed (Atkin & Gorely, 2012; Shiffman et al., 2008) but limitations of EMA include the potential for reactivity, mainly through the intense 'self-monitoring' that it entails, and compliance may be challenging given the high degree of participant burden (Atkin & Gorely, 2012; Shiffman et al., 2008). Also, the economic costs associated with data entry and processing limit the applicability of EMA-based methods in large-scale studies (Shiffman et al., 2008).

Exclusive to the field of sedentary behavior research, assessment of the type of behavior being undertaken is complicated by the phenomenon of concurrent behaviors (i.e., an individual may be engaged in TV viewing and computer use at the same time). Therefore, data collection using global measures of self-reported sedentary behavior rather than specific behavior types may have greater utility in epidemiological research.

2.6.2. OBJECTIVE METHODS

To address some of the limitations associated with the subjective methods to estimate sedentary behavior, objective methods of measurement are increasingly being used. This section summarizes the literature on the use of such devices in the epidemiological context.

Accelerometers

Accelerometers, small lightweight devices that are usually worn on an elastic belt positioned on the hip or lower back, become an increasingly popular tool to measure the frequency and amplitude of acceleration of the body segment to which they are attached and often integrate this information in the form of movement ‘counts’ (Chen & Bassett, 2005). Accelerometers can be used to estimate the total volume of sedentary behavior through the accumulation of low movement counts at specified cut points. They can also be used to detect short incidental breaks in sedentary time, defined by periods where movement counts exceed the specified threshold, which may not be feasibly recorded by self-report measures (Healy, Dunstan, et al., 2008).

In addition, as the collected information is stamped with real time, specific segments of the day or week can be extracted, such as after school or time at work. There are many accelerometers on the market suitable for use in epidemiological research, although the ActiGraph (ActiGraph, Pensacola, FL, USA) has been the most widely used to date. Key issues in the use of accelerometry for the assessment of sedentary time relate to device initialization, post-processing, signal feature extraction and inference of specific outcome variables. There is a lack of consensus as to the most appropriate accelerometer data-processing protocol, limiting comparability between studies and hindering evidence synthesis. Nonetheless, accelerometers are being used to assess sedentary time in large-scale surveillance studies (Colley et al., 2011; Matthews et al., 2012).

Previously, it was necessary to specify the sampling frequency (epoch) during device initialization, but in newer accelerometer models (e.g., ActiGraph GT3X+) that record raw acceleration data, the epoch is overlaid during post-processing. A significant effect of epoch length on accelerometer-determined sedentary time has been reported

(Aibar & Chanal, 2015), but findings are inconsistent, and the most appropriate sampling frequency for determining sedentary time has yet to be established (Edwardson & Gorely, 2010).

In general, it is beneficial for researchers to collect data in as short epoch as possible, as this provides information on exposure at the highest possible resolution (see example on Figure 2.1). One study analyzed the effect that epoch length (1, 2, 3, 5, 10, 15, 30 and 60 seconds) may have on different PA intensities in physical education lessons of 1912 students (Aibar & Chanal, 2015). This study found that longer epochs were associated with significantly higher levels of LIPA, MVPA and lower levels of sedentary activity. For example, the percentage of time spent in sedentary behavior during physical education lessons decreased from 53% (1s epoch) to 15% while using 60 seconds epochs (Aibar & Chanal, 2015).

Moreover, data collected under shorter epochs can be summed into longer epochs, facilitating the process of directly comparing findings across studies. Importantly, data collected using longer epochs cannot be partitioned into shorter time frames. In the absence of a consensus regarding optimal epoch length, data collection using the shortest possible epoch provides an opportunity for data to be re-integrated and compared between studies that would not otherwise be possible.

The monitoring period for accelerometer-based assessments of sedentary time has typically been of 7 days (Hagstromer, Oja, & Sjostrom, 2007; Healy, Wijndaele, et al., 2008), with participants included in subsequent analyses if they provided sufficient data for at least 3–5 days. In older adults, it has been suggested that 5 days are sufficient to accurately predict average daily sedentary time by accelerometry (Hart, Swartz, Cashin, & Strath, 2011). Further work is required to examine between-day variability in sedentary behavior patterns (e.g., weekday versus weekend) and possible seasonal variation, both of which will have implications for the monitoring period required.

Patterns of sedentary behavior: Insights from observational and experimental studies on body composition and energy expenditure

Time	Demo File (10s epochs)			Demo File (60s epochs)	
	Epoch Value	Epoch Value x6 (scaled up)	Cutpoint Category (Time)	Epoch Value	Cutpoint Category (Time)
06:00:00	200	1200	Lifestyle (10s)	1100	Lifestyle (60s)
06:00:10	100	600	Light (10s)		
06:00:20	100	600	Light (10s)		
06:00:30	200	1200	Lifestyle (10s)		
06:00:40	400	2400	Moderate (10s)		
06:00:50	100	600	Light (10s)		
06:01:00	0	0	Sedentary (10s)	1030	Lifestyle (60s)
06:01:10	10	60	Sedentary (10s)		
06:01:20	10	60	Sedentary (10s)		
06:01:30	10	60	Sedentary (10s)		
06:01:40	1000	6000	Vigorous (10s)		
06:01:50	0	0	Sedentary (10s)		
06:02:00	1600	9600	Very Vigorous (10s)	3140	Moderate (60s)
06:02:10	40	240	Light (10s)		
06:02:20	150	900	Lifestyle (10s)		
06:02:30	350	2100	Moderate (10s)		
06:02:40	1000	6000	Vigorous (10s)		
06:02:50	0	0	Sedentary (10s)		
06:03:00	20	120	Light (10s)	90	Sedentary (60s)
06:03:10	0	0	Sedentary (10s)		
06:03:20	0	0	Sedentary (10s)		
06:03:30	0	0	Sedentary (10s)		
06:03:40	70	420	Light (10s)		
06:03:50	0	0	Sedentary (10s)		
06:04:00	400	2400	Moderate (10s)	2400	Moderate (60s)
06:04:10	400	2400	Moderate (10s)		
06:04:20	400	2400	Moderate (10s)		
06:04:30	400	2400	Moderate (10s)		
06:04:40	400	2400	Moderate (10s)		
06:04:50	400	2400	Moderate (10s)		

Totals for 10s Epoch File	
Category	Time Spent in Category
Sedentary	1m 40s
Light	1m
Lifestyle	30s
Moderate	1m 20s
Vigorous	20s
Very Vigorous	10s

Totals for 60s Epoch File	
Category	Time Spent in Category
Sedentary	1m
Light	0m
Lifestyle	2m
Moderate	2m
Vigorous	0m
Very Vigorous	0m

Figure 2.1. Categorization of "Demo File". The same file is categorized as a 10-second epoch file and a 60-second epoch file for comparison purposes. Available on <https://help.theactigraph.com/entries/22225385-How-are-Cut-Points-Calculated->

In adults, a minimum of 10 hours of wear time has usually been required (Hagstromer et al., 2007; Healy et al., 2007). Identification of non-wear time is typically conducted by selecting a period of consecutive zero counts above which it is deemed that the device must have been removed. These segments of zero counts are then removed from further analysis. In studies concerned with estimating sedentary time, non-wear criteria have varied from 10 to 60 min of consecutive zero counts (Matthews et al., 2012; Sardinha et al., 2008).

Using the ActiGraph, a count threshold of < 100 counts per min (CPM) is commonly applied to denote sedentary behavior in adults (Hagstromer et al., 2007; Healy et al., 2007; Matthews et al., 2012). This cut point has also been proposed for the classification of sedentary behavior using the Actical activity monitor (Mini-Mitter, Bend, OR, USA) (Wong, Colley, Connor Gorber, & Tremblay, 2011). However, despite the widespread use of this cut point, this value was not empirically derived, and studies reporting the validity of this cut point in adults are limited (Kozey-Keadle et al., 2011).

Recently, Kozey-Keadle et al., (2011) assessed the criterion validity of a number of ActiGraph (GT3X) cut points (50, 100, 150, 200 and 250 CPM) for defining sedentary time against direct observation in a small sample of adults (N=20). Findings indicated that the ActiGraph 100 CPM cut point underestimated sedentary time by 4.9% (Kozey-Keadle et al., 2011). The cut point with the lowest bias was 150 CPM, which overestimated sedentary time by 1.8%. Another study (Oliver, Schofield, Badland, & Shepherd, 2010) investigated sedentary behavior cut points for the Actical accelerometer (hip mounted), using the ActivPAL (thigh mounted; PAL Technologies Ltd, Glasgow, UK) device as the criterion measure and concluded that a threshold of 0 counts/15 s epoch provided the most accurate estimates of sedentary time.

A key limitation of traditional (count based) accelerometers as a measure of sedentary behavior is that they assess intensity of movement and thus are less able to distinguish between postures, such as sitting and lying or standing still. Consequently, periods of standing still may be misclassified as sedentary behavior and vice versa (Clemes et al., 2012; Hart, Ainsworth, & Tudor-Locke, 2011). Newer models of the ActiGraph accelerometer (GT3X and GT3X+) include an inclinometer function, which classifies participants' posture into four categories (device removed, standing, lying and sitting). Preliminary evidence, however, indicates that the validity of this function is limited and may be influenced by point of attachment (Clemes et al., 2012; Hart, Ainsworth, et al., 2011).

Posture monitors

The ActivPAL is a small lightweight electronic device worn under clothing. It is attached directly to the skin on the midline of the anterior aspect of the thigh. The ActivPAL determines posture on the basis of an inclinometer, including the gravitational component and uses proprietary algorithms (Intelligent Activity Classification) to classify time as sitting/lying, standing or stepping. Information on cadence, number of steps taken, sit-to-stand and stand-to-sit transitions and estimates of EE are also provided.

Adult validation studies have reported the ActivPAL to have excellent reliability and validity of posture and motion during everyday activities compared to direct observation determined by video analysis (Busse, van Deursen, & Wiles, 2009; Dahlgren, Carlsson, Moorhead, Hager-Ross, & McDonough, 2010; Grant, Dall, Mitchell, & Granat, 2008; Maddocks, Petrou, Skipper, & Wilcock, 2010; Ryan, Grant, Tigbe, & Granat, 2006). However, relatively few studies have explored the criterion validity of the ActivPAL for measuring sitting time (Hart, Ainsworth, et al., 2011; Kozey-Keadle et al., 2011).

A recent validation study found the ActivPAL to be a more precise measure of sitting time compared to the ActiGraph (Kozey-Keadle et al., 2011). Twenty office workers were observed for two periods of six hours whilst wearing an ActivPAL and ActiGraph accelerometer (Kozey-Keadle et al., 2011). Validity was assessed using a range of accelerometer cut-points from 50 to 250 CPM and ActivPAL output of time spent sitting/lying against direct observation of sitting/lying and non-sedentary behavior (Kozey-Keadle et al., 2011).

The correlation between the ActivPAL and direct observation of sitting/lying time was considerably higher in comparison to that of the ActiGraph utilising ≤ 100 CPM threshold ($r^2=0.94$ and $r^2=0.39$ respectively for ActivPAL and Actigraph). Another validation study found a mean percentage difference of 0.19% (limits of agreement: -0.68% to 1.06%) between the ActivPAL monitor and direct observation for total time spent sitting (Grant, Ryan, Tigbe, & Granat, 2006). Although limited in number, these studies provide promising preliminary evidence that the ActivPAL may be a valid tool for the assessment of sedentary behavior in adults.

However, future research should aim to establish the validity, reliability, and responsiveness of ActivPAL for measuring sedentary behavior in different populations and in different settings. Similar to other accelerometer-based methods, the ActivPAL does not provide information on the type of behavior being undertaken or the social or environmental context in which it occurs.

Combined heart rate and movement sensing

All strengths and limitations of HR monitoring and movement sensing apply equally to combined sensing data when these data streams are analysed separately. At this point, the specific utility of combined sensing data for assessing sedentary behavior when the HR and movement data are analysed together is referred. This includes the initial inference on whether the monitor is worn, which can be made with greater certainty in the presence of both biomechanical and physiological sensor information (Atkin & Gorely, 2012).

Several studies have investigated the utility of combined HR and movement sensing to accurately assess physiological intensity across a wide range of daily activities (Brage et al., 2007; Crouter, Churilla, & Bassett, 2008; Strath, Brage, & Ekelund, 2005). Defining sedentary behavior in caloric terms (e.g., time spent at 1.5 metabolic equivalent or below) enables sedentary outcome variables to be derived from these methods. Time spent in the lowest branch of the branched model may be used as a pragmatic measure of sedentary behavior, irrespective of its ability to estimate PA intensity (Brage et al., 2004). To date, the utility of combined HR and movement sensing as a measure of sedentary behavior has not been fully explored. Further work exploring the validity of this approach in diverse populations and settings is warranted.

2.6.3. CRITERION MEASURE: DIRECT OBSERVATION

Direct observation has been served as the criterion measure to assess total sedentary time and breaks from sedentary time (Kozey-Keadle et al., 2011; Lyden, Kozey-Keadle, Staudenmayer, & Freedson, 2012). Usually, a trained observer met the participants in their natural environment (e.g., place of work, school, home) and participants are observed for approximately 10 consecutive hours. A hand-held personal digital assistant (PDA) programmed for focal sampling and duration coding is used to record participant behavior (Kozey-Keadle et al., 2011; Lyden et al., 2012). Every time body position changes (e.g., from sitting to standing) the observer records this in the PDA. Each entry is time stamped and the length of each behavior bout is automatically recorded in the PDA (Lyden et al., 2012).

The start and stop of each behavior recorded by the direct observer is then exported from the PDA using a custom software (e.g., Noldus: Observer 9.0). During the 10-hour observation, participants are generally allow to have “private time” when needed. Reasons for “private time” include behaviors such as using the restroom and changing clothes. During these activities, the observer codes “private” on the PDA (Kozey-Keadle et al., 2011; Lyden et al., 2012).

The software (Noldus: Observer 9.0) used to conduct the direct observation is a commercially available tool (Noldus Information Technology; Netherlands), and it is programmed to capture specific behaviors of interest (e.g., sitting, standing). This technique relies on several observers that work in 2–4 hour shifts. Observers have to complete an extensive verbal, written and video training and testing before observing participants in a free-living environment. The training material focus on a specific protocol to avoid disrupting free-living behavior and to accurately record sedentary time and breaks from sedentary time.

Upon completion of training, the ability of each observer to identify activity type (e.g., sit, stand, walk) and intensity (e.g., 3 METs) is tested using a ~15 minute video of free-living behavior. The video is first coded by a group of experienced observers and study observer responses (activity type and MET value) are compared with the experienced observers’ responses. To be considered “in agreement” study observers need to correctly identify both the type and intensity of the activity, and present a very high level of agreement between the study observers’ responses and the experienced observers’ responses (mean $\kappa = 0.92$) (Lyden et al., 2012).

In conclusion, in this section, we have described and evaluated the various methods of measuring sedentary behavior applicable in the epidemiological context, highlighted the areas in need for further study, and discussed new and emerging themes in this field. Assessment of sedentary behavior by self-reports is limited by, among other things, the ubiquitous nature of these behaviors, which may be unremarkable, intermittent and incidental and therefore difficult to recall. Traditional survey methods may be surpassed by new technologies that can provide, for all population groups, second-by-second information on posture, movement (or lack of movement) and patterns within and between days.

Specific behavioral measures remain essential nonetheless for monitoring compliance with screen time recommendations and for providing additional information on the environmental context in which the behavior occurs. Therefore, new measures and analytic methods may be needed to capture nuanced features of the behavior and future developments, advances in sedentary behavior assessment, particularly with regard to objective monitoring, will likely mirror those observed in computing and information technology. Accordingly, 3 emergent trends can be identified, namely the miniaturization of new devices, interoperability of existing devices and advanced computational methods. Here, it was not a goal to develop these specific new tools but to present them, as trends that may influence sedentary behavior assessment in the future.

2.7. The aim of the investigation

The present dissertation presents six research studies conducted under the scope of sedentary behavior.

Study 1 (chapter 4) is a methodological study that was conducted to examine the validity of two objective motion sensors in estimating total sedentary time and breaks in sedentary time. This is particularly important, given that one of the alternative devices (Actigraph accelerometer) is the most widely used method for assessing PA and more recently, sedentary time. To overcome some of the accelerometers' limitations, a combined HR with accelerometer device (Actiheart) has been used to estimate EE. Regardless of the advantages that Actiheart presents for MVPA estimation, the accuracy of this device for sedentary time and patterns assessment is still unknown. Therefore, the purpose of study 1 (chapter 4) was to examine the validity of GT3X and Actiheart in estimating changes in daily sedentary time and breaks, during free-living settings, using ActivPAL as the reference.

Moving beyond the methodological area of sedentary behavior and considering that older people are often engaged in long periods of sedentary behavior, the aim of **study 2** (chapter 5) was to investigate the cross-sectional associations for objectively measured uninterrupted sedentary bouts of different durations and respective patterns

with abdominal obesity in older adults. In addition, study 2 also aimed to understand if these associations were independent of sex and MVPA levels.

Study 3 (chapter 6) was conducted to understand if the associations for sedentary behavior with total and abdominal adiposity measures exist, when considering a highly active population, and if these associations remain independently of the higher MVPA levels observed in this population group. This study presents a novelty, since it was the first to put this question and to examine the relationships previously found, between sedentary behavior and obesity measures, applied to a highly trained population.

Results from quantifying the metabolic and energy cost associated with "sitting" and "standing" have produced equivocal results. **Study 4** (chapter 7) also brings an innovation to the field by taking a step toward aiming to analyse the impact of transitioning from sit/stand/sit on metabolic and energetic cost, independent of sex and body composition profiles.

Regarding that study 4 will provide the energy cost of breaking up sedentary time and recognizing that obesity results from an energy imbalance (higher EI vs lower EE) that favors a positive balance with a concomitant increase of the energy stores (adipose tissue). The purpose of **study 5** (chapter 8) was to examine the associations of total sedentary time and breaks in sedentary time with abdominal obesity in older adults, the most sedentary group in the population.

Finally, **study 6** (chapter 9), gathers the information resulting from the previous studies (1, 2, 3, 4, 5) and seeks to report the short-term effectiveness of reducing and breaking up overall daily sitting time in physically-inactive overweight/obese working adults using a multi-component intervention simultaneously addressing workplace and leisure time contexts. This pilot intervention study will offer valuable insight for the rapidly growing field of research for reducing sedentary time and increasing the number of activity breaks throughout the whole day, highlighting some of the challenges that future interventions may encounter.

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CHAPTER 3

Methodology

A brief description of the sample and study protocol will be provided in this chapter, however further specific details of the methods will be provided in each study (chapter 4 to 9).

3.1. Study design and sampling

All studies included in the present thesis were approved by the Faculty of Human Kinetics, University of Lisbon Ethics Committee and conducted in accordance with the Declaration of Helsinki. Studies 1 and 6 (chapters 4 and 9) result from a crossover randomized clinical trial registered at the ClinicalTrials.gov (ID:NCT02007681). Studies 2 and 5, (chapter 5 and 8) result from cross-sectional analysis using a non-institutionalized Portuguese Caucasian older adults database. For study 3 (chapter 6), cross-sectional data was collected in a project including athletic male population in the competitive period of the season. Finally, study 4 (chapter 7) results from a crossover randomized experiment. In Table 3.1 are summarized the basic characteristics of each study regarding sampling and design.

Table 3.1. Basic characteristics of each study: sampling and design

Study	Sample	Sex	Age range	Design
1	Overweight/obese adults	5 M & 5 F	37 – 65 yrs	Crossover randomized clinical trial (ClinicalTrials.govID:NCT02007681)
2	Older adults	121 M & 230 F	≥ 65 yrs	Cross-sectional
3	Adult athletes	82 M	18 – 38 yrs	Cross-sectional (competitive period)
4	Adults	25 M & 25 F	20 – 64 yrs	Crossover randomized experiment (ClinicalTrials.govID:NCT02377037)
5	Older adults	111 M & 190 F	≥ 65 yrs	Cross-sectional
6	Overweight/obese adults	5 M & 5 F	37 – 65 yrs	Crossover randomized clinical trial (ClinicalTrials.govID:NCT02007681)

Abbreviations: F, female; M, males; yrs, years

3.2. Body composition measurements

All studies, with the exception of studies 1 and 6 have body composition as their main outcome. In studies 2 and 5, the whole body level of body composition was considered and WC was the dependent variable in both studies. Furthermore, study 3 considered both the whole body level (WC), and the molecular level of body composition, by including DXA to assess fat mass (FM), fat-free mass (FFM), and regional FM components such as trunk FM and abdominal FM (AFM). Finally, DXA was also included in study 4 to estimate FM and FFM. A more detailed explanation for the methods used to assess body composition will be presented below.

3.2.1. WHOLE BODY LEVEL OF BODY COMPOSITION

Anthropometry

Weight and height

Weight and height were assessed across all studies presented in this dissertation (chapters 4 to 9). Participants were weighed without shoes to the nearest 0.01 kg minimal clothes on an electronic scale connected to the plethysmograph computer (BOD POD[®] COSMED, Rome, Italy) (chapters 4, 6, and 9) or in a scale coupled with a stadiometer (Seca, Hamburg, Germany) (chapters 5, 7, and 8). Based on 10 young active adults (5 males and 5 females), the coefficient of variation for body mass in our laboratory using BOD POD's electronic scale is 0.07% and using Seca's scale is 0.08%. Height was measured to the nearest 0.1 cm with a stadiometer (Seca, Hamburg, Germany), according to standardized procedures (Lohman, Roche, & Martorell, 1988). Based on 10 adults the coefficient of variation for height is 0.04%. BMI was calculated as weight (kg) divided by the square of the height (m).

Waist circumference

In chapters 5, 6, and 8 waist circumference (WC) was measured at minimal respiration by positioning an inelastic tape parallel to the floor and immediately above the iliac crest, according to the National Institute of Health (NIH) procedures (NIH,

1998) and reported to the nearest 0.1 cm. An anthropometric tape (Seca, Hamburg, Germany) was used in chapters 5 and 8 and another anthropometric tape (Cescorf, Brazil) was used in chapter 6. Measurements were conducted by the same anthropometrist and the coefficient of variation for WC is 0.20%.

3.2.2. MOLECULAR LEVEL OF BODY COMPOSITION

Traditionally body composition at the molecular level of analysis was studied as the sum of two compartments, where the body mass equals the sum of FM and FFM (Behnke, Feen, & Welham, 1942; Brozek, Grande, Anderson, & Keys, 1963; Pace & Rathbun, 1945; Siri, 1961). However, at the molecular level FFM can be partitioned into several molecular components, including water, mineral, and protein (Wang, Pierson, & Heymsfield, 1992).

Many stable relationships are recognized at the molecular level. These associations are crucial to the body composition methodology area. The calculated and assumed constant densities of combined molecular level components are the basis of two, three, and four molecular components level models (Heymsfield, Wang, Baumgartner, & Ross, 1997). The basic 2-component models (densitometric and hydrometric based techniques) lie on the premise that the body can be divided into two chemically distinct compartments, FM and FFM, with FFM corresponding to all the remaining molecular components (Wang et al., 1992). In these models it is assumed that the densities of FM and FFM are 0.9007 g/cm^3 and 1.100 g/cm^3 , respectively (Brozek et al., 1963) and also that the $\text{FFM/TBW}=0.732$ (Wang et al., 1999). Body composition research progressed and models that partition body mass up to six components are now available. By including more than 2-component, multi component models typically account for more biological variability (Wang, Shen, Whithers, & Heymsfield, 2005; Whithers et al., 1998), providing more accurate body composition measurements.

The DXA body composition approach assumes that the human body consists of three components that are distinguishable by their X-ray attenuation properties: FM, bone mineral, and lean-soft tissue (LST). This method was used in studies 3 and 4, and will be further described below.

Dual-energy X-ray absorptiometry

Single photon absorptiometry was introduced in the early 1960s as a way of quantifying bone mass. Dual photon absorptiometry methods first became clinically available in the early eighties, referred to as DXA (Pietrobelli, Formica, Wang, & Heymsfield, 1996). DXA provides whole body and regional assessment of FM, FFM and, also the estimation of bone mineral that can be used in multi-component models.

The fundamental principle of DXA is the measurement of the transmission of X-rays through the body at two different energy levels, low and high (typically 40 and 70 keV), which passes through tissues and is attenuate at rates related to its elemental composition (density and thickness of the human tissues through which they pass) (Figure 3.1). The extent to which photon energy is attenuated is a function of the initial photon energy of the X-ray beam, the mass per unit area of the absorber material, and the mass attenuation coefficient (μ_m) of the absorber. Photons of two different energies (e.g., 40 and 70 keV) are passed through an absorber. For a homogeneous absorber, R is a function of mass attenuation coefficient and mass fraction of each component (Pietrobelli et al., 1996). Therefore each element has a characteristic mass attenuation coefficient and an R value at a given energy. For instances, bone is rich in highly attenuating minerals (Ca and P), and is readily distinguished from soft tissues (Pietrobelli et al., 1996).

The DXA body composition approach assumes that the human body consists of three components that are distinguishable by their X-ray attenuation properties: FM, bone mineral, and LST. In theory, solving for three unknown components requires measurement at three different photon energies. However, in practice, DXA can only resolve the fractional masses of a two-component mixture. Thus, DXA first separates pixels into those with soft tissue only (FM and LST) and those with soft-tissue plus bone mineral, based on the two different photon energies. This means that in pixels with bone mineral, soft tissue is not separately analyzed and the equipment assumes FM and LST content of the adjacent area analyzed. (Pietrobelli et al., 1996). Normally, 40% to 45% of the whole body scan contains bone in addition to soft tissue thus, a systematic individual error is introduced as there might be variations in body composition between measured and non measured areas (Lohman, 2005). For example, the influence of the

arm and thorax on body composition estimation can be underrepresented due to the relatively large areas of bone in those regions (Roubenoff, Kehayias, Dawson-Hughes, & Heymsfield, 1993). This source of systematic error can be increased when tracking body composition compartments (Kiebzak, Leamy, Pierson, Nord, & Zhang, 2000).

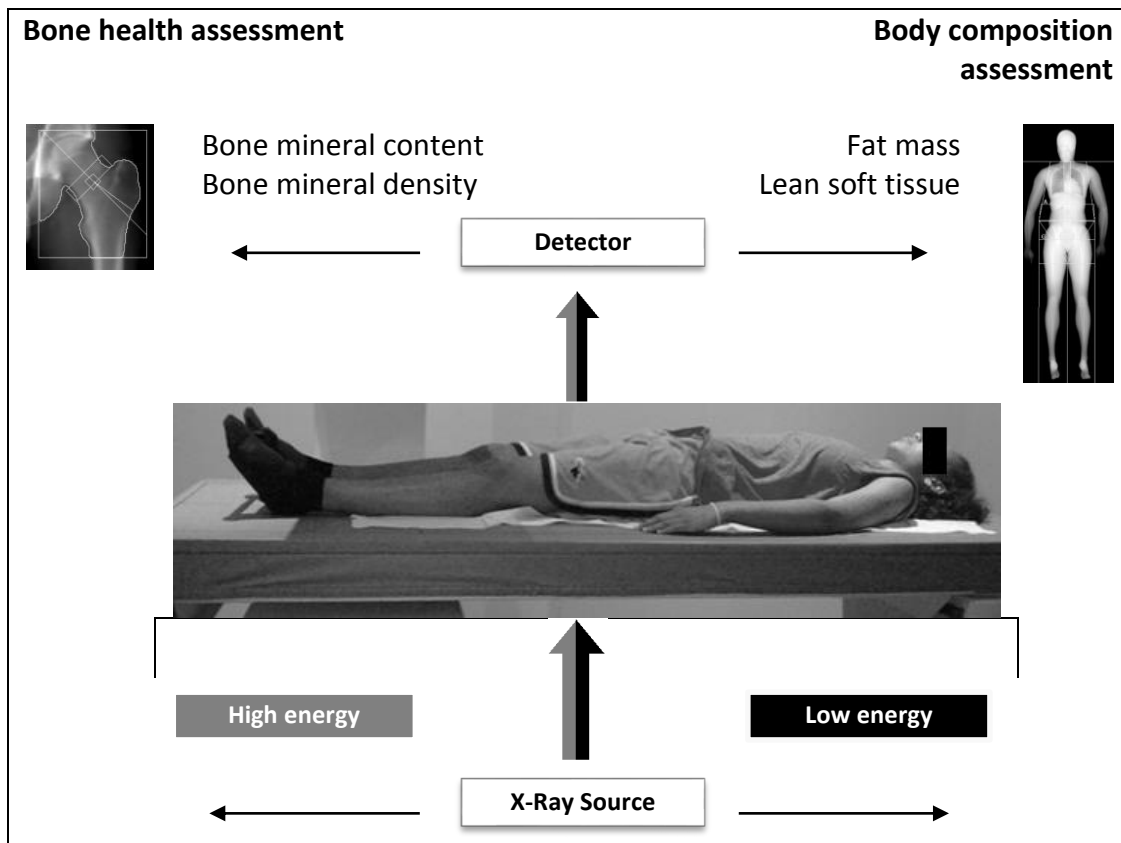


Figure 3.1. Fundamental principle of dual-energy X-ray absorptiometry (DXA): the DXA measures the transmission of X-rays through the body at high and low energies. The X-ray beam energy is attenuated with the passage through tissue. The DXA body composition approach assumes that humans consist of three components that are distinguishable by their X-ray attenuation properties: bone mineral, fat tissue, and lean soft tissue (LST). (Toombs, Ducher, Shepherd, & De Souza, 2012)

Despite DXA's accuracy, precision, reliability, high speed, and non-invasive estimates with minimal radiation exposure (Haarbo, Gotfredsen, Hassager, & Christiansen, 1991; Toombs et al., 2012; Tothill, 1995), DXA is not without limitations. The main limitations pointed to this method are: algorithms calculations differ between manufacturers and are not published; pencil and fan-beam densitometers differ in accuracy; and limited active scan area (Ackland et al., 2012). This last limitation

particularly affects athletes involved in sports where height is a major factor of performance, such as basketball and volleyball. Considering that it may be critical to measure people taller than the DXA scan area, alternative procedures are required to allow complete whole body scans (Santos et al., 2013).

Participants underwent a whole-body DXA scan according to the procedures recommended by the manufacturer on a Hologic Explorer-W, fan-beam densitometer (Hologic, Waltham, Massachusetts, USA). The equipment measures the attenuation of X-rays pulsed between 70 and 140 kV synchronously with the line frequency for each pixel of the scanned image. Following the protocol for DXA described by the manufacturer, a step phantom with six fields of acrylic and aluminium of varying thickness and known absorptive properties was scanned to serve as an external standard for the analysis of different tissue components.

The same technician positioned the participants, performed the scan and executed the analysis (software QDR for Windows version 13.3, Hologic, Waltham, Massachusetts, USA) according to the operator's manual using the standard analysis protocol. The DXA measurements included whole body or regional measurements of bone mineral content, bone mineral density, absolute fat mass, percent fat mass, fat-free mass, and lean soft tissue (chapters 6 and 7).

On chapter 6, for athletes who's height exceeded the scan area an alternative method was performed, with two scans already validated by our group (Santos et al., 2012), specifically: a) a head scan, where the DXA scan length (95 cm) was set at a height sufficient to scan from the top of the head to the lower jaw; and b) a trunk and limbs scan, where the participant was positioned with the head slightly out of the scan area. The scan length was set as the normal length for the trunk and limbs scan (195 cm). The sum of head and trunk plus limbs was used as an alternative procedure to assess bone mineral content, fat mass and lean soft tissue.

In chapter 6, abdominal fat mass was also assessed. Abdominal fat mass, which includes intra-abdominal fat plus subcutaneous fat, can be distinguished using DXA by identifying a specific region of interest (ROI) within the analysis program. Specific DXA ROIs for abdominal regional fat were defined as follows: ROI 1, the upper edge

of the second lumbar vertebra (approximately 10 cm above the L4 to L5) to above the iliac crest and laterally encompasses the entire breadth of the abdomen, thus determining total abdominal fat mass (Park, Heymsfield, & Gallagher, 2002); ROI 2 have the same upper and inferior edges than ROI 1 and laterally excludes subcutaneous fat in the lateral region of the abdomen. The difference between ROI 1 and ROI 2 thus provides an estimate of lateral subcutaneous fat. The same technician positioned the participants, performed the scans and executed the analysis according to the operator's manual using the standard analysis protocol. Based on test-retest using ten participants, the coefficient of variation (CV) in our laboratory for total abdominal fat mass is 0.01% (Pimenta, Santa-Clara, Sardinha, & Fernhall, 2012) and the values for fat mass, fat-free mass, appendicular lean soft-tissue, and trunk fat mass are presented in Table 3.2 (Santos et al., 2010).

Table 3.2. Coefficients of variation in our laboratory for dual-energy X-ray Absorptiometry measurements

	Whole-body	Sub-total	Appendicular	Trunk
Absolute FM	1.7 %	1.8 %	2.8 %	4.3 %
Percent FM	1.6 %	1.7 %	2.1 %	3.6 %
FFM	0.8 %	0.6 %	1.6 %	1.2 %
LST	0.8 %	0.6 %	1.2 %	1.3 %

Abbreviations: FM, fat-mass; FFM, fat-free mass; LST, lean soft tissue

3.3. Energy expenditure measurements

3.3.1. ENERGY EXPENDITURE COMPONENTS

Physical activity (PA) is defined as any bodily movement produced by skeletal muscles that result in EE. The term exercise was used interchangeably with PA. In fact, both have a number of common elements, yet, exercise and PA are not synonyms; exercise is a subcategory of PA. Exercise is PA that is planned, structured, repetitive, and purposive in the sense that aims to improve or maintain one or more components of physical fitness. Both PA and exercise have in common a resulting increase in EE (Caspersen, Powell, & Christenson, 1985).

Total EE (TEE) can be described as the sum of resting EE (REE), activity EE (AEE) and the diet-induced thermogenesis (DIT) (Donahoo, Levine, & Melanson, 2004). REE represents the minimum amount of energy required to sustain vital bodily functioning in the post-absorptive awakened state (Gallagher & Elia, 2005). DIT is the increase in EE associated with the digestion, absorption, and storage of food and accounts for approximately 10% of TEE (D'Alessio et al., 1988). AEE can be further separated into exercise activity thermogenesis and NEAT. The NEAT is the EE in all activities that are not sleeping, eating or sports-like, which includes all occupation, leisure, sitting, standing, and ambulation (Levine, 2004).

EE must equal EI (the sum of energy from foods, fluids, and supplement products) to achieve energy balance (Rodriguez, Di Marco, & Langley, 2009). Energy balance is usually calculated over longer periods of time and represents the difference between EI and TEE. When the balance is positive it will result in weight gain, whereas if a negative balance occurs, individuals will lose weight (Jeukendrup & Gleeson, 2004). The majority of the people are often under a positive energy balance, and sedentary behavior plays an important role in this harmful unbalance.

EE measurements were conducted in study 4 (chapter 7). Participants came to the laboratory in the morning after an 8 hours fasting, not to engage in any exercise or ingest any caffeine or take any other stimulants 48 hours prior to the visit.

3.3.2. RESTING ENERGY EXPENDITURE (REE)

In chapter 7, measurements were performed between 7:00 and 10:00 a.m. Prior to the REE measurements, the participants lied supine for 10 min covered with a blanket in a quiet room at an environmental temperature and humidity of $\pm 22^{\circ}\text{C}$ and 40–50%, respectively. The MedGraphics CPX Ultima (MedGraphics Corporation, Breezee Software) indirect calorimeter was used to measure breath-by-breath oxygen consumption ($\dot{V}\text{O}_2$) and carbon dioxide production ($\dot{V}\text{CO}_2$) using a facial mask. One trained technician conducted all measurements. The oxygen and carbon dioxide analysers were calibrated in the morning before testing using a known gas concentration. The flow and volume were measured using a pneumotachograph calibrated with a 3 L-syringe (Hans Rudolph, inc.TM). The auto calibration was

performed between participants. Before testing participants were instructed about all the procedures and asked to relax, breath normally, not to sleep, and not to talk during the evaluation.

Total rest duration was 60 min, participants lied supine for 30 min covered with a blanket and the calorimeter device was then attached to the mask and breath by breath $\dot{V}O_2$ and $\dot{V}CO_2$ were measured for another 30 min period. Outputs of $\dot{V}O_2$, $\dot{V}CO_2$, respiratory exchange ratio (RER), and ventilation were collected and averaged over 1 min intervals for data analysis. The first and the last 5 min of data collection were discarded and the mean of a 5 min steady state interval between the 5 and the 25 min with RER between 0.7 and 1.0 was used to determine REE. Steady state was defined as a 5 min period with $\leq 10\%$ CV for $\dot{V}O_2$ and $\dot{V}CO_2$ (Compher, Frankenfield, Keim, & Roth-Yousey, 2006). The mean $\dot{V}O_2$ and $\dot{V}CO_2$ of 5 min steady states were used in the Weir equation (Weir, 1949) and the period with the lowest REE used for data analysis. Based on test-retest using seven participants, the CV in our laboratory for REE is 4.0%.

3.3.3. METABOLIC COST DURING EXPERIMENTAL CONDITIONS

Also in chapter 7 (study 4) the same equipment described in REE measurement, the MedGraphics CPX Ultima (MedGraphics Corporation, Breezeex Software) was used to measure ventilation, CO_2 production by computer interfaced with gas analyzers, during each of the three conditions. The initial 5 min of each condition allowed for steady state $\dot{V}O_2$ to be achieved. Mean $\dot{V}O_2$ and RER were then determined from the ensuing 5 min. EE (in kilocalories per min) were estimated with the use of the caloric equivalent for a liter of O_2 . Participants wore a pulse oximeter that is attached to the MedGraphics system to capture HR min by min. Conditions were performed continuously, with no interruptions allowed. To avoid an overestimation of $\dot{V}O_2$ on the first min of each condition as a result of a potential carryover from the previous condition to the next, only the second 5 min of each condition were analyzed and the first 5 min discarded. $\dot{V}O_2$ was presented in milliliters of oxygen consumption per kg of body mass per min ($ml \cdot kg^{-1} \cdot min^{-1}$) and milliliters of oxygen consumption per kg of FFM per min ($ml \cdot kg_{FFM}^{-1} \cdot min^{-1}$). Relative METs were calculated by dividing mean oxygen consumption ($ml \cdot kg^{-1} \cdot min^{-1}$) per activity by mean oxygen consumption during

lying down at rest. Absolute METs were calculated by the common practice of dividing the relative $\dot{V}O_2$ in $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ by $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$.

3.4. Dietary measurements

Dietary measurements were performed in study 6 (chapter 9). Energy and nutrient intake were assessed in 3-days (one weekend-day) in each condition week, using a 24 hour diet records. Participants were instructed regarding portion sizes, supplements, food preparation aspects (boiling, grilled, frying), and others aspects (e.g., fried in olive oil or butter) pertaining to an accurate recording of their EI. At the last visit, records were turned in and reviewed for liquids ingestion, macro nutrient composition and total EI by the same technician. Diet records were analyzed using a specific software (Food Processor SQL).

3.5. Sedentary behavior and PA measurements

Sedentary behavior and PA were assessed using objective methods in all studies (chapters 4, 5, 7, 8, and 9), except for the third study (chapter 6) where a subjective method was used. The objective methods involved 4 different devices: GT1M accelerometer (chapters 5 and 8); GT3X+ accelerometer (chapters 4 and 9); ActivPAL inclinometer (chapters 4 and 9); and Actiheart (chapter 4).

3.5.1. SUBJECTIVE MEASUREMENTS

In chapter 6, sedentary behavior was assessed using IPAQ self-administered short-IPAQ sitting items (Rosenberg, Bull, Marshall, Sallis, & Bauman, 2008) that consisted of a single question regarding the time spent in sedentary behavior (watching TV, computer use, transport, and other sitting or reclining activities) in a weekday during the waking period.

For the total weekly training time participants were asked to report the number of hours in which they engaged in field or gymnasium training.

3.5.2. ACTIVPAL MEASUREMENTS

ActivPAL Professional (PAL Technologies Ltd., Glasgow, UK) monitor was considered the primary method for the main variables in chapters 4 and 9, as it provides a reliable method for differentiating sitting/lying, standing and stepping activities (Godfrey, Culhane, & Lyons, 2007), with a high accuracy for time spent sitting, compared with direct observation (Kozey-Keadle, Libertine, Lyden, Staudenmayer, & Freedson, 2011). The ActivPAL is a uniaxial piezoresistive accelerometer and inclinometer that is small (35 mm × 53 mm × 7 mm) and lightweight (20 g) worn on the middle-anterior line of the right thigh that provides a range of objectively measured and objectively processed variables, including total time spent sitting/lying, standing and stepping and sit/stand transitions.

The device was attached to the skin with a manufacturer-supplied non-allergenic and non-waterproof adhesive tape (PALstickie) and used continuously for 24 hours a day for 14 days, except for water-based activities such as showering. After showering or bathing participants were instructed to re-attach the ActivPAL with an additional piece of the same adhesive tape that was provided. Prior to the trial they were taught exactly how, where and the correct positioning to attach the device. None of the participants performed any activity like swimming or any other water dependent activity. Therefore, a valid-day was defined as having ≥ 22 hours of monitor wear, corresponding to the minimum daily use except for showering and bathing. Participants were asked to record waking/sleeping hours and wear-time in a logbook. This information was used to determine ActivPAL's waking period and therefore deduct sleeping hours from total sitting/lying time. They were asked to record timing and reasons for every occasion the ActivPAL was removed.

Data were collected at a predetermined 10 Hz and in 15 seconds intervals. Recorded output from the ActivPAL monitor was downloaded, processed, and classified into sitting, standing, and walking by using manufacturer-supplied ActivPAL's software (version 5.9.1.1, PAL Technologies, Glasgow, United Kingdom).

Patterns of sedentary time

In chapter 9, from the ActivPAL raw data it was possible to extract prolonged and uninterrupted periods of time spent sitting, standing and stepping of different durations (bouts of ≤ 4 min; 5-9; 10-19; 20-29; 30-59; and at least 60 min) by manually counting the number of bouts in which participants were sitting, standing or stepping in the bout's duration categories (Dowd, Harrington, Bourke, Nelson, & Donnelly, 2012). Because the past three bout categories were infrequent for the standing bouts, they were combined into one category (≥ 20 min).

3.5.3. ACTIGRAPH ACCELEROMETER MEASUREMENTS

In chapters 4, 5, 8, and 9, all participants were asked to wear an accelerometer ActiGraph, GT1M model, Fort Walton Beach, FL (chapters 5 and 8) and Actigraph, GT3X+ model, Pensacola, FL (chapters 4 and 9) on the right hip, near the iliac crest, during waking hours, and requested to remove it only during water-based activities such as showering and swimming (Trost, McIver, & Pate, 2005). The processing was performed using the software Actilife (v.6.9.1). A valid-day was defined as having 600 or more min (≥ 10 hours) of monitor wear time, corresponding to the minimum daily use of the accelerometer (Ward, Evenson, Vaughn, Rodgers, & Troiano, 2005). As well as reported monitor non-wear time (i.e., when it was removed for sleeping or water activities), periods of at least 60 consecutive min of zero activity intensity counts were also considered as non-wear-time (Colley, Connor Gorber, & Tremblay, 2010).

The amount of activity assessed by accelerometer was expressed as min per day spent in different intensities. The cutoff values used to define the intensity of PA and therefore to quantify the mean time in each intensity (sedentary, light, moderate or vigorous) were: sedentary: < 100 counts \cdot min $^{-1}$; light: 100-2019 counts \cdot min $^{-1}$; moderate: 2020-5998 counts \cdot min $^{-1}$ (corresponding to 3-5.9 METs); vigorous: ≥ 5999 counts \cdot min $^{-1}$ (corresponding to ≥ 6 METs) (Troiano et al., 2008). There are no cutoffs for the sedentary time using the three-axial information from this new generation Actigraph GT3X+ accelerometer; therefore the previous cutoffs were used which utilize the vertical-axis only. Actigraph break was considered as any bout of time in which the

accelerometer count rose up to or above $100 \text{ counts} \cdot \text{min}^{-1}$ and which stayed within the LIPA range ($< 2020 \text{ counts} \cdot \text{min}^{-1}$).

The delivery and fitting of both devices to the participants were conducted face-to-face (Ward et al., 2005). The devices were activated on the first day at 6:00 a.m. and data were recorded in 15 seconds epochs. Participants were asked to record timing and reasons for every occasion the devices were removed. Although it would be useful to differentiate working from leisure time periods, participants were not told to record the times they entered and finished work.

3.5.4. ACTIHEART MEASUREMENTS

In chapter 4, Actiheart (Actiheart, CamNtech Limited, UK), a lightweight (10 g) combined HR and movement (uniaxial accelerometer oriented to measure acceleration along the body's longitudinal axis) sensor that utilizes both piezoelectric accelerometer and HR data synchronously was used. This sensor is capable of storing time-sequenced data for several days and was worn on an adapted polar band placed on the chest. The Actiheart software allows two types of calibration; an individual calibration using a standardized step test that consists of step up and down a 15 cm high step, progressively increasing step frequency from 15 to 32.5 body lifts per min (rate of change: 2.5 body lifts per min^2) and a group calibration inbuilt function.

Given that some of the participants were not able to finish the step test, a group calibration that is available in the software (version 4.0.99) was performed. The Actiheart was started at the long term mode to record HR and acceleration with 15 seconds' epochs. Participants wore the Actiheart 24 h·day⁻¹ for 14 days and a valid day was defined as having 600 or more min ($\geq 10 \text{ h}$) of monitor wear during waking hours. Data from the Actiheart were downloaded into the commercial software. The camNtech software algorithm allowed data cleaning, recovering, and interpolation of missing and noisy HR. Using the raw data from the branched combined model that uses activity (acceleration) and HR, it was possible to extract and quantify the daily sedentary time ($< 1.5\text{METs}$). Participants were also instructed to register the periods in which they removed the device for water activities.

3.5.5. SEDENTARY PATTERNS

In chapter 4, sedentary time from the three devices (Actigraph, ActivPAL, and Actiheart) was accounted by the total time spent in sedentary behavior while considering the same awake hours in the three devices. For ActivPAL, sedentary time was created based on posture (sitting/reclining). For GT3X, the traditional < 100 counts \cdot min $^{-1}$ intensity cut off was used to estimate sedentary time. Finally, for Actiheart, the presumed MET cut point for sedentary time (< 1.5 METs) based on accelerometry+HR was used. A break in sedentary time was considered whenever participants were above the aforementioned cut offs.

For the comparisons between devices, the 15 seconds epochs' data from GT3X, Actiheart, and ActivPAL were reintegrated in 1 min epochs for data analyses. GT3X was only worn during waking hours and removed for sleeping. Therefore, to be able to distinguish sleeping hours (recorded in Actiheart and ActivPAL as sedentary time) from actual sedentary time spent during waking hours, only the hours from the three devices corresponding to the waking period were matched and synchronized in each participant. Thus, the variable sedentary time (min \cdot day $^{-1}$) is the sum of the time spent in sedentary time in all the valid hours during the waking period for each participant. The days that were simultaneously valid in all three monitors were considered.

In chapter 5, continuous bouts of sedentary time were assessed by accelerometry (ActiGraph, GT1M model, Fort Walton Beach, FL). A bout was considered as a specific period of time (x) in continuous sedentary time in which the accelerometer count down from 100 counts \cdot min $^{-1}$ and no interruption was allowed (> 100 counts \cdot min $^{-1}$). For example, a bout of ≥ 60 min of sedentary time is not an accumulation of 6 or more shorter bouts ($5 \leq \text{min} < 10$) but instead a period of at least 60 min in which the participants were continuously in sedentary time. In other words, longer bouts are not an accumulation of shorter bouts categories once it is not allowed any interruption during the bout period and when an interruption occurs another bout begins. Data processing derived in the following variables: daily number of bouts of $5 \leq \text{min} < 10$, $10 \leq \text{min} < 20$, $20 \leq \text{min} < 30$, $30 \leq \text{min} < 60$, ≥ 60 min of continuous sedentary time.

In chapter 8, breaks in sedentary time and PA were assessed by accelerometry (ActiGraph, GT1M model, Fort Walton Beach, FL). A break in sedentary time was considered as any bout of time in which the accelerometer count rose up to or above 100 counts·min⁻¹ and which stayed within the LIPA range (< 2020 counts·min⁻¹). The difference between LIPA and the daily breaks in sedentary time variable is that whereas LIPA is the total cumulative daily time spent in LIPA per day (min·day⁻¹), breaks in sedentary time represents the number of times sedentary time was broken by LIPA (breaks·day⁻¹). Data processing also derived the following variables: bouts of at least 1, 5, and 10 min of LIPA (bouts·day⁻¹); hourly breaks in sedentary time calculated as follows (60 x daily breaks in sedentary time)/daily accelerometer wear time in min.

In chapter 9, the primary outcomes were ActivPAL's total waking time spent sitting, standing, stepping, number of steps, and the number of bouts (\leq 4 min; 5-9; 10-19; 20-29; 30-59; and at least 60 min) of uninterrupted sitting. As secondary outcome measures the number of bouts (\leq 4 min; 5-9; 10-19; 20-29; 30-59; and at least 60 min) of ActivPAL's standing and stepping and the Actigraph accelerometer's breaks in sedentary time were also considered.

3.6. Statistical analysis

Data analyses were performed using the following softwares: IBM SPSS Statistics (SPSS Inc., an IBM Company, Chicago, Illinois, USA) version 21.0 (chapters 5, 6, 8, and 9) or 22.0 (chapters 4 and 7); MedCalc Statistical Software version 11.1.1.0, 2009 (Mariakerke, Belgium) (chapter 4); GPower software, version 3.1.9.2 (chapter 7).

The statistical procedures common to all studies are presented in this section (Chapter 4 to 9), as follows:

Descriptive statistics including means and standard deviation were performed for all outcome measurements. Normality of the outcome variables was analyzed using the Kolmogorov-Smirnov test.

Additionally, statistical analyses that were specific to each of the studies were included according to the objectives that were proposed for each investigation.

Mean comparisons for two groups were performed using independent sample t-test (chapter 8) while comparisons for three or more groups was performed using One-way ANOVA (chapters 4, 6, and 8) or repeated measures ANOVA (chapter 9). Paired sample t-tests were used to compare measures from paired samples (chapters 4 and 9).

In study 1 (chapter 4) specific statistical procedures were used to test the accuracy of the alternative methods as described in detail in chapter 4.

In studies 2 and 5 (chapters 5 and 8) backwards linear regression analyses were performed to examine the associations of continuous sedentary main variables (bouts and breaks, respectively), total sedentary time, and MVPA ($\text{min}\cdot\text{day}^{-1}$) with waist circumference (continuous variable). Backwards binary logistic analyses were performed to examine associations of continuous sedentary bouts/breaks ($\text{number}\cdot\text{day}^{-1}$), total sedentary time ($\text{min}\cdot\text{day}^{-1}$), and MVPA ($\text{min}\cdot\text{day}^{-1}$) with the odds of abdominal obesity. Both linear and logistic adjusted models were additionally included to adjust for covariates removed in backwards elimination. In study 2, Goodness-of-fit tests such as the Log Likelihood ratio, the Cox & Snell R Square statistic and the Hosmer and Lemeshow Test were used as indicators of model appropriateness, and the Wald statistic was used to test the significance level of individual independent predictor variables. Interactions for gender with bouts of continuous sedentary time from distinct lengths to predict abdominal adiposity were tested. Interactions that were considered to be significant if $p < 0.05$ were followed with stratified analyses.

In study 3 (chapter 6) multiple partial regressions analysis were performed for the overall sample and by sport' groups, adjusting for covariates. Prior to the regression analysis, normality and multi-co linearity tests were conducted.

In study 4 (chapter 7) a repeated measures ANCOVA with post hoc analysis was used to compare the differences between conditions (conditions x 3), adjusting for potential covariates and considering the order of conditions' randomization and sex as between-subject effects. Multicollinearity for the covariates was also examined. To test the sphericity or homogeneity of variances, the Mauchly's statistical test was performed. If the test was non-significant ($p \geq 0.05$), the F-ratios produced by SPSS

were considered. If the test was significant ($p < 0.05$), no homogeneity of variances existed, then the Greenhouse and Geisser's test was considered.

3.7. References

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CHAPTER 4

Validity of GT3X and Actiheart to estimate sedentary time and breaks using ActivPAL as the reference in free-living conditions¹

¹ **Judice, P. B.**, Santos, D. A., Hamilton, M. T., Sardinha, L. B., & Silva, A. M. (2015). Validity of GT3X and Actiheart to estimate sedentary time and breaks using ActivPAL as the reference in free-living conditions. *Gait Posture*, 41(4), 917-922. doi: 10.1016/j.gaitpost.2015.03.326. **2.75** Impact Factor

Validity of GT3X and Actiheart to estimate sedentary time and breaks using ActivPAL as the reference in free-living conditions

Pedro B. Júdice, Diana A. Santos, Marc T. Hamilton, Luís B. Sardinha, Analiza M. Silva

4.1. Abstract

Aim. Sedentary time, specifically sitting/reclining, is a risk factor for many non-communicable diseases and premature mortality. Inclinometers have been used as a valid measurement of sedentary time and its patterns; however, there is a lack of information regarding the validity of alternative accelerometry and heart rate methods. The validity of GT3X and Actiheart in estimating changes in daily sedentary time and breaks, during free-living settings, using ActivPAL as the reference was examined.

Methods. A crossover randomized control trial of an intervention that aimed to reduce ~ 3 hours \cdot day $^{-1}$ of sitting time included 10 overweight/obese adults (37-65 years). Participants had a total of 74 valid days for the three devices (29 controls; 45 interventions). For ActivPAL, sedentary time was measured directly based upon posture (sitting/reclining); Actiheart, the presumed MET cutpoint for sedentary time (< 1.5 METs) based on accelerometry+heart rate; GT3X, the traditional < 100 counts \cdot min $^{-1}$. A break in sedentary time was defined as when the participants were above the aforementioned cutoffs.

Results. GT3X overestimated and Actiheart underestimated sedentary time (bias=135 min; bias= -156 min, respectively) and both methods overestimated breaks in sedentary time (bias=78; bias=235 breaks, respectively). The GT3X method was in better agreement with the ActivPAL sedentary time ($r^2=0.70$; concordance correlation coefficient (CCC)=0.56) than the Actiheart ($r^2=0.24$; CCC=0.31).

Conclusions. The present results highlight the magnitude of potential errors in estimating sedentary time and breaks from common alternative methods other than ActivPAL. Because misclassification errors from the commonly used surrogates are potentially large, this raises concern that alternative methods used in many

epidemiological observations may have underestimated the true effects caused by too much sitting. (ClinicalTrials.govID:NCT02007681).

***Keywords:** Sedentary patterns, motion sensor, inclinometer, objective methods, intervention*

4.2. Introduction

Sedentary behavior and PA are distinct entities and the lack of moderate-to-vigorous PA (MVPA) does not directly imply higher sedentary time. A paradigm shift first proposed in 2004 by Hamilton et al. (Hamilton, Hamilton, & Zderic, 2004) and updated since (Hamilton, Hamilton, & Zderic, 2007) states that behaviors and physiology of sitting inactive (inactivity physiology) is qualitatively different from what has been the traditional focus of much less frequent, more brief, and generally more vigorous PA associated with exercise. This has raised the need for being able to quantify behaviors like sitting and light activity that historically have not been measured objectively. One of the most heavily studied aspects comes from the possibility that many common diseases are caused by large amounts of sitting behaviors, which are potentially preventable by replacing them with non-fatiguing low intensity PA, separate from traditional exercise recommendations (Hamilton, Hamilton, & Zderic, 2004, 2007; Hamilton, Healy, Dunstan, Zderic, & Owen, 2008). Recently, there has been an emergence in an appreciation for studies that focus on sitting time. However, devices used to quantify sitting time and breaks have relied less often on methods actually designed to directly measure postural allocation (such as ActivPAL) than the more indirect surrogate measures. Thus, with some exceptions (Hart, McClain, & Tudor-Locke, 2011; Kozey-Keadle, Libertine, Lyden, Staudenmayer, & Freedson, 2011; Lyden, Kozey Keadle, Staudenmayer, & Freedson, 2012; Ryde, Gilson, Suppini, & Brown, 2012), there is still much to learn regarding how well existing commercial technologies commonly used in the epidemiological studies estimate sedentary time and breaks in the free-living condition.

Accelerometers have been the preferred method to study patterns of PA. The ActiGraph GT3X and earlier versions of similar devices have been utilized and, in

general, have been quite useful for estimating MVPA (Prince et al., 2008). However, when considering sedentary time, ActivPAL (an inclinometer-based device that detects postures) has been presented as the best alternative due to its high precision and accuracy compared to gold standard methods such as direct observation (Kozey-Keadle et al., 2011). ActivPAL also allows for longer data collection periods (Aguilar-Farias, Brown, & Peeters, 2013; Grant, Ryan, Tigbe, & Granat, 2006; Ryan, Grant, Gray, Newton, & Granat, 2008). Accelerometers (count-based data) have been presented as less accurate for detecting low intensity behaviors (Kozey-Keadle et al., 2011; Oliver et al., 2013) because they do not discern sitting from non-sitting time. Rather, accelerometers estimate sedentary time based on a lack of movement ($< 100 \text{ counts} \cdot \text{min}^{-1}$), which may often erroneously incorporate light PA behaviors (standing) as sedentary time. One study found GT3X to accurately detect changes in sedentary time and PA comparable with ActivPAL (Swartz, Rote, Cho, Welch, & Strath, 2014). Conversely, evidence suggests that the GT3X may not be able to identify breaks in sedentary time given its biased and imprecise estimates of total sedentary time (Kozey-Keadle et al., 2011).

To overcome some of the accelerometers' limitations, a combined heart rate (HR) with accelerometer device (Actiheart) (Loney, Standage, Thompson, Sebire, & Cumming, 2011; Villars et al., 2012) has been used to estimate energy expenditure (EE) (Silva et al., 2014). Actiheart utilizes both accelerometer and HR, and calculates AEE by differently weighting the data from the two components depending on the dominance of activity or HR using a validated branched model calculation. Essentially, when both accelerometer and HR are low, the accelerometer AEE estimates have more weight, whereas when accelerometer and HR values are high, the HR AEE estimates are the predominant contributor to AEE. To minimize the influence of HR increase not related to PA, the normal HR data weighting is reduced where HR increases in the absence of sufficient counts (Silva et al., 2014).

Actiheart has been shown to accurately estimate AEE compared to the gold standard doubly labeled water technique (Silva et al., 2014). By combining accelerometer and HR data, Actiheart may prevent accelerometer only misclassification when low body movement (but high HR) exists. Regardless, the advantages that

Actiheart presents for MVPA estimation are still to be investigated when examining sedentary time patterns, with no data for the accuracy of Actiheart in sedentary time estimations. Therefore, the aim of this study was to examine the agreement between GT3X and Actiheart with ActivPAL for capturing sedentary time and breaks in overweight/obese adults engaged in a free-living intervention to reduce sedentary time.

4.3. Methods

4.3.1. STUDY DESIGN

The study was approved by the Ethics Committee from Faculdade de Motricidade Humana, Universidade de Lisboa, (approval number:14/2013) and conducted in accordance with the Ethical Standards in Sport and Exercise Science (Harriss & Atkinson, 2013). Written informed consent was obtained from each participant. Inclusion criteria consisted of: currently employed in a full time academic or administrative role that involves > 7 hours \cdot day $^{-1}$ of computer based work; aged 18-65 years old; body mass index (BMI) > 25.0 kg \cdot m $^{-2}$; not taking medication or dietary supplements; physically inactive (not meeting the MVPA recommendations and not exceeding 5000 steps \cdot day $^{-1}$); and free from any major disease.

This was a crossover randomized clinical trial (ClinicalTrials.govID: NCT02007681). Participants were randomly assigned for two treatment arms (intervention/control) by an automated computer generated randomization scheme (a detailed description available as supporting information; CONSORT flow diagram and checklist). Data were collected between September-December 2013 and analyzed in 2014.

4.3.2. PARTICIPANTS

To ensure that participants were physically inactive (< 30 min \cdot day $^{-1}$ of MVPA and ~ 5000 steps \cdot day $^{-1}$) and to assess habitual steps \cdot day $^{-1}$, PA, and sedentary time, participants were fitted with a pedometer (Omron Hj-113 Pocket Pedometer, Walking Style-II) and an accelerometer ActiGraph GT3X+ (ActiGraph, Pensacola, FL) prior to intervention. The trial consisted of two one-week conditions performed in a random

order, both under free-living conditions: intervention (3 h reductions in sitting time) and control (habitual sitting time). Participants were instructed to maintain the same eating patterns during the trial.

The intervention included a software program (Workrave, GitHub) that gave hourly alerts to participants to break up their sitting time for 7 min. During transportation/home/domestic leisure time contexts, individual goals for number of steps·day⁻¹ were set, based on an expected step cadence for ambulatory activities (~ 90-120 min·day⁻¹) and by adding 6000 steps to their initial habitual daily amount.

Anthropometric variables were measured according to the standardized procedures described elsewhere (Lohman, Roche, & Martorell, 1988). BMI was calculated as body mass (kg)·height⁻² (m).

4.3.3. ACTIVPAL MEASUREMENTS

The ActivPAL Professional (Pal Technologies Ltd., Glasgow, UK) was worn on the middle anterior line of the right thigh and provided objectively processed variables, including total time spent sitting/lying. From the ActivPAL raw data, it was possible to extract the periods of time spent in sedentary behavior. The device was sealed with a non-allergenic adhesive tape attached to the skin and used continuously for 24 h for 14 days, except for water-based activities such as showering and swimming. Data was recorded in 15 seconds epochs. Participants were asked to record waking/sleeping hours and ActivPAL wear time in a logbook. A valid day was defined as having 600 or more min (≥ 10 h) of monitor wear during waking hours. They were also asked to record timing and reasons for every occasion the ActivPAL was removed.

4.3.4. GT3X+ MEASUREMENTS

Participants wore an accelerometer ActiGraph GT3X+ (ActiGraph, Pensacola, FL) on the right hip, near the iliac crest programmed to collect data from the vertical axis in 15 seconds epochs and initialized using the normal filter (AG-Norm). Accelerometers were worn for 14 days during all waking hours and removed for sleeping and during water-based activities (Troost, McIver, & Pate, 2005). The delivery and fitting of the accelerometers was conducted face to face (Ward, Evenson, Vaughn,

Rodgers, & Troiano, 2005). The device activation/download/processing were performed using the Actilife software (v.6.9.1). A valid day was defined as having 600 or more min (≥ 10 h) of monitor wear (Ward et al., 2005). The cutoff value used to define sedentary time was < 100 counts \cdot min⁻¹ (Troiano et al., 2008). Participants were asked to record waking/sleeping hours and accelerometer' wear time in a logbook. They were also asked to record timing and reasons for every occasion the accelerometer was removed.

4.3.5. ACTIHEART MEASUREMENTS

The Actiheart (Actiheart, CamNtech Limited, UK) is a lightweight (10 g) combined HR and movement (uniaxial accelerometer oriented to measure acceleration along the body's longitudinal axis) sensor that utilizes both piezoelectric accelerometer and HR data synchronously. This sensor is capable of storing time-sequenced data for several days and was worn on an adapted polar band placed on the chest. The Actiheart software allows two types of calibration; an individual calibration using a standardized step test that consists of step up and down a 15 cm high step, progressively increasing step frequency from 15 to 32.5 body lifts per min (rate of change: 2.5 body lifts per min) and a group calibration inbuilt function.

Given that some of the participants were not able to finish the step test, a group calibration that is available in the software (version 4.0.99) was performed. The Actiheart was started at the long term mode to record HR and acceleration with 15 second epochs. Participants wore the Actiheart 24 h \cdot day⁻¹ for 14 days and a valid day was defined as having 600 or more min (≥ 10 h) of monitor wear during waking hours. Data from the Actiheart were downloaded into the commercial software. The camNtech software algorithm allowed data cleaning, recovering, and interpolation of missing and noisy HR. Using the raw data from the branched combined model that uses activity (acceleration) and HR, it was possible to extract and quantify the daily sedentary time (< 1.5 METs). Participants were also instructed to register the periods in which they removed the device for water activities.

Sedentary time from the three devices was accounted for by the total time spent in sedentary behavior while considering the same awake hours in the three devices. For

ActivPAL, sedentary time was created based on posture (sitting/reclining). For GT3X, the traditional $< 100 \text{ counts} \cdot \text{min}^{-1}$ intensity cut off was used to estimate sedentary time. Finally, for Actiheart, the presumed MET cut point for sedentary time ($< 1.5 \text{ METs}$) based on accelerometry+HR was used. A break in sedentary time was considered whenever participants were above the aforementioned cut offs.

For the comparisons between devices, the 15 seconds epochs' data from GT3X, Actiheart, and ActivPAL were reintegrated in 1 min epochs for data analyses. GT3X was only worn during waking hours and removed for sleeping. Therefore, to be able to distinguish sleeping hours (recorded in Actiheart and ActivPAL as sedentary time) from actual sedentary time spent during waking hours, only the hours from the three devices corresponding to the waking period were matched and synchronized in each participant. Thus, the variable sedentary time ($\text{min} \cdot \text{day}^{-1}$) is the sum of the time spent in sedentary time in all the valid hours during the waking period for each participant. The days that were simultaneously valid in all three monitors were considered.

To ensure that no sleeping hours were considered in the analysis, data from the three devices were crossed with the information reported in the logbooks.

4.3.6. STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS Statistics for Windows version 22.0, 2012 (SPSS Inc., an IBM Company, Chicago IL, USA). Descriptive analysis included means \pm standard deviation (SD). To assess differences between devices' estimations, we used paired samples t-test. The participants' random effects for the differences between methods were tested using the univariate analysis of variance model. To assess validity, the coefficient of determination (r^2) and standard error of estimate (SEE) were used to assess the predictive power and the association between methods, respectively.

To examine the amount of agreement for GT3X and Actiheart sedentary time estimates using ActivPAL as a reference, we calculated the concordance correlation coefficient (CCC) using the Lin approach (Lin, 1989) with MedCalc Statistical Software version 11.1.1.0, 2009 (Mariakerke, Belgium). The CCC (ρ_c) contains a measurement of precision ρ and accuracy ($\rho_c = \rho C_b$), where ρ is the Pearson correlation

coefficient and C_b is a bias correction factor. As CCC is defined without ANOVA assumptions, we also calculated the intraclass correlation coefficient (ICC) which has been traditionally used for assessing reliability between multiple methods. Definitions of different versions of ICCs depend on the assumptions of specific ANOVA models. Therefore, type A ICC was calculated using an absolute agreement definition for the two-way mixed models available on SPSS.

Agreement between methods was assessed using the Bland-Altman method (Bland & Altman, 1986). The Pearson coefficient of correlation (ρ) was also used to test if the differences between methods were related with the mean of the methods. Statistical significance was set at $p < 0.05$.

4.4. Results

There was approximately 13% lost data for the GT3X (insufficient daily wear time), and approximately 35% of lost days for the Actiheart (no HR data). All 10 participants completed both trial conditions but due to lost data, we finished with a total of 7 participants and 74 valid days (29 control; 45 intervention). For both total sedentary time and breaks in sedentary time, the unit of analysis was the participant/day. One participant was overweight and 6 were obese, and the sample was not equally distributed according to gender (5 women; 2 men). Mean age was 49.7 ± 12.6 (range=37-65) years; mean BMI was 34.7 ± 5.07 (range=29-41).

The difference in sedentary time between control and intervention valid days was not significant (-18.5 ± 38.5 min) (Table 4.1). Participants significantly increased MVPA (control: 22.1 ± 10.7 min vs intervention: 47.4 ± 21.6 min, $p < 0.001$) and daily steps (control: 5618 ± 2193 steps·day⁻¹ vs intervention: 11355 ± 2196 steps·day⁻¹, $p < 0.001$).

Table 4.1 presents the means and the differences between methods for the daily sedentary time and breaks in sedentary time estimations obtained by GT3X and Actiheart methods using ActivPAL as the reference.

Table 4.1. Means and differences for sedentary time and breaks in sedentary time estimations for GT3X and Actiheart using ActivPAL as the reference, by condition

	Intervention			Control		
	Estimation (Mean \pm SD)	Alternative-Reference (Mean \pm SD; <i>P</i>)		Estimation (Mean \pm SD)	Alternative-Reference (Mean \pm SD; <i>P</i>)	
Sedentary time (min·day⁻¹)						
	ActivPAL (496 \pm 172)			ActivPAL (515 \pm 142)		
GT3X	636 \pm 138	140 \pm 83; <0.001		642 \pm 94	127 \pm 97; <0.001	
Actiheart	342 \pm 158	-154 \pm 144; <0.001		356 \pm 126	-159 \pm 174; <0.001	
Breaks in sedentary time (number·day⁻¹)						
	ActivPAL (53.7 \pm 15.2)			ActivPAL (46.6 \pm 16.7)		
GT3X	136 \pm 35	82 \pm 30; <0.001		128 \pm 44	81 \pm 47; <0.001	
Actiheart	305 \pm 79	251 \pm 77; <0.001		258 \pm 80	211 \pm 79; <0.001	

The total number of valid-days for the three methods comparison was 74 days; 29 days of control and 45 days of intervention. ActivPAL was used as the reference for the comparisons with GT3X and Actiheart.

Abbreviations: Actiheart, combined heart rate and motion sensor; ActivPAL, inclinometer; GT3X, accelerometer; SD, standard deviation.

As shown in Table 4.1, GT3X significantly overestimated while Actiheart underestimated ActivPAL's sedentary time. Both alternative methods overestimated breaks in sedentary time compared with ActivPAL.

No significant interaction for the condition with the differences between both alternative and reference methods was observed ($p > 0.05$). Significant random effects for the participants' factor with the differences between methods and the reference were observed ($p < 0.001$) for both sedentary time and breaks in sedentary time.

The results from the regression analyses are presented in Table 4.2.

Table 4.2. Regression for GT3X and Actiheart using ActivPAL as the reference for the daily sedentary time and breaks in sedentary time estimations

	r	r²	slope	Intercept	SEE	95% CI	Trend	CCC	ICC[§]
Sedentary time (min·day⁻¹)									
GT3X	0.84*	0.70	1.10	-199	88.1	0.93 – 1.27	0.45 [#]	0.56	0.72
Actiheart	0.48*	0.24	0.54	317	141	0.31 – 0.76	0.11	0.31	0.48
Breaks in sedentary time (number·day⁻¹)									
GT3X	0.28*	0.08	0.13	37.7	16.8	0.03 – 0.23	0.68 [#]	0.05	0.09
Actiheart	0.23*	0.05	0.32	414	15.8	0.00 – 0.09	0.93 [#]	0.01	0.02

* Significant correlation for the alternative method with the reference method.

Significant trend for the differences and the means for the alternative method with the reference method.

§ Intraclass correlation coefficient using an absolute agreement definition for two-way mixed effects model.

The total number of valid days for the three methods comparison was 74 days; 29 days of control and 45 days of intervention.

ActivPAL was used as the reference for the comparisons with GT3X and Actiheart.

Abbreviations: Actiheart, a combined heart rate and motion sensor; ActivPAL, inclinometer; r, coefficient of correlation; r², coefficient of determination; CI, confidence intervals; CCC, concordance correlation coefficient; ICC, intraclass correlation coefficient; GT3X, accelerometer; SEE, standard error of estimation.

As presented in Table 4.2, significant associations were observed for the GT3X and Actiheart estimations with ActivPAL sedentary time and breaks in sedentary time. However, while GT3X and Actiheart explained 70% and 24% of ActivPAL’s sedentary time, the two devices only explained 8% (GT3X) to 5% (Actiheart) of ActivPAL’s breaks in sedentary time estimation. Additionally, for both GT3X and Actiheart, the estimation obtained by each method and the reference method differed from the line of identity. Indeed, considering ICC and CCC values (Table 4.2), GT3X presented the best agreement with ActivPAL’s sedentary time estimation with a precision of 0.84 and an accuracy of 0.66, whereas Actiheart had a precision and accuracy of 0.46 and 0.66, respectively. For the breaks in sedentary time, both devices presented lower ICCs and CCCs. A precision of 0.28 and accuracy of 0.17 were observed for GT3X, whereas a precision of 0.22 and an accuracy of 0.03 were observed using Actiheart.

The agreement for GT3X and Actiheart’s sedentary time estimations with ActivPAL as the reference is shown in panel A of Figure 4.1. A significant trend was found between the differences and the mean of the alternative, and the reference method for GT3X ($p < 0.001$) but not for Actiheart ($p=0.337$). Wide limits of agreement were

observed for both methods to predict ActivPAL's sedentary time (panel A of Figure 4.1).

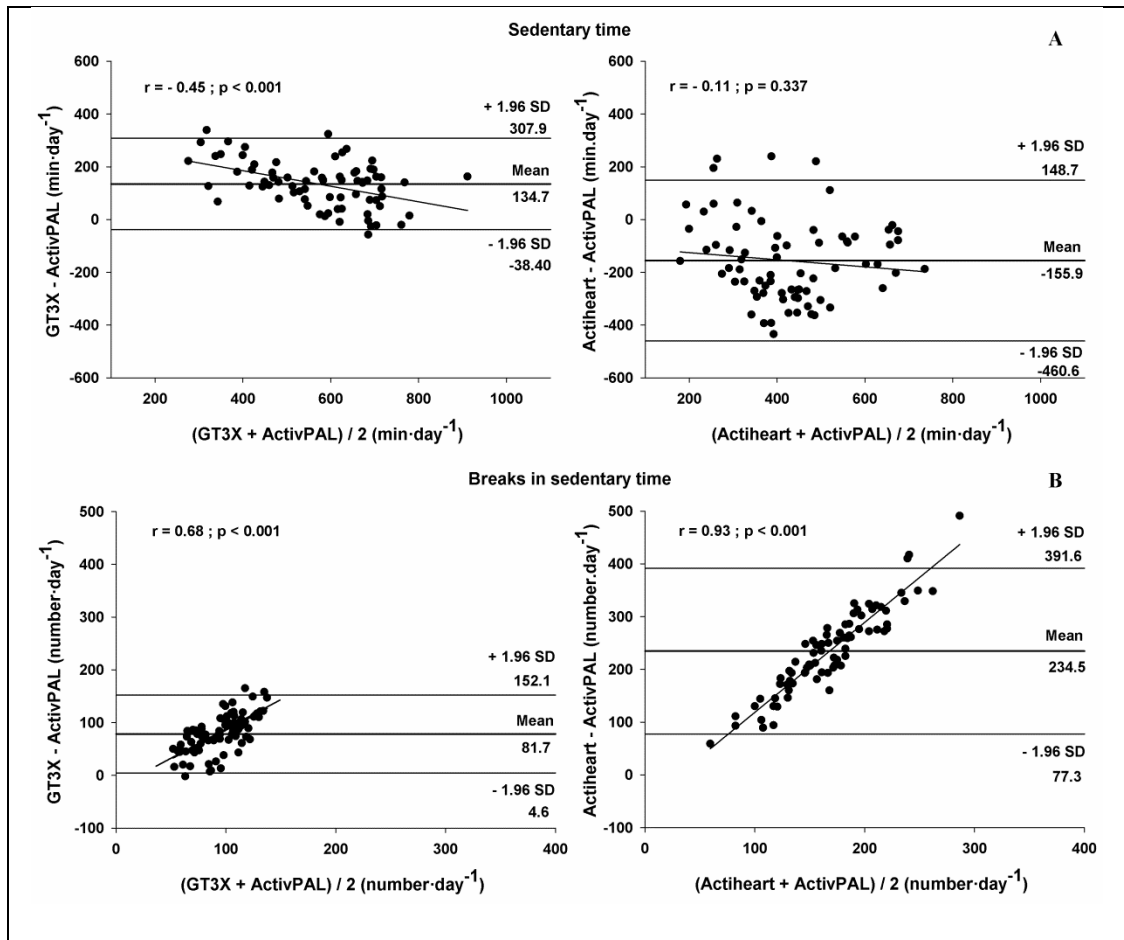


Figure 4.1. A Bland-Altman analysis of between-methods agreement in estimate daily sedentary time and breaks in sedentary time. The middle solid line represents the mean differences between both methods. The upper and lower lines represent ± 2 standard deviations (SD) from the mean, that is, 95% limits-of-agreement (± 1.96 SD). The trend line represents the association between the differences of the methods and the mean of both methods.

For the breaks in sedentary time estimations, agreement for GT3X and Actiheart with ActivPAL as the reference is shown in panel B of Figure 4.1. A significant trend was found between the differences and the mean of both alternative and reference methods for both GT3X and Actiheart ($p < 0.001$). Wide limits of agreement were observed for both methods to predict ActivPAL's breaks in sedentary time (panel B of Figure 4.1).

4.5. Discussion

The present study examined the validity of GT3X and Actiheart to estimate daily sedentary time and breaks in sedentary time using ActivPAL as the reference method, in physically inactive overweight/obese working adults engaged in a multi component intervention to reduce sedentary time. An empirical evaluation and comparison of these tools will further inform research aiming to measure and interpret sedentary time and its associated health outcomes. This is of particular importance given that ActiGraph was the tool used in many studies providing evidence that breaks from sedentary time might be favorably related to health (Healy et al., 2008; Healy, Matthews, Dunstan, Winkler, & Owen, 2011).

Some studies have assessed the validity of GT3X in estimating sedentary time, with ActivPAL as the reference (Kozey-Keadle et al., 2011; Ryan et al., 2008) without as much prior understanding regarding comparisons with Actiheart outcomes (accelerometry+HR). The comparison of three distinct methods to estimate sedentary time and breaks in sedentary time in free-living conditions provides new insights to this recent scientific area of study. The inclusion of a device that combines HR and accelerometry information (a method without background in the evaluation of sedentary time) makes this comparison especially meaningful. Our comparison is of particular interest since observational findings regarding the independent associations of sedentary time with disease outcomes have been obtained by using distinct analytical approaches to measure sedentary time and generally not used ActivPAL or other validated devices to measure postural allocation.

The results showed Actiheart to significantly underestimate sedentary time compared to ActivPAL (~ 155 min). In addition, the ICC and CCC between Actiheart and the reference method were low with Actiheart explaining only 24% of ActivPAL's sedentary time total variability. Despite the low association between equipment and the significant bias, Actiheart underestimated ActivPAL's sedentary time independently on the magnitude of sedentary time values (panel-A of Figure 4.1). This means that Actiheart underestimated sedentary time in a constant manner, with no influence of sedentary time levels in the error between methods.

Actiheart combines the information from accelerometry and HR monitor and uses one of four branched equations. Normally in the branched model, the contribution to EE from accelerometry and HR is weighted epoch by epoch according to certain activity and HR thresholds. At running speeds, HR is a very reliable measure of EE. On the other hand, for sedentary and low intensity activities, HR is a poor measure of intensity; movement registration is more reliable. Thus, HR is weighted 10% on the HR-EE relationship. Therefore, with 90% of sedentary time estimation being dependent on accelerometry data only, it was expected that Actiheart would overestimate sedentary time similarly to what occurs in GT3X. However, the 10% inclusion of HR in the branched equations associated with a different wearing position (chest) may explain why Actiheart underestimated sedentary time compared to ActivPAL. Participants were obese and physically inactive with generally poor fitness. Therefore, even when sitting they were more susceptible to external stimulus and may have presented an elevated HR which would be classified as non-sedentary time (≥ 1.5 METs) by the Actiheart.

The large limits of agreement and the lack of precision presented in panel A of Figure 4.1 indicate that Actiheart is not a good method for estimating sedentary time, both at group or individual level. Actiheart can be suitable to estimate sedentary time if accounting for the constant bias, once no trend along the magnitude of sedentary time levels was found.

Positive but weak association was found for the breaks in sedentary time estimated by Actiheart compared to ActivPAL. However, Actiheart significantly overestimated ($235 \text{ breaks} \cdot \text{day}^{-1}$) the number of daily breaks in sedentary time. The Bland-Altman plots showed a trend between the difference and the mean of both methods (panel B of Figure 4.1) with large limits of agreement and lack of precision. Therefore, Actiheart is not valid both at individual and group levels for the breaks in sedentary time. Actiheart combines information from accelerometry and HR, and the vulnerability of this former parameter to external stimulus may explain the higher number of transitions from sedentary time to light PA that could be independent of postural changes (sit to stand) and, therefore, justify the discrepancies with ActivPAL's breaks estimation.

Data comparing and validating accelerometer estimates of sedentary time against ActivPAL are accumulating (Harrington, Welk, & Donnelly, 2011; Lyden et al., 2012). However, the findings are equivocal, with studies finding good agreement between these two methods (Feito, Bassett, & Thompson, 2012; Godfrey, Culhane, & Lyons, 2007; Matthews et al., 2013) and others showing weak concordance, specifically because GT3X output of count thresholds is less sensitive to detect sitting/standing transitions compared to ActivPAL (Lyden et al., 2012; Oliver, Schofield, Badland, & Shepherd, 2010). These controversial results can be partially explained by the variability in studies' conditions (laboratory or free-living), and the fact that previous studies have used different cutoffs to define sedentary time when using accelerometry. In addition, there is a basic difference inherent to what these two types of devices evaluate. While GT3X evaluates intensity of movement, the ActivPAL assesses postures.

For the comparison of GT3X with ActivPAL, our results are in accordance with former studies that found accelerometry to overestimate sedentary time compared to ActivPAL. A significant trend was revealed (panel B of Figure 4.1), with a higher overestimation of sedentary time for the lower sedentary levels and a better agreement between methods for the higher sedentary levels. Therefore, in opposition to what occurred with Actiheart, the error between GT3X and ActivPAL was not constant along sedentary time levels. This is of great importance, since the reliability of GT3X to measure sedentary time seems to vary with sedentary levels. Therefore, interventions that aim to examine sedentary time changes over time may be weakened or enhanced by this inconsistent error. The ICC between GT3X and ActivPAL methods was 0.72, indicating that despite the mean bias of GT3X overestimating ActivPAL, there is a moderate to high agreement between the two methods. Furthermore, GT3X explained 70% of ActivPAL's sedentary time total variability, providing a much higher power to explain ActivPAL's variability compared to Actiheart.

The discrepancies between GT3X and ActivPAL estimations of sedentary time may be explained by an important limitation of using accelerometry counts alone to define sedentary time. Much of the standing time demanding muscular activity without high amounts of hip acceleration may be inadequately included by the hip mounted

accelerometer as sedentary time, resulting in a sedentary time overestimation. For example, the GT3X monitor output for standing activities such as cooking or washing dishes can be below 100 counts per min, and these activities are not sedentary.

In general, the ability of GT3X to distinguish between sedentary time and LIPA time is not known. Moreover, although GT3X is a triaxial accelerometer, only the information from the vertical axis was considered, because there are still no cutoffs for sedentary time using the triaxial information. While for some activities in the sitting position, the antero-posterior and mediolateral axes are able to record accelerations, the vertical axis indicates acceleration equal to zero. Therefore, we can only assume that the poor agreement observed for GT3X with ActivPAL was specific to its uniaxial measure, since only information on the vertical axis was considered. A positive but weak association was found for the breaks in sedentary time estimated by GT3X compared to ActivPAL, with GT3X overestimating (81.5 breaks·day⁻¹) daily breaks in sedentary time. A trend between the difference and the mean of both methods (panel B of Figure 4.1) with large limits of agreement and lack of precision was found. Therefore, GT3X showed poor agreement with ActivPAL both at individual and at a group level for the breaks in sedentary time. These results are in accordance with previous findings that found GT3X to significantly overestimate breaks in sedentary time compared to direct observation with good accuracy for the ActivPAL method (Lyden et al., 2012).

This study has some limitations that should be noted. Our results showed significant random effects for the participant factor with the differences between both GT3X and Actiheart with ActivPAL estimations for both sedentary time and breaks in sedentary time. This was in addition to the fact that the sample was restricted to overweight/obese participants, and that limits the generalizability of these results to a broader population. As mentioned before, another limitation was that the low agreement observed for GT3X with ActivPAL is specific to its uniaxial measure, since no information from the other two axes was considered. Using GT3X's triaxial information could improve the accuracy of this method to estimate sedentary time and breaks, but this still needs to be investigated in future studies (when thresholds for the triaxial information of the GT3X are developed).

Finally, although ActivPAL has been validated in the laboratory compared with a criterion measure (direct observation) and found to be 100% accurate for measuring sitting, standing, and walking, it cannot be considered a criterion measure for sedentary time assessment. Therefore, introducing a reference method like direct observation would enrich this study.

There are important strengths to this study. We were able to collect more than 750 free-living hours of valid data in all three devices. As an additional strength, we assessed each monitor's accuracy to detect change in behavior by examining breaks from sedentary time in all three devices. To our knowledge, no other study has examined the ability of a combined motion sensor and HR device to estimate sedentary time or breaks in sedentary time, which represents a novel finding in this field.

4.6. Conclusions

The present results suggest a relatively low agreement for GT3X and Actiheart with ActivPAL as the reference for sedentary time and breaks in sedentary time estimations. However, at the group level, the GT3X provided acceptable validity in estimating sedentary time. When comparing the effectiveness of free-living interventions to reduce sedentary time, especially if assessing sedentary time patterns, one must be careful when interpreting findings or making conclusions about sedentary behavior when using these alternative methods.

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CHAPTER 5

Sedentary bout durations are associated with abdominal obesity in older adults ²

² **Judice, P. B.**, Silva, A. M., & Sardinha, L. B. (2015). Sedentary Bout Durations Are Associated with Abdominal Obesity in Older Adults. *J Nutr Health Aging*, 19(8), 798-804. doi: 10.1007/s12603-015-0501-4. **3.00** Impact Factor

Sedentary bout durations are associated with abdominal obesity in older adults

Pedro B. Júdice, Analiza M. Silva, Luís B. Sardinha

5.1. Abstract

Aim: In older adults, sedentary behavior has been positively associated with obesity and impaired metabolic health, additional to low moderate-to-vigorous physical activity (MVPA). Further to the total time spent in sedentary behavior, the manner in which it is accumulated – number of continuous sedentary bouts of different extends – may also be relevant. The association for objectively measured uninterrupted sedentary bouts and respective patterns with abdominal obesity in older adults was examined.

Method: A cross-sectional study that included 351 older adults (230 women) with a mean age of 75-years. Community-based older people were recruited in each region of Portugal. Data collection was performed between September, 2007 and May, 2009.

Sedentary time was measured by an accelerometer ($\text{counts} \cdot \text{min}^{-1} < 100$), worn during waking hours for 4 consecutive days. Continuous sedentary bouts of $5 < \text{min} < 10$, $10 < \text{min} < 20$, $20 < \text{min} < 30$, $30 < \text{min} < 60$, > 60 min length were treated ($\text{counts} \cdot \text{min}^{-1} < 100$). Abdominal obesity was defined by waist circumference (men > 102 cm; women > 88 cm).

Results: There were positive and escalating linear associations for the continuum of sedentary bouts' lengths with waist circumference. Logistic regression showed that for each additional sedentary bout of $10 < \text{min} < 20$ the odds of being abdominally obese increased by 6.8% (OR=1.07, 95% CI: 1.02 – 1.13) up to 48% (OR=1.48, 95% CI: 1.07 – 2.03) for each 1 hour sedentary bout increment, after controlling for age, gender, total sedentary time, MVPA time, total wear time, movement counts within the sedentary bouts, socio-demographic and other behavioral attributes, and medical history.

Conclusions: These findings indicate positive graded associations for continuous sedentary bouts with abdominal obesity. Public health recommendations regarding

breaking up sedentary time more often, potentially avoiding very prolonged bouts of sedentary time, are expected to be relevant for older adults.

Key Words: Prolonged sedentary time; waist circumference; physical activity; older adults; abdominal obesity

5.2. Introduction

A large population-based study found that the transition to retirement was consistently associated with substantial increases in time spent engaged in sedentary behaviors (Barnett, van Sluijs, Ogilvie, & Wareham, 2014), defined as time spent sitting or reclining during waking hours (Dunstan, Howard, Healy, & Owen, 2012; Owen, Healy, Matthews, & Dunstan, 2010). Older adults have higher levels of sedentary time (Evenson, Buchner, & Morland, 2012; Jefferis et al., 2014) which has been positively associated with excess adiposity (Bann et al., 2014; Vandelanotte, Sugiyama, Gardiner, & Owen, 2009). Body mass index (BMI) has been used as a measure of general nutritional status and adiposity in the elderly (Kumanyika et al., 2008). However, the optimal BMI and effects of being underweight or overweight on the risk of mortality of the elderly remain controversial (Flegal, Kit, Orpana, & Graubard, 2013; Lin et al., 2010) because of its inability to discern or detect age-related body fat redistribution (Chang, Beason, Hunleth, & Colditz, 2012). Among the potential measures of adiposity, waist circumference is a valuable indicator of abdominal obesity (Klein et al., 2007) and a strong and independent marker of health risk (Chang et al., 2012; Turcato et al., 2000). Even among people participating in high levels of moderate-to-vigorous physical activity (MVPA), the association of sedentary time with waist circumference still remains (Gennuso, Gangnon, Matthews, Thraen-Borowski, & Colbert, 2013). This suggests that regular physical activity may not fully protect against the risks associated with older adults' sedentary time (Gennuso et al., 2013; Larsen et al., 2014; Levine, Vander Weg, Hill, & Klesges, 2006), specifically in relation to abdominal obesity (Swartz, Tarima, et al., 2011).

Older adults are the most sedentary group in the population – spending about 70% (9 to 10 hours·day⁻¹) of their waking hours in sedentary time (Baptista et al., 2012;

Evenson et al., 2012; Healy et al., 2011) and the least amount of time in MVPA. They are also the age group that has the highest prevalence of abdominal obesity, which is positively associated with multiple comorbidities (Sardinha et al., 2012). In older adults, positive associations have been found for overall sedentary time with increased BMI (Bell, Kivimaki, Batty, & Hamer, 2014; Nicklas et al., 2014; Stamatakis, Hirani, & Rennie, 2009), body fat mass (Chastin, Ferriolli, Stephens, Fearon, & Greig, 2012; Larsen et al., 2013; Swartz, Tarima, et al., 2011), and waist circumference (Stamatakis et al., 2009; Swartz, Tarima, et al., 2011), but only one study has examined how the pattern in which total sedentary time is accumulated may partially attenuate the negative effects of sedentary time (Chastin et al., 2012). This study using an objective method for assessing sedentary time (ActivPAL) found sedentary time fragmentation (calculated as the ratio of the number of sedentary bouts divided by the total sedentary time), to be inversely associated with the percentage of body fat. The different durations of uninterrupted bouts of sedentary time could be related with adiposity but was not investigated. Therefore, little is known about the thresholds for prolonged time spent in sedentary behavior or how long sedentary time must be interrupted before it exacerbates abdominal obesity odds. This knowledge may provide an insight into the patterns through which sedentary time influences this cardiovascular disease risk phenotype. In addition, this information may also have potential implications for novel strategies designed to decrease this behavior. Therefore, we sought to characterize the associations between physical activity dimensions and if different durations of continuous sedentary bouts were associated with the odds for abdominal obesity, in older adults.

5.3. Methods

5.3.1. PARTICIPANTS

This study included a sample of non-institutionalized Portuguese Caucasian older adults, aged 65–103 years. Participants were selected by proportionate stratified random sampling taking into account the number of people by age and gender in each region of mainland Portugal (Alentejo, Algarve, Centro, Lisboa and Norte), excluding the Madeira and Açores regions (Portuguese Archipelagos). Data collection was

performed between September 2007 and May 2009. A total of 401 participants with an independent physical functioning were evaluated, of which 351 participants aged 65 or older (121 men and 230 women) had valid records of PA (\geq three days (including one weekend day), with \geq 10 h of wear time per day). The sample recruitment was carried out in senior universities, parish councils, city halls, day care centers, and health promotion fairs. All participants were informed about the possible risks of the investigation before giving their written informed consent to participate. All procedures were approved by the Ethics Committee of the Faculdade de Motricidade Humana, Universidade de Lisboa, and were conducted in accordance with the Declaration of Helsinki for human studies ("World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects," 2013) .

5.3.2. ANTHROPOMETRY

Participants were weighed to the nearest 0.01 kg while wearing minimal clothes and without shoes and height was measured to the nearest 0.10 cm with a scale coupled with a stadiometer (Seca, Hamburg, Germany) according to the standardized procedures (Lohman, Roche, & Martorell, 1988). BMI was calculated as body mass (kg)/ height² (m). Waist circumference was measured according to NIH procedures used in the third U.S. National Health and Nutrition Examination Survey (NHANES III 1988–1994) protocol with a flexible anthropometric tape (Seca, Hamburg, Germany) at minimal respiration and reported to the nearest 0.10 cm by positioning a tape parallel to the floor and immediately above the iliac crest. Waist circumference was then dichotomized into normal or increased relative risk (men >102 cm; women: > 88 cm) (National Institutes of Health, 1998).

5.3.3. CONTINUOUS BOUTS OF SEDENTARY TIME

Actigraph monitors have been presented as accurate methods to measure PA patterns and sedentary time (Hagstromer, Oja, & Sjostrom, 2007; Matthews et al., 2008; Montoye, Pfeiffer, Sutton, & Trost, 2014). Continuous bouts of sedentary time were assessed by accelerometry (ActiGraph, GT1M model, Fort Walton Beach, FL). The accelerometer used is a small device that measures the acceleration of normal human

movements ignoring high frequency vibrations associated with mechanical equipment. All participants were asked to wear the accelerometer on the right hip, near the iliac crest for four consecutive days, including two weekdays and two weekend days. The devices were activated on the first morning day and data were recorded in 15 seconds epochs. Participants were included if they had a total of at least three valid days (including one weekend day) of accelerometer data. A valid day was considered as at least 600 min of wear time. Considering the previous inclusion/exclusion criteria, from 401 participants that were evaluated, 351 participants had valid records of PA, and 50 participants were excluded. Apart from accelerometer non-wear time (i.e., when it was removed for sleeping or water activities), periods of at least 60 consecutive min of zero activity intensity counts were also considered as non-wear time. Each min that the accelerometer counts were <100 was considered sedentary time; total sedentary time was the sum of sedentary min while the accelerometer was worn. A bout was considered as a specific period of time (x) in continuous sedentary time in which the accelerometer count down from $100 \text{ counts}\cdot\text{min}^{-1}$ and no interruption was allowed ($> 100 \text{ counts}\cdot\text{min}^{-1}$). For example, a bout of ≥ 60 min of sedentary time is not an accumulation of 6 or more shorter bouts ($5 \leq \text{min} < 10$) but instead a period of at least 60 min in which the participants were continuously in sedentary time. In other words, longer bouts are not an accumulation of shorter bouts categories once it is not allowed any interruption during the bout period and when an interruption occurs another bout begins. Accelerometer counts ≥ 100 per min were classified as active time, with further differentiation to identify separately light-intensity physical activity (LIPA); (100 to $2019 \text{ counts}\cdot\text{min}^{-1}$) and MVPA; $\geq 2020 \text{ counts}\cdot\text{min}^{-1}$. Data processing derived in the following variables: daily number of bouts of $5 \leq \text{min} < 10$, $10 \leq \text{min} < 20$, $20 \leq \text{min} < 30$, $30 \leq \text{min} < 60$, ≥ 60 min of continuous sedentary time. Movement counts per min (CPM_x) within the continuous sedentary bouts for each one of the bouts' lengths were calculated as $(\text{total counts in bout}_x / \text{total time in bout}_x)$.

5.3.4. COVARIATES

Self-reported socio-demographics, behavioral, and medical covariates were assessed via interviewer-administered questionnaires. Employment was dichotomized as employed or unemployed (includes retired) and educational attainment was categorized as: 1) no education; 2) elementary school (up to 4 years of education); 3) middle school (up to 9 years of education); 4) high school (up to 12 years of education; and 5) higher education (more than 12 years of education). Geographical location of participants according to each region of mainland Portugal (Alentejo, Algarve, Centro, Lisboa and Norte) was also introduced as a covariate. Smoking status and alcohol dependence was reported and dichotomized in two categories (no or yes). Medical history for hypertension, elevated cholesterol and hiperglycemia, current medication, and the presence of any long-standing condition such as diabetes, asthma, cancer or cardiac disease were also reported and classified in two categories (no or yes).

5.3.5. STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS Statistics for Windows version 21.0, 2012 (SPSS Inc., an IBM Company, Chicago IL, USA). Descriptive analyses included means \pm standard deviation (SD) for all measured variables and linear correlations of sedentary time, LIPA, and MVPA. Backwards linear regression analyses were performed to examine the associations of continuous sedentary bouts (number \cdot day⁻¹), total sedentary time, and MVPA (min \cdot day⁻¹) with waist circumference (continuous variable). Backwards binary logistic analyses were performed to examine associations of continuous sedentary bouts (number \cdot day⁻¹), total sedentary time (min \cdot day⁻¹), and MVPA (min \cdot day⁻¹) with the odds of abdominal obesity. This method begins with a full or saturated model and variables are eliminated from the model in an iterative process. Variables making no significant contribution were eliminated from the final model using a backward stepwise approach.

Using this approach the criterion for inclusion of a predictor is significant at $P \leq 0.05$, while the removal criteria is set at $P > 0.10$. Both linear and logistic adjusted models were additionally included to adjust for covariates removed in backwards elimination (age, wear time, total sedentary time, employment, educational attainment,

geographical location, smoking status, alcohol dependence, medical history for chronic disease, hypertension, elevated cholesterol and glycemia, current medication status), and MVPA ($\text{min}\cdot\text{day}^{-1}$) or continuous bouts of sedentary time ($\text{number}\cdot\text{day}^{-1}$). Goodness-of-fit tests such as the Log Likelihood ratio, the Cox & Snell R Square statistic and the Hosmer and Lemeshow Test were used as indicators of model appropriateness, and the Wald statistic was used to test the significance level of individual independent predictor variables. Interactions for gender with bouts of continuous sedentary time from distinct lengths to predict abdominal adiposity were tested. Interactions that were considered to be significant if $P < 0.05$ would be followed with stratified analyses. Statistical significance was set at $P < 0.05$.

5.4. Results

No interactions for gender with continuous bouts of sedentary time to predict abdominal adiposity were found ($P > 0.05$). Therefore, men and women were pooled together. The participants' characteristics are shown in Table 5.1. On average participants spent 72% of their waking hours sedentary, 25% in LIPA and 3% in MVPA. From the daily overall sedentary time, 11% of the continuous sedentary bouts had less than 5 min, 29% ($5 < \text{min} < 10$), 15% ($10 < \text{min} < 20$), 17% ($20 < \text{min} < 30$), 10% ($30 < \text{min} < 60$), and 18% (> 60 min). There were 48% of the participants in the normal weight category and 52% in the abdominal obesity category.

Table 5.1. Mean and standard deviation values for participants' characteristics, waist circumference, and physical activity by gender

	Total (N=351)	Male (N=121)	Female (N=230)
Age (years)	74.6 ± 7.0	74.6 ± 6.8	74.6 ± 7.1
Height (cm)	157.7 ± 8.7	166.1 ± 6.3	153.2 ± 6.2
Body mass (kg)	68.1 ± 11.2	74.6 ± 10.7	64.6 ± 9.8
Waist circumference (cm)	94.1 ± 11.0	96.3 ± 10.4	92.9 ± 11.1
Sedentary time (min·day⁻¹)	576.0 ± 117.0	592.1 ± 107.7	567.6 ± 121.0
LIPA (min·day⁻¹)	199.0 ± 89.0	187.3 ± 85.1	205.3 ± 90.6
MVPA (min·day⁻¹)	23.0 ± 23.0	28.4 ± 24.8	20.7 ± 22.3
Continuous sedentary bouts (number·day⁻¹)			
5 ≤ min < 10	156.2 ± 27.0	156.5 ± 23.8	156.2 ± 28.7
10 ≤ min < 20	40.0 ± 14.0	44.0 ± 13.7	38.2 ± 14.6
20 ≤ min < 30	16.0 ± 7.5	18.1 ± 7.0	14.8 ± 7.5
30 ≤ min < 60	6.0 ± 3.9	7.0 ± 3.8	5.4 ± 3.8
≥ 60 min	1.3 ± 1.2	1.6 ± 1.2	1.2 ± 1.2

Abbreviations: N, number of participants; LIPA, light intensity physical activity; MVPA, moderate-to-vigorous physical activity; min, min.

The linear regression analyses showed significant correlations of total sedentary time, LIPA, and MVPA with waist circumference ($r=0.14$; $r=-0.11$; and $r=-0.20$, respectively, $P < 0.05$). The correlations for the continuum of daily sedentary bouts of $10 < \text{min} < 20$, $20 < \text{min} < 30$, $30 < \text{min} < 60$, > 60 min lengths with waist circumference were significant ($r=0.17$; $r=0.18$; $r=0.19$; and $r=0.18$, respectively, $P < 0.001$), whereas no significant correlation was found for $5 < \text{min} < 10$ sedentary bout, ($r=0.08$, $P=0.121$).

Table 5.2 shows the beta coefficients for the independent variables that remained in the model with waist circumference. Both total sedentary time, continuous sedentary bouts of $10 < \text{min} < 20$, $20 < \text{min} < 30$, $30 < \text{min} < 60$, > 60 min lengths and MVPA were significantly and independently related with waist circumference for the non-adjusted model and remained in the model. However, when adjusting for the several covariates there were no significant associations for the total sedentary time ($r=0.03$, $P=0.789$) and > 60 min sedentary bouts ($r=0.10$, $P=0.068$) with waist circumference.

Table 5.2. Linear associations of total sedentary time, MVPA and sedentary bouts with waist circumference

Independent variables	Non-adjusted model		Adjusted model	
	β (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>
Total sedentary time (min·day⁻¹)	0.01 (0.00, 0.02)	0.011	0.02 (-0.12, 0.16)	0.789
MVPA (min·day⁻¹)	-0.09 (-0.14,-0.05)	<0.001	-0.12 (-0.18,-0.05)	<0.001
Continuous sedentary bouts (number·day⁻¹)				
10 ≤ min <20	0.13 (0.05, 0.21)	0.001	0.25 (0.01, 0.49)	0.042
20 ≤ min <30	0.26 (0.11, 0.41)	0.001	0.39 (0.03, 0.74)	0.032
30 ≤ min <60	0.53 (0.24, 0.82)	<0.001	0.59 (0.09, 1.09)	0.022
≥ 60 min	1.67 (0.73, 2.62)	0.001	1.38 (-0.10, 2.86)	0.068

Using the backwards regression model, only MVPA and continuous sedentary bouts longer than 10 min remained in the model as significant variables that associated with waist circumference (cm). Regardless of sedentary time has been removed from the model as it is a variable of interest so it is presented here.

Data are β coefficient (95% confidence interval) for the non-adjusted model and adjusted for the covariates removed in backwards elimination (age, gender, sedentary time, LIPA, CPM, employment, educational attainment, geographical location, smoking status, alcohol dependence, medical history for chronic diseases, hypertension, elevated cholesterol and hipeglycemia, and current medication status), and MVPA (min·day⁻¹) or continuous bouts of sedentary time (number·day⁻¹).

Abbreviations: MVPA, moderate-to-vigorous physical activity; LIPA, light intensity physical activity; CPM, counts per min for the 10 < min < 20, 20 < min < 30, 30 < min < 60, and > 60 min of continuous sedentary bouts; min, minutes.

The binary logistic regression showed the associations for predictor variables with the odds for abdominal obesity. Both non-adjusting and adjusting for the covariates the only variables that significantly predict the odds for abdominal obesity were gender, the 5 ≤ min < 10, 10 ≤ min < 20, 20 ≤ min < 30, 30 ≤ min < 60, ≥ 60 continuous min sedentary bouts, and MVPA. No associations were found for total sedentary time with the odds of being abdominally obese (OR=1.00, 95% CI: 1.00 – 1.00). The odds of a woman having abdominal obesity were 6.99 times higher than those of a man (OR=6.99, 95% CI: 3.90 – 12.54). Each min increment in MVPA was associated with a 2% lower (OR=0.98, 95% CI: 0.97 – 0.99) odds of being abdominally obese. As presented in Figure 5.1., for each additional continuous sedentary bout of 10 ≤ min < 20, the odds of being abdominally obese increase by 7% (OR=1.07, 95% CI: 1.02 – 1.13), for each 20 ≤ min < 30 sedentary bout the odds for abdominal obesity increase 12% (OR=1.12, 95% CI: 1.04 – 1.21), 16% (OR=1.16, 95% CI: 1.04 – 1.30) for each additional prolonged sedentary bout of 30 ≤ min < 60, and 48% (OR=1.48, 95%

CI: 1.07 – 2.03) for the prolonged sedentary bout of at least 1 hour. In opposition, for each additional sedentary bout of $5 \leq \text{min} < 10$, the odds of being abdominally obese decrease by 3% (OR=0.97, 95% CI: 0.95 – 1.00). We used post-hoc power analyses to estimate the statistical power of these logistic regressions. Because our goal was to examine if the odds of being abdominally obese were driven primarily by continuous sedentary bouts, we computed the odds ratio of the regressions for the prolonged sedentary bout of $30 \leq \text{min} < 60$, the mean and standard deviation and coefficient of determination for this independent variable. Using a large sample approximation method (Demidenko, 2007) and significance criterion (α) of 0.05, the analyses revealed that with the current sample size (351), the statistical power was high (0.998). For reference, a power of 0.80 is conventionally considered sufficient (Cohen, 1992).

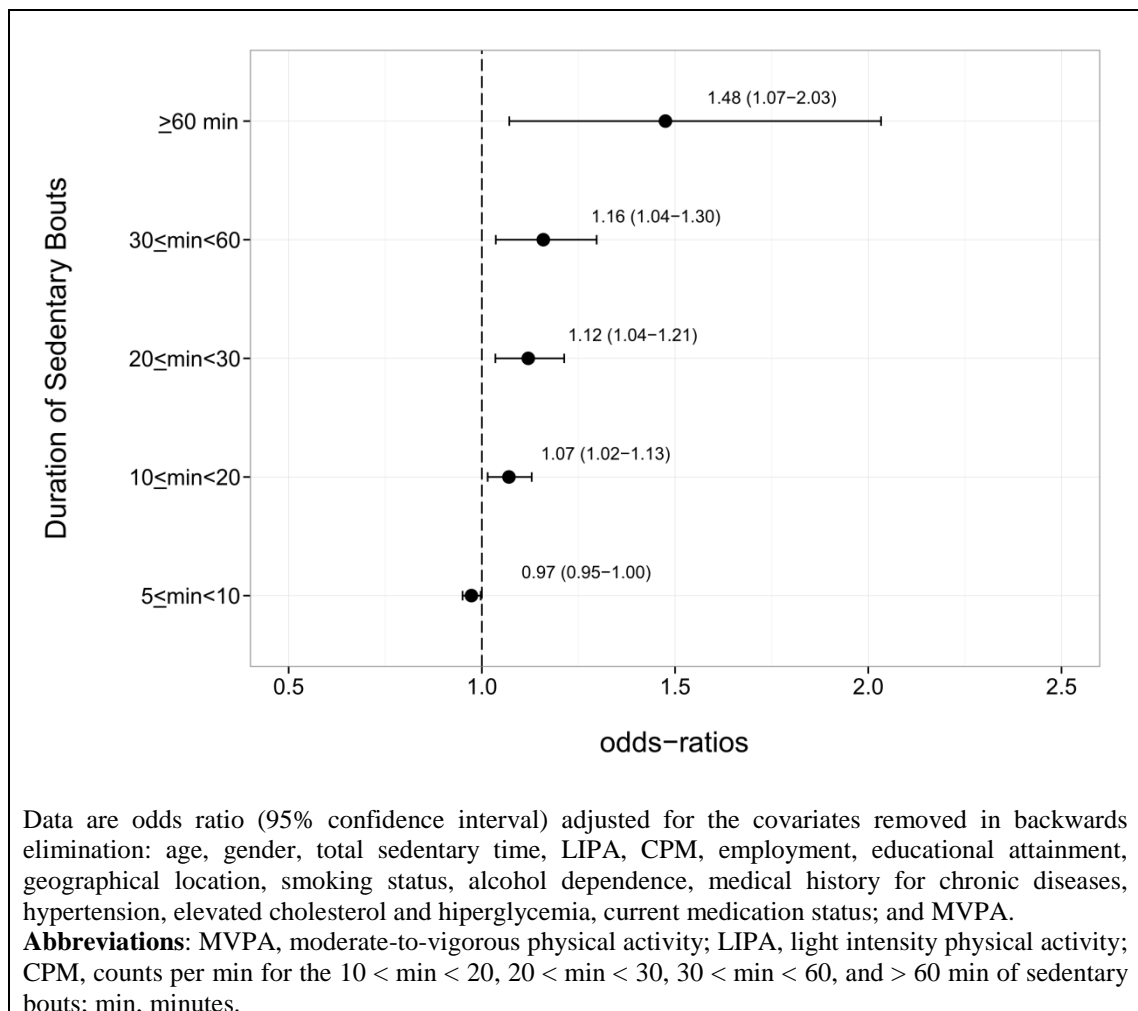


Figure 5.1. The odds of abdominal obesity for the continuous sedentary bouts of distinct durations (N=351).

5.5. Discussion

This study used a novel approach investigating the independent associations of duration of continuous sedentary bouts with abdominal obesity of older adults (men: > 102 cm; women: > 88 cm). The results from the present study found gender, continuous sedentary bouts of $10 \leq \text{min} < 20$, $20 \leq \text{min} < 30$, $30 \leq \text{min} < 60$, ≥ 60 min, and MVPA to be the most important predictive variables for the odds of having abdominal obesity, in older adults. Indeed, it was found that older adults who perform long periods of continuous sedentary time are more likely to be abdominally obese, independently of total sedentary time itself, MVPA and movement counts within the continuous sedentary bouts.

These results further extend the findings from a previous study (Chastin et al., 2012) which also found the pattern of accumulation of sedentary time to be important with less fragmented sedentary time associated with higher total body and lower limb adiposity for both men and women, indicating that individuals who break up their sedentary time have lower body fat compared with those who engage in more prolonged periods of sedentary time. However, the former study did not consider the characteristics of the fragmentation or how long sedentary time was accumulated in between breaks from sedentary time. Therefore, this novel finding in older adults is relevant for breaking sedentary behaviors (such as sitting time) to improve abdominal obesity phenotype and adds further information about the thresholds for time spent in sedentary time or how long sedentary time must be interrupted before it raises the odds for abdominal obesity. Furthermore, these results seem to indicate that the risk for abdominal obesity increases alongside sedentary bout duration starting on 10 min length, with no further risk for abdominal obesity when considering the $5 \leq \text{min} < 10$ continuous sedentary bouts. Extending upon findings of linear associations (Henson et al., 2013) we observed a significant graded-relationship for continuous sedentary bouts with abdominal obesity. The logistic regression analyses showed that the odds of abdominal obesity were 7% higher for each $10 \leq \text{min} < 20$ of uninterrupted sedentary time, 11% higher for each $20 \leq \text{min} < 30$ continuous sedentary bout, 15% higher for each $30 \leq \text{min} < 60$ of uninterrupted sedentary time with the most significant increases for the ≥ 60 min prolonged sedentary bout (48%).

In other words, these results seem to indicate that older adults must avoid spending more than 10 min of continuous sedentary time, with progressively higher odds for abdominal obesity if they spend more than 20, 30 and 60 min in continuous sedentary time. Moreover, based on the higher increments for the odds of abdominal obesity for each 1 hour prolonged sedentary bout compared to the shorter sedentary bouts' lengths and knowing that breaking up sedentary time every 10 min can be less feasible, the message should be that older adults must avoid spending more than 1 prolonged hour in sedentary time and if possible introduce small LIPA breaks, every 10, 20, or 30 min of continuous sedentary time.

In accordance with previous studies (Henson et al., 2013; Santos et al., 2012) in older adults, our results showed that higher levels of MVPA were associated with lower odds of abdominal obesity. In contrast, for every additional continuous sedentary bout increase, independent of sedentary time itself ($\text{min}\cdot\text{day}^{-1}$), movement counts within the continuous sedentary bouts ($\text{counts}\cdot\text{min}^{-1}$), MVPA ($\text{min}\cdot\text{day}^{-1}$), demographics, behavioral and medical covariates, the odds of having abdominal obesity were higher for more prolonged sedentary bouts. These findings are indirectly supported by previous studies, that presented breaks in sedentary time to be strongly inversely associated with waist circumference (Cooper et al., 2012; Healy et al., 2011; Healy et al., 2008; Henson et al., 2013) and adds information regarding the minimal thresholds for breaking up sedentary time.

These findings demonstrate that bouts of continuous sedentary time shorter than 10 min did not increased the odds of abdominal obesity; however, bouts of greater than 10 min raised the odds ratio of abdominal obesity significantly and must be avoided.

It would be natural to assume that long sedentary periods entail a long total sedentary time. Interestingly, total sedentary time itself was not associated with the odds of having abdominal obesity. The associations for prolonged sedentary bouts with the odds for abdominal obesity independent of total sedentary time itself ($\text{min}\cdot\text{day}^{-1}$) suggest that prolonged bouts of sedentary time, rather than total sedentary time or total LIPA (which were removed from the model) may be a relevant indicator for abdominal obesity risk (Chastin et al., 2012). If confirmed in future prospective studies, these cross-sectional findings together with findings on other metabolic health markers,

provide preliminary evidence that reducing long uninterrupted sedentary periods may be important to target in the prevention of abdominal obesity in older adults (Chastin et al., 2012). Findings from a small intervention study support this possibility, suggesting that regular variations in posture allocation may be an influential factor in the regulation of energy homeostasis (Swartz, Squires, & Strath, 2011), a key factor in the development of obesity. Previous findings have demonstrated that sedentary time can be easily reduced by following a brief intervention based on goal setting and behavioral self-monitoring in older adults (Gardiner, Eakin, Healy, & Owen, 2011).

An important strength of this study was that sedentary time was objectively measured by accelerometry (Prince et al., 2008; Swartz, Rote, Cho, Welch, & Strath, 2014). There are some limitations, such as accelerometers are not sensitive to detect all activities such as biking, standing, and upper-body movement and they do not discern sitting from non-sitting time. The cross-sectional design of this study limits inference about the direction of causality between the continuous sedentary bouts and abdominal obesity. We cannot rule out the possibility that more prolonged bouts of sedentary time result from higher levels of adiposity.

Nevertheless of potential confounders (age, smoking, alcohol dependence, occupation, educational level, medical history, and also geographic location) have been included in the logistic regression, residual confounding from potentially important unmeasured covariates like diet were not taken into account. This represents a major limitation once diet and EI are a cornerstone when making inferences related with obesity and due to a lack of data presenting the interactions of sedentary behavior patterns and diet related changes which somehow influence the associations we found in this study.

Although no differences between genders were found and the large sample size, the different proportion of men and women included in this study limits inference about potential differences that may exist for the response of men and women to sedentary behavior patterns. Another limitation is related to the use of waist circumference as a measure of abdominal obesity. Regardless of its recognized validity, persons with different subcutaneous/visceral fat distribution profiles may present the same waist circumference and therefore it is not possible to distinguish these two types of adipose

tissue. Future research should prospectively explore the association for the continuum of prolonged sedentary bouts with abdominal obesity.

5.6. Conclusions

These findings provide additional objective evidence that in older adults, total sedentary time may not be the most important predictor for abdominal obesity but that additional to time spent in MVPA, avoiding sedentary periods longer than 10 min may have potential public health implications for the prevention of abdominal obesity in older adults.

Intrinsically, programs engaged exclusively on MVPA may overlook an area that is of vital importance to obesity control. Along with recommendations to accumulate at least 150 min·week⁻¹ of MVPA, such interventions might be more effective if individuals are further encouraged to avoid very prolonged bouts of sedentary time.

5.7. References

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CHAPTER 6

Sedentary behavior and adiposity in elite athletes³

³ **Judice, P. B.**, Silva, A. M., Magalhaes, J. P., Matias, C. N., & Sardinha, L. B. (2014). Sedentary behaviour and adiposity in elite athletes. *J Sports Sci*, 32(19), 1760-1767. doi: 10.1080/02640414.2014.926382. **2.25** Impact Factor

Sedentary behavior and adiposity in elite athletes

Pedro B. Júdice, Analiza M. Silva, João P. Magalhães, Catarina, N. Matias, Luís B. Sardinha

6.1. Abstract

Aim. Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a health risk. Even in athletes an increased adiposity affects health and performance. Sedentary behavior has been associated with higher levels of adiposity, independent of moderate-to-vigorous physical activity. However, it is unclear whether this independent relationship still exists in highly active individuals. The aim of this study was to examine the association for sedentary behavior with body fatness in elite athletes.

Methods. Cross-sectional data from 82 male athletes (mean age 22-years) was used. Total and regional body composition was measured by dual energy X-ray absorptiometry. Self-reported time spent in sedentary behavior and weekly training time were assessed in all participants at one time point and multiple regression analyses were used.

Results. Sedentary behavior predicted total fat mass ($\beta=0.77$; 95% CI: 0.36 – 1.19, $p=0.000$) and trunk fat mass ($\beta=0.25$; 95% CI: 0.07 – 0.43, $p=0.007$), independent of age, weekly training time, and residual mass (calculated as weight - dependent variable) but not abdominal fat. Also, no associations for sedentary behavior with fat-free mass, appendicular lean soft-tissue, and body mass index were found.

Conclusion. These findings indicate that athletes with higher amounts of sedentary behavior presented higher levels of total and trunk fatness, regardless of age, weekly training time, and residual mass. Therefore, even high moderate-to-vigorous physical activity levels do not mitigate the associations between sedentary behavior and body fatness in highly trained athletes.

Key words: *body composition, fat mass, trunk fat mass, physical activity, athletes*

6.2. Introduction

Obesity is a serious growing health problem and several international organizations are adopting preventive strategies to tackle this disease (Fitzgerald, 2013; Flegal, Carroll, Kit, & Ogden, 2012; Mitchell, Catenacci, Wyatt, & Hill, 2011). Athletes are not immune to this major public health issue with higher adiposity being associated with serious health complications including metabolic syndrome (Buell et al., 2008; Guo, Zhang, Wang, Guo, & Xie, 2013) and cardiovascular diseases (Tucker et al., 2009). Additionally, in athletic populations, increased levels of adiposity have been demonstrated to negatively influence performance (Fedor & Gunstad, 2013; Willeumier, Taylor, & Amen, 2012).

Engaging in regular physical activity at a moderate-to-vigorous intensity has been identified to be effective in preventing high levels of adiposity (Gonzalez-Gross & Melendez, 2013; Maher, Mire, Harrington, Staiano, & Katzmarzyk, 2013). Conversely, physical inactivity has been associated with increased levels of adiposity (Vandelanotte, Sugiyama, Gardiner, & Owen, 2009). However, there is still some confusion in the literature regarding the concept of physical inactivity. This term is commonly used to either describe those who are performing insufficient amounts of moderate-to-vigorous physical activity but also the time spent in sedentary behaviors, which are two distinct conceptions. A person can be highly physically active (2 hours of exercise training per day) but also spend the rest of the day mostly in sedentary behavior (8-9 hours·day⁻¹).

Time spent in sedentary behavior reflects the accumulated amount of time spent sitting, reclining, or lying down at home, at work, at school, in transit, and during leisure time. Athletes perform high levels of moderate-to-vigorous physical activity compared with non-athletes but a previous study found that non-exercise activity thermogenesis did not differ between sedentary people and athletes (Almeras, Mimeault, Serresse, Boulay, & Tremblay, 1991) suggesting that sedentary behavior is not so different between these two groups. As a result, the risk of an increased adiposity may occur even among athletes. In addition, independent of adiposity, sedentary behavior has also been associated with negative metabolic impacts (Wijndaele et al., 2014). A new body of information is beginning to focus on the negative impact of

sedentary behavior on adiposity (Delmas et al., 2007; Gomez-Cabello et al., 2012; Janz, Burns, & Levy, 2005; Larsen et al., 2013). In athletes, adiposity is a source of concern as it impacts on both health (Batista & Soares, 2013; Buell et al., 2008; Tucker et al., 2009) and performance (Fedor & Gunstad, 2013) and a healthier body composition profile is expected in this population (Grund et al., 2001; Malina, 2007; Silva, Petroski, & Peres, 2012).

It has been recognized that even for those individuals that do engage in regular moderate-to-vigorous physical activity, the risk of having increased adiposity is increased by simply being more sedentary (sitting, watching TV, etc.) (Hu, Li, Colditz, Willett, & Manson, 2003; So, 2012; Stamatakis, Hirani, & Rennie, 2009). One study found the time spent in moderate-to vigorous physical activity to be independent of sedentary time (Craft et al., 2012), and reinforced the idea that these are two distinct behavioral domains and that exclusively looking at moderate-to-vigorous domain may overlook an area that is of vital importance to adiposity control. Therefore, to understand the impact of spending more time in sedentary behavior in athletes, regardless of the amount of time spent in their exercise training sessions, the aim of this investigation was to examine the independent association of sedentary behavior with body composition in a group of male elite athletes from different sports.

6.3. Methods

6.3.1. PARTICIPANTS

A total of 82 elite male athletes from different disciplines volunteered to participate in this study. The different sports were categorized in three groups, the first two groups are according to Ackland et al. classification (Ackland et al., 2012), and the third group included the sports that were not comprehended in this classification, as follows: a) Gravitational sports in which mass restricts performance due to mechanical (gravitational) reasons. Among these are long distance running, road cycling, and triathlon; b) Weight class sports in which unhealthy short-term mass reduction behavior, associated with extreme dehydration, can be observed because the athletes anticipate an advantage when they are classified in a lower weight category. This group includes

wrestling, judo, and taekwondo; c) non-weight sensitive sports that include swimming, sail, tennis, handball, track and field athletics, and pentathlon.

The inclusion criteria were: 1) age ≥ 18 years; 2) more than 5 years of experience competing in both national and international championships; 3) deemed to be not taking any performance enhancing agents. Medical screening indicated that all athletes were in good health, without endocrine abnormalities that would limit their participation in the study. All participants were informed about the possible risks of the investigation before giving their written informed consent to participate. All procedures were approved by the Ethics Committee of the Faculty of Human Kinetics, Technical University of Lisbon, and were conducted in accordance with the declaration of Helsinki for human studies (World Medical Association, 2008).

6.3.2. EXPERIMENTAL DESIGN

All evaluations were performed on a single moment, in a crucial time of the competitive season (e.g., the last days before engaging in an international competition). Participants were required to fast for at least 8 h prior to the visit, avoid alcohol consumption for 24 h, and consume a normal evening meal the night before the visit. All measurements were carried out in the morning of a week day. In brief, the procedures adopted were as follows:

6.3.3. BODY COMPOSITION MEASUREMENTS

Anthropometric variables

Participants wearing minimal clothes and without shoes were weighed to the nearest 0.01 kg, on an electronic scale connected to a plethysmograph computer (BOD POD[®], COSMED, Rome, Italy). Height was measured to the nearest 0.1 cm with a stadiometer (Seca, Hamburg, Germany) according to the standardized procedures described elsewhere (Lohman, Roche, & Martorell, 1988). Body mass index (BMI) was calculated as body mass (kg)/ height² (m). Waist circumference was measured with a flexible anthropometric tape (Cescorf, Brasil) at the end of an expiration and reported to

the nearest 0.1 cm by positioning a tape parallel to the floor and immediately above the iliac crest, according to NIH procedures (NIH, NHLBI, & NAASO, 2000).

Dual-Energy X-Ray Absorptiometry (DXA)

Dual energy X-ray absorptiometry (DXA) (Hologic Explorer-W, fan-beam densitometer, software QDR for windows version 13.3, Waltham, Massachusetts, USA) was used to estimate fat-free mass, appendicular lean soft-tissue, fat mass, trunk fat mass, and total abdominal fat mass. The equipment measures the attenuation of X-rays pulsed between 70 and 140 kV synchronously with the line frequency for each pixel of the scanned image. Following the protocol for DXA described by the manufacturer, a step phantom with six fields of acrylic and aluminium of varying thickness and known absorptive properties was scanned to serve as an external standard for the analysis of different tissue components. For the athletes who's height exceeded the scan area we performed an alternative method with two scans already validated by our group (Santos et al., 2012), specifically: a) a head scan, where the DXA scan length (95 cm) was set at a height sufficient to scan from the top of the head to the lower jaw; and b) a trunk and limbs scan, where the participant was positioned with the head slightly out of the scan area. The scan length was set as the normal length for the trunk and limbs scan (195 cm). The sum of head and trunk plus limbs was used as an alternative procedure to assess bone mineral content, fat mass and lean soft tissue.

Total abdominal fat, which includes intra-abdominal fat plus subcutaneous fat, can be distinguished using DXA by identifying a specific region of interest within the analysis program. Specific DXA ROIs for abdominal regional fat were defined as follows: ROI 1, the upper edge of the second lumbar vertebra (approximately 10 cm above the L4 to L5) to above the iliac crest and laterally encompasses the entire breadth of the abdomen, thus determining total abdominal fat mass (Park, Heymsfield, & Gallagher, 2002); ROI 2 have the same upper and inferior edges than ROI 1 and laterally excludes subcutaneous fat in the lateral region of the abdomen. The difference between ROI 1 and ROI 2 thus provides an estimate of lateral subcutaneous fat.

The same technician positioned the participants, performed the scans and executed the analysis according to the operator's manual using the standard analysis

protocol. Based on test-retest using ten participants, the coefficient of variation (CV) in our laboratory for fat mass, fat-free mass, appendicular lean soft-tissue, and trunk fat mass are 1.7%, 0.8%, 1.2%, and 0.01%, respectively (Santos et al., 2010), and 0.01% for total abdominal fat mass (Pimenta, Santa-Clara, Sardinha, & Fernhall, 2012).

6.3.4. SEDENTARY BEHAVIOR AND WEEKLY TRAINING TIME ASSESSMENT

Sedentary behavior was assessed using the self-administered short-IPAQ sitting items (Rosenberg, Bull, Marshall, Sallis, & Bauman, 2008) that consisted of a single question regarding the time spent in sedentary behavior (watching TV, computer use, transport, and other sitting or reclining activities) in a week day during the waking period.

6.3.5. STATISTICAL ANALYSIS

Statistical analysis was performed using IBM-SPSS Statistics for Windows version 21.0, 2012 (SPSS Inc., an IBM Company, Chicago IL, USA). Descriptive analysis included means \pm SD for all measured variables.

To evaluate the associations between sedentary behavior and the main body composition variables, multiple partial regressions analyses were performed for the overall athletes and by sport' groups, adjusting for weekly training time, age, and residual mass. The residual mass was calculated for each model as body weight minus the dependent variable (total, trunk and abdominal fat mass; fat free mass and appendicular lean soft tissue). Prior to the regression analysis, normality and multi-collinearity tests were conducted and the results fell within the acceptable range. To examine the differences in sedentary time and weekly training time between the sports' categories, a one-way analysis of variance (ANOVA) was used.

Statistical significance was set at $p < 0.05$.

6.4. Results

The athletes' characteristics, body composition, sedentary behavior and weekly training time are presented in Table 6.1.

Table 6.1. Athletes' characteristics, body composition, sedentary behavior, and weekly training time

	(N=82)	
	Mean \pm SD	Range
Age (years)	21.8 \pm 4.8	18 - 38
Height (m)	1.79 \pm 0.07	1.64 - 2.04
Body mass (kg)	77.5 \pm 13.5	57.8 - 117.8
BMI (kg·m⁻²)	24.0 \pm 3.60	18.6 - 36.9
Fat mass (%)	14.3 \pm 4.90	7.80 - 27.2
Trunk fat mass (kg)	4.90 \pm 2.80	2.30 - 14.2
Total abdominal fat mass (kg)	1.13 \pm 0.62	0.46 - 3.74
Fat-free mass (kg)	66.1 \pm 9.00	51.7 - 89.2
Appendicular lean soft-tissue (kg)	30.7 \pm 4.60	23.1 - 44.6
Waist circumference (cm)	81.1 \pm 7.90	68.8 - 108.8
Sedentary behavior (hours·week·day⁻¹)	7.70 \pm 2.70	2.00 - 15.0
Weekly training time (hours·week⁻¹)	17.2 \pm 7.30	4.00 - 34.0

Abbreviations: BMI, body mass index; N, number of participants; SD, standard deviation.

Multiple regression analyses were performed to understand the associations for sedentary behavior with the main body composition variables (Table 6.2).

Table 6.2. Associations for sedentary behavior with the main body composition variables

	Sedentary behavior					
	Non-adjusted model			Adjusted model		
	β (95% CI)	ρ	<i>P</i> -value	β (95% CI)	ρ	<i>P</i> -value
FM (kg)	0.96 (0.53, 1.38)	0.44	0.000	0.77 (0.36, 1.19) ^{a)}	0.39	0.000
TFM (kg)	0.39 (0.18, 0.60)	0.38	0.000	0.25 (0.07, 0.43) ^{a)}	0.30	0.007
TAF (kg)	0.07 (0.02, 0.11)	0.29	0.009	0.00 (-0.04, 0.04) ^{a)}	0.10	0.930
FFM (kg)	0.88 (0.17, 1.58)	0.27	0.015	-0.33 (-1.09, 0.44) ^{a)}	-0.10	0.394
ALST (kg)	0.39 (0.02, 0.76)	0.23	0.038	-0.28 (-0.61, 0.05) ^{a)}	-0.19	0.095
WC (cm)	0.75 (0.13, 1.37)	0.26	0.018	-0.01 (-0.36, 0.35) ^{b)}	-0.00	0.971
BMI (kg m⁻²)	0.32 (0.04, 0.60)	0.25	0.026	0.29 (-0.05, 0.64) ^{c)}	0.19	0.096

Notes: ^{a)} Adjusted for age, weekly training time, and residual mass; ^{b)} adjusted for age, weekly training time, and total body mass; ^{c)} adjusted for age and weekly training time.

Abbreviations: ρ , Pearson correlation coefficient; ALST, appendicular lean soft-tissue; BMI, body mass index; CI, confidence interval; FFM, fat-free mass; FM, fat mass; TAF, total abdominal fat; TFM, trunk fat mass; WC, waist circumference.

As presented in Table 6.2, sedentary behavior was positively associated with total and regional fatness and waist circumference, in athletes. For the adjusted models only the fat mass and trunk fat mass were significantly associated with sedentary behavior, adjusting for age, weekly training time, and residual mass.

No significant associations for sedentary behavior with fat-free mass and appendicular lean soft-tissue were found after controlling for age, weekly training time, and residual mass. Also no relation was found for sedentary behavior with BMI after controlling for age and weekly training time.

Figure 6.1 illustrates the relationship for sedentary behavior with waist circumference, total fat mass and its regional components, specifically trunk fat mass and total abdominal fat mass, for the different sports.

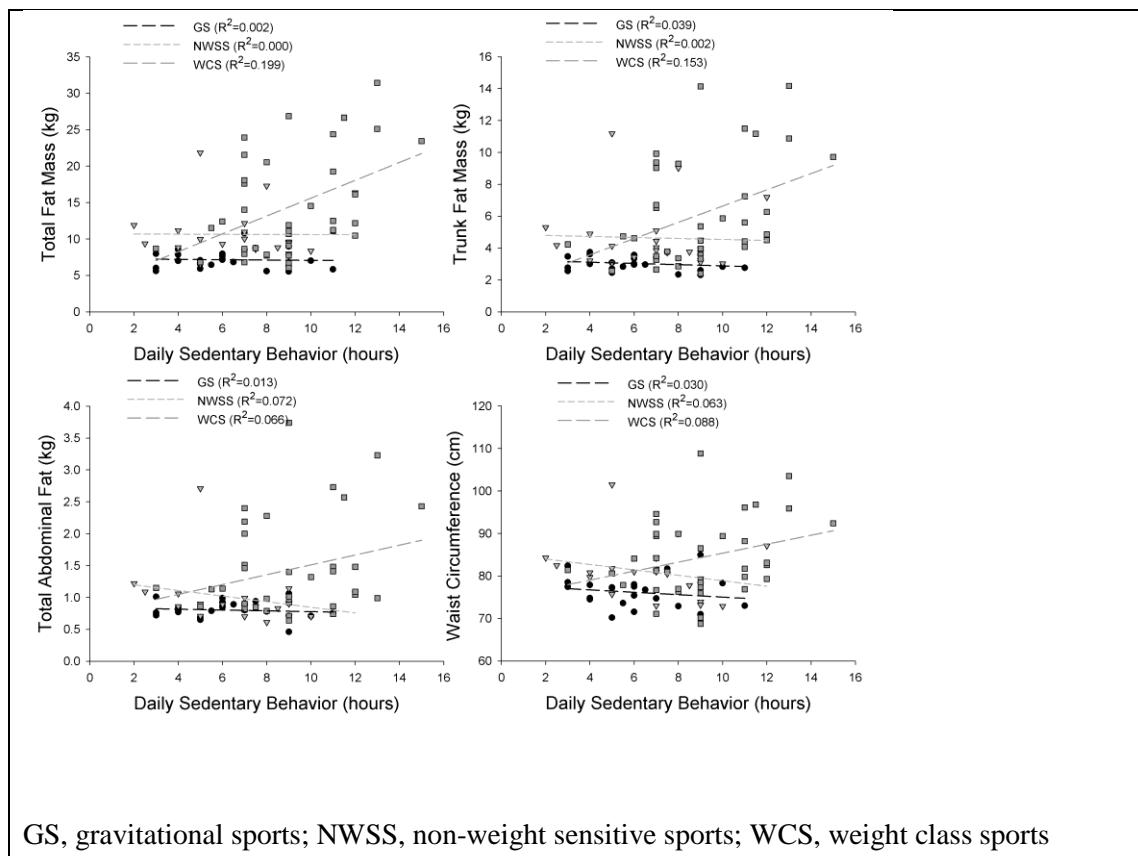


Figure 6.1. Associations for total, regional fat mass, and waist circumference with sedentary behavior, for the different sports.

As demonstrated in Figure 6.1, weight class sports is the sport category that is responsible for the association for sedentary behavior with body fatness ($\beta=0.82$; 95%

CI: 0.02 – 1.63, $\rho=0.35$), compared to the non-weight sensitive sports ($\beta=0.78$; 95% CI: 0.38 – 1.18, $\rho=0.71$), or the gravitational sports ($\beta=-0.02$; 95% CI: -0.34 – 0.30, $\rho=-0.03$) that did not presented significant associations.

The results from ANOVA showed that weight class sports category simultaneously presented significantly higher time spent in sedentary behavior (approximately 9 hours·day⁻¹) compared to the non-weight sensitive sports (approximately 7 hours·day⁻¹; 95% CI for difference: 0.73 – 3.38, effect size $\rho=0.38$, $p=0.008$) and gravitational sports (approximately 6 hours·day⁻¹; 95% CI for difference: 1.48 – 4.10, effect size $\rho=0.50$, $p \leq 0.001$); and lower weekly training time (~ 13 hours·week⁻¹) compared to the non-weight sensitive sports (approximately 17 hours·week⁻¹; 95% CI for difference: -6.71 – -0.28, effect size $\rho=-0.26$, $p=0.004$) and gravitational sports (approximately 24 hours·week⁻¹; 95% CI for difference: -13.3 – -6.96, effect size $\rho=-0.71$, $p \leq 0.001$).

6.5. Discussion

This study examined the association between sedentary behavior and body fatness in elite Portuguese athletes. Although there was only a small explanation for the variance in adiposity by sedentary behavior, the present investigation reveals a novel finding within the field of sports science, showing that sedentary behavior predicts some of the total and regional body fatness in the athletic population, regardless of weekly training time. No other study to date has aimed to explore these associations in the athletic field. Our results extend the findings of other studies (Vandelanotte, Sugiyama, Gardiner, & Owen, 2009; Wagner et al., 2012) that found associations between sedentary behavior and body fatness to be independent of moderate-to-vigorous physical activity levels in non-athletic adults.

It is worth noting that reported weekly training time from our elite athletic sample averaged 17.2 hours·week⁻¹ which is far above the moderate-to-vigorous physical activity recommendations for the general population (2.5 hours·week⁻¹) or the highest active group defined in a previous study (Vandelanotte et al., 2009) (3 or more hours·week⁻¹). Nevertheless, weekly training hours did not mediate the associations

between sedentary behavior and body fatness variables for the overall athletic population but when considering the sport groups the associations were only significant for the weight class sports. This category includes sports like judo and taekwondo that simultaneously presented higher time spent in sedentary behavior (approximately 9 hours·day⁻¹) and lower weekly training time (~ 13 hours·week⁻¹) compared to the two other groups (sedentary behavior ~ 7 hours·day⁻¹ and weekly training time ~ 20 hours·week⁻¹). Our cross sectional findings generate the hypothesis that sedentary behavior should be considered an independent risk factor from moderate-to-vigorous physical activity for fat mass accumulation in highly trained people. However based on the non-significant associations for sedentary behavior with fat mass accumulation found in the two sport groups that also performed higher weekly training times, some caution should exist when referring to athletes with substantial hours of training (> 20 hours·week⁻¹), as the higher levels of moderate-to vigorous physical activity may compensate the amount of time spent in sedentary behavior. In spite of this independent relationship for sedentary behavior with adiposity, few studies have examined the associations between objectively measured sedentary or sitting time and moderate-to-vigorous physical activity (Craft et al., 2012). The lack of objective measures to quantify sedentary behavior or moderate-to-vigorous physical activity is a major weakness of this study and the extent to which weekly training time directly affects the time spent in sedentary behavior remains unknown. The literature concerning this issue is scarce and has reported, using self-report measures, equivocal associations (Bauman et al., 2011; Brown, Ryde, Gilson, Burton, & Brown, 2013; Burton, Khan, Brown, & Turrell, 2012).

Moderate-to-vigorous physical activity participation may result in an increase in sedentary behavior, by reducing the drive to be active in non-exercise periods (Rowland, 1998) whereas adults who exercise regularly may generally have more energy, or have enhanced feelings of vigor, and decrease sedentary behavior (Puetz, 2006). However this last argument may not be adequate in athletes as daily high levels of moderate-to-vigorous physical activity are required to achieve a certain level of performance. Furthermore, one study has shown that the exercise-induced increase in daily energy requirements is not compensated by a more sedentary lifestyle during the

other daily activities in trained men (Almeras et al., 1991). These results suggest that promoting a healthier balance between sedentary behavior and light intensity physical activity may determine a healthier body composition regulation in elite athletes but the assumption that athletes should be encouraged to reduce sedentary behavior on non-training periods may blunt regenerative processes and contribute to the accumulation of ongoing fatigue (Edwards, Hill, Jones, & Merton, 1977). However, previous data showed that the addition of light intensity physical activity to the rest period did not adversely affect physiological recovery and had a significantly beneficial effect on psychological recovery (Suzuki et al., 2004).

The association between sedentary behavior and total abdominal fat did not remain significant after adjusting for age, residual mass, and weekly training time which is in accordance with the findings from a recent investigation (Saunders et al., 2013) reporting that sedentary behavior was not associated with changes in visceral adiposity. Another explanation might be related with a selective effect of exercise in reducing visceral fat (Ross et al., 2000), as the high levels of moderate-to-vigorous physical activity may have blunted the deleterious effects of sedentary behavior.

Evidence has found that moderate-to-vigorous physical activity levels decreased with increasing BMI and in opposition sedentary behavior increased with increasing BMI, in a non-athletic population (Scheers, Philippaerts, & Lefevre, 2012). Lack of information still exists regarding these trends in highly trained individuals but it is hypothesized that a similar trend could be found in this population for the sedentary behavior, since their non-exercise activity thermogenesis was similar to sedentary individuals (Almeras et al., 1991; Drenowatz, Eisenmann, Pivarnik, Pfeiffer, & Carlson, 2013). Previous investigations have found BMI to mislead inferences about fatness in highly trained people (Lambert et al., 2012) which may explain the lack of association between sedentary behavior and BMI in our athletic population.

Appendicular lean soft tissue assessed by DXA has been suggested to be a good indicator of skeletal muscle mass (Kim et al., 2004; Rolland, Perry, Patrick, Banks, & Morley, 2007). For athletic populations that incorporate strength training into their weekly trainings, sedentary behavior might have an important role on the skeletal muscle mass recovery (Candow & Burke, 2007) which may justify higher amounts of

resting time in sedentary behavior. The positive associations observed between total body mass and sedentary behavior led us to investigate the associations for sedentary behavior with fat-free mass and appendicular lean soft-tissue. However, sedentary behavior was not associated with fat-free mass and appendicular lean soft-tissue, after adjusting for age, weekly training hours, and residual mass.

Previous studies have found a positive association between sedentary behavior and waist circumference in a non-athletic population (Wijndaele et al., 2009). Still, the results from the present investigation did not find an association between sedentary behavior and waist circumference. In fact, waist circumference is not a good indicator of body fatness in athletes or highly trained persons (Burton, 2010), because the higher skeletal muscle mass in the trunk area might increase the measurement without a corresponding elevation in total abdominal fat.

It is important to mention some limitations and strengths of the current investigation. First, the cross sectional design of the study does not allow for conclusions about causality between sedentary behavior with total and regional fatness. Therefore, future research is required to explore this relationship in both prospective and experimental studies. Questionnaires comprehend a natural error due to a possibility of under or overestimating sedentary behavior since it is based on self-reported information. However, self-reported measurements have been found to accurately estimate sedentary behavior compared to motion sensors (Bauman et al., 2011). Specifically, the world wide used self-administered short-IPAQ sitting items seem to have acceptable reliability on estimating sedentary behavior compared to accelerometry (Rosenberg et al., 2008). The use of self-reported hours for training load is also a main limitation of this study as the type and intensity of the training session is not reported. Still, reported weekly training duration give us the total volume of the exercise sessions. Finally, our findings are only generalized to male athletes, therefore further research should be conducted in female athletes.

The major strengths of this study include the state-of-the-art methods for precision and accuracy of body composition assessment, specifically the DXA and its use for ROI analysis that allowed total abdominal fat mass estimation. According to a previous investigation, DXA ROI used in the present study (L2 – upper iliac crest) and

conventional trunk measurements significantly correlated with total visceral adipose tissue from magnetic resonance imaging in non-obese men (Park et al., 2002). Also, this study included a unique population of highly trained athletes of different sports competing in national and international championships.

6.6. Conclusions

The results from this study indicate that similarly to what occurs in the general population, individuals with high levels of moderate-to-vigorous physical activity presented a positive association between time spent in sedentary behavior with total and trunk adiposity, regardless of exercise training volume. Therefore, to promote healthier body composition athletes should be encouraged to reduce time spent in sedentary behavior by shifting it to low intensity physical activity.

6.7. References

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CHAPTER 7

What is the metabolic and energy cost of sitting, standing and sit/stand transitions?⁴

⁴ **Judice, P. B.**, Hamilton, M. T., Sardinha, L. B., Zderic, T. W., & Silva, A. M. (2015). What is the metabolic and energy cost of sitting, standing and sit/stand transitions? *Eur J Appl Physiol*. doi: 10.1007/s00421-015-3279-5. **2.19** Impact Factor

What is the metabolic and energy cost of sitting, standing and sit/stand transitions?

Pedro B. Júdice, Marc T. Hamilton, Luís B. Sardinha, Theodore W. Zderic, Analiza M. Silva

7.1. Abstract

Aim: Modern lifestyles require people to spend prolonged periods of sitting, and public health messages recommend replacing sitting with as much standing as is feasible. The metabolic/energy cost (MEC) of sitting and standing is poorly understood, and MEC associated with a transition from sitting to standing has not been reported. Thus, we carefully quantified the MEC for sitting, standing and sit/stand transitions, adjusting for age and fat free mass (FFM) in a sample of adults with no known disease.

Methods: Participants (N=50; 25 women), 20-64 years, randomly performed 3 conditions for 10 min each (sitting, standing, 1 sit/stand transition·min⁻¹ and then sitting back down). MEC was measured by indirect calorimetry and FFM by dual energy X-ray absorptiometry.

Results: $\dot{V}O_2$ (ml·kg⁻¹·min⁻¹) for sitting (2.93±0.61; 2.87±0.37 in men and women respectively), standing (3.16±0.63; 3.03±0.40), and steady-state cost of repeated sit/stand transitions (1·min⁻¹) (3.86±0.75; 3.79±0.57) were significantly different regardless of sex and weight ($p < 0.001$). EE (kcal·min⁻¹) also differed from sitting (1.14±0.18; 0.88±0.11), to standing (1.23±0.19; 0.92±0.13), and sit/stand transitions (1·min⁻¹) (1.49±0.25; 1.16±0.16). Heart-rate increased from sitting to standing (~ 13 bpm; $p < 0.001$). Neither sex nor FFM influenced the results ($p > 0.05$).

Conclusion: This study found in a sample of adults with no known disease that continuous standing raised MEC 0.07 kcal·min⁻¹ above normal sitting. The transition from sitting to standing (and return to sitting) had a metabolic cost of 0.32 kcal·min⁻¹ above sitting. Therefore, public health messages recommending to interrupt sitting frequently should be informed of the modest energetic costs regardless of sex and body composition.

Key Words: Sedentary behavior; Expenditure; Body composition; Breaks; Heart rate

7.2. Introduction

Sedentary behavior—as defined since 2004 as too much sitting as distinct from too little physical activity—has increasingly been considered as one of the major contributors for the low activity energy expenditure (EE) that contributes to obesity (Hamilton, Hamilton, & Zderic, 2007), and it seems to be adversely associated with cardiometabolic health and premature mortality (Dempsey, Owen, Biddle, & Dunstan, 2014; Hu, Li, Colditz, Willett, & Manson, 2003; Wilmot et al., 2012). Although these studies have found sedentary behavior to be an independent risk factor from moderate-to-vigorous physical activity (Matthews et al., 2012), few explored the causality between sedentary behavior and health parameters (Helajarvi et al., 2014). Therefore, more prospective studies are needed to better understand the direction of these associations.

The interpretation regarding the associations between sedentary time and metabolic health indicators are equivocal. One recent study reported that there was no association for sedentary behavior with cardiometabolic biomarkers once analyses were adjusted for “total physical activity” (Maher, Olds, Mire, & Katzmarzyk, 2014). This supports the logical hypothesis first raised in 2007, that sitting with relatively idle muscles for too much time promotes metabolic unfitness because it limits the otherwise high volume of intermittent non-exercise muscular activity in everyday life, which mostly involves low intensity physical activity below 3 METs during standing and light muscular movement (Hamilton et al., 2007). A systematic review (van Uffelen et al., 2010) found that five of ten cross-sectional studies showed a positive association between occupational sitting and body mass index (BMI), but four studies found no association, and one study found a negative association. Therefore, there is still uncertainty about the influence of replacing occupational sitting with increasing suggestions such as taking breaks from prolonged sitting to use sit to stand desks, at least in terms of significantly influencing energy balance and weight control (van Uffelen et al., 2010). Regardless of weight, low EE demanding behaviors when sitting

have been consistently related to risk of diabetes and cardiovascular risk factors independent of BMI (Hamilton, Hamilton, & Zderic, 2014).

Adults spend ~ 65% of waking hours in sedentary behavior and have dozens of transitions between each posture (Baptista et al., 2012; Craft et al., 2012; Evenson, Buchner, & Morland, 2012; Healy, Clark, et al., 2011). In one of the larger studies to date using inclinometry (ActivPAL device in 91 adult women), the average weekly sitting time was 64 hours and the average weekly standing time (non-stepping) was 27 hours (Craft et al., 2012). Thus, the amount of time people spend sitting and standing is large enough to result in meaningful cumulative effects on some metabolic processes, and knowing the energy demand of standing and in sit/stand transitions will be important to understand human energetics.

Results from quantifying the metabolic and energy cost (MEC) associated with "sitting" and "standing" have produced equivocal results (Torbeyns, Bailey, Bos, & Meeusen, 2014). One study found no differences for the EE between sitting and standing (Speck & Schmitz, 2011). In opposition, Reiff and colleagues (Reiff, Marlatt, & Dengel, 2012) found EE to increase from sitting to standing ($0.34 \text{ kcal}\cdot\text{min}^{-1}$). More recently, another study (Buckley, Mellor, Morris, & Joseph, 2014) found that compared to sitting, EE during an afternoon of standing work was 174 kcals greater ($0.83 \text{ kcals}\cdot\text{min}^{-1}$). Therefore, a large variation between the mean values for the MEC of standing versus sitting seems to exist (Reiff et al., 2012; Schuna et al., 2014).

Sedentary behavior related content is emerging in the mainstream media (Knight & Intzandt, 2015; Knox, Biddle, Esliger, Piggin, & Sherar, 2014). Public health and work related reports suggest that "simply standing burns considerably more calories than sitting", and this justifies why standing desks are becoming an alternative for socially conscious employers (Schuna et al., 2014). However, supporting research often compares sitting to a variety of exercise devices (treadmill desks, cycling desks, and Yoga balls) (Elmer & Martin, 2014; Schuna et al., 2014) instead of defining the MEC for the type of standing that characterizes standing still when a person might for example be typing at a standing desk or standing in an office meeting.

Much scientific interest has been emerging about the possible metabolic benefits of interrupting sitting time to stand frequently throughout the workday (Healy, Matthews, Dunstan, Winkler, & Owen, 2011; Henson et al., 2013; Peddie et al., 2013). However, studies have not examined the MEC associated with these sit/stand transitions. There is a need to carefully quantify these behaviors in a group of both men and women while accounting for body weight and body composition. Fat free mass (FFM) is highly associated with resting EE (REE) (Muller, Bosy-Westphal, Kutzner, & Heller, 2002) and it would be important to account for this covariate.

As such, using indirect calorimetry to measure MEC and dual energy X-ray absorptiometry (DXA) to assess FFM, the present study aimed to determine the differences in MEC and heart rate (HR) between sitting, standing per se, and the action of getting up and returning to a seated position (sit/stand transition·min⁻¹). By including this methodological approach, we were able to estimate the additional contribution of performing a sit/stand transition on MEC and HR that is needed in the literature. It is important to understand the energetics of sit to stand desks and the very common act of transitioning between sitting and standing that takes place about an average of 40-60 times each day (Craft et al., 2012; Reiff et al., 2012; Smith et al., 2015).

7.3. Methods

7.3.1. PARTICIPANTS

For sample and power calculations we used the (GPower software, version 3.1.9.2) and considered the differences in MEC between sitting motionless and standing motionless conditions. Based on a pilot study (N=15) using indirect calorimetry we obtained an effect size of approximately 0.385 for the differences between sitting and standing with a repeated measures ANOVA. Therefore, we needed to study 50 participants to be able to reject the null hypothesis with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

Fifty adults (25 women) (20-64 years) completed the study. Participants were recruited through posting and advertisements placed nearby the University and from announcements in classes. Participants were included if they were apparently healthy,

not taking any medications that impact metabolism, and had no locomotion limitation. Participants were excluded if they had any metabolic, cardiovascular, or pulmonary diseases.

7.3.2. *STUDY DESIGN*

The study took place at the Exercise and Health Laboratory in Faculdade de Motricidade Humana, Universidade de Lisboa. This was a crossover randomized experiment that included a 2 hour visit to the laboratory. Participants were asked not to consume any food or calorie containing beverages 8 hours prior to the visit, not to engage in any exercise, ingest any caffeine or take any other stimulants 48 hours prior to the visit. General health and ability to participate in the study (inclusion criteria) were examined. The assessments started with the measurement of body height and total mass followed by DXA and REE assessment. After REE assessment, participants were enrolled in an experiment with 3 conditions administered in a random order. Each condition lasted for 10 min and consisted of: 1) spending 10 continuous min seated in a chair motionless with hands on thighs; 2) spending 10 continuous min standing motionless with arms resting down alongside the body; 3) seated at a chair motionless with hands on thighs and performing a sit/stand transition each min during the 10 min. Participants stood up from the seated position and returned to the seated position in one single action movement at the 30 second mark of each min, therefore they performed a total of 10 sit/stand transitions. The order in which participants performed the three conditions was randomly assigned by an automated computer-generated randomization scheme. The study was approved by the Faculty Ethics Committee (approval number: 14/2013) and conducted in accordance with the Declaration of Helsinki (World Medical Association, 2008). Written informed consent was obtained from each participant prior to entry into the trial.

7.3.3. *BODY COMPOSITION MEASURES*

Participants were weighed to the nearest 0.01kg wearing minimal clothes and without shoes, and height was measured to the nearest 0.1cm on a digital scale with

integrated stadiometer (Seca, Hamburg, Germany). BMI was calculated as weight (kg) divided by the square of the height (m).

DXA (Hologic Explorer-W, fan-beam densitometer, software QDR for windows version 13.3, Waltham, Massachusetts, USA) was used to estimate FFM and fat mass (FM). The equipment measures the attenuation of X-rays pulsed between 70 and 140 kV synchronously with the line frequency for each pixel of the scanned image. Following the protocol for DXA described by the manufacturer, a step phantom with six fields of acrylic and aluminium of varying thickness and known absorptive properties was scanned to serve as an external standard for the analysis of different tissue components. The same technician positioned the participants, performed the scans and executed the analysis according to the operator's manual using the standard analysis protocol. Based on test-retest using 10 participants, the coefficients of variation (CV) in our laboratory for FM and FFM were 1.7% and 0.8%, respectively.

7.3.4. RESTING ENERGY EXPENDITURE

Assessment of REE was performed in the morning (7:00 – 10:00 a.m.) when fasted (≥ 8 hours). All measurements were performed in the same room at an environmental temperature and humidity of approximately 22°C and 40-50%, respectively. The MedGraphics CPX Ultima (MedGraphics Corporation, Breezeex Software) indirect calorimeter was used to measure breath-by-breath oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) using a facial mask. One trained technician conducted all measurements. The oxygen and carbon dioxide analyzers were calibrated in the morning before testing using known gas concentration. The flow and volume were measured using a pneumotachograph calibrated with a 3 L syringe (Hans Rudolph, inc.TM). The auto calibration was performed between participants. Before testing, participants were instructed about all the procedures and asked to relax, breathe normally, not to sleep, and not to talk during the evaluation. Total rest duration was 60 min, participants lay supine for 30 min covered with a blanket and the calorimeter device was then attached to the mask and breath-by-breath $\dot{V}O_2$ and $\dot{V}CO_2$ were measured for another 30 min period. Outputs of $\dot{V}O_2$, $\dot{V}CO_2$, respiratory exchange ratio (RER), and ventilation were collected and averaged over 1

min intervals for data analysis. The first and the last 5 min of data collection were discarded and the mean of a 5 min steady state interval between the 5 and the 25 min with RER between 0.7 and 1.0 was used to determine REE. Steady state was defined as a 5 min period with $\leq 10\%$ CV for $\dot{V}O_2$ and $\dot{V}CO_2$ (Compher, Frankenfield, Keim, & Roth-Yousey, 2006). The mean $\dot{V}O_2$ and $\dot{V}CO_2$ of 5 min steady states were used in Weir equation (Weir, 1949) and the period with the lowest REE used for data analysis.

Based on test-retest using seven participants, the CV in our laboratory for REE is 4.0%.

7.3.5. EXPERIMENTAL CONDITIONS

The same equipment described in REE measurement was used to measure ventilation (CO_2 production by computer interfaced with gas analyzers) during each of the three conditions. The initial 5 min of each condition allowed for steady state $\dot{V}O_2$ to be achieved. Mean $\dot{V}O_2$ and RER were then determined from the ensuing 5 min.

Studies show that approximately 4.82 kcal release when a blend of carbohydrate, lipid, and protein burns in one liter of oxygen (McArdle, 1981). Even with large variations in the metabolic mixture, this caloric value for oxygen varies only slightly (within 2% to 4%). Regardless, EE (in kilocalories per min) was estimated with the use of the specific caloric equivalent for a liter of O_2 considering the RER of each test and assuming a non-protein metabolic mixture (McArdle, 1981).

Participants wore a pulse oximeter that was attached to the MedGraphics system to capture HR min by min. Conditions were performed continuously, with no interruptions allowed. To avoid an overestimation of $\dot{V}O_2$ on the first min of each condition as a result of a potential carryover from the previous condition to the next, only the second 5 min of each condition were analyzed and the first 5 min discarded. $\dot{V}O_2$ was presented in milliliters of oxygen consumption per kg of body mass per min ($ml \cdot kg^{-1} \cdot min^{-1}$) and milliliters of oxygen consumption per kg of FFM per min ($ml \cdot kg_{FFM}^{-1} \cdot min^{-1}$). Relative METs were calculated by dividing mean oxygen consumption ($ml \cdot kg^{-1} \cdot min^{-1}$) per activity by mean oxygen consumption during lying down at rest. Absolute METs were calculated dividing the relative $\dot{V}O_2$ in $ml \cdot kg^{-1} \cdot min^{-1}$ by 3.5

$\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. Also, the percentage above resting (Table 7.2) and percentage above sitting (Figure 7.1, panel B and Figure 7.2) were calculated for the main variables.

7.3.6. STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS Statistics version 22.0, 2013 (SPSS Inc., New York, NY). Descriptive statistics (mean \pm SD) were calculated for all outcome measurements. Normality was verified using the Kolmogorov-Smirnov test. A repeated measure ANCOVA with post hoc analysis was used to compare the differences between conditions (conditions \times 3), adjusting for potential covariates (FFM and age) and considering the order of conditions' randomization and sex as between-subject effects. Multicollinearity for the covariates was also examined. To test the sphericity the Mauchly's statistical test was performed. If the test was non-significant ($p \geq 0.05$) we considered the F-ratios produced by SPSS. If the test was significant ($p < 0.05$), no homogeneity of variances existed, then the Greenhouse and Geisser's test was considered. Statistical significance was set at ($p < 0.05$).

7.4. Results

The sample was equally distributed according to sex (25 women; 25 men). There were no interactions for sex among the changes in MEC variables and HR between the different postures ($p \geq 0.05$). However, because of differences in body composition profiles, the absolute values were different. Therefore, results are presented separately by sex. Participants' characteristics are shown in Table 7.1. Based on BMI, 48% of men were in the normal weight category (BMI < 25) and 52% were overweight or obese (BMI ≥ 25). In women, 72% were normal weight and 28% were overweight or obese.

Table 7.1. Participants' characteristics, by sex (N=50)

	Men (N=25) (Mean ± SD)	Women (N=25) (Mean ± SD)
Age (years)	32.5 ± 11.4	38.0 ± 15.7
Height (m)	1.76 ± 0.05	1.60 ± 0.07
Body mass (kg)	79.1 ± 11.6	62.4 ± 12.1
BMI (kg·m⁻²)	25.6 ± 3.19	24.4 ± 4.99
FM (%)	20.7 ± 7.09	33.1 ± 8.19
FM (kg)	16.5 ± 7.37	20.9 ± 8.46
FFM (kg)	61.5 ± 7.41	40.5 ± 5.81
REE (kcal·day⁻¹)	1476 ± 246	1164 ± 162
REE (kcal·min⁻¹)	1.03 ± 0.17	0.81 ± 0.11
REE $\dot{V}O_2$ (ml·kg⁻¹·min⁻¹)	2.73 ± 0.52	2.64 ± 0.33
REE $\dot{V}O_2$ (ml·kg_{FFM}⁻¹·min⁻¹)	3.50 ± 0.68	4.04 ± 0.49
Resting HR (bpm)	56.8 ± 9.47	63.5 ± 8.82

Abbreviations: SD, standard deviation; BMI, body mass index; FM, fat mass; FFM, fat free mass; REE, resting energy expenditure; HR, heart rate; bpm, beats per min.

Table 7.2 shows men and women's mean values for $\dot{V}O_2$ (ml·kg⁻¹·min⁻¹, ml·kg_{FFM}⁻¹·min⁻¹, % above resting), EE (kcal·min⁻¹, kcal·kg⁻¹·min⁻¹), relative and absolute METs, and HR (bpm and % above resting) and ANOVA differences for the three conditions.

As presented in Table 7.2, differences in $\dot{V}O_2$, EE and METs were found for all the three conditions ($p < 0.001$). Considering HR, sitting differed from standing and sit/stand transition·min⁻¹ conditions ($p < 0.001$), but no differences were found between standing and sit/stand transition·min⁻¹ ($p \geq 0.05$). Neither the randomly assigned order of treatment nor the treatment by groups' interaction influenced the differences ($p \geq 0.05$). MEC and HR significantly increased from sitting to standing but only MEC increased from standing to the sit/stand transition·min⁻¹ condition ($p < 0.001$), with no differences for HR ($p \geq 0.05$). After the adjustment for age and FFM (no multicollinearity found between these two covariates), the ANCOVA differences remained the same for all the main variables (Figure 7.1).

Table 7.2. Differences in oxygen consumption, EE, METs, and HR for the three conditions, in both men and women

	Experimental conditions			One-way ANOVA
	Sitting on a chair (continuous) (Mean ± SD)	Standing (continuous) (Mean ± SD)	Sit/stand transitions (rate of 1·min ⁻¹) (Mean ± SD)	p-value
Men (N=25)				
$\dot{V}O_2$ (ml·kg ⁻¹ ·min ⁻¹)	2.93 ± 0.61	3.16 ± 0.63	3.86 ± 0.75	<0.001**
$\dot{V}O_2$ (ml·kg _{FFM} ⁻¹ ·min ⁻¹)	3.75 ± 0.75	4.06 ± 0.83	4.96 ± 0.98	<0.001**
$\dot{V}O_2$ % above Resting	7.57 ± 9.23	16.3 ± 10.1	42.1 ± 13.5	<0.001**
RER	0.89 ± 0.06	0.89 ± 0.07	0.88 ± 0.07	≥0.05
EE (kcal·min ⁻¹)	1.14 ± 0.18	1.23 ± 0.19	1.49 ± 0.25	<0.001**
EE (kcal·kg ⁻¹ ·min ⁻¹)	0.014 ± 0.003	0.016 ± 0.003	0.019 ± 0.003	<0.001**
Absolute METs	0.84 ± 0.18	0.90 ± 0.18	1.10 ± 0.21	<0.001**
Relative METs	1.08 ± 0.09	1.16 ± 0.10	1.42 ± 0.14	<0.001**
HR (bpm)	62.8 ± 10.9	76.8 ± 15.9	76.3 ± 10.4	<0.001*
HR % above Resting	10.8 ± 12.8	35.9 ± 25.3	34.5 ± 15.1	<0.001*
Women (N=25)				
$\dot{V}O_2$ (ml·kg ⁻¹ ·min ⁻¹)	2.87 ± 0.37	3.03 ± 0.40	3.79 ± 0.57	<0.001**
$\dot{V}O_2$ (ml·kg _{FFM} ⁻¹ ·min ⁻¹)	4.39 ± 0.51	4.63 ± 0.53	5.79 ± 0.76	<0.001**
$\dot{V}O_2$ % above Resting	8.89 ± 7.70	15.0 ± 8.03	43.7 ± 13.3	<0.001**
RER	0.89 ± 0.06	0.88 ± 0.06	0.88 ± 0.07	≥0.05
EE (kcal·min ⁻¹)	0.88 ± 0.11	0.92 ± 0.13	1.16 ± 0.16	<0.001**
EE (kcal·kg ⁻¹ ·min ⁻¹)	0.014 ± 0.002	0.015 ± 0.002	0.019 ± 0.003	<0.001**
Absolute METs	0.82 ± 0.11	0.87 ± 0.11	1.08 ± 0.16	<0.001**
Relative METs	1.09 ± 0.08	1.14 ± 0.08	1.44 ± 0.13	<0.001**
HR (bpm)	68.8 ± 7.71	80.1 ± 9.68	80.1 ± 7.52	<0.001*
HR % above Resting	8.95 ± 7.85	27.4 ± 16.3	27.4 ± 13.1	<0.001*

Abbreviations: SD, standard deviation; $\dot{V}O_2$, oxygen consumption; EE, energy expenditure; FFM, fat free mass; HR, heart rate; bpm, beats per min. Relative METs were calculated by dividing mean oxygen consumption (ml·kg⁻¹·min⁻¹) per activity by mean oxygen consumption during lying down at rest, because of the overestimation of actual resting $\dot{V}O_2$. Absolute METs were calculated by dividing the relative $\dot{V}O_2$ in ml·kg⁻¹·min⁻¹ by 3.5 ml·kg⁻¹·min⁻¹.

** Significant differences between all conditions; * Significant differences for sitting with standing and sit/stand transition·min⁻¹ conditions but not between standing and sit/stand transition·min⁻¹ conditions. Each condition lasted for 10 min and participants fasted for at least 8 hours previous to the conditions' assessment. For the sit/stand transition the participants stood up and immediately sat back down once per min for 10 min.

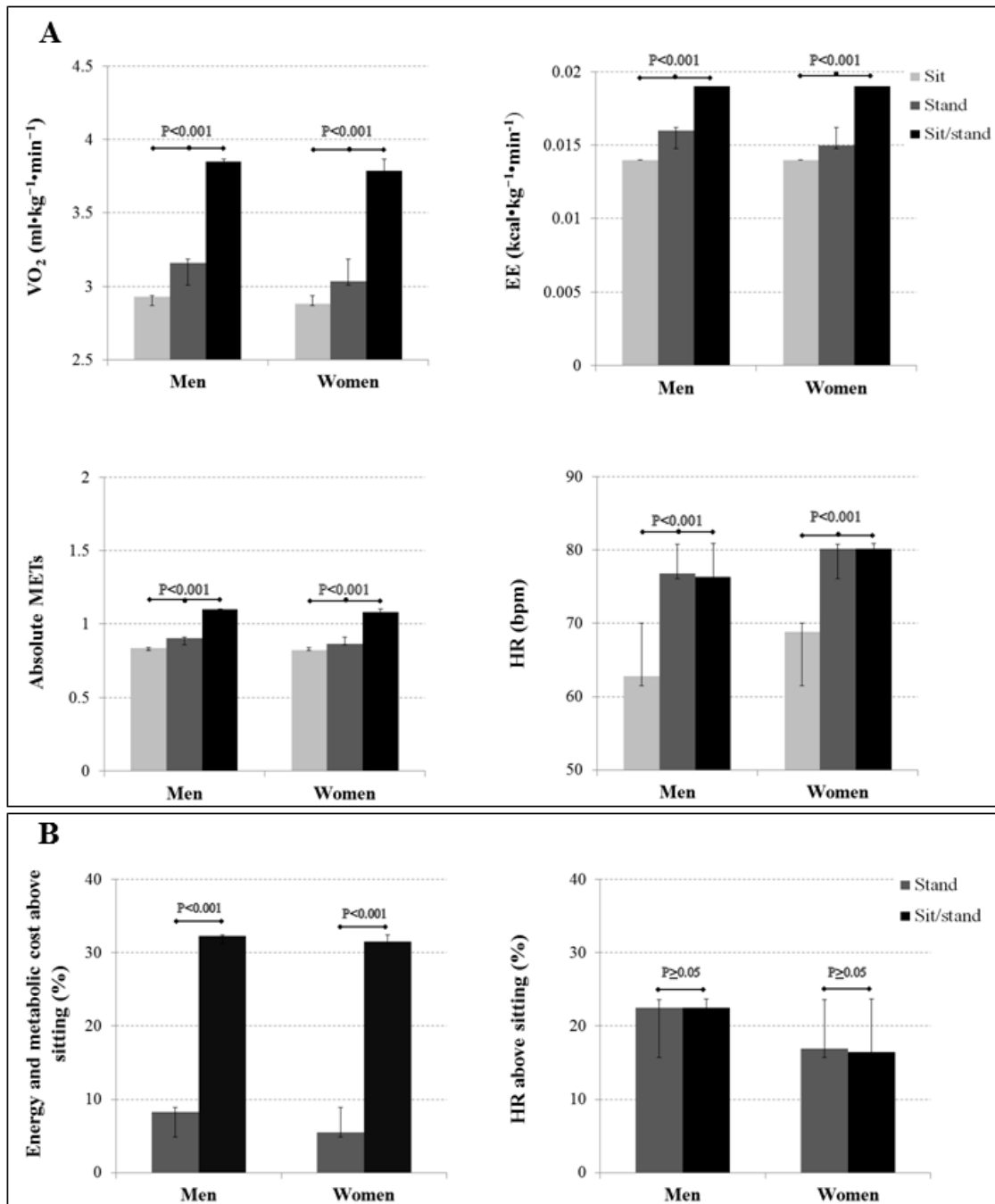


Figure 7.1. Oxygen consumption (ml·kg⁻¹·min⁻¹), EE (kcal·kg⁻¹·min⁻¹), Absolute METs, and HR (bpm) for the three conditions, adjusting for age and FFM in both men and women.

Each condition lasted for 10 min and participants fasted for at least 8 hours previous to the conditions' assessment. **For the sit/stand transition the participants stood up and immediately sat back down once per minute for 10 min.** Data collected between 11/2014 and 02/2015 and analyzed in 2015. Bars represent the average value for the sitting, standing, and sit/stand transition·min⁻¹ conditions and standard deviations across men and women (**panel A**). In **panel B**, bars represent the increase above sitting levels for the metabolic/ energy cost and heart rate during the standing and sit/stand transition·min⁻¹ conditions and standard deviations. Absolute METs were calculated by the common practice of dividing the relative $\dot{V}O_2$ in ml·kg⁻¹·min⁻¹ by 3.5 ml·kg⁻¹·min⁻¹.

As presented in Figure 7.2, we tested whether the changes in MEC between conditions differed for the two BMI categories (normal weight and overweight/obese), adjusted for age and FFM.

In women, there were no differences for the two BMI groups, on the % increase above sitting in the MEC values for the standing or sit/stand transition·min⁻¹ conditions ($p \geq 0.05$). Compared to the normal weight group, overweight or obese men had an additional ~ 13% increase in MEC values from sitting to standing ($p < 0.001$), but similar MEC responses for the sit/stand transition·min⁻¹ condition ($p \geq 0.05$).

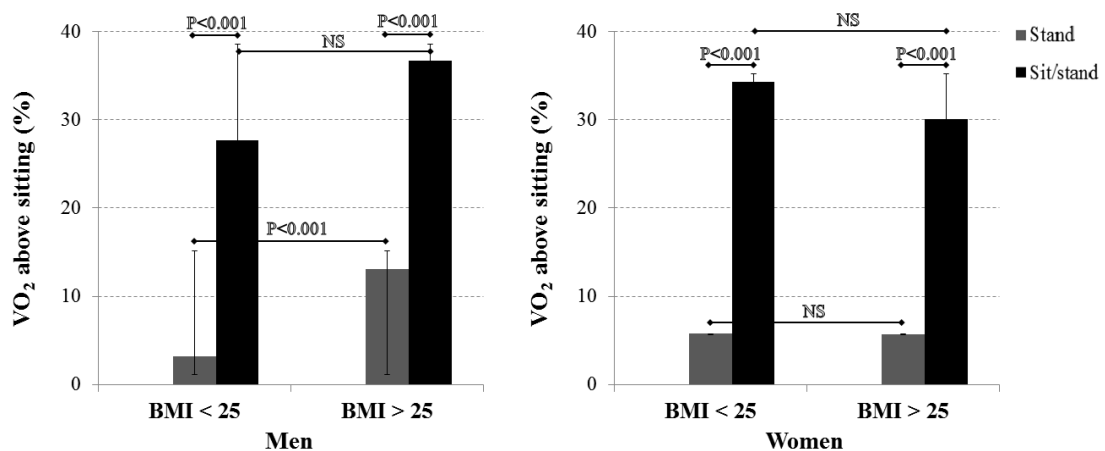


Figure 7.2. Oxygen consumption (% above sitting) for the normal weight vs overweight/obese in both men and women, adjusting for age and FFM.

Each condition lasted for 10 min and participants fasted for at least 8 hours previous to the conditions' assessment. **For the sit/stand transition the participants stood up and immediately sat back down once per minute for 10 min.** Data collected between 11/2014 and 02/2015 and analyzed in 2015. Bars represent the increase above sitting levels for the metabolic/ energy cost during the standing and sit/stand transition·min⁻¹ conditions and standard deviations. BMI < 25 represents the normal weight category and BMI ≥ 25 the participants in the overweight or obesity category.

7.5. Discussion

People spend dozens of hours each week sitting and standing without ambulation (Craft et al., 2012) and thus the potential cumulative effects of taking more sit/stand transitions on EE could be important if there are even modest differences in metabolic rate (Miles-Chan, Sarafian, Montani, Schutz, & Dulloo, 2013). In addition, there has been much speculative interest in the metabolic effects of breaking up long periods of sitting with intermittent standing and walking, but no study until the present

has yet examined the associated EE with the simple sit/stand transition or carefully examined influences of body composition and sex.

The present study quantified these issues and based on the acute effects (5 min condition) found in our experiment it can be extrapolated that for every 10 sit/stand transitions (sit to stand followed by a stand to sit movement), the metabolic rate is increased modestly (~ 3.2 kcals) but significantly above normal sitting ($p < 0.001$). Smith and colleagues (Smith et al., 2015) investigated the usual number of sit/stand transitions measured in a sample of office workers and found that they performed approximately 52 sit/stand transitions/day. Based on our findings, the daily EE related to the sit/stand transitions of these office workers would be 16.6 kcal and if they increased 10%, 20%, and 50% of their regular number of daily transitions, an additional 8.4, 16.7, and 41.6 kcals would be spent in a work week.

The present results also suggest that working at a standing desk will produce a modest but statistically significant rise in EE in both normal weight and overweight/obese ~ 8% (men) and ~ 6% (women) compared with sitting. Based on REE (1476 kcal for men; 1164 kcal for women) and the magnitude of MEC increases between sitting and standing, if an individual would theoretically expend 50% of an 8 hour working day standing an additional 20 kcal (men) and 12 kcal (women) per working day or 100 kcal (men) and 57 kcal (women) in a 5 day working week would be spent. However, a recent study (Chau et al., 2014) reported that a standing desk based intervention reduced daily time spent sitting and increased standing time at work only by 65 min. This would translate to an additional EE of 5.1 kcals during a work day, which is negligible. Previous studies found that the relative differences in the energy demand of standing and sitting have been misleading because the absolute differences are relatively small (Schuna et al., 2014; Torbeyns et al., 2014) and there could be inter-individual differences (Miles-Chan et al., 2013). However, our results seem to confirm previous findings (Reiff et al., 2012; Speck & Schmitz, 2011; Torbeyns et al., 2014) that sitting and standing have a significantly different MEC (Table 7.2).

We further examined if the MEC responses were influenced by the BMI categories (normal weight or overweight/obese), adjusting for age and FFM in both men and women. We concluded that BMI did not alter the relative MEC responses

(expressed as percentage changes from sitting) for the two postural conditions, in women. However, overweight/obese men had a higher increase in the percent change in MEC from sitting to standing than those with normal BMI.

Church and colleagues (Church et al., 2011) argued the possibility that a modest reduction in occupational EE may have accounted for a large portion of the observed increase in mean U.S. weight over the last 5 decades (Church et al., 2011). Their analysis estimated that daily occupation related EE has decreased about 100 calories in both women and men, underscoring the potential larger than expected public health impact of modest differences in low intensity energy expenditure if habitual and sustained for decades. Thus, regardless of the statistical significance, the magnitude of changes for the EE between standing and sitting was small but not totally insignificant compared to total EE if uncompensated by other components of energy balance. However small, we also recognize that there is individual variability, and the cumulative small effects of reducing sitting time over long periods of time could contribute to the sometimes significant associations between postural allocation (reducing sitting time) and body composition (Levine et al., 2005).

As mentioned before, no study until the present has yet examined the associated EE with the simple sit/stand transition that could potentially contribute to the reported metabolic health benefits of taking more breaks from sitting independent of total sitting time. Our study found a considerably higher MEC for the sit/stand transition when performed once per min compared with sitting (35%) and standing (28%), ($p < 0.001$) in both normal weight and overweight/obese men and women. Based on participants' REE, if an individual simply stood up and returned to the seated position (sit/stand transition) an additional 10 times every hour during an 8 hour working day, it would theoretically expend 120 kcal or more in a full 5 day working week. The cumulative effect of increasing time spent standing and the number of sit/stand transitions would also be a good alternative. If we add the effect of 10 additional sit/stand transitions every hour (120 Kcal) with an additional 80 kcal from spending 40% of an 8 hour working day standing, a worker would theoretically spend an additional 200 Kcal in a full 5 day working week.

It is widely accepted that FFM explains the majority of the REE variability. In fact, FFM alone explained 80 (Sparti, DeLany, de la Bretonne, Sander, & Bray, 1997), 84 (Gallagher et al., 1998) and 85% (Illner, Brinkmann, Heller, Bosy-Westphal, & Muller, 2000) of the variance in REE.

In our sample, men had lower body fat percentage and 13% higher FFM compared to women, although both were highly variable within each sex. We examined whether there was an interaction between postural conditions with regard to sex and included FFM as a covariate. The results showed that there were no interactions for sex ($p \geq 0.05$). This is a novel finding, and no previous investigation had adjusted for FFM. This indicates that the MEC responses to the three postural conditions were independent of body composition or sex.

In the present study, HR increased from resting to sitting (~ 6 bpm) and from sitting to standing (~ 13 bpm) ($p < 0.001$). However, the additional increase in the MEC of the sit/stand transition $\cdot \text{min}^{-1}$ compared to standing was not accompanied by an even greater HR (~ 0.4 bpm) ($p \geq 0.05$). During postural change a number of complex physiological processes are undertaken to regulate the body's cardiovascular and musculoskeletal responses. Standing is one of the most common conscious physical activities in which we partake, but the metabolic response appears to be anything but simple (Miles-Chan et al., 2013). Confirming the results from a previous study (Miles-Chan et al., 2013), HR had a large variance (from 47 to 113 bpm) in the standing condition, followed by moderate variance compared with sitting (45-89 bpm) and sit/stand transition $\cdot \text{min}^{-1}$ (57-100 bpm). This means that some participants had a sustained 50% increase in HR above rest; others showed a little increase of 3% above rest HR during the standing condition.

Although energetically distinct, there is uncertainty about the metabolic benefits of standing and sit/stand transitions. The first study that experimentally reduced sitting time (a single day of mostly standing to replace mostly sitting all day) observed a significant difference for insulin action (Stephens, Granados, Zderic, Hamilton, & Braun, 2011). One recent study (Bailey & Locke, 2015) suggests that interrupting sitting time with standing did not impart beneficial postprandial responses that may enhance cardiometabolic health. Two other recent studies that examined replacing

prolonged acute sitting with standing found there was a lowering of plasma glucose concentration (Buckley et al., 2015; Duvivier et al., 2013; Thorp et al., 2014). Regardless, interventions have been more effective on shifting sitting time for standing behaviors instead of walking behaviors (Chau et al., 2014) and recently, an international group of experts convened to provide guidance for employers to promote the avoidance of prolonged periods of sedentary work. The set of recommendations was developed from the totality of the current evidence, including long term epidemiological studies and interventional studies; they recommend workers to stand and/or move more frequently (Buckley et al., 2015). Based on our findings focusing from the energetic point of view, the recommendation might best be to include more sit/stand transitions and more movement when standing instead of standing too still, as stated recently, “similar to the risks of prolonged static seated positions, so too should prolonged static standing postures be avoided” (Buckley et al., 2015).

7.5.1. STUDY LIMITATIONS AND STRENGTHS:

It is important to make note of the limitations in the current investigation. First, while men were equally distributed according to BMI (50% normal weight and 50% overweight/obese), the majority of women were in the normal weight category. Regardless, as mentioned before, no interactions for the differences between conditions with sex were found. Finally, our findings are only generalized to healthy male and female adults with no diagnosed disease.

We carefully considered the duration of measurement. Previous research (Compher et al., 2006) found that a 10 min test duration with the first 5 min discarded and the remaining 5 min having a CV < 10% gives an accurate measure of MEC. Furthermore, MEC measurements should be taken when participants are undisturbed. The fact that participants performed a 30 min REE followed by three 10 min conditions implied participants to spend a total of 60 min using the mask attached to face. Therefore, longer condition length would extend the assessment period and possibly generate stress that could influence the results. Nonetheless, the 10 min testing period can be considered a limitation as it is not known if extended periods would show slightly different metabolic responses.

Although well controlled, the time frame and scripted postures also limit the generalizability of our results, and these laboratorial settings combined with the fact that participants were fasting should also be noted. The fasting conditions we studied would be associated with a lower absolute EE (by ~ 20%) than in the postprandial period due to the thermic effects of feeding (Newton, Han, Zderic, & Hamilton, 2013). One recent study took feeding and time of day into consideration when quantifying the metabolic rate of sedentary behaviors over an 8 hour day in a metabolic chamber (Newton et al., 2013). That study helps us to interpret the potential limitation of our subjects being relatively motionless while seated or standing without much opportunity to “fidget”. It was shown that when 25 people were housed in a whole room metabolic chamber and allowed to spontaneously fidget or to be motionless, the average EE when sitting to read, type, or watch TV was ~ 1.1 kcal·kg⁻¹·hr⁻¹ (~ 3.65 ml·kg⁻¹·min⁻¹), which is not much greater than the present study after accounting for the thermic effect of feeding in the postprandial period. Therefore, fidgeting while seated or standing that characterizes real life settings, and the fact that people are not typically fasting may alter the absolute metabolic rate; however, it might not be of major importance to the changes reported in the present study caused by standing.

Another finding from this study was the overestimation of the actual resting $\dot{V}O_2$ when using the assumption of 1 MET equivalent to 3.5 ml·kg⁻¹·min⁻¹ as our results observed a mean value of 2.7 ml·kg⁻¹·min⁻¹. This seems to go along with findings from a previous study with approximately 800 adults and found the average $\dot{V}O_2$ and energy cost corresponding with rest of 2.6 ml·kg⁻¹·min⁻¹ (Byrne, Hills, Hunter, Weinsier, & Schutz, 2005).

The major strengths of this study include: the valid methods for assessing body composition, specifically DXA that enabled FFM to be further explored as a covariate in the models; and the inclusion of a third condition to understand the energetics of the common act of taking a sit/stand transition (i.e., the simple action of getting up and return to a seated position), which was something not measured before.

Confirming previous findings, this study found a great variability on the metabolic and energy response associated with the standing alone posture (Miles-Chan et al., 2013). As suggested previously (Miles-Chan et al., 2013), this means that while

some people may be able to increase their EE by shifting sitting time with prolonged standing, others will not energetically benefit by performing this postural change. Recent investigations have been recommending people to break up sedentary behavior more often, based on the metabolic health benefits. Moreover, the present study brings important quantitative results to the field by taking a step toward helping to elucidate the impact of transitioning from sit/stand/sit on metabolic and energetic cost.

7.6. Conclusions

The results from the present study lead us to conclude that the rise in metabolic rate when standing is not elevated by a great amount (5-8%) when compared to continuous sitting and is significantly independent of sex and body composition. Although the observed differences are not large on a percentage basis, it cannot be ignored because of the high duration that people stand each day and the ubiquitous nature of these behaviors.

This was also the first study to determine the metabolic cost of a single sit/stand transition and found it to be about 0.32 kcal (35% above sitting). Therefore, emerging public health messages recommending the suggestion to frequently interrupt sitting should be informed by understanding these modest energetic costs regardless of sex and body composition.

7.7. References

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CHAPTER 8

Associations of breaks in sedentary time with abdominal obesity in Portuguese older adults⁵

⁵ **Judice, P. B.**, Silva, A. M., Santos, D. A., Baptista, F., & Sardinha, L. B. (2015). Associations of breaks in sedentary time with abdominal obesity in Portuguese older adults. *Age (Dordr)*, 37(2), 23.
DOI: 10.1007/s11357-015-9760-6. **3.39** Impact Factor

Associations of breaks in sedentary time with abdominal obesity in Portuguese older adults

Pedro B. Júdice, Analiza M. Silva, Diana A. Santos, Fátima Baptista, Luís B. Sardinha

8.1. Abstract

Aim: In older adults, sedentary time is positively associated with obesity. The manner in which it is accumulated, i.e. – the number of breaks in sedentary time – might be also important. We examined the cross-sectional associations of breaks in sedentary time with abdominal obesity in 301 older adults (111 men and 190 women) aged 75.0 ± 6.8 years.

Methods: Sedentary time ($\text{counts} \cdot \text{min}^{-1} < 100$) and physical activity were objectively measured by accelerometry, worn during waking hours for at least three consecutive days. A break was defined as an interruption ($\geq 100 \text{ counts} \cdot \text{min}^{-1} < 2020$) in sedentary time while performing light intensity physical activities. Sedentary time was expressed as the number of daily breaks in sedentary time or hourly breaks in sedentary time. Abdominal obesity was defined by waist circumference (men > 102 cm; women > 88 cm).

Results: Using binary logistic regression analyses, the odds for abdominal obesity decreased 7% for each additional hourly break in sedentary time in women (OR=0.93, 95% CI: 0.87 – 0.99), but not men, independently of total sedentary time and moderate-to-vigorous physical activity. The odds for abdominal obesity were 3.21 times higher ($p=0.039$) for women in quartile 1 ($< 225 \text{ breaks} \cdot \text{day}^{-1}$) of daily breaks in sedentary time compared to those in quartile 4 ($> 353 \text{ breaks} \cdot \text{day}^{-1}$) of daily breaks in sedentary time.

Conclusion: These findings indicate that older women who interrupt their sedentary time more frequently are less likely to present abdominal obesity. Public health recommendations regarding breaking up sedentary time complementary to those for physical activity are likely to be relevant.

Key Words: Breaks; sedentary time; waist circumference; physical activity; older adults; abdominal obesity

8.2. Introduction

Physical activity and sedentary behaviors are complex and distinct entities and the lack of moderate-to-vigorous physical activity (MVPA) does not directly imply higher sedentary time. A paradigm shift proposes that inactivity physiology is qualitatively different from exercise physiology (Hamilton, Hamilton, & Zderic, 2007), groundbreaking a new conceptual framework based on epidemiological evidence linking sedentary behaviors directly with adverse health outcomes (Owen, Salmon, Koohsari, Turrell, & Giles-Corti, 2014). Sedentary time' patterns are generally represented by breaks in sedentary time considered in terms of how frequently sedentary bouts are interrupted. For example, two older adults may exhibit the same total amount of sedentary time but have different accumulation or breaking patterns during the day (Lord et al., 2011).

Geriatric population are the most sedentary group in the population – spending about 70% (9 to 10 hours·day⁻¹) of their waking hours in sedentary time (Baptista et al., 2012; Evenson, Buchner, & Morland, 2012; Healy, Clark, et al., 2011) and the least amount of time in MVPA (Baptista et al., 2012). They are also the age group that has the highest prevalence of abdominal obesity (Sardinha et al., 2012) which is associated with multiple co-morbidities (Kohrt, 1998).

The associations of sedentary time with obesity have been reported for older adults independent of MVPA (Gennuso, Gangnon, Matthews, Thraen-Borowski, & Colbert, 2013; Inoue et al., 2012; Swartz et al., 2012). Nevertheless, there are inconsistent findings concerning the role of sedentary time in abdominal obesity, with some studies in adults reporting no relation between overall sedentary time and abdominal fatness (McGuire & Ross, 2012; Saunders et al., 2013). Disparities in associations for older adults have also been reported, with studies reporting an association of sedentary time with the presence of abdominal obesity in older women, but not in older men (Healy, Matthews, Dunstan, Winkler, & Owen, 2011; Scheers,

Philippaerts, & Lefevre, 2012a). Understanding the pattern in which sedentary time is accumulated has been identified as a research priority and may explain these disparities in older adults (Lord et al., 2011; Swartz et al., 2012).

Recent studies using general samples of adults have found that, independent of MVPA levels and total sedentary time, more breaks in sedentary time are associated with lower adiposity (Ayabe et al., 2013; Chastin, Ferriolli, Stephens, Fearon, & Greig, 2012; Healy, Matthews, et al., 2011; Oliver et al., 2012). One study has found relationships of breaks in sedentary time with overall fat mass among older adults (Chastin et al., 2012). However, no studies with older adults have examined how breaks in sedentary time are associated with being in the at-risk category for abdominal obesity. Based on this new paradigm and conceptual framework of a plausible independent role of sedentary time on adverse health outcomes, the purpose of this study was to examine the associations of total sedentary time and breaks in sedentary time with waist circumference – defined abdominal obesity in older adults.

8.3. Methods

8.3.1. PARTICIPANTS

This study included a sample of non-institutionalized Portuguese Caucasian older adults, aged 65–103 years. Participants were selected by proportionate stratified random sampling taking into account the number of people by age and gender in each region of mainland Portugal (Alentejo, Algarve, Centro, Lisboa e Norte), excluding the Madeira and Açores regions (Portuguese Archipelagos). A total of 401 participants were evaluated, of whom 301 aged 65 years or older (111 men and 190 women) had valid accelerometer data (\geq three days, including one weekend day, with \geq 10 h of wear time·day⁻¹). The sample recruitment was carried out in senior universities, parish councils, city halls, day care centers, and health promotion fairs. Participants were included if they had independent physical functioning, determined by responses to the 12-item of Composite Physical Functioning Scale (Rikkli and Jones, 1998): able to perform all basic and instrumental activities of daily living. All participants were informed about the possible risks of the investigation before giving their written

informed consent to participate. All procedures were approved by the Ethics Committee of the Faculty of Human Kinetics, University of Lisbon, and were conducted in accordance with the Declaration of Helsinki for Human Studies (World Medical Association, 2008).

8.3.2. ANTHROPOMETRY

Participants were weighed to the nearest 0.01 kg while wearing minimal clothes and without shoes and height was measured to the nearest 0.1 cm with a stadiometer (Seca, Hamburg, Germany) according to the standardized procedures described elsewhere (Lohman, Roche, & Martorell, 1988). Body mass index (BMI) was calculated as body mass (kg)/height² (m) and classified into normal (< 25 kg·m⁻²), overweight (25–29.9 kg·m⁻²), or obesity (≥ 30 kg·m⁻²) (National Institutes of Health, 1998). Waist circumference was measured according to NIH procedures used in the third U.S. National Health and Nutrition Examination Survey (NHANES III 1988–1994) protocol (National Center for Health Statistics, 1996) with a flexible anthropometric tape (Seca, Hamburg, Germany) at minimal respiration and reported to the nearest 0.1 cm by positioning a tape parallel to the floor and immediately above the iliac crest. Waist circumference was then dichotomized into normal or at risk category for abdominal obesity (men > 102 cm; women > 88 cm) (National Institutes of Health, 1998).

8.3.3. BREAKS IN SEDENTARY TIME AND PHYSICAL ACTIVITY

Breaks in sedentary time and physical activity were assessed by accelerometry (ActiGraph, GT1M model, Fort Walton Beach, FL). The accelerometer is a small device that measures the acceleration of normal human movements ignoring high frequency vibrations associated with mechanical equipment. All participants were asked to wear the accelerometer on the right hip, near the iliac crest for at least three consecutive days, including two weekdays and one weekend day. The devices were activated on the first morning day and data were recorded in 15 seconds epochs. Apart from accelerometer non-wear time (i.e., when it was removed for sleeping or water activities), periods of at least 60 consecutive min of zero activity intensity counts were also considered as non-wear time. A valid day was defined as having 600 min (10 h) or

more of monitor wear, and the study included the results from participants with at least three valid days (including one weekend day). Each min during which the accelerometer counts were below 100 was considered sedentary time; total sedentary time was the sum of sedentary min while the accelerometer was worn. A break in sedentary time was considered as any bout of time in which the accelerometer count rose up to or above 100 counts·min⁻¹ and which stayed within the light-intensity physical activity (LIPA) range (< 2020 counts·min⁻¹). Accelerometer counts $\geq 100 \cdot \text{min}^{-1}$ were classified as active time, with further differentiation to identify separately LIPA (100 to 2019 counts·min⁻¹) and MVPA; $\geq 2020 \text{ counts} \cdot \text{min}^{-1}$. The difference between LIPA and the daily breaks in sedentary time variable is that whereas LIPA is the total cumulative daily time spent in LIPA per day (min·day⁻¹), breaks in sedentary time represents the number of times sedentary time was broken by LIPA (breaks·day⁻¹). Data processing also derived the following variables: bouts of at least 1, 5, and 10 min of LIPA (bouts·day⁻¹); hourly breaks in sedentary time calculated as follows (60* daily breaks in sedentary time)/daily accelerometer wear time in minutes.

8.3.4. COVARIATES

Self-reported socio-demographics, behavioral, and medical covariates were assessed via interviewer-administered questionnaires. Employment was dichotomized as employed or unemployed (includes retired) and educational attainment was categorized as: 1) no education; 2) 4 years of education; 3) 9 years of education; 4) 12 years of education; and 5) higher education. Geographical location of participants according to each region of mainland Portugal (Alentejo, Algarve, Centro, Lisboa e Norte) was also introduced as a covariate. Smoking status and alcohol dependence was reported and dichotomized in two categories (no and yes). Medical history for hypertension, elevated cholesterol and glycemia, current medication, and the presence of any long-standing condition such as diabetes, asthma, cancer or cardiac disease were also reported and classified in two categories (no or yes).

8.3.5. STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS Statistics for Windows version 21.0, 2012 (SPSS Inc., an IBM Company, Chicago IL, USA). Descriptive analyses included means \pm SD for all measured variables. Bivariate correlations of sedentary time, LIPA, and MVPA were performed to verify the associations between physical activity variables. Binary logistic regression analyses were performed to examine associations of MVPA, quartiles of daily breaks in sedentary time (breaks·day⁻¹), and measured hourly breaks in sedentary time (breaks·hour⁻¹) with the odds for abdominal obesity (National Institutes of Health, 1998), adjusting for covariates retained in backwards elimination ($p < 0.1$): age, accelerometer wear time, total sedentary time (min·day⁻¹), employment, educational attainment, geographical location, smoking status, alcohol dependence, medical history for chronic disease, hypertension, elevated cholesterol and glycemia, current medication status, and MVPA (min·day⁻¹) or daily breaks in sedentary time (breaks·day⁻¹). Goodness-of-fit tests including the Log Likelihood ratio, the Cox & Snell R Square statistic and the Hosmer and Lemeshow Test were used as indicators of model appropriateness, and the Wald statistic was used to test the significance level of individual independent predictor variables. To examine the differences in waist circumference between quartiles of daily breaks in sedentary time (breaks·day⁻¹) and test for linear effect of the association, a one-way analysis of variance (ANOVA) was used. To examine the differences in covariates between the two women's subgroups, T-Tests were used.

8.4. Results

All results are reported by gender, as a significant gender x breaks in sedentary time interaction was observed ($p=0.016$). Participants' characteristics, according to gender are shown in Table 8.1. On average, men and women spent 72% and 71% of their waking hours sedentary, 24% and 26% in LIPA, and 3.6% and 2.6% in MVPA, respectively. The linear correlations of breaks in sedentary time with total sedentary time, LIPA, and MVPA were ($r=-0.35$; $r=0.67$; and $r=0.30$, respectively, $p \leq 0.001$) for men and ($r=-0.37$; $r=0.64$; and $r=0.29$, respectively, $p \leq 0.001$), for women. Of the

women, 68% were classified as abdominally obese; 28% of the men were abdominally obese.

Table 8.1. Participants' characteristics according to gender

	Men (N=111) (mean \pm SD) or % (N)	Women (N=190) (mean \pm SD) or % (N)
Age (years)	74.5 \pm 6.78	75.0 \pm 7.06
Employment (%)		
Employed	24 (27)	36 (68)
Retired	76 (84)	64 (122)
Education (%)		
None	4.5 (5)	6.3 (12)
Primary school (4 years)	65 (72)	67 (128)
Secondary school (9 years)	13 (14)	11 (21)
High school (12 years)	6.3 (7)	3.7 (7)
Higher education (>12 years)	7.2 (8)	3.2 (6)
Smoker (%)	4.5 (5)	1.1 (2)
Alcohol dependent (%)	2.7 (3)	0.5 (1)
Medical conditions (%)		
Hypertensive	42 (47)	53 (100)
Hypercholesterolemia or impaired fasting glucose	32 (35)	50 (95)
Take medication	89 (99)	91 (173)
Known chronic disease	36 (40)	35 (66)
Anthropometrics		
Height (m)	1.66 \pm 0.06	1.53 \pm 0.06
Body mass (kg)	75.2 \pm 11.0	64.8 \pm 10.0
BMI (kg·m⁻²)	27.4 \pm 3.49	27.7 \pm 3.83
Waist circumference (cm)	97.0 \pm 10.3	93.5 \pm 10.8
Accelerometer variables		
Total sedentary time (min·day⁻¹)	598 \pm 114	583 \pm 122
LIPA (min·day⁻¹)	200 \pm 90	214 \pm 95
MVPA (min·day⁻¹)	30 \pm 29	21 \pm 23
Daily breaks in sedentary time (breaks·day⁻¹)	259 \pm 81	308 \pm 91
Hourly breaks in sedentary time (breaks·hour⁻¹)	19 \pm 5.6	23 \pm 6.7
>1 min LIPA bouts (bouts·day⁻¹)	83 \pm 44	88 \pm 49
>5 min LIPA bouts (bouts·day⁻¹)	3.5 \pm 4.4	3.2 \pm 4.2
>10 min LIPA bouts (bouts·day⁻¹)	0.5 \pm 0.8	0.4 \pm 0.8

Abbreviations: n, number of participants; SD, standard deviation; LIPA, light intensity physical activity; MVPA, moderate-to-vigorous physical activity.

The associations of total sedentary time, MVPA, and hourly breaks in sedentary time with the odds for abdominal obesity are shown in Table 8.2.

Table 8.2. Association of total sedentary time, LIPA, MVPA, and hourly breaks in sedentary time with abdominal obesity, by gender

Independent variables	Men (N=111)			Women (N=190)		
	β (SE)	OR (95% CI)	<i>P</i>	β (SE)	OR (95% CI)	<i>P</i>
Total sedentary time (min·day⁻¹)	0.001 (0.001)	1.00 (0.99-1.01)	0.251	0.010 (0.01)	1.00 (0.99-1.04)	0.297
LIPA (min·day⁻¹)	-0.001 (0.001)	1.00 (0.99-1.00)	0.135	-0.001 (0.001)	1.00 (0.99-1.00)	0.135
MVPA (min·day⁻¹)	-0.040 (0.020)	0.96 (0.92-0.99)	0.020	-0.020 (0.001)	0.98 (0.97-0.99)	0.041
Hourly breaks in sedentary time (breaks·hour⁻¹)	-0.120 (0.070)	0.89 (0.78-1.01)	0.071	-0.070 (0.040)	0.93 (0.87-0.99)	0.043

Data are unstandardized β co-efficient \pm standard error (SE) or odds ratio (OR) 95% confidence interval (CI) adjusted for age, wear time, total sedentary time, employment, educational attainment, geographical location, smoking status, alcohol dependence, medical history for chronic disease, hypertension, elevated cholesterol and glycemia, and current medication status.

Abbreviations: LIPA, light intensity physical activity; MVPA, moderate-to-vigorous physical activity.

For each additional hourly break in sedentary time, the odds of being abdominally obese decreased by 7% (OR=0.93, 95% CI: 0.87 - 0.99) for women, but was not significant for men (Table 8.2). Each daily one min in MVPA was associated with a 4% (OR=0.96, 95% CI: 0.93 - 0.99) and 2% lower (OR=0.98, 95% CI: 0.97 – 0.99) odds of abdominal obesity in men and women, respectively (Table 8.2). There were no significant associations of sedentary time or LIPA with abdominal obesity, for both men and women ($p > 0.05$). Being employed was associated with an 81% higher (OR=2.24, 95% CI: 1.05 - 4.82) odds of abdominal obesity in women but no associations with employment were found for men. Also, no associations of total sedentary time, LIPA, MVPA, daily or hourly breaks in sedentary time with BMI were found (data not shown; $p > 0.05$). The characteristics of the two women's subgroups were similar for most sociodemographic and medical covariates (Table 8.3).

Table 8.3. Women characteristics according to subgroups: abdominal obese vs no abdominal obesity

	No abdominal obese (N=59) (mean \pm SD) or % (N)	Abdominal obese (N=131) (mean \pm SD) or % (N)	T-Test <i>P</i>
Age (years)	73.8 \pm 6.54	75.5 \pm 7.49	0.130
Employment (%)			0.228
Employed	29 (17)	37 (49)	
Retired	71 (42)	62 (81)	
Education (%)			0.005
None	3.4 (2)	7.6 (10)	
Primary school (4 years)	63 (37)	73 (95)	
Secondary school (9 years)	17 (10)	9.2 (12)	
High school (12 years)	10 (6)	0.8 (1)	
Higher education (>12 years)	6.8 (4)	3.1 (4)	
Smoker (%)	0.00 (0)	1.5 (2)	0.343
Alcohol dependent (%)	0.00 (0)	0.8 (1)	0.508
Medical (%)			
Hypertensive	42 (25)	56 (73)	0.089
Hypercholesterolemia or impaired fasting glucose	46 (27)	48 (63)	0.846
Take medication	88 (52)	91 (119)	0.364
Known chronic disease	19 (11)	41 (54)	0.001
Anthropometrics			
Height (m)	1.53 \pm 0.06	1.53 \pm 0.07	0.780
Body mass (kg)	58.5 \pm 7.86	68.2 \pm 9.27	<0.001
BMI (kg·m ⁻²)	24.9 \pm 2.93	29.0 \pm 3.45	<0.001
WC (cm)	81.7 \pm 5.13	99.1 \pm 7.70	<0.001
Accelerometer variables			
Total sedentary time (min·day ⁻¹)	572 \pm 99.4	594 \pm 132	0.258
LIPA (min·day ⁻¹)	232 \pm 85.0	203 \pm 98.0	0.054
MVPA (min·day ⁻¹)	26 \pm 24	18 \pm 20	0.018
Daily breaks in sedentary time (breaks·day ⁻¹)	325 \pm 84	295 \pm 94	0.038
Hourly breaks in sedentary time (breaks·hour ⁻¹)	24 \pm 5.9	22 \pm 7.0	0.113
>1 min LIPA bouts (bouts·day ⁻¹)	93 \pm 46	84 \pm 50	0.222
>5 min LIPA bouts (bouts·day ⁻¹)	3.1 \pm 3.1	3.0 \pm 4.6	0.911
>10 min LIPA bouts (bouts·day ⁻¹)	0.4 \pm 0.7	0.4 \pm 0.8	0.963

Abbreviations: *n*, number of participants; SD, standard deviation; BMI, body mass index; WC, waist circumference; LIPA, light intensity physical activity; MVPA, moderate-to-vigorous physical activity.

The odds for being abdominally obese were significantly higher in the lowest quartile of daily breaks in sedentary time compared to the highest quartile, for women (OR=3.21, 95% CI: 1.06 - 9.75) but not for men (OR=4.33, 95% CI: 0.81 - 23.3)

(Figure 8.1). The ANOVA results showed significant differences in waist circumference between quartile 1 of daily breaks in sedentary time (lowest number of breaks) and quartiles 2, 3, and 4 with mean differences of 4.21 cm ($p=0.048$), 4.92 cm ($p=0.015$), and 4.74 cm ($p=0.018$) for women, but no significant differences in men ($p > 0.05$). After adjustment for covariates, only the difference between the 4th and 1st quartiles (mean 7.15 cm) remained significant ($p=0.042$).

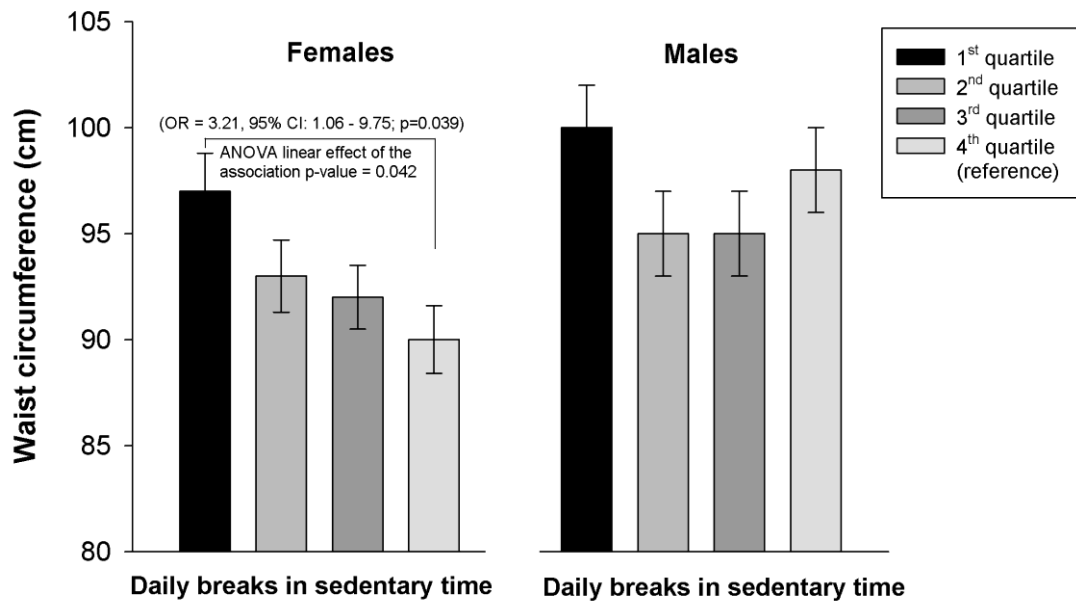


Figure 8.1. Waist circumference among quartiles of daily breaks in sedentary time, by gender.

Adjusted for age, total sedentary time, MVPA, total wear time, employment, educational attainment, geographical location, smoking status, alcohol dependence, medical history for the presence of chronic diseases, hypertension, elevated cholesterol and glycemia, and current medication status

Abbreviations: MVPA, moderate-to-vigorous physical activity; OR, odds ratio.

*Significant OR for abdominal obesity between quartiles and the differences between quartiles' waist circumference averages using one-way analysis of variance (ANOVA) to test for linear effect of the association are presented.

Note: Quartiles of daily breaks in sedentary time: Quartile 1 (< 225 breaks \cdot day $^{-1}$); quartile 2 (225 to 297 breaks \cdot day $^{-1}$); quartile 3 (297 to 353 breaks \cdot day $^{-1}$); quartile 4 (> 353 breaks \cdot day $^{-1}$).

8.5. Discussion

The prevalence of obesity increases with age whereas waist circumference is a good indicator of abdominal obesity. Among elderly, it has been suggested that the use of this anthropometric indicator predicts morbidity and mortality. Furthermore, abdominal obesity is strongly and inversely associated with regular physical activity. However, few studies have examined the independent associations of sedentary time and breaks in sedentary time with abdominal obesity in geriatric population. Grounded on the new paradigm of a plausible independent role of sedentary time on adverse health outcomes and consistent with the findings of previous studies on the associations of breaks in sedentary time with adiposity indices (Ayabe et al., 2013; Healy, Matthews, et al., 2011; Oliver et al., 2012; Scheers, Philippaerts, & Lefevre, 2012b), we found that older women who frequently interrupted their sedentary time were less likely to be in the higher range of abdominally obesity risk category, after controlling for total sedentary time, MVPA, socio-demographic and medical covariates. While there were non-significant associations for men, there were 7% lower odds of having abdominal obesity for every additional hourly break in sedentary time for women. For MVPA, there were significant associations with the odds for abdominal obesity, for both men and women, with each daily min in MVPA being associated with 4% and 2% lower odds for abdominal obesity in men and women, respectively.

The different distribution of men and women being classified as having abdominal obesity (28% of men and 68% of women) may in part explain why there were no significant associations for breaks in sedentary time with the odds for abdominal obesity in men. Only 28% of men compared to 68% of women were abdominally obese which may have weakened the associations for the breaks in sedentary time with the odds for abdominal obesity. However, similar results were reported in a previous study that examined the linear associations of breaks in sedentary time with measures of total body fat mass (Chastin et al., 2012) and found these associations to be present only in women. Therefore, a potential gender dimorphism for the associations of breaks in sedentary time with abdominal obesity risk may exist (Scheers et al., 2012a), with women benefiting the most through more breaks in sedentary time. However, considering the different distribution of men and women

within the abdominal obesity categories in our sample, our study is not powered to identify whether there is or is not a significant difference in the gender response to the breaks in sedentary time. This is a limitation that should be addressed in future investigations. Regardless, the present study showed that women who broke up sedentary time no more than 17 times an hour ($225 \text{ breaks} \cdot \text{day}^{-1}$) had an odds of being abdominally obese of 3.21, relative to those who broke up sedentary time more than 26 times an hour ($353 \text{ breaks} \cdot \text{day}^{-1}$).

We observed a significant inverse association of breaks in sedentary time with the odds of being in the abdominal obesity risk category. This finding is consistent with a previous study that examined linear associations of breaks in sedentary time with continuous measures of waist circumference, which also had a similar number of daily breaks in sedentary time (current study: 288 ± 88 ; (Henson et al., 2013): 273 ± 60). The odds for abdominal obesity were significantly lower in the highest quartile compared to the first quartile. The differences in waist circumference between daily breaks in sedentary time quartile 1 (lowest number of breaks) and quartiles, 2, 3, and 4 (4.2, 4.9, and 4.7 cm lower waist circumference, respectively) are supported by a previous study in adults that found a similar trend (Quartiles 2, 3, and 4 were all significantly different from Quartile 1) (Healy, Matthews, et al., 2011).

Similar to previous studies of older adults (Henson et al., 2013; Santos et al., 2012), lower MVPA but not total sedentary time or LIPA were associated with higher odds of abdominal obesity for both men and women. Moreover, the inverse association of MVPA with abdominal obesity was stronger in men compared to women, which in addition to the weaker associations of breaks in sedentary time with abdominal obesity in men, seemed to indicate that MVPA, rather than breaks in sedentary time may be of greater importance for controlling abdominal obesity in men. Since both the quartile categories of daily breaks in sedentary time and the continuous measures of breaks in sedentary time were associated with the odds for abdominal obesity, breaks in sedentary time, rather than total sedentary time or total LIPA, may be more relevant for abdominal obesity risk (Ando et al., 2013; Chastin et al., 2012). These cross-sectional findings together with findings on the metabolic syndrome (Bankoski et al., 2011) provide preliminary evidence that breaking up sedentary time may be important to target in the

prevention of abdominal obesity in a geriatric population, especially for women (Chastin et al., 2012). These results should be confirmed in future prospective studies.

Findings from a small intervention study support this possibility, suggesting that regular variations in posture allocation may be an influential factor in the regulation of energy homeostasis (Swartz, Squires, & Strath, 2011), a key factor in the development of obesity. Previous findings have demonstrated that sedentary time can be reduced by following a brief intervention based on goal setting and behavioral self-monitoring in older adults (Gardiner, Eakin, Healy, & Owen, 2011).

A randomized controlled trial (Ando et al., 2013) also found that breaking sedentary time more often may lead to efficient utilization of ingested fat by preventing decreased fat oxidation and as a result reduces fat deposition. Decreased fat oxidation with prolonged sedentary time has been observed in rats as a result of decreased heparin-releasable LPL activity, which directs consumed fat toward muscle (Zderic & Hamilton, 2006). Recent human studies have been found that regular walking breaks of light intensity activities were more effective than continuous physical activity at decreasing postprandial glycemia and insulinemia in healthy, normal-weight adults (Dunstan et al., 2012; Peddie et al., 2013). Another study found that alternating standing and sitting in 30 min bouts results in modest beneficial effects on postprandial glucose responses in overweight/obese adults (Scheers et al., 2012a). Lower postprandial glycemia is indicative of a more efficient response to glucose ingestion and has been shown to be inversely associated with abdominal fat deposition (Khoury et al., 2010; Nakatsuji et al., 2010). These physiological changes may be underlying the associations of breaks in sedentary time with abdominal obesity and should be addressed in future investigations.

An important strength of our study is that sedentary time was objectively measured by accelerometry, but still there is some limitation as accelerometers are not sensitive to detect all activities such as biking, standing, and upper-body movement. Although the criteria that we considered to validate accelerometer data, (\geq three days, including one weekend day, with ≥ 10 h of wear time·day⁻¹) has been used in large scale studies, this criteria may be less reliable than a 7-day period and therefore must be presented as a limitation. The cross-sectional design of this study limits inference about

the direction of causality between the breaks in sedentary time and abdominal obesity. We cannot rule out the possibility that more breaks in sedentary time result from lower levels of adiposity. Moreover, based on the cutoffs for waist circumference (men > 102 cm; women > 88 cm), on average women were abdominally obese while men were in the normal category. The fact that men had lower levels of abdominal obesity may underlie the lack of significant associations of breaks in sedentary time with abdominal obesity in men.

The majority of participants in our study was retired and had no specific work context. Women who were employed had 81% higher odds of being abdominal obese, compared with the retired women. We hypothesized that women who were retired may have more free-time and therefore more opportunities to be physically active and break sedentary time more often. Also, the fact that women usually do more housework may justify why retired women present less odds for abdominal obesity compared with employed women.

The lack of association between employment and the odds for abdominal obesity in men may be explained by a lower contribution in housework and therefore a similar pattern can be found in both work and leisure time settings.

Another potential limitation is that considering only 36% of our sample had medical problems like diabetes, asthma, cancer or cardiac disease our results cannot be generalized to people who have health problems. We also cannot rule out the possible residual confounding from potentially important unmeasured covariates like diet. Future studies would benefit from prospective designs to examine the association of breaks in sedentary time with abdominal obesity in both men and women.

These findings might have potential implications for the prevention of abdominal obesity in older adults. Our findings provide objective evidence that in older women, total sedentary time may not be the most important determinant for abdominal obesity but that additional to time spent in MVPA, the fragmentation of sedentary time may attenuate the development of abdominal obesity, especially in women. As such, programs engaged exclusively on MVPA may overlook an area that is of also of importance to obesity control. Along with messages related to accumulating at least 150

min·week⁻¹ of MVPA, older adults could also be encouraged to sit less and stand/walk more often, even with light intensity levels.

8.6. Conclusions

The present findings revealed an inverse association for the breaks in sedentary time with abdominal obesity in older women, using cross-sectional data. Therefore, older women that interrupted sedentary time more often were less likely to be abdominal obese independently of total sedentary time itself and MVPA levels.

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CHAPTER 9

Randomized controlled pilot of an intervention to reduce and break-up overweight/obese adults' overall sitting time⁶

⁶ **Judice, P. B.**, Hamilton, M. T., Sardinha, L. B., & Silva, A. M. (2015). Randomized controlled pilot of an intervention to reduce and break-up overweight/obese adults' overall sitting-time. *Trials*, 16(1), 490. doi: 10.1186/s13063-015-1015-4. **1.73** Impact Factor

Randomized controlled pilot of an intervention to reduce and break-up overweight/obese adults' overall sitting time

Pedro B Júdice, Marc T Hamilton, Luís B Sardinha, Analiza M Silva

9.1. Abstract

Aim: Too much prolonged sitting is a prevalent health-risk among adults. Interventions have focused mainly on the workplace, with limited attention to non-work settings. The effectiveness of a short-term intervention to reduce and break up sitting time in overweight/obese adults was examined. This pilot study sought to determine the feasibility of interrupting sitting to stand/ambulate objectively with ActivPAL devices which provide a valid measurement of sit/stand transitions.

Methods: This is a cross-over-randomized-controlled-pilot that included 10 participants (aged 37-65 years) and while a small and short term intervention (one-week intervention; no washout) further informs about the feasibility of interventions in a larger scale. At the workplace, screen-delivered hourly alerts prompted participants to break up sitting time through adopting walking behaviors ($\sim 30\text{-}60 \text{ min}\cdot\text{day}^{-1}$). During transportation/home/leisure time individual goals for $\text{steps}\cdot\text{day}^{-1}$ were set and sitting-reduction strategies (including behavioral self-monitoring) were delivered through text-messages each-day.

Change in inclinometer-derived sitting time is the main outcome. Standing, stepping, number of sit/stand transitions and participant satisfaction were also examined.

Results: For the intervention compared to the control-week (mean difference [95% confidence interval]; p-value), participants had less sitting time (1.85 h [0.96 – 2.75]; $p=0.001$), more standing (0.77 h [0.06 – 1.48]; $p=0.036$), and more stepping (1.09 h [0.79 – 1.38]; $p < 0.001$). Importantly, there was no change in the total number of sit/stand transitions (3.28 [-2.33 – 8.89]; $p=0.218$) despite successfully reducing sitting time and increasing time spent standing and walking.

Conclusion: Sitting time in overweight/obese adults can be reduced following a brief multi-component intervention based on prompts, telephone-support, goal setting and behavioral self-monitoring. However, the results from this pilot study provide new insight that when overweight/obese adults attempted to reduce sedentary time by walking and standing for ~ 2 hours·day⁻¹ more than usual, they did not actually get up from sitting more often (i.e., increasing the number of sit/stand transitions), but instead remained on their feet for longer during each non-sitting bout. This behavioral resistance to make more sit/stand transitions (i.e., get-up from sitting more often) may have important implications for future modification programs and supports the concept that when overweight/obese people are sitting, people seem to prefer not to interrupt the sedentary behavior to get-up from sitting.

Trial registration: November 26, 2013, ClinicalTrials.govID:NCT02007681 (first participant was randomized in 2 September 2013).

Key Words: *Sedentary time; leisure time; reduction; breaks; physical activity; workplace*

9.2. Introduction

Sedentary behavior – time spent sitting or reclining during waking hours (Dunstan, Howard, Healy, & Owen, 2012) – is a specific occupational hazard in office workers. Prolonged sitting is associated with obesity (Vandelanotte, Sugiyama, Gardiner, & Owen, 2009), metabolic disorders (Healy et al., 2008) and all-cause mortality (van der Ploeg, Chey, Korda, Banks, & Bauman, 2012) and observational (Oliver et al., 2013) and experimental evidence (Dunstan, Kingwell, et al., 2012; Latouche et al., 2013) suggest that interrupting sitting time may be associated with better health outcomes. Adults spend most of their time in sedentary behaviors, some 65% of waking hours; 8 to 11 hours·day⁻¹ (Healy et al., 2011) and one of the features of modern life is that work has become less physically-active and more sedentary (Church et al., 2011) and has more leisure time engaged in sitting related pursuits (Aadahl et al., 2013).

There is a lack of studies that aimed to understand how the two desirable dimensions from these interventions (total sitting time reductions and increases in sit/stand transitions) would in fact interact in real life settings. The workplace is an important context to introduce strategies for reducing and break up periods of prolonged sitting (Alkhajah et al., 2012). However, leisure time and non-working days also comprise a large portion of a working adults' week (Aadahl et al., 2013). Recent trials have shown significant reductions in workplace sedentary time, using sit/stand workstations (Alkhajah et al., 2012), educational sessions (Adams, Davis, & Gill, 2013) and multi-component interventions (Cooley, Pedersen, & Mainsbridge, 2013). These multi-component interventions are likely to provide the most effective approach to reduce workplace sedentary time (Carr, Karvinen, Peavler, Smith, & Cangelosi, 2013; Healy et al., 2013). In addition, interventions using prompts to disrupt sitting time and increase physical activity (PA) at work have been shown to effectively increase the number of breaks in sitting time and reducing the number of bouts in prolonged sedentary time (Evans et al., 2012; Pedersen, Cooley, & Mainsbridge, 2014; Swartz et al., 2014). Distinct prompt's frequencies have been previously used (Evans et al., 2012; Pedersen et al., 2014; Swartz et al., 2014) but regardless of a generalized increase in the number of breaks, shorter prompt's frequencies (one prompt every 30 min) seemed not to reduce overall sitting time (Evans et al., 2012). Therefore, in this pilot study we considered hourly prompts to enhance overall sitting time reduction while at work.

Recent investigation has been shown that workers that spend more time in sedentary pursuits during working hours do not compensate by being more active on non-working periods (Clemes, Patel, Mahon, & Griffiths, 2014). Prior interventions aiming to increase physical activity in employees have been found to be of benefit (Chau et al., 2010; Freak-Poli, Cumpston, Peeters, & Clemes, 2013). To reduce overall daily sitting time, there is a need for interventions that, additional to focusing on the workplace context, also target leisure time contexts (Clemes et al., 2014).

Furthermore, a recent systematic review (Shrestha, Ijaz, Kukkonen-Harjula, Kumar, & Nwankwo, 2015) showed that overweight/obese people are an understudied population group in interventions that target reductions in sitting time (Shrestha et al., 2015) with only two studies (Healy et al., 2013; Verweij, Proper, Weel, Hulshof, & van

Mechelen, 2012) including overweight/obese people (BMI > 25 kg·m⁻²). In fact, those are the persons that are at higher risk of several diseases (Ghoorah, Campbell, Kent, Maznyczka, & Kunadian, 2014) therefore this pilot study tried to fill this gap by examining the short-term effectiveness of reducing and breaking up overall daily sitting time of physically-inactive overweight/obese working adults using a multi-component intervention simultaneously addressing workplace and leisure time contexts.

9.3. Methods

9.3.1. SAMPLE POWER CALCULATION

For sample and power calculations we considered one of the main outcomes from this pilot study whether not reported here (the energy expenditure assessed by doubly labeled water (DLW) technique). Based on a previous intervention (Bergouignan et al., 2010), the energy expenditure assessed by DLW within each participant group was normally distributed with a standard deviation (SD) of 1.09. If the true difference in the experimental and control means was -1.31 MJ·day⁻¹, we would need to study 10 experimental participants to be able to reject the null hypothesis that the population means of the experimental and control were equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

9.3.2. PARTICIPANTS

The study was approved by the Faculty of Human Kinetics, University of Lisbon Ethics Committee (approval number: 14/2013) and conducted in accordance with the Declaration of Helsinki (World Medical Association, 2008). Written informed consent was obtained prior to entry into the trial. After a careful analysis of the work patterns of several academic and administrative sectors of the University and surrounded workplaces [N=50], an invitation email was sent to each potential workplace limiting the participation to one person per workplace to avoid behavioral coupling or contamination between participants. Therefore, an invitation email was sent to 50 potential participants working in full-time that involved prolonged computer-based

work while sitting. Details of the study were explained to respondents [N=30] via telephone call and participants who expressed interest [N=20] attending a 30 min face-to-face screening session.

Inclusion criteria consisted of: currently employed in a full-time academic or administrative role that involves greater than 7 hours·day⁻¹ computer-based work; 18-65 years-old; Body mass index (BMI) greater than 25.0 kg·m⁻²; not taking any medication or dietary-supplements; physically inactive (not meeting the moderate-to-vigorous PA (MVPA) recommendations and with approximately 5000 steps·day⁻¹); and free from any major disease that inhibited their ability to participate in the study. Based on eligibility criteria we tested 10 participants (5-women and 5-men) (Figure 9.1). Considering the 10 participants' occupation, 5 had an administrative role in 5 different departments of the University. Two participants worked on a bank (distinct banks). One was a lawyer working on a private company and the last two participants were independent architects working on their private studios. There was no drop-out during the trial.

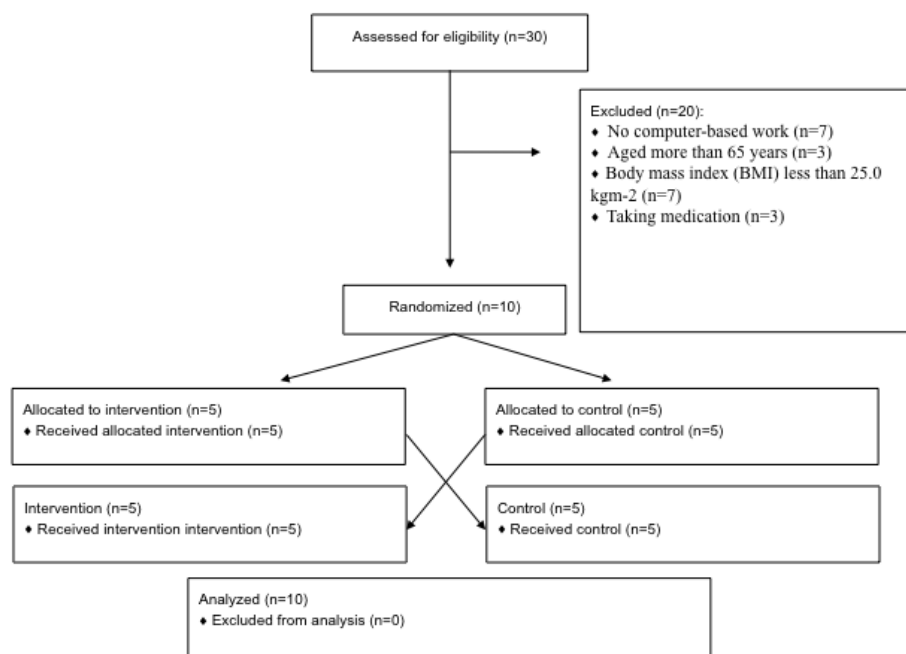


Figure 9.1. Screening, enrollment and interventions of the study participants.

The pilot study design consisted on a crossover-randomized-clinical-trial (ClinicalTrials.govID: NCT02007681). A baseline measurement period (one week), followed later (with approximately a week break) by a 2 week period of measurement, where one week was the intervention and one the control (with the order of intervention and control randomized by an automated computer-generated randomization scheme). Data were collected between September-December 2013 and analyzed in 2014.

To ensure that participants were physically inactive ($< 30 \text{ min}\cdot\text{day}^{-1}$ of MVPA and $\sim 5000 \text{ steps}\cdot\text{day}^{-1}$) and to assess habitual $\text{steps}\cdot\text{day}^{-1}$, PA and sedentary time, participants were fitted with an accelerometer (Actigraph GT3X+, Actigraph, Pensacola, FL) prior to the intervention. The pilot trial consisted of two one-week conditions performed in a random order, both under free-living conditions: intervention (asked to make a 3 h reduction in sitting time) and control (asked to undertake habitual sitting time). In each condition participants were instructed to maintain the same eating patterns while wearing an accelerometer (Actigraph GT3X+) and an inclinometer (ActivPAL, PAL Technologies Ltd., Glasgow, UK). Both these devices do not allow participants to have a real-time feedback on their PA levels. Therefore, a pedometer (OMRON, Walking style II, HEALTHCARE Ltd., Qyoto, Japan) was used on the right hip, near the iliac crest, during waking hours, and requested to remove it only during water-based activities such as showering and swimming, so that participants could control the number of steps they were performing during the day.

Regardless of the randomization order, participants were verbally told in person to maintain their habitual PA levels and sedentary patterns on both working hours and non-working periods during the control week. We reinforced them the importance of never to exceed the daily step goal for this condition (the number of $\text{steps}\cdot\text{day}^{-1}$ performed at baseline) by using telephone-calls and messages throughout the day as well as checking on adherence to these individual daily steps goal, and reminding participants to report their daily steps in a diary.

To avoid carryover of behavioral strategies to reduce sitting time adopted during the intervention week, those participants who were randomly allocated to the intervention condition during the first week were explicitly instructed to follow their normal work and non-work routines on the first day of the control week. Furthermore,

on the last day of the intervention week, an investigator met the participants and verbally in person explained them that starting on the next day (beginning of control week), it was critical that they did not perform any efforts to change their habitual activity patterns (prior to the study started).

The intervention at the workplace to reduce sitting time included a software program (Workrave, GitHub) that gave hourly alerts to participants to break up their sitting time for approximately 7 min through taking part in walking (to accumulate 30-60 min·day⁻¹). This software was installed in the work computers and automatically alerted the participants to break up working while seated by presenting a warning message that covered and locked the screen entirely. When this alert appeared in the screen, participants had the option to postpone for 5 min, but at the second time they did not have any option but stop working and perform a break for at least 7 min (the time the computer screen was locked).

During transportation/home/domestic-leisure time contexts, individual goals for number of steps·day⁻¹ were set, based on an expected step cadence for ambulatory activities (~ 90-120 min·day⁻¹) and by adding 6000 steps to their initial habitual daily amount. Also, generic strategies to reduce and break up sitting time were suggested, and participants identified strategies specific to their circumstances in their work, transport, and home contexts, for attaining their goal (3 h-reduction in sitting time).

Daily adherence during the intervention week was managed by using motivational telephone-calls and messages throughout the day as well as checking on adherence to the individual daily steps goal, and reminding participants to report their daily steps in a diary, which also worked as part of the intervention.

Participant satisfaction with the program was rated during the post-intervention assessment on a scale of 1–10, with 1 being extremely displeased and 10 being extremely satisfied. They also had to select one of the three strategies (screen-based prompts; daily steps goal, and behavioral strategies personally delivered) and one from the two domains (work/leisure time) as the most effective for reducing sitting time.

9.3.3. ANTHROPOMETRY

Anthropometric variables were measured according to the standardized procedures described elsewhere (Lohman, Roche, & Martorell, 1988). BMI was calculated as body mass (kg)·height⁻² (m).

9.3.4. SEDENTARY TIME AND PHYSICAL ACTIVITY MEASUREMENTS

ActivPAL Professional (PAL Technologies Ltd., Glasgow, UK) monitor was considered the primary method for the main variables in this study, as it provides a reliable method for differentiating sitting/lying, standing and stepping activities (Godfrey, Culhane, & Lyons, 2007), with a high accuracy for time spent sitting, compared with direct observation (Kozey-Keadle, Libertine, Lyden, Staudenmayer, & Freedson, 2011). The ActivPAL is a uniaxial piezoresistive accelerometer and inclinometer that is small (35 mm × 53 mm × 7 mm) and lightweight (20 g) worn on the middle-anterior line of the right thigh and provides a variety of objectively measured and objectively processed variables, including total time spent sitting/lying, standing and stepping and sit/stand transitions. Data was collected at a predetermined 10 Hz and the 15 seconds interval output was used for data analysis. Recorded output from ActivPAL monitor was downloaded, processed, and classified into sitting, standing, and walking by using manufacturer-supplied ActivPAL software (version 5.9.1.1, PAL Technologies, Glasgow, United Kingdom).

From the 15 seconds interval output it was possible to extract prolonged and uninterrupted periods of time spent sitting, standing and stepping of different durations (bouts of ≤ 4 min; 5-9; 10-19; 20-29; 30-59; and at least 60 min) by manually counting the number of bouts in which participants were sitting, standing or stepping in the bout's duration categories (Dowd, Harrington, Bourke, Nelson, & Donnelly, 2012). Because the past three bout categories are infrequent for the standing bouts, they were combined into one category (≥ 20 min).

The device was attached to the skin with a manufacturer-supplied non-allergenic and non-waterproof adhesive tape (PALstickie) and used continuously for 24 hours a day for 14 days, except for water-based activities such as showering and bathing. After

showering or bathing participants were instructed to re-attach ActivPAL with an additional piece of the same adhesive tape that we provided. Prior to the trial we taught them exactly how, where and the correct positioning to attach the device. None of the participants performed any activity like swimming or any other water dependent activity. Therefore, a valid-day was defined as having ≥ 22 hours of monitor wear, corresponding to the minimum daily use except for the showering and bathing. Participants were asked to record waking/sleeping hours and wear-time in a logbook. The information provided in the diary was used to determine ActivPAL's waking period and therefore assess sedentary time between waking and bed times. All ActivPAL's main variables including the sit/stand transitions, and the number of bouts in which participants were sitting, standing or stepping do not include sleeping hours. They were asked to record timing and reasons for every occasion the ActivPAL was removed.

All participants were asked to additionally wear an accelerometer Actigraph GT3X+ (Actigraph, Pensacola, FL) on the right hip, near the iliac crest, during waking hours, and requested to remove it only during water-based activities such as showering and bathing (Trost, McIver, & Pate, 2005). The device activation, download, and processing were performed using the software Actilife (v.6.9.1). A valid-day was defined as having 600 or more min (≥ 10 hours) of monitor wear, corresponding to the minimum daily use of the accelerometer (Ward, Evenson, Vaughn, Rodgers, & Troiano, 2005). As well as reported monitor non-wear time (i.e., when it was removed for sleeping or water activities), periods of at least 60 consecutive min of zero activity intensity counts were also considered as non-wear-time (Colley, Connor Gorber, & Tremblay, 2010).

The amount of activity assessed by the Actigraph accelerometer was expressed as min per day spent in different intensities. The cutoff values used to define the intensity of PA and therefore to quantify the mean time in each intensity (sedentary, light, moderate or vigorous) were: sedentary: < 100 counts \cdot min $^{-1}$; light: 100-2019 counts \cdot min $^{-1}$; moderate: 2020-5998 counts \cdot min $^{-1}$ (corresponding to 3-5.9 METs); vigorous: ≥ 5999 counts \cdot min $^{-1}$ (corresponding to ≥ 6 METs) (Troiano et al., 2008). There are no cutoffs for the sedentary time using the three-axial information from this new generation Actigraph GT3X+ accelerometer; therefore we used the previous

cutoffs which utilize the vertical-axis only. Actigraph break was considered as any bout of time in which the accelerometer count rose up to or above 100 counts·min⁻¹ and which stayed within the light-intensity physical activity (LIPA) interval (< 2020 counts·min⁻¹).

The delivery and fitting of both devices (ActivPAL and Actigraph GT3X+) to the participants were conducted face-to-face (Ward et al., 2005). The devices were activated on the first day at 6:00 a.m. and data were recorded in 15 seconds epochs. Participants were asked to record timing and reasons for every occasion the devices were removed. Although it would be useful to differentiate working from leisure time periods, participants were not told to record the times they entered and finished work.

The primary outcomes were ActivPAL's total waking time spent sitting, standing, stepping, number of steps, and the number of bouts (\leq 4 min; 5-9; 10-19; 20-29; 30-59; and at least 60 min) of uninterrupted sitting. As secondary outcome measures the number of bouts (\leq 4 min; 5-9; 10-19; 20-29; 30-59; and at least 60 min) of ActivPAL's standing and stepping and the Actigraph accelerometer's breaks in sedentary time were considered.

9.3.5. COVARIATES

Energy and nutrient intake were assessed in 3-days (one weekend-day) in each condition week, using a 24 hour diet records. Participants were instructed regarding portion sizes, supplements, food preparation aspects (boiling, grilled, frying), and others aspects (e.g., fried in olive oil or butter) pertaining to an accurate recording of their energy intake. At the last visit, records were turned in and reviewed for liquids ingestion, macro nutrient composition and total energy intake by the same technician. Diet records were analyzed using Elizabeth Stewart Hands and Associates (ESHA's) Food Processor Nutrition Analysis software for Windows version 10.0, 2013 (SQL Inc., an ESHA Company, Salem, OR, USA).

9.3.6. STATISTICAL ANALYSIS

Statistical analysis was performed using PASW Statistics for Windows version 21.0, 2010 (SPSS Inc., an IBM Company, Chicago, IL, USA). Descriptive analysis included means, SD for all measured variables. Changes in the main primary and secondary variables between control and intervention conditions and for the week-days with weekend days were individually assessed using paired sample *t*-tests. Day-by-day variations in sitting time and treatment by condition interactions were examined by repeated measures ANOVA. The distributional assumptions for ANOVA are for the normal distribution of the residuals. Therefore, normality was found for the residuals from all the main variables. To test if the randomly assigned order of treatment or the treatment by group interaction influenced the differences between conditions, the order of randomization was entered as between-subject variable and interaction with the main variables changes were checked. Statistical significance was set at 0.05.

9.4. Results

All participants completed both trial conditions and no adverse events were reported. Of the 10 participants (5-women; 5-men), 2 were overweight and 8 were obese. Mean age was 50.4 (SD=11.5; min-max=37-65) years; mean BMI was 32.6 kg·m⁻² (SD=5.50; min-max=25-41). Actigraph measured daily mean sedentary time at baseline was 688 (SD=91.2; min-max=565-846) min; mean LIPA was 170 (SD=25.4; min-max=130-193) min; MVPA was 28.1 (SD=12.4; min-max=8-27) min; and the daily mean number of steps was 4783 (SD=1365; min-max=1274-5803).

Table 9.1. Differences in sitting, standing, stepping, daily steps, and bouts of sitting, standing, stepping from different durations (N=10)

	Intervention	Control	Intervention minus Control difference	
	(Mean , SD)	(Mean , SD)	(Mean , SD)	P
During overall waking time				
Sitting time (hours·day⁻¹)	9.55 , 1.80	11.40 , 1.48	-1.85 , 1.25	0.001
Standing time (hours·day⁻¹)	5.16 , 1.82	4.39 , 1.40	0.77 , 0.99	0.036
Stepping time (hours·day⁻¹)	2.33 , 0.37	1.24 , 0.29	1.09 , 0.41	<0.001
Sit/stand transitions (number·day⁻¹)	56.90 , 9.06	53.60 , 11.00	3.28 , 7.84	0.218
Steps (number·day⁻¹)	12076 , 1934	5712 , 1335	6363 , 1953	<0.001
Sitting ≤ 4 min bouts (number·day⁻¹)	31.20 , 8.74	26.40 , 10.80	4.83 , 9.68	0.149
Sitting 5-9 min bouts (number·day⁻¹)	9.60 , 2.67	7.92 , 2.46	1.68 , 2.79	0.088
Sitting 10-19 min bouts (number·day⁻¹)	9.58 , 3.07	7.62 , 1.00	1.96 , 3.00	0.069
Sitting 20-29 min bouts (number·day⁻¹)	4.31 , 1.55	3.81 , 1.24	0.50 , 1.50	0.320
Sitting 30-59 min bouts (number·day⁻¹)	4.09 , 1.86	3.95 , 1.03	0.14 , 1.78	0.805
Sitting ≥60 min bouts (number·day⁻¹)	3.13 , 1.46	3.33 , 1.36	-0.21 , 1.03	0.542
Standing ≤ 4 min bouts (number·day⁻¹)	491 , 88.50	365 , 78.50	125 , 104	0.004
Standing 5-9 min bouts (number·day⁻¹)	5.56 , 2.92	5.55 , 2.44	0.01 , 2.51	0.995
Standing 10-19 min bouts (number·day⁻¹)	1.29 , 0.84	1.49 , 1.37	-0.21 , 0.89	0.480
Standing ≥ 20 min bouts (number·day⁻¹)	1.70 , 2.12	2.10 , 3.96	-0.40 , 3.78	0.745
Stepping ≤ 4 min bouts (number·day⁻¹)	19.10 , 6.67	3.00 , 2.71	16.10 , 6.95	<0.001
Stepping 5-9 min bouts (number·day⁻¹) *	2.94 , 1.03	0.46 , 0.42	2.48 , 1.07	<0.001
Actigraph breaks (100 counts·min⁻¹ threshold, number·day⁻¹)	506 , 106	477 , 128	29.10 , 7.50	0.085

Abbreviations: SD, standard deviation.

* The participants had no stepping bouts longer than 10 uninterrupted min on both control and intervention weeks. Therefore, the means and differences were not presented for these bouts lengths as it would be all zero.

All variables were obtained with ActivPAL except for Actigraph breaks which were obtained with Actigraph GT3X+.

For both intervention and control weeks there were no differences between week-days and weekend-days for any of the ActivPAL variables, therefore week and weekend-days were pooled together. Also, no differences were found for the dietary patterns between conditions, (mean, SD control; mean, SD for the intervention-control,

p-value); energy intake (1828, 635 Kcal; -105, 439 Kcal, 0.468), carbohydrates (239, 169 g; -36.2, 134 g, 0.416), fat (63.9, 22.9 g; -5.67, 20.8 g, 0.533), and protein (78.3, 26.2 g; -1.93, 25.8 g, 0.818).

Daily overall waking time during control week was 16.4 hour·day⁻¹ and 17.0 hour·day⁻¹ for the intervention week. Individually, reductions in waking hours sitting time varied from 4.8% (0.56 hour·day⁻¹) to 36% (4.16 hour·day⁻¹), standing time varied from 1.0% reduction (-0.05 hour·day⁻¹) to 62% increase (2.71 hour·day⁻¹), and stepping time increased from 41% (0.51 hour·day⁻¹) to 145% (1.80 hour·day⁻¹). Sitting time in 2 participants was reduced more than the target of three hours·day⁻¹ reductions, 6 reduced sitting more than one hour·day⁻¹ and 2 achieved a reduction in sitting time of less than one hour·day⁻¹.

As presented on Table 9.1, for the intervention week compared to the control week, there were significantly less daily hours spent sitting and significantly more time spent standing, stepping and a greater number of daily steps. There were no significant differences in ActivPAL-determined daily sit/stand transitions. Because the number of sit/stand transitions was not reduced, most commonly the additional standing and walking bouts were occurring continuously (i.e., slightly longer non-sitting bouts for the cumulative duration of ~ 1.85 hour·day⁻¹). This resulted in greater number of bouts of ≤ 4 min of standing and ≤ 4 and 5-9 min bouts of stepping (Table 9.1). There were no significant differences between conditions for any of the sitting bouts, standing bouts longer than 5 min, stepping bouts longer than 10 min and Actigraph breaks as defined by > 100 counts·min⁻¹. Neither the randomly assigned order of treatment nor the treatment by groups' interaction had any statistically-significant effect on these differences ($p > 0.05$). The (mean, SD) for the overall sitting time in the control and intervention conditions were 11.99, 1.19 and 10.23, 1.64 hours·day⁻¹, respectively in the group that started in the control condition followed by the intervention. The participants who performed the two conditions in an inverse order (intervention first and control afterwards) spent 10.82, 1.51 hours·day⁻¹ of sitting time during the control condition and 8.82, 2.19 hours·day⁻¹ in the intervention period.

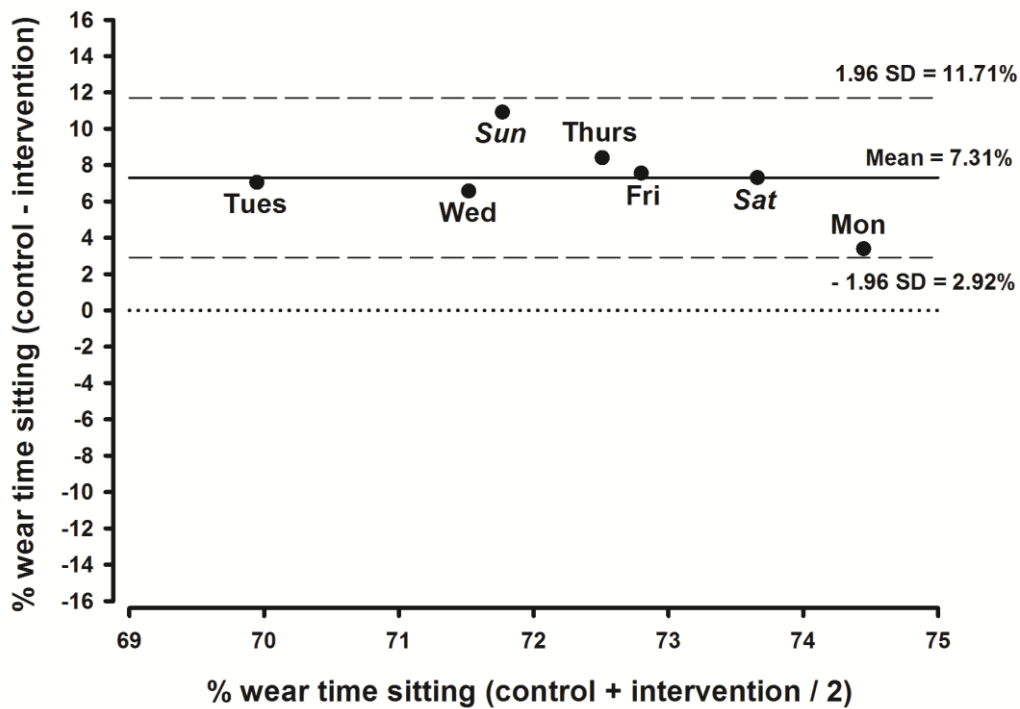


Figure 9.2. Percentage of sitting from wear-time within the trial for control and intervention weeks.

No significant day-by-day variations in sitting time ($p > 0.05$) were observed in either the control or intervention week (Figure 9.2).

On a scale of 1–10, with 1 being extremely displeased and 10 being extremely satisfied, six of the ten participants rated the program 10, (median=9.5, min-max: 8–10). The 10 participants rated the daily steps goal as the best strategy to achieve the sitting time reduction and 7 reported leisure time to be the greatest domain to perform sitting time changes.

9.5. Discussion

The results from this pilot intervention showed a reduction of $110 \text{ min}\cdot\text{day}^{-1}$ of sitting time in overweight/obese adults following a brief multi-component intervention based on prompts, telephone support, goal setting and behavioral self-monitoring.

Along with the findings from previous interventions (Barwais & Cuddihy, 2015; Pedersen et al., 2014) on the effectiveness for shifting sedentary time by walking and standing for $\sim 2 \text{ hour}\cdot\text{day}^{-1}$, we extended these results by finding that participants did not actually get up from sitting more often. While a small and short term intervention, this pilot study offers valuable insight for the rapidly growing field of research taking aim at reducing sedentary time and increasing the number of activity breaks throughout the whole day. Using the most validated device (Godfrey et al., 2007; Grant, Ryan, Tigbe, & Granat, 2006; Kozey-Keadle et al., 2011) for measuring sit/stand transitions (ActivPAL), we found that people in the real world did not get up from sitting many times per day for activity breaks.

Previous interventions that also aimed to interrupt sitting time have been effective to increase the number of daily sit/stand transitions (Evans et al., 2012; Swartz et al., 2014) but the concomitant overall reduction in sitting time was not always verified (Evans et al., 2012). Therefore, it is not yet clear how the various metrics of number and total duration of sitting time should be interpreted. However, only the numbers of sitting bouts within particular ranges of bout duration were reported in the present study and not the mean time in each of these bout length categories. While this gives a reasonable cross-sectional description of the pattern of sitting, it is less good as identifying the sorts of changes in the duration of sitting bouts falling within the ranges selected. For example, a reduction of a single sitting bout from 58 min to 31 min would be a reduction in total sitting time of 27 min, but this would result in no change in the number of sitting bouts in the 30-59 min range. Therefore, the sedentary bout categories and the selected ranges must be considered a limitation.

From our interviews with participants and the ActivPAL data regarding stepping, it appears that much of the extra non-sitting time was spent when participants went out on a slow walk. Examples of behaviors where people would perform slow and intermittent stepping and standing include more time shopping, cooking, and light non-exercise strolls in leisure time. This behavioral resistance to make more sit/stand transitions in the present study (from 54 per day to 57 per day from before to during the intervention) and other interventions (Aadahl et al., 2014) (i.e., get up from sitting more often) would be consistent with an important potentially new concept regarding human

sedentary behaviors, namely, that once people are engaged in a seated activity such as using the computer, reading a book, watching a movie, etc, people do not want to be interrupted to perform another activity even if it is potentially healthy for them (Shrestha et al., 2015).

Reflecting on the habitual number of > 60 min sitting bouts found in this workers (~ 3 bouts \cdot day $^{-1}$) and the hourly prompts for breaking sitting time it would be expected that participants did not increase the number of sit/stand transitions in a greater extent. The mean number of sit/stand transitions based on ActivPAL was about 55 \cdot day $^{-1}$ and participants did not take enough “breaks” to do their standing and walking to result in any detectable change (3.3 sit/stand transitions) in this pattern of sitting and non-sitting time. Regardless of the non-statistical differences, a similar magnitude of change in sit/stand transitions was found significant in a previous study (Smith et al., 2015). Therefore, it is curious that considering the mean daily number of > 60 min sitting bouts in the present study (~ 3 bouts \cdot day $^{-1}$), three sit/stand transitions would be sufficient to interrupt these periods of prolonged sitting time (> 60 min). Nevertheless, and acknowledging this is a pilot study, the finding that the number of sit/stand transitions did not increase during this pilot intervention may be valuable for informing the many upcoming sedentary behavior interventions taking aim at evaluating health outcomes to be more cautious about assuming that less total daily sitting time will be effectively spread throughout the whole day as desired.

Moreover, the 7.31% reduction in overall sitting time was four times greater than for previously reported sitting-reduction interventions in overweight/obese adults using treadmill working desks (Schuna et al., 2014) or by using a lock-out device to reduce TV viewing time (3.8%) (Otten, Jones, Littenberg, & Harvey-Berino, 2009). We acknowledge that the differences between our findings and these studies might be due to the fact that those studies considered a longer intervention period but also because the present study considered both work and leisure time settings (Swartz et al., 2014). Studies have been using ActivPAL in sitting-reduction interventions (Healy et al., 2013), which is a more valid measurement for distinguishing sitting from LIPA (Harrington, Welk, & Donnelly, 2011). However, in contrast to a workplace intervention that included both normal weight and overweight/obese adults, also used

ActivPAL devices, a multi-component intervention, and reduced sitting time by 89 min/8 hour workday and 33 min in the workstations-only group (Neuhaus, Healy, Dunstan, Owen, & Eakin, 2014), the present results (110 min·day⁻¹) show a major reduction in overall daily sitting time, suggesting that focusing not only on workplace but also considering strategies to reduce sitting time in non-work settings may enhance the effectiveness of these interventions (Swartz et al., 2014). Another study that considered work, commute and leisure time was able to reduce muscle inactivity time by 33 min·day⁻¹ with a simple tailored counseling in both normal weight and overweight/obese adults (Pesola et al., 2014). Therefore, the multiuse of different strategies to reduce sitting time in the present pilot study seemed to improve the effectiveness of these sitting-reduction interventions on reducing total sitting time but not to increase the number of activity breaks throughout the day.

Considering leisure time only interventions, based on the actual daily step change (~ 6000 steps) we anticipate that the inclusion of higher daily step goal than have been purposed (1500-2000 steps·day⁻¹) (Adams et al., 2013) would result in higher stepping times, which could indirectly contribute for reducing sitting time (Tudor-Locke, Burton, & Brown, 2009). The number of breaks in sedentary time showed no significant differences between the two conditions (0.60 breaks sedentary·hour⁻¹) but Actigraph measurement of “breaks” is not a measurement of sitting to standing transitions but rather it is the transition from being motionless to moving, which occurs during standing also. Thus the large number of breaks by acceleration is a metric of change in movement rather than posture. Regardless, our findings were similar to a previous study (0.64 breaks sedentary·hour⁻¹, p=0.005) including overweight/obese adults (Parry, Straker, Gilson, & Smith, 2013) which reinforces the idea that people are resistant to increase the number of breaks in sitting time even though significantly reducing total time spent sitting. There were also no differences in the number of prolonged sitting bouts of any duration between the two weeks, but the absence of these differences may be explained by a shortening of the sedentary bouts within the duration categories (e.g., a change from 58 to 31 min in prolonged sitting time) as opposed to across them (e.g., a change from 31 to 29 min). Likewise the example presented above, similar cases would justify the significant reduction in total sitting time without a

correspondent change in the number of prolonged sitting bouts. However the number of ≤ 4 min bouts of standing and ≤ 4 and 5-9 min bouts of stepping were significantly higher in the intervention week compared to control week. While there are hundreds of standing bouts, there are only 50-60 sitting bouts. Therefore standing bouts are broken predominantly by stepping bouts (usually < 1 min step bouts).

The lack of significant differences for the sitting bouts may also be related to the large variability concerning the free-living conditions and the small sample size. In fact, this study was not powered for this hypothesis, representing a limitation. Furthermore, the fact that our daily step goal was higher than in previous interventions may justify the need for participants to perform longer walking bouts and consequentially they had fewer opportunities to break up sitting time. Methods to induce more breaks in sedentary time over the whole day are challenging in free-living conditions and the present pilot study shows that it will be harder than expected to change this than simply getting people to go on one or two longer strolls/standing bouts.

The nonexistence of a washout period between the two conditions could be considered a fair limitation to this study given that, it is a lifestyle intervention and some behavioral carryover might exist for the group that started with the intervention condition and then participants would continue the intervention regardless of being in the control group. This possible response would lower the difference in sitting time between the two conditions. However, neither the randomly assigned order of treatment nor the treatment by groups' interaction had any statistically-significant effect on these differences and no carryover existed, as in fact, the group that started with the intervention condition was the one presenting higher differences between control and intervention conditions. Regardless, there was a trend for this group to present lower overall (control and intervention) sitting time compared to the group that started with the control condition.

The lack of a good measure to distinguish work-time from leisure time makes it difficult to objectively understand in which domain the major changes in sitting time occurred and also what strategy from this multi-component intervention was more successful. These are some limitations that future interventional studies should be awareness about. Regardless, based on participants' choices, the daily step goals was

the most easy understood strategy for reducing sitting time and leisure time the setting in which 7 in 10 reported as being easily to reduce sitting time. The small sample-size and the short-term duration of the trial are probably the main limitations of this pilot study. However the results are important for guiding the rapidly emerging field because we found with the most valid measurement tools for sitting time and breaks from sitting, that even when making moderate reductions in overall sitting time of almost 2 hours·day⁻¹, overweight/obese people did not to get up from sitting more frequently than normal. While small effectiveness studies could obviously use prompts (“alarms”, text messages, or other reminders) throughout the day to get up from sitting, it is perhaps important for scalable behavioral change in large numbers to carefully design behavioral studies that recognize that getting up from sitting when engaged in most tasks may be the hardest measure of sedentary behavior to make long-term changes.

Strengths of our pilot intervention include the cross-over randomized controlled trial design, the focus on overweight/obese adults (who are an understudied population group in interventions that target reductions in sitting time) the use of a multi-component intervention that extended strategies to the non-work settings, and also the use of objective and accurate measures of sitting time (ActivPAL) (Godfrey et al., 2007; Grant et al., 2006; Kozey-Keadle et al., 2011). Non-work days and leisure time activities like TV viewing time or computer screen-time also contribute to overall sedentary profile (Otten et al., 2009) and the present study adds to the scientific findings by taking a broader approach to influencing overall sitting time. Also, a strength of this study was the fact that changes in dietary patterns were monitored and no differences were observed between conditions, meaning that participants did not increase their food intake in response to a higher activity level.

9.6. Conclusions

The results from this pilot study suggest that a multi-component intervention focusing not only on the work environment but also on the reduction of sitting time throughout the whole day may result in greater changes than single-context interventions. The magnitude of sitting time changes in this pilot study along with the poor increases in the number of sit/stand transitions and the utilization of objective

measures justify future investigations aiming to replicate the present approach on a larger scale and understand if most effective real world interventions are going to be found easily.

9.7. References

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CHAPTER 10

General Discussion

10.1. Overview

In the past decade, PA and public health research has shifted its focus to the harms of sedentary behavior. Despite meaningful advances in the investigation of sedentary behavior and its deleterious effects, the majority of the information comes from cross-sectional data and used poor measures of sedentary behavior. Therefore, there is still uncertainty as to its forms of accumulation may or may not affect certain health parameters (Chastin, Egerton, Leask, & Stamatakis, 2015; Larsen et al., 2015). In a way, some of the uncertainty that exists on sedentary behavior research area is explained by the lack of well-designed studies (Chastin et al., 2015) and the possibility of reverse causation (i.e., does sedentary behavior cause disease or vice versa), lack of a widely accepted and consistently applied operational definition of sedentary behavior, a general lack of physiologically based studies, and finally reliance on self-reported estimates instead of objective measures of sedentary behavior (Barreira, Zderic, Schuna, Hamilton, & Tudor-Locke, 2015).

Several objective methods to measure sedentary time and its patterns have been currently used in the past years but studies aiming to specifically assess the validity of these methods to detect interruptions in these behaviors (breaks) are lacking (Barreira et al., 2015). The first study on this thesis sought to assess the validity of the widely used objective method in the field (Actigraph accelerometer) and estimate the error associated with its use, specially for sedentary behavior patterns of accumulation (breaks from sedentary time). Additionally, this study aimed to examine the validity of a motion sensor that combines the information from accelerometry and HR (Actiheart) which has been shown to accurately estimate PAEE compared to the gold standard doubly labeled water technique (Silva et al., 2014).

By combining accelerometer and HR data, Actiheart may prevent accelerometer misclassification when low body movement (but high HR) exists and regardless of being a recognized device to estimate MVPA it was never utilized for sedentary behavior assessment. From this methodological study it was concluded that Actigraph accelerometer presented a better agreement with the reference method than Actiheart. Regardless of the potential error in estimating sedentary time and breaks from sedentary

time at the individual level, Actigraph accelerometer was valid at a group level. Furthermore, adding a physiological indicator (HR) to the accelerometry information did not improve sedentary behavior estimation or enhance sensitivity for detecting interruptions in sedentary pursuits.

Overweight affects more than a billion adults worldwide. Both general and abdominal obesity have been shown to be a risk factor for morbidity and mortality, and all health organizations have focused increasingly on a perceived obesity epidemic said to pose drastic threats to public health. Recently, a group of experts was invited by Public Health of England and a UK community interest company to provide guidelines for employers to avoid prolonged periods of sedentary work (Buckley et al., 2015). The set of recommendations was developed from the totality of the current evidence, including largely observational and retrospective studies and short-term interventional studies of getting workers to stand and/or move more frequently (Buckley et al., 2015). While longer term intervention studies are required, the level of consistent evidence accumulated to date and the public health context of rising chronic diseases suggest initial guidelines are justified (Buckley et al., 2015).

The problem of overweight and obesity has therefore proceeded as one of the most regular global issues and results from excessive fat mass accumulation resulting from an energy imbalance, favoring increases in EI, decreases in EE or a combination of both. Therefore, using the Actigraph accelerometers in a representative sample of Portuguese older adults, study 2 contributed to the evidence accumulated to date by adding more specific information on the associations for objectively measured sedentary patterns (bouts of sedentary time of distinct durations) with abdominal obesity. Older people are the most sedentary and understudied group in the population and also the ones presenting higher obesity levels. Thus, regardless of the cross-sectional data, this study added important information on how prolonged sedentary time may be positively associated with abdominal obesity in older adults. However, clear recommendations as to the amount and duration of bouts spent in sedentary behavior to avoid compromising health does not exist yet.

In addition to the methods' choice limitation, there is another concern that has not been addressed yet. Despite suspecting that the hazards of spending too much time

in sedentary behavior are not offset by greater MVPA, whether this independence remains when a much higher MVPA exists was never investigated. Recent epidemiological evidence suggests that sedentary behavior may increase risk for early mortality even if individuals perform regular defined exercise (van der Ploeg, Chey, Korda, Banks, & Bauman, 2012). These data are difficult to reconcile. Does this mean that an elite endurance athlete with very high aerobic capacity who spends 1-2 hours a day performing exercise training is at an increased risk for disease if they spend the rest of their day in sedentary pursuits (office job)?

Therefore, the third study represents a novelty as it explored the associations for sedentary behavior with adiposity measures in a highly active population for the first time. It was found that in highly trained athletes, the amount of sedentary behavior was positively associated with total and trunk fat mass measured by DXA. This study suggests that even performing high levels of MVPA, the low EE that characterizes sedentary behavior together with the excessive amount of time spent in these behaviors may explain the associations found for sedentary behavior with total and regional fatness.

Although there is research on the EE associated with some types of NEAT behaviors, such as sitting, standing, or even some specific forms of these behaviors (e.g., sitting to read, sitting using computer, standing writing), no study have examined the EE associated with the highly proclaimed “breaks” or the simple act of transitioning between sitting and standing, an action that happens several times during the day and that has been the target of some recent interventions. Therefore, study 4 represents an innovation to the field by addressing this issue.

The findings from study 4, showed a modest energetic cost associated with breaks from sedentary time but considering the experimental evidence on the metabolic benefits of these interruptions, study 5 examined the associations for the number of breaks from sedentary time with abdominal obesity in older adults. Again, the elderly are the most sedentary group in the population and the ones presenting higher obesity levels. Therefore, this study added relevant information by finding a cross-sectional inverse association for the number of breaks from sedentary time with WC, independently of MVPA and total sedentary time, in older women only.

Finally, with a small and acute intervention (study 6) it was possible to understand the main barriers and difficulties when the aim is to reduce and break up sedentary behavior by increasing NEAT, in overweight/obese sedentary adults, using a multicomponent intervention that focus on both workplace and leisure time settings.

To better understand the interconnection established between the six research studies included in this thesis, Figure 10.1 illustrates and summarizes the rationale for the sequence and organization of such studies within the thesis.

In summary, the present thesis focused on sedentary behavior and added to the scientific knowledge by exploring: 1) the validity of two objective methods to estimate total sedentary time and its patterns; 2) the associations for sedentary time and its patterns with body composition in three observational studies (studies 2 and 5 considering the whole-body level of body composition analysis and study 3 the molecular level of body composition analysis); and finally 3) two experimental studies, one EE basic science related study, and a pilot study that aimed to assess the effectiveness of an intervention to alter sedentary behavior and its patterns, considering both work and leisure time settings.

An exhaustive discussion of each of the six studies' main findings was included in the respective chapters. The rationale of this section was to gather and integrate the contributions of the six studies, by summarizing the main results and globally reflecting on the implications for future research and practical applications. Limitations of these studies and future research avenues are also disclosed.

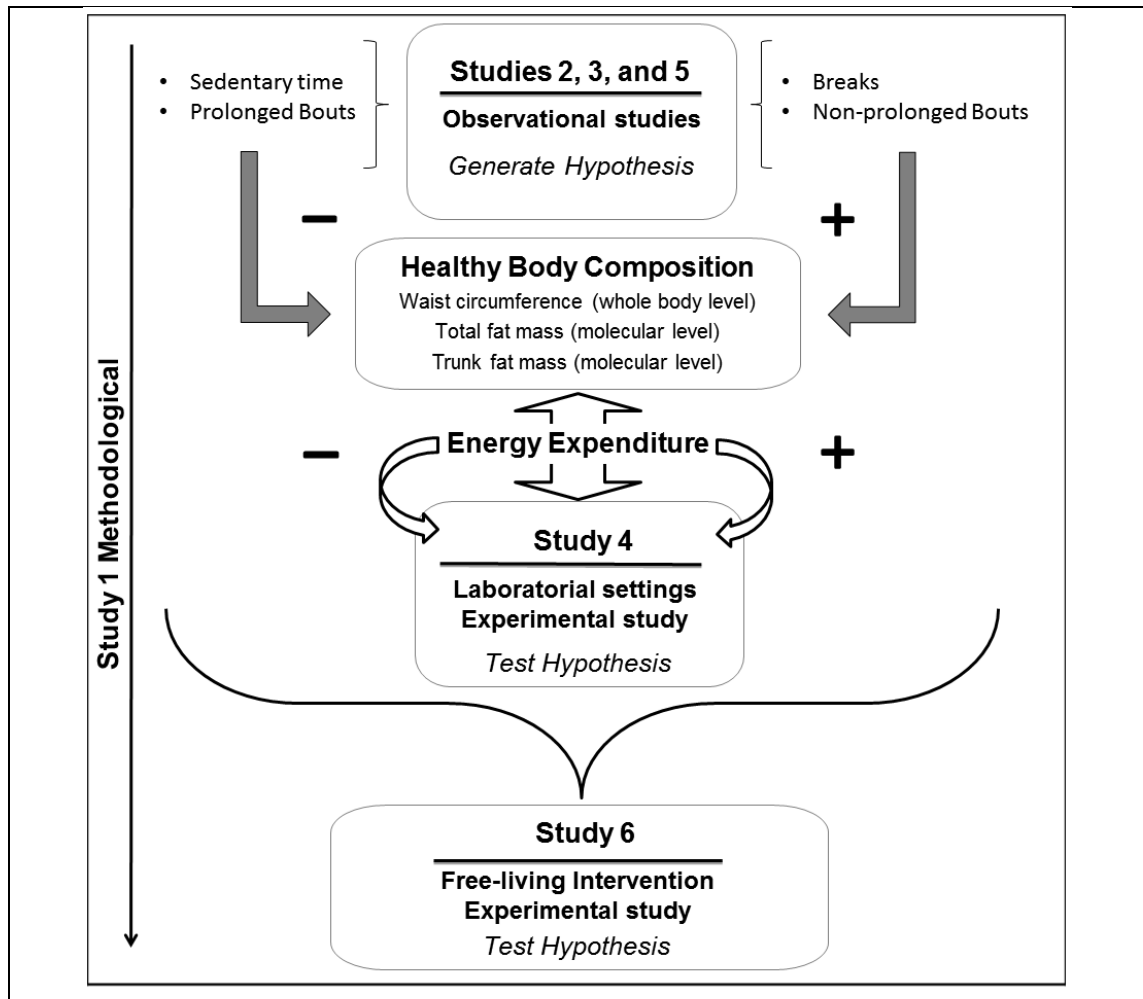


Figure 10.1. Interconnection between the six studies from the present dissertation.

10.2. Main research findings

There is still some tendency to cogitate sedentary behavior as a lack of MVPA. However, MVPA represents only a small fraction of total daily movement (Colley et al., 2011) and does not compete with sedentary time (Tikkanen et al., 2013), a behavior that adults engage approximately 9.5 hours per day (69% of waking hours) (Colley et al., 2011). Evidence have been shown that sedentary behavior has deleterious effects on human's health and suggest that these effects are responsible for an increase in the risk for obesity (Chau, van der Ploeg, Merom, Chey, & Bauman, 2012; Church et al., 2011; Hamilton, Hamilton, & Zderic, 2007; Hu, Li, Colditz, Willett, & Manson, 2003; Inoue et al., 2012; Thorp et al., 2010), cardiovascular impairments (Ford & Caspersen, 2012; Grontved & Hu, 2011; Helajarvi et al., 2014; Kim, Wilkens, et al., 2013; Wilmot et al.,

2012), and metabolic harms, that are independent of whether adults meet MVPA guidelines (Alkahtani, Elkilany, & Alhariri, 2015; Bankoski et al., 2011; Chastin et al., 2015; Chau et al., 2015; Gennuso, Gangnon, Thraen-Borowski, & Colbert, 2015; Kim, Tanabe, Yokoyama, Zempo, & Kuno, 2013; Kozey Keadle et al., 2014).

However, as presented in chapter 2, both observational and experimental studies have found contradicting results and a recent meta-analysis indicates that, among other reasons, the confusing findings may be explained by the reliance on self-reported estimates instead of objective measures for sedentary behavior (Barreira et al., 2015). In the present thesis, three different objective measures were used to examine sedentary behavior: sedentary time (hip mounted accelerometers and chest mounted accelerometers combined with HR) and sitting time (thigh mounted inclinometers). The relevance of utilising these measures is reflected in Australia's Physical Activity and Sedentary Behavior Guidelines, (The Department of Health 2014) which comprises both a recommendation for limiting screen time and one for reducing and breaking up sitting time, thereby requiring an objective measure of postural allocation.

ActiGraph accelerometer was one of the measures of sedentary behavior used in this thesis. This method enables to examine bout lengths and breaks in sedentary time as it provides objective date and time stamped information, however studies examining its accuracy in measuring sedentary patterns are scarce. It is unlikely that this type of behavioural information could be captured by self-report, and that is one of the advantages of using these objective methods. The updated definition of sedentary behavior (SBRN 2012) reflects the value of additionally utilising different types of measures for sedentary behavior, with a component that addresses EE (≤ 1.5 METs) and postural allocation (sitting).

Furthermore, Actiheart is a combined HR and motion sensor that was already shown to be an accurate method in estimating EE compared to a gold standard (doubly labeled water) (Santos et al., 2014) but was never used to specifically estimate sedentary behavior or breaks from sedentary time. The use of the ActivPAL device in sedentary behavior research has increased rapidly in recent years (460% increase from 2008 to 2014 on the Scopus citation database), and it has been presented as the best objective method to assess sedentary behavior, more specifically sitting time and transitions

between sitting and non-sedentary behaviors (Dahlgren, Carlsson, Moorhead, Hager-Ross, & McDonough, 2010; Dowd, Harrington, Bourke, Nelson, & Donnelly, 2012). Therefore, study 1 adds to the methodological field of sedentary behavior by examining the validity of GT3X and Actiheart to estimate sedentary time and breaks from sedentary time, using ActivPAL as the reference, in free-living conditions.

For ActivPAL, sedentary time was measured directly based upon posture (sitting/reclining); Actiheart, the presumed MET cutpoint for sedentary time (< 1.5 METs) based on accelerometry + HR; GT3X, the traditional < 100 counts \cdot min $^{-1}$. A break in sedentary time was defined as when the participants were above the aforementioned cutoffs. The findings from this study showed that GT3X overestimated and Actiheart underestimated sedentary time (bias=135 min; bias=-156 min, respectively), and both methods overestimated breaks from sedentary time (bias=78; bias=235 breaks, respectively). This study presented a relatively low agreement for both GT3X and Actiheart with ActivPAL for sedentary time and breaks in sedentary time estimations. However, at the group level, GT3X provided acceptable validity in estimating sedentary time.

The main conclusion from this methodological study was that breaks in sedentary time are typically inferred from time-stamped accelerometer data indicating a transition from lack of movement (recording of < 100 activity counts \cdot min $^{-1}$) to relatively more movement (≥ 100 activity counts \cdot min $^{-1}$). Therefore, these breaks do not actually represent sit-to-stand postural transitions and accelerometers do not precisely record the end of a sedentary behavior bout, but rather estimate it via a count threshold, which has been shown to have low accuracy (Barreira et al., 2015).

This might in part explain the lack of consistent evidence regarding the associations for sedentary patterns with health parameters, and future research should consider using measurement instruments such as posture sensors to more accurately detect the end of sedentary behavior bouts and correctly estimate interruptions in sedentary time. Additionally, the new finding that a method combining accelerometry with HR data (Actiheart) did not improve the accuracy of the accelerometry-only method to estimate sedentary behavior or sedentary patterns is relevant to inform future studies in the sedentary behavior research area. Furthermore, study 1 confirmed

previous findings (Santos et al., 2014) that Actiheart has a considerable rate of equipment failure, which limits its usefulness.

Evidence from "inactivity physiology" laboratory studies have identified unique mechanisms that are distinct from the biologic bases of exercising (Hamilton, Healy, Dunstan, Zderic, & Owen, 2008) and one of the driving hypothesis is that the lack of frequent engagement of the antigravity muscles, particularly the large muscles of the lower limbs, results in detrimental physiological processes and adverse cardiometabolic profile (Hamilton et al., 2008). The protective effect of MVPA on health outcomes relates to improvements in cardiorespiratory fitness through increased oxygen supply to the myocardium and improved myocardial contraction, as well as lower blood pressure, improved LPL profile, and increased insulin sensitivity (Page, Peeters, & Merom, 2015). The main biological mechanism proposed for sedentary behavior relates to cardiometabolic changes associated with decreased LPL activity (associated with increases in plasma triglycerides and decreases in HDL-cholesterol) (Hamilton, Hamilton, & Zderic, 2004), which are associated with coronary heart disease, type 2 diabetes and obesity (Saleh et al., 2015).

It is hypothesized that chronic exposure to sedentary behavior reduces skeletal muscle contractile activity (Pesola et al., 2015) which, independently of MVPA and concomitant changes in LPL messenger RNA (Hamilton et al., 2004), evokes a process of suppressing the amount of capillary LPL in the muscle (Page et al., 2015). However, the association between muscle inactivity and cardiometabolic outcomes has not been shown with direct measures (Pesola et al., 2015). Interestingly, a recent study (Pesola et al., 2015) examined the associations between electromyography (EMG)-derived muscle inactivity and activity patterns and cardiometabolic biomarkers in healthy, physically active adults, and found that muscles were inactive for 65% of the measurement time and that compared to those in the lowest muscle inactivity quartile (< 56% of measurement time), those in the highest quartile (> 75% of measurement time) had lower HDL cholesterol and higher triglycerides independent of moderate-to-vigorous muscle's EMG activity (Pesola et al., 2015).

Conventionally, sedentary time is measured as a lack of impact (accelerometer), as a systemic response to movement (HR), or as a postural difference over a certain

time period (inclinometer). In this study however, sedentary time was defined as a lack of any muscular activity in major locomotor muscles providing a measure which is the primary source for the outcomes assessed by the conventional methods (Pesola et al., 2015). Additionally, another study using EMG (Tikkanen et al., 2013) found that thigh muscles were also inactive over 65% of the time and only a fraction of muscle's maximal voluntary strength capacity is used during normal daily life (4%), which is below the mean EMG level required for walking (Tikkanen et al., 2013). These two studies suggest that the daily amount of sedentary behavior assessed by EMG is in accordance with the findings from accelerometry data also showing the same amounts of daily time in sedentary behavior. So using accelerometers to estimate sedentary behavior may be reasonable.

Irrespective of the consistent findings for the metabolic harms of prolonged sedentary behavior, the associations with obesity and adiposity measures are not so clear, with some studies reporting no relation between adults' overall sedentary time and total fat mass (Foong et al., 2014) or abdominal obesity (McGuire & Ross, 2012; Saunders et al., 2013). A recent intervention (Saleh et al., 2015) found that those who decreased sedentary time by 30 min or more per day had a greater reduction in body weight and BMI than those who did not (Saleh et al., 2015), but how sedentary patterns may affect obesity was not investigated in this study. Similarly, studies examining how sedentary patterns associate with obesity parameters in the elderly are scarce.

Therefore, the present thesis makes a contribution to the evidence base concerning total and accumulated sedentary behavior and associations with obesity risk. Studies 2 and 5 contributed to the literature by generating the hypothesis that in older adults, total sedentary time may not be the most important predictor for abdominal obesity but instead the pattern of accumulation seems to play a key role in abdominal obesity, independently of MVPA and total sedentary time. In study 2, it was found that in addition to time spent in MVPA, avoiding sedentary periods longer than 10 min may have potential public health implications for the prevention of abdominal obesity in older adults. The 10 min threshold might be the more conservative estimate to capture the prolonged nature of sedentary behavior.

Regardless of the cross-sectional data, our findings are confirmed by a recent study that found the same threshold when considering a representative adult sample (Kim, Welk, Braun, & Kang, 2015), indicating that durations longer than 10 min were generally associated with increased risk factors (Kim et al., 2015). Furthermore, study 2 showed progressively higher odds for abdominal obesity if they spend more than 20, 30 and 60 min in continuous sedentary time. Based on the higher increments for the odds of abdominal obesity for each 1 hour prolonged sedentary bout (48%) compared to the shorter sedentary bouts' lengths and knowing that breaking up sedentary time every 10 min can be less feasible, the message should be that older adults must avoid spending more than 1 hour prolonged sedentary time.

Recent guidelines (Buckley et al., 2015) state that workers must aim to initially accumulate at least 2 hours·day⁻¹ of standing and LIPA (light walking) during working hours, eventually progressing to a total accumulation of 4 hours·day⁻¹. Additionally, seated-based work should be regularly broken-up with standing-based work and vice versa. Although these recommendations did not find sufficient evidence to establish specific thresholds for the highest duration of sedentary bouts, they stated that it is important to break up sedentary time more often (Buckley et al., 2015).

Our cross-sectional findings that prolonged sedentary bouts are deleterious to the risk of abdominal obesity (study 2) and that introducing LIPA breaks in sedentary behavior will reduce the risk of abdominal obesity (study 5) generate the hypothesis that interrupting sedentary behavior more frequently must be recommended in older adults. In fact, findings from a recent experimental study (Takahashi, Miyashita, Park, Sakamoto, & Suzuki, 2015) confirm these hypothesis and showed that one day of sitting elevated the postprandial oxidative stress on the next day, but interrupting sitting time with standing bouts and acute exercise prevented an elevation of the postprandial oxidative stress markers (Takahashi et al., 2015), thus suggesting that the benefits of interrupting sedentary behavior not only manifest acutely.

Older adults, are the age group that most suffers from chronic conditions and also the ones presenting lower functional independence. Thus, it may be difficult to increase their levels of MVPA due to some physical incapacity and also because of social drive to be inactive (Chastin, Fitzpatrick, Andrews, & DiCroce, 2014). Therefore,

the findings that increasing the number of LIPA breaks in sedentary behavior is associated with metabolic and physiological benefits, independent of MVPA, are very important in this population group. Our results on the associations for prolonged sedentary bouts with abdominal obesity risk being independent from LIPA and MVPA go along with recent findings (Loprinzi, 2015) that sedentary behavior is associated with multimorbidity (independent of LIPA and adherence to MVPA guidelines), which underscores the importance of minimizing prolonged sedentary behavior (in addition to promoting PA).

In line with this, study 3 brings a novelty to the field of sedentary behavior research by indicating that similarly to what occurs in the general population, individuals with high levels of MVPA (highly active athletes) also presented a positive association between reported time spent in sedentary behavior and total and trunk adiposity, regardless of the weekly exercise training. This was the first study examining the associations for sedentary behavior with adiposity measures in a highly active population group and contributed to the field by showing that the associations found for sedentary behavior with adiposity outcomes, remained independent of MVPA, even when high levels of exercise are considered.

Thus, programs engaged exclusively on MVPA may overlook an area that is of vital importance to obesity control. Along with recommendations to accumulate at least 150 min·week⁻¹ of MVPA, such interventions might be more effective if individuals are further encouraged to avoid very prolonged bouts of sedentary time. Moreover, the fact that sedentary behavior was found to be associated with higher adiposity, even when considering an highly active population, suggests that the low EE associated with sedentary behaviors (Pulsford, Stamatakis, Britton, Brunner, & Hillsdon, 2015) seems to somehow explain and favour a positive energy balance. Therefore, understanding what is in fact the metabolic and energy cost of sitting, standing and sit/stand transitions or breaks in sedentary time is a priority.

Additionally, the cross-sectional nature of the majority of studies that found positive associations for the breaks in sedentary time with health parameters do not allow to understand if the observed effects could be attributed to the introduction of LIPA rather than to the act of breaking up sedentary time. If breaking sedentary

behavior is the key component, then standing breaks would be expected to have similar effect to walking breaks, which was not the case in a recent meta-analysis (Chastin et al., 2015). Similarly, to date, none of the experimental studies presented a measure of EE, therefore it is not clear if the effects reported are owing to a reduction in sitting, the addition of activity, or the action of breaking.

Understanding the effects of interrupting sedentary behavior is challenging as the number, duration, and intensity of breaks can all be manipulated. Ideally, one of the parameters (breaks' dose) should be tested while controlling for the others. However, this was rarely seen in the studies reviewed, leaving a lot of uncertainty. Study 4 added that the low metabolic rate when standing is not altered much (5-8%) when compared to continuous sitting, and that this is independent of sex and body composition. More importantly this was the first study to determine the metabolic cost of a single sit/stand transition and found it to be about 0.32 kcal. A significantly higher MEC for the sit/stand transition when performed once per min compared with sitting (35%) and standing (28%), in both normal weight and overweight/obese men and women was found. If an individual simply stood-up and returned to the seated position (sit/stand transition) an additional 10 times every hour during an 8 hour working day, it would theoretically expend an additional 120 kcal or more in a full 5 day working week.

Although the aforementioned example appears to be unrealistic, it must be emphasized that standing or walking breaks that comprise minutes of “non-working” time are not being contemplated but the inclusion of brief breaks “stand-up and return to the seated position” actions, which would only take approximately 3-5 seconds. Based on the previous question whether the benefit came from the act of breaking or the introduction of activity resulting from those breaks, our findings seem to indicate that from the energetic point of view, the gain is associated with the breaking behavior itself. In fact, as stated in chapter 2, research have been presenting that some metabolic pathways benefit with the simple act of breaking up sedentary time, with muscle contraction playing a relevant role on human metabolic health (Pesola et al., 2015).

Along with some other recent findings (Chastin et al., 2015; Kim et al., 2015; Lyden, Keadle, Staudenmayer, Braun, & Freedson, 2015), the emphasis must be placed on the recommendation to break sedentary behavior more often rather than shifting

great amounts of sedentary behavior for standing activities. Additionally, there is evidence that similar to the risks of prolonged static seated positions, so too should prolonged static standing postures be avoided (Buckley et al., 2015; Pope, Goh, & Magnusson, 2002).

Recent trials have shown significant reductions in workplace sedentary behavior (Adams, Davis, & Gill, 2013; Alkhajah et al., 2012; Cooley, Pedersen, & Mainsbridge, 2013). Also, interventions using prompts to disrupt sitting time and increase PA at work have been shown to effectively increase the number of breaks in sitting time (Parry, Straker, Gilson, & Smith, 2013), and reducing the number of bouts in prolonged sedentary time (Evans et al., 2012; Pedersen, Cooley, & Mainsbridge, 2014; Swartz et al., 2014). After conducting a retrospective of the main findings resulting from the other five studies in this thesis, the knowledge gained throughout the process was used, and the natural step was to carry out and examine the effectiveness of an intervention to reduce and break up sitting time (study 6).

Based on the findings from study 2 it would be logic to target the inclusion of a break in sedentary time every 10 min, however this would not be feasible in the workplace settings, therefore reducing sitting time at the workplace by breaking up their sitting time for approximately 5-10 min every hour through taking part in LIPA activities (standing and walking) was aimed. During transportation/home/domestic-leisure time contexts, individual goals for the number of steps·day⁻¹ were set by adding 6000 steps to their initial habitual daily amount. Also, generic strategies to reduce and break up sitting time were suggested and participants identified strategies specific to their circumstances in their work, transport, and home contexts, for attaining their goal (3 h-reduction in sitting time).

The main findings from study 6 suggest that a multi-component intervention focusing not only on the work environment but also on the reduction of sitting time throughout the day may result in greater changes than single-context interventions. This short-term intervention resulted in a mean reduction of approximately 2 hours of sedentary time per day, which significantly exceeded the results from previous interventions (Burke et al., 2013; Martin et al., 2015; Prince, Saunders, Gresty, & Reid,

2014), and is in accordance with the new set of recommendations from the expert statement commissioned by Public Health England (Buckley et al., 2015).

A recent publication (Gardner, Smith, Lorencatto, Hamer, & Biddle, 2015) identified studies through existing literature reviews, and interventions were categorised as 'very promising', 'quite promising', or 'non-promising' according to observed behavior changes. Twenty-six eligible studies reported thirty-eight interventions, of which twenty (53%) were worksite-based. Fifteen interventions (39%) were very promising, eight quite promising (21%), and fifteen non-promising (39%). Very or quite promising interventions tended to have targeted sedentary behavior instead of PA (Gardner et al., 2015). Interventions based on environmental restructuring, persuasion, or education were most promising. Self-monitoring, problem solving, and restructuring the social or physical environment were particularly promising behavior change techniques (Gardner et al., 2015). Therefore, the results from our intervention seem to go along with these findings, once it was also found that interventions might most fruitfully incorporate self-monitoring and goals to succeed.

Furthermore, the good results found in this intervention and the fact that leisure time was considered, support recent findings (Walsh, Umstadd Meyer, Stamatis, & Morgan, 2015) that sedentary time in one segment of life (work) predicts time spent sitting in other areas of life (leisure time) and that workers who spend more time in sedentary pursuits during working hours do not compensate by being more active on non-working periods (Clemes, Patel, Mahon, & Griffiths, 2014). Thus, the two domains must be target when aiming to reduce overall sedentary time. Regardless, few interventions have considered the non-work domains (weekday's leisure time and weekend days) (Miller & Brown, 2004; Tudor-Locke, Burton, & Brown, 2009) and there is a need for more interventions that additional to focusing on the workplace context, also target leisure time contexts (Clemes et al., 2014).

Finally, the magnitude of sitting time changes in study 6 were not accompanied by increases in the number of sit/stand transitions. Regardless of using a specific strategy to break up sedentary time (computer prompts), the low prompting frequency (one prompt every hour) may justify the non-significant increases in the number of daily breaks. Another reason might be, a natural resistance to break up sitting time more

often, even when significantly reducing sedentary behavior. In fact, a similar trend was observed in a recent intervention that also aimed to reduce sedentary time and increase the number of breaks (Rosenberg et al., 2015). Thus, future investigations aiming to replicate the present approach on a larger scale are needed to understand if most effective real world interventions to break up sedentary behavior are going to be found easily.

In order to gain further insight into interventions targeting sedentary time, the effect of behavioral change needs to be studied across the whole PA spectrum with objective measures. Given that the key mechanism proposed for the associations of sedentary time with health is lack of muscular activity, it is important to measure the changes in this outcome. Thus, a recent study (Pesola et al., 2014) examined whether an intervention designed to reduce and break up sedentary time, decreased muscle inactivity measured by EMG (Pesola et al., 2014). The findings showed that a simple tailored counseling was able to reduce muscle inactivity time by 33 min, which was reallocated to 21 min of light muscle activity (Pesola et al., 2014). By extending the findings from previous interventions (Walsh et al., 2015) this study concluded that selecting more specific measures of sedentary time (e.g., EMG) may improve susceptibility to detect changes resulting from these interventions.

10.2.1. CONCLUSIONS

This thesis adds relevant information to the literature related to sedentary behavior by including observational studies that generated important questions, and experimental studies addressing basic knowledge about EE-related sedentary patterns and translational knowledge, by testing the effectiveness of manipulating sedentary patterns. At the methodological level, Actigraph accelerometers presented modest but significant accuracy to estimate sedentary behavior and its patterns compared to ActivPAL but Actiheart did not. A cross-sectional study including older adults found associations for prolonged sedentary time with abdominal obesity independent of MVPA, and another study raised the hypothesis that breaks from sedentary time were inversely associated with abdominal obesity in older women but not men. Additionally,

an association for sedentary behavior with body fatness was observed in a population engaged in high levels of PA.

The determination of the metabolic and energy cost associated with a transition or "break" (35% above sitting) was conducted in a basic experimental study that also found standing not to elevate energy cost by a great amount compared to sitting. Finally, a pilot intervention found that considering strategies that target more than only the work environment will bring advantages, as some resistance for participants to perform a greater number of "breaks", seems to exist. Finally, the most important elements of experimental studies are manipulation and control. Manipulation means that something is purposefully changed by the researcher in the environment and control is used to prevent outside factors from influencing the study outcome. In our opinion, sedentary behavior's research area needs more studies to manipulate and control the outcomes, in order to be more confident that the manipulation "caused" the outcome.

10.3. Practical implications and future directions

In this section, the practical findings derived from the studies were summarized to the real-world settings.

10.3.1. FROM THE METHODOLOGICAL STUDY

- Although different methods may have acceptable validity to measure sedentary time, it is important to understand that they measure different phenomena. Therefore, caution must be taken once comparing sedentary estimates from distinct methods.
- Sedentary behavior and its limits are better defined by changes in posture than intensity, however GT3X accelerometer is a valid method at group level.
- Actiheart, an accelerometer coupled with a physiological indicator (HR), is not a valid method for sedentary behavior or breaks from sedentary time estimations.

10.3.2. FROM OBSERVATIONAL STUDIES (HYPOTHESIS)

- For obesity control, sedentary time should not be seen as a whole, but rather the sum of the parts. That is, the focus should be on how sedentary time is accumulated instead of the total time spent in this behavior.
- Older people must avoid spending prolonged sedentary time and introduce frequent LIPA breaks.
- There are associations for sedentary behavior with measures of adiposity even in highly active population.
- Breaks from sedentary time are inversely associated with abdominal obesity in women but not men.

10.3.3. FROM EXPERIMENTAL STUDIES

- The metabolic and energetic cost associated with the simple act of breaking sedentary time is 35% higher than sitting.
- The rise in metabolic rate when standing is not elevated by a great amount (5–8 %) when compared to continuous sitting, regardless of sex and body composition.
- A multi-component intervention focusing not only on the workplace domain but also including strategies to reduce and break up sedentary behavior in the leisure time is more effective.
- When overweight/obese adults attempted to reduce sedentary time by walking and standing more than usual, they did not actually get up from sitting more often. There seems to be a behavioral resistance to make more sit/stand transitions.

10.4. References

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CHAPTER 11

Appendices