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Title	Exploring the relationship between patterns of physical activity, sedentary behaviour and cardiometabolic health in middle-aged Irish adults
Authors	Dillon, Christina B.
Publication date	2016
Original Citation	Dillon, C. 2016. Exploring the relationship between patterns of physical activity, sedentary behaviour and cardiometabolic health in middle-aged Irish adults. PhD Thesis, University College Cork.
Type of publication	Doctoral thesis
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Download date	2026-11-04 15:36:15
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EXPLORING THE RELATIONSHIP BETWEEN PATTERNS OF PHYSICAL ACTIVITY, SEDENTARY BEHAVIOUR AND CARDIOMETABOLIC HEALTH IN MIDDLE-AGED IRISH ADULTS

A thesis submitted to the National University of Ireland for the degree of Doctor of Philosophy in the Department of Epidemiology and Public Health, School of Medicine.

September 2016



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Version 15/09/2016

ABSTRACT

Background and Study Rationale

Being physically active is a major contributor to both physical and mental health. More specifically, being physically active lowers risk of coronary heart disease, high blood pressure, stroke, metabolic syndrome (MetS), diabetes, certain cancers and depression, and increases cognitive function and wellbeing. The physiological mechanisms that occur in response to physical activity and the impact of total physical activity and sedentary behaviour on cardiometabolic health have been extensively studied. In contrast, limited data evaluating the specific effects of daily and weekly patterns of physical behaviour on cardiometabolic health exist. Additionally, no other study has examined interrelated patterns and minute-by-minute accumulation of physical behaviour throughout the day across week days in middle-aged adults.

Study Aims

The overarching aims of this thesis are firstly to describe patterns of behaviour throughout the day and week, and secondly to explore associations between these patterns and cardiometabolic health in a middle-aged population. The specific objectives are to:

1. Compare agreement between the International Physical Activity Questionnaire-Short Form (IPAQ-SF) and GENEActiv accelerometer-derived moderate-to-vigorous (MVPA) activity and secondly to compare their associations with a range of cardiometabolic and inflammatory markers in middle-aged adults.
2. Determine a suitable monitoring frame needed to reliably capture weekly, accelerometer-measured, activity in our population.

3. Identify groups of participants who have similar weekly patterns of physical behaviour, and determine if underlying patterns of cardiometabolic profiles exist among these groups.
4. Explore the variation of physical behaviour throughout the day to identify whether daily patterns of physical behaviour vary by cardiometabolic health.

Methods

All results in this thesis are based on data from a subsample of the Mitchelstown Cohort; 475 (46.1% males; mean aged 59.7±5.5 years) middle-aged Irish adults. Subjective physical activity levels were assessed using the IPAQ-SF. Participants wore the wrist GENEActiv accelerometer for 7 consecutive days. Data was collected at 100Hz and summarised into a signal magnitude vector using 60s epochs. Each time interval was categorised based on validated cut-offs. Data on cardiometabolic and inflammatory markers was collected according to standard protocol. Cardiometabolic outcomes (obesity, diabetes, hypertension and MetS) were defined according to internationally recognised definitions by World Health Organisation (WHO) and Irish Diabetes Federation (IDF).

Results

The results of the first chapter suggest that the IPAQ-SF lacks the sensitivity to assess patterning of activity and guideline adherence and assessing the relationship with cardiometabolic and inflammatory markers. Furthermore, GENEActiv accelerometer-derived MVPA appears to be better at detecting relationships with cardiometabolic and inflammatory markers.

The second chapter examined variations in day-to-day physical behaviour levels between- and within-subjects. The main findings were that Sunday differed from all other days in the week for sedentary behaviour and light activity and that a large within-

subject variation across days of the week for vigorous activity exists. Our data indicate that six days of monitoring, four weekdays plus Saturday and Sunday, are required to reliably estimate weekly habitual activity in all activity intensities.

In the next chapter, latent profile analysis of weekly, interrelated patterns of physical behaviour identified four distinct physical behaviour patterns; Sedentary Group (15.9%), Sedentary; Lower Activity Group (28%), Sedentary; Higher Activity Group (44.2%) and a Physically Active Group (11.9%). Overall the Sedentary Group had poorer outcomes, characterised by unfavourable cardiometabolic and inflammatory profiles. The remaining classes were characterised by healthier cardiometabolic profiles with lower sedentary behaviour levels.

The final chapter, which aimed to compare daily cumulative patterns of minute-by-minute physical behaviour intensities across those with and without MetS, revealed significant differences in weekday and weekend day MVPA. In particular, those with MetS start accumulating MVPA later in the day and for a shorted day period.

Conclusion

In conclusion, the results of this thesis add to the evidence base regards an optimal monitoring period for physical behaviour measurement to accurately capture weekly physical behaviour patterns. In addition, the results highlight whether weekly and daily distribution of activity is associated with cardiometabolic health and inflammatory profiles. The key findings of this thesis demonstrate the importance of daily and weekly physical behaviour patterning of activity intensity in the context of cardiometabolic health risk. In addition, these findings highlight the importance of using physical behaviour patterns of free-living adults observed in a population-based study to inform and aid health promotion activity programmes and primary care prevention and

treatment strategies and development of future tailored physical activity based interventions.

AUTHOR DECLARATION

I declare that the work presented in this thesis is that of my own and was carried out in collaboration with a team of researchers and supervisors who are duly acknowledged in the text of this thesis. This work has not been submitted for any academic award, at this or any other educational establishment. Where the use has been made of the work of others, it has been fully acknowledged and referenced.

_____

Christina Dillon **September 2016**

ACKNOWLEDGEMENTS

I sincerely thank my PhD supervisors. Catherine, thank you for your constant support throughout my PhD, I have learnt so much from you, thank you for your patience I know I tested it quite a lot! I would like to thank Tony for your support, encouragement and advice. Thank you both for believing in me, if you didn't I would not have had this amazing experience. I aspire to be as supportive and encouraging to my students as you both have been to me. Alan, thank you for coming on board my supervisory team, I have enjoyed working with you and your team in UL. Your guidance and support will always be appreciated.

Darren, thank you for putting up with my questions and most of all having to deal with my stubbornness with statistics, your patience is greatly appreciated. Also thank you for inspiring me to go further with statistical analysis and to be inspired by my own work. It has been a pleasure to work with all four of you. I would also like to thank Ivan for giving me the opportunity to do a PhD. Your guidance, support and motivating speeches have been inspirational! Thank you Xia for processing the data, I would have been lost without you. Thank you Kirsten for your impeccable advice and guidance, your support and role in my PhD will never be forgotten.

To the PhD evaluation committee, thank you for your advice and most of all, thank you for believing in me. To the Cork and Kerry, Mitchelstown Cohort team members, I really enjoyed working with you. To my fellow PhD students, thank you for your advice and support but most of all for listening to all my complaining!

Last but not least, thank you to my family. Shane you have been amazingly supportive and understanding in the last five years, I couldn't have done it without you. Mom, Dad, my brother Thomas, your strength and encouragement has always helped me through. It will never be forgotten.

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LIST OF ABBREVIATIONS

ABBREVIATION	TERM
ACDC	Adiponectin
ACE	Adverse Childhood Events
AIC	Akaike Information Criterion
ANOVA	Analysis of variance
BIC	Bayesian Information Criterion
BMI	Body mass Index
C3	Complement component c3
CDC	Centre for Disease Control
CHD	Coronary Heart Disease
CHOL	Cholesterol
cm	Centimetres
COSMIN	Consensus-based standards for the selection of health measurement instruments
CRFs	Clinical Report Forms
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
EVA	exposure variation analysis
FFQ	Food frequency questionnaire
FPG	Fasting plasma glucose
GHQ	General health questionnaire
GP	General Practitioner
HDL-C	High density lipoprotein cholesterol
HOMA	Homeostasis model assessment
ICC	Intraclass correlations
IL6	Interleukin-6
IPAQ-SF	International Physical Activity Questionnaire-Short form
KG	Kilograms
LCR	Latent Class Regression
LDL-C	Low density lipoprotein cholesterol
LMR	Lo Mendell Rubin
LPA	Latent profile analysis
METs	Metabolic equivalents
MetS	Metabolic syndrome
MIN	Minute
ML	Millilitres
MM	Millimetres
MVPA	Moderate-to-vigorous activity
NCDs	Non-communicable diseases
NHANES	National Health and Nutrition Survey
OR	Odds ratio
QUICKI	Quantitative insulin sensitivity check index
SBP	Systolic blood pressure

SD	Standard deviation
SOP	Standard operating procedures
SSA-BIC	Sample Size Adjusted Bayesian Information Criterion
TAG	Triglyceride
TNF-α	Tumor Necrosis Factor alpha
UK	United Kingdom
USA	United States of America
WHO	World Health Organisation
ß	Beta

CHAPTER ONE - BACKGROUND

Problem

The WHO now recognises physical inactivity as one of the leading global risk factors for morbidity and premature mortality (1). Physical inactivity is defined as “not achieving the recommended 150 minutes of moderate activity a week” (2) and in 2008, was found to cause 6-10% of all deaths from non-communicable diseases (NCDs) and 9% of premature mortality (3). Moreover physical inactivity is thought to be responsible for approximately 21-25% of breast and colon cancers, 27% of diabetes and 30% of ischaemic heart disease burden (4). It is estimated that if physical inactivity was eliminated, the life expectancy of the world’s population would increase by 0.68 years, and in Ireland life expectancy would increase by 0.87 years (5). Even modest levels of physical activity are beneficial. For example, Wen et al. (2011) concluded that 15 minutes a day or 90 minutes a week of moderate-intensity exercise are beneficial in terms of all-cause mortality, even for individuals at risk of cardiovascular disease (CVD) (6). The benefits of physical activity are extensive. Being physically active is a major contributor to both physical and mental health. More specifically, being physically active reduces the risk of a range of conditions including coronary heart disease (CHD), high blood pressure, stroke, MetS, diabetes, colon and breast cancer, depression and increases cognitive function and wellbeing (4, 7-16).

The relationship between sedentary behaviour, physical activity and health is complex. Sedentary behaviour is defined as “any waking behaviour involving little or no energy expenditure (1–1.5 METs) while in a sitting or reclining posture and includes sitting during transport, at work, in leisure time and at home” (17). Sedentary behaviour is associated with poor health and mortality (12, 18-21). Evidence is now emerging that excessive bouts of prolonged sedentary behaviour negatively impact on health (22-

26). Avoiding these lifestyle behaviours could significantly increase total life expectancy and CVD–free life expectancy (27).

The National Survey of Lifestyles Attitudes and Nutrition (SLÁN) showed that only 41% of Irish adults took part in moderate activity for at least 20 minutes three or more times a week (28). This level of activity has not changed greatly over the years with 40% of the population reaching these levels in 2002 and 38% in 1998 (29). In 2009 the Health Service Executive and Department of Health and Children produced 'The National Guidelines on Physical Activity for Ireland' (29). These existing guidelines do not include recommendations on light and sedentary activities. In 2011, Canadian physical activity guidelines included recommendations on light and sedentary activities, however these have only been created for children and youth (30). In addition, the findings to support these guidelines are based on questionnaire data.

Questionnaires and accelerometers are widely used to assess physical activity in epidemiological studies. Numerous physical activity questionnaires exist, all varying in complexity and length. Questionnaires are inexpensive, easy to administer and feasible in large epidemiological studies while in contrast, accelerometers are expensive, time consuming and not always feasible in large studies. Nonetheless accurate measurements of physical activity are central to successfully determine the relationship between physical activity and health outcomes. The IPAQ-SF, which is used in this study, has been validated in multiple populations against several objective methods and overall results have indicated poor validity (31, 32). Despite this, the IPAQ-SF continues to be extensively used in epidemiological studies. Current findings have suggested that the IPAQ-SF is not a suitable indicator of relative or absolute physical activity (31). Hence, the evidence to support the use of the IPAQ-SF to investigate the intricate relationships between physical activity and health when

examining total time spent in physical activity and physical activity guideline adherence is questionable. Accelerometers can record activity continuously throughout the day. They provide details on intensity of activity, minutes spent in activity, breaks in activity transition, duration of bouts of activity between activity transitions and time of day when activity occurred i.e. morning, afternoon or evening.

Relevance to Public Health

Physical activity and sedentary behaviour are easily and inexpensively modifiable lifestyle factors. As already stated physical activity impacts on both physical and mental health. Evidence shows that physical inactivity increases the risk of NCDs and shortens life expectancy. In 2008, approximately 31% of adults worldwide did not meet physical activity recommendations (33). Due to high levels of physical inactivity worldwide this presents a major global public health issue. In Europe, it is estimated that physical inactivity is costing €150 – 300 per citizen per year (34). In the UK in 2006-2007, it was estimated that physical inactivity cost the health care system £0.9 billion (35). In Ireland, the SLÁN survey of lifestyle, attitudes and nutrition showed 38% of Ireland's population is overweight and 23% is classed as obese. A major factor contributing to this is physical inactivity, with approximately 59% of Irish adults not meeting recommended levels (28). The scale of physical inactivity in Ireland together with the high economic cost of obesity alone, highlight the importance of making physical inactivity a national public health priority(36).

Gap in Research

To date, accelerometer-based studies in adults have examined averaged daily physical activity and sedentary behaviour levels during weekday and weekend days

or total weekly estimates (19, 37). Physical behaviour intensities are interrelated, in that a change in the time spent in one intensity directly affects time spent in the other intensities. In addition, few studies have examined all physical behaviour intensities combined. No study to date has examined the combined interrelated patterns of physical activity and sedentary behaviour levels throughout the week or daily distribution of activity across week days in adults. Despite the ability of accelerometers to investigate minute-by-minute patterns of physical activity and sedentary behaviour only six studies have examined physical activity patterns in adults using continuous hourly estimates or minute-by-minute accelerometry data (38-43). Arvidsson et al. (2013) investigated both the mean daily physical activity and the hour-by-hour physical activity patterns across the day (38). Hansen et al. (2013) evaluated hourly physical activity patterns across body mass index (BMI) categories (39). Cooper et al. (2000) determined levels (minutes per day) and hourly patterns of daily physical activity in BMI categories using minute-by-minute data (40). Lee et al. (2012) used cluster analysis to identify characteristic hourly patterns of physical activity (41). Metzger et al. (2010) used latent class analysis (LCA) to assess weekly patterns of minutes spent in moderate activity, vigorous activity, and moderate-to-vigorous physical activity (MVPA) accumulated in bouts greater than 10 minutes using NHANES data (42). A previous paper by Metzger et al. (2008) examined whether certain patterns of continuous minutes spent in moderate and vigorous physical activity were associated with risk factors of MetS using LCA (43).

Thus research on the distribution of physical behaviour using minute-by-minute data across days and interrelated weekly patterns of physical behaviour in middle-aged adults is lacking.

Thesis Structure

This thesis examines and describes patterns of physical behaviour measured by the GENEActiv accelerometer both throughout the day and week and explores associations between these patterns and cardiometabolic health defined by a range of traditional CVD risk markers, inflammatory biomarkers and internationally recognised definitions. Chapter 1 provides a brief introduction to the research topic while highlighting the gaps in the research, and primary aims and novelty of this thesis. Chapter 2 presents a comprehensive review of the literature on the relevance and role of physical behaviour in cardiometabolic health. Chapter 3 outline the study methodology of the thesis. Chapter 4 investigates the levels of agreement between the IPAQ-SF and the GENEActiv accelerometer in determining which measurement method is most sensitive to capture time spent in physical activity and to ascertain physical activity guideline adherence in middle-aged adults. Chapter 5 determines the number of weekday and weekend days of accelerometer monitoring required to reliably capture accelerometer-measured habitual activity in our population by examining between and within subject variation in physical behaviour across days. Chapter 6 uses Latent Profile Analysis (LPA) to identify groups of participants based on how they accumulate weekly physical activity and sedentary behaviour and determines if different cardiometabolic profiles exist among these groups. Chapter 7 explores whether daily, cumulative patterns of physical activity and sedentary behaviour vary by cardiometabolic health status. Finally, in Chapter 8 the overall results of the thesis, strengths and limitations, together with potential implications of these findings and future recommendations are discussed.

Novelty of Research

The Mitchelstown Cohort Phase One is one of few general population-based cohort studies nationally to include an accelerometer-based objective measure of physical behaviour. This study is one of the first studies in Ireland to use tri-axial raw acceleration data in adults, one other study exists in adults however that study uses uni-axial accelerometer data. Tri-axial accelerometry data offers the potential to improve the accuracy of energy expenditure of activities such as cycling, a common leisure time activity in Ireland which a uni-axial device cannot capture. The Mitchelstown Cohort includes a wide array of health-related variables including subjective and objective physical behaviour data, dietary data, plasma biomarkers of diabetes and CVD including lipids and inflammatory markers, anthropometric measures, 24-hour ambulatory blood pressure, adverse childhood events, medical history, depression and well-being scores. To the best of our knowledge, the current body of work is the first to examine combined interrelated patterns of weekly physical behaviour and daily cumulative variation of minute-by-minute physical behaviour associated with cardiometabolic health using accelerometry data in middle-aged adults.

Aims and Objectives

The overarching aims of this thesis are firstly to describe patterns of physical behaviour throughout the day and week, and secondly to explore associations between these patterns and cardiometabolic health.

The specific objectives of this study are to:

1. Compare the agreement between the IPAQ-SF and GENEActiv accelerometer-derived MVPA activity and secondly to compare their associations with a range of cardiometabolic and inflammatory markers in middle-aged adults.
2. Determine the number of weekday and weekend days of accelerometer monitoring needed to reliably capture weekly, accelerometer-measured, habitual activity in our population.
3. Identify groups of participants who have similar weekly patterns of physical activity and sedentary behaviour, and determine if underlying patterns of cardiometabolic profiles exist among these groups.
4. Explore variations in physical activity and sedentary behaviour throughout the day to identify whether daily patterns of physical activity and sedentary behaviour vary by cardiometabolic health status.

CHAPTER TWO - INTRODUCTION

History and Epidemiology of Sedentary Behaviour and Physical Activity

Sedentary Behaviour and Physical Activity Definitions

Many definitions of sedentary behaviour exist. Previously Pate et al. (2008) defined sedentary behaviour as “activities that do not increase energy expenditure substantially above that of resting level and includes activities such as sleeping, sitting, lying down and watching television and other screen-based entertainment. However recently sedentary behaviour was defined in the literature by Tremblay et al. (2012) as “any waking behaviour involving little or no energy expenditure (1–1.5 METs) while in a sitting or reclining posture and includes sitting during transport, at work, in leisure time and at home” (25, 44). Overall, these definitions are analogous. In this thesis, sedentary behaviour is quantified as daily time (minutes) spent in sedentary behaviour. Physical activity is a complex, multidimensional behaviour. Everyone performs physical activity in order to sustain life. The amount of physical activity performed on a daily or weekly basis can vary from person to person and also for a given person over time e.g. throughout the day or within the week. Physical activity is most often defined as “any bodily movement produced by skeletal muscles that results in energy expenditure” (45). However, with new technological advancements in the measurement of habitual behaviour, the appropriateness of this definition has started to be questioned. According to Bussmann et al. (2013) physical activity defined in this way does not cover all aspects of behaviour, such as sitting and standing, that are relevant to health and thus it cannot be used as an umbrella term. Bussmann et al. propose ‘physical behaviour’ as a suitable umbrella term, which includes the behaviour of a person in terms of body postures, movement and daily activities, and this is how physical behaviour will be referred throughout this thesis (46).

History of Physical Activity

Physical behaviour levels have evolved over time. Since the Stone Age, shifts from hunting and gathering to agriculture and then to industry, have significantly changed physical behaviour patterns. During this time, human health and longevity has improved (47). In the past, the most common causes of death were due to communicable diseases such as typhoid, cholera, smallpox, polio, yellow fever and diphtheria. The introduction of vaccination programs in the 1800's to present-day worldwide vaccination programs have led to low prevalence rates and, in some cases, total eradication of these diseases e.g. smallpox. Today, the most common causes of morbidity and mortality are associated with NCDs such as cancers and heart disease. Since the start of the Industrial Age, labour-saving machines have been developed. The adverse effects of these labour saving developments on public health became evident as diseases such as CHD, diabetes, osteoporosis and cancer became highly prevalent worldwide (47).

In the late 1940's and early 1950's, Professor Jeremy Morris and his associates tested the hypothesis that participation in physical activity protects against CHD. They demonstrated an apparent protection against CHD among bus conductors in that the bus conductors experienced roughly half the number of heart attacks and 'sudden death' due to hear attacks as the drivers (48). Subsequent studies on civil workers found postmen to have increased protection against CHD compared to their less active counterparts, postal clerks. In both of these civil service surveys, Morris and colleagues demonstrated strong associations between moderate and vigorous exercise and reduced levels of CHD. By the 1960's, Morris speculated that because occupations were becoming more sedentary, any future role of physical activity in the protection of CHD would have to be related to leisure time activity outside of one's

occupation (47, 48). In 1967, Morris and colleagues established the 'Whitehall I' study to test this theory. Collectively this early research laid the foundation of physical behaviour research examining the relationship with health outcomes. However some shortfalls of these studies can be identified including the use of subjective measures such as job classification, surveys, questionnaires, logs and diaries to quantify physical behaviour. Subsequently numerous weaknesses and limited research applications of such measurement methods have been identified (49).

Physical Behaviour Measurements

Physical behaviour plays a major role in the aetiology of many NCDs (25, 50-53). Thus monitoring physical behaviour levels would be useful in assessing how health behaviours of a population influence morbidity and mortality. In current epidemiological studies, both self-reported questionnaires and accelerometers are widely used to assess physical behaviour. The most appropriate method for measuring physical behaviour depends on the population under study, time-frame of interest, available finances and outcome of interest (54). However, most of the evidence highlighting the role of physical behaviour on health status has come from studies using self-reported questionnaires which are subjective measures and prone to bias (55). Accurately measuring habitual physical behaviour is crucial to truly understanding the relationship between frequency, duration, type and amount of physical behaviour and health. In order to be accurate in the measurement of physical behaviour, a questionnaire needs to be both reliable and valid. Reliability is defined by the COSMIN (COnsensus-based Standards for the selection of health Measurement INstruments) panel as "the degree to which the measurement instrument is free from measurement error" (56).

Validity is defined as “the degree to which the scores of a health-related-patient reported outcome instrument measures the construct(s) it purports to measure” (56). Accurately measuring physical behaviour is central to epidemiological research for many reasons. These include the monitoring of physical behaviour trends, measuring the effects of physical behaviour interventions, to estimate more accurate effect sizes, to specify which aspect of physical behaviour is important for a particular health outcome and to properly inform public health policies to develop physical behaviour guidelines (57, 58).

Self-reported Measurements of Physical Behaviour - Questionnaires

A physical behaviour questionnaire is a research instrument consisting of a series of questions with the purpose of gathering information from respondents on their physical behaviour levels. Physical behaviour questionnaires vary greatly in the amount of detail they provide and typically consist of four components (49, 59). Firstly, the time-frame the participants are asked to remember, e.g. the last 7 days, past 2 weeks. Secondly, the nature and detail of the physical behaviours; participants are asked to report the frequency, duration and intensity of their physical behaviour or specific activities such as swimming or walking. The third component is the way in which data is collected, this could involve personal interviews, telephone interviews or self-reported information. The final component involves the calculated summary estimate which could include a simple continuous variable (energy expenditure per day), an arbitrary summary variable (exercise units) or an ordered ranking scaled variable which scores a person according to their physical behaviour level e.g. low, moderate and high (49, 59). Numerous physical behaviour questionnaires exist, all varying in complexity and length. Overall, questionnaires show limited reliability and validity (54,

59). The IPAQ-SF was developed in 1998 to aid in national and international surveillance of physical activity and to facilitate global comparisons (60, 61). The IPAQ-SF has been validated in multiple populations against several objective methods and overall results have indicated poor validity (31, 32). However, the IPAQ-SF continues to be extensively used as a sole, subjective measure of habitual physical activity in epidemiological studies (62-65) .

Reliability and Validity of the IPAQ-SF

The reliability and validity of the IPAQ-SF for physical activity assessment has been studied extensively. Craig et al. (2003) examined the reliability and validity of the IPAQ-SF in 14 samples across 12 countries (32). They reported the IPAQ-SF to be both reliable and valid for physical activity assessment and strongly recommended the use of the IPAQ-SF for national public health surveillance in middle-aged adults (32). More specifically they concluded that the IPAQ has “acceptable measurement properties, at least as good as other established self-reported questionnaires” (32). However, that study has a number of limitations. The study sample consisted generally of volunteer samples. Those who agreed to take part in the study might have been healthy volunteers, with different physical activity patterns from those who choose not to participate, leading to conflicting findings. Furthermore, the study reported a wide range of Spearman correlations between countries (0.02-0.47). Craig et al. (2003) stated that considering the diversity of the samples and countries studied; these results were satisfactory for the acceptance of the use of the IPAQ-SF for physical activity measurement in middle-aged adults. However, the wide variability between correlation estimates raises concerns of variability in validity across different populations (32).

A systematic review by Lee et al. (2011) on the validity of the IPAQ-SF reported the questionnaire to have negligible to small correlations in total activity level when compared to objective measuring devices including pedometers, accelerometers and actometers (31). In relation to specific levels of intensity of activity by the IPAQ-SF, time spent walking seemed to correlate best with accelerometer counts. The study reported that the correlations for the overall scale on the IPAQ-SF and any index never reached the standard correlation (0.5) for acceptable self-reported physical activity questionnaires (31, 66). More specifically, values obtained for moderate and vigorous activity correlated weakly with measures from objective devices (31). In addition to weak correlations between IPAQ-SF and accelerometer data, the study by Lee et al. (2011) found the IPAQ-SF to over-report activity by between 36-106% while only one study was found to under-reported activity (67-72). Furthermore, it is important to note that the IPAQ-SF was not developed to study aetiological relationships with health outcomes.

Strengths and Limitations of the IPAQ-SF

In the past, most population-level physical behaviour data collection involved self-reported questionnaires. As already stated, these were often used due to their low cost, feasibility, low participant burden and general acceptance (32, 42). Today, questionnaires are still used in large epidemiological studies because of the high cost associated with large scale use of accelerometers. Despite these strengths, questionnaires has numerous limitations. Questionnaires are prone to various degrees of measurement error and bias (42). For example, a common limitation of the IPAQ-SF is over-reporting of physical activity levels by study participants, this is often due to social desirability bias (73-75). Many questionnaires suffer from floor effects, the

instrument does not account for activities that are less intense than brisk walking or that have a duration of less than 10 minutes (54, 59, 76, 77). Thus, questionnaires lack emphasis on light intensity activities and often do not take into account the fragmentation of physical behaviour episodes (78, 79). Other major limitations which are of particular concern for public health surveillance worldwide is the potential for differential measurement error between countries (question interpretation may differ across different cultures and languages), 'likely question order effect', over- and under-reporting of physical behaviour levels and high variance between study samples (meaning small sample studies will be under-powered to detect group differences) (60, 73, 80, 81).

Additionally, if physical behaviour questionnaires are to be used to measure adherence to physical activity guidelines then they must be able to capture and summarise information on bout duration, breaks between bouts and moderate and vigorous activity accurately (79). However due to the previously stated limitations such as over-reporting and recall bias this would prove difficult. In addition, measuring moderate and vigorous activity is a challenge for questionnaires because of the need to assess many activities of short duration that occur as part of everyday habitual activity. Physical activity guidelines suggest physical activity to occur in bouts of 10 minutes or more. In addition to the 'floor effects' these problems are amplified by issues with rounding-up bias and recall bias since questionnaire responses rely on the perception, encoding, storage and retrieval of information about previous physical behaviours (82). In addition many questionnaires focus on the absolute rather than the relative intensity of individual physical activities which may be of particular concern in the study between physical behaviour and health (59).

Objective Measurements of Physical Behaviour -Accelerometers

Accelerometers are devices that measure the acceleration of bodily movements over time and provide researchers with real time, accurate and objective measures of physical behaviour. Most researchers are now turning to objective physical behaviour measurement methods due to lowering costs, coupled with the rich, accurate, time-stamped and detailed data obtained. In the last few decades, objective measurements of physical behaviour have significantly improved. Devices have become smaller, data storage capacity has increased, battery consumption has decreased and location of wear has become more practical. Previous accelerometers processed recorded acceleration data internally and saved the data as 'counts'. Present day accelerometers, such as the GENEActiv accelerometer, collect data as raw acceleration and store the data as g units for offline analysis. This allows for efficient data cleaning, management of spurious data, and the application of various known data processing algorithms post-data collection. These sensors detect accelerations in three axis (mediolateral (x), vertical (y) and anteroposterior (z)), Figure 1 (83).

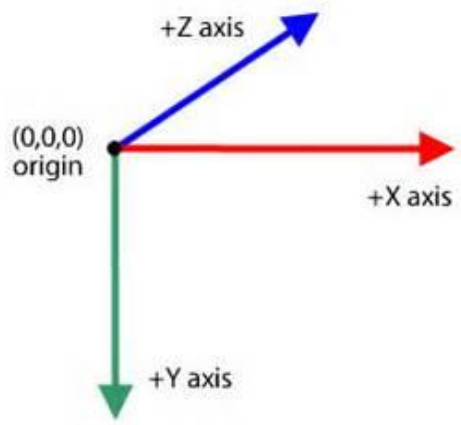


Figure 1: Directions of movements measured by tri-axial accelerometers

In these accelerometer designs, forces created from acceleration causes crystals to become stressed, which in turn generate an electric charge proportional to the magnitude of the acceleration force. The generated electric charge is filtered and converted by the accelerometer into raw acceleration signals taken multiple times every second, depending on the chosen recording frequency (84). These signals or raw data are stored as g units by internal memory and then downloaded through computer ports. These raw data are unitless and dimensionless and thus need to be processed and calibrated to be interpretable i.e. sedentary behaviour, light activity and MVPA.

Reliability and Validity of the GENEActiv Accelerometer

Esliger et al. (2010) examined the technical reliability and validity of the GENEA accelerometer using a mechanical shaker (85). The GENEA accelerometer was reported to be highly reliable with mean intra- and inter-instrumental coefficients of variation of 1.8% and 2.4% respectively. The device was also found to have excellent criterion validity against maximum oxygen consumption and excellent concurrent validity compared to the Actigraph and the RT3 (85). It should be noted that the GENEA accelerometer and the GENEActiv accelerometer are essentially identical with the exception of extended measurement frequency (GENEA accelerometer had a recording range of 10-80Hz while the GENEActiv accelerometer has a recording range of 10-100Hz) and wider recording range (GENEA had a recording range of ±6*g* whereas the GENEActiv accelerometer has a recording range of ±8*g*).

Strengths and Limitations of the GENEActiv Accelerometer

Accelerometers allow for the objective measurement of physical behaviour and thus avoid reporting errors created by translation, misinterpretation and social desirability bias (86). The GENEActiv accelerometer measures and stores physical behaviour data as raw acceleration units (*g*), allowing for post-data collection processing of data, while older accelerometers processes the data internally and store data as counts which hinders between model comparisons and prohibits post-data processing (85). Accelerometers have now made it possible to examine physical behaviour over long periods of time. They are helpful for capturing intermittent, ambulatory activities preformed through the day, week and month (87). More specifically, they provide details on intensity of activity, minutes spent in activity, breaks in activity transition, duration of bouts of activity between activity transitions, time of day when activity occurs, i.e. morning, afternoon or evening, and have the potential to examine how weekly and daily patterns of physical behaviour contribute to health status. Most research to date has examined the relationship between physical behaviour and health outcomes using summary estimates (46). While summary estimates have made huge contributions to our understanding of physical behaviour, accelerometers now enable us to look at physical behaviour in more novel ways than ever before (88, 89). In physical behaviour studies, data are often summed or averaged over whole measurement periods which may lead to real effects going undetected (46, 90). This would suggest that examining the relationship between daily and weekly physical behaviour patterns may highlight relationships not previously examined. Accelerometers have the potential to examine how variation in daily and weekly patterns of physical behaviour differ by health status and thus provide an opportunity for more complete physical behaviour profiles to be evaluated.

While accelerometers are advantageous in minimising reporting bias, they are not without limitations. It has been suggested that wrist worn devices are poor at capturing lower body movement. Devices such as the activPAL and ActiGraph are placed on the thigh and hip and are thus better at capturing lower body movement. There are also concerns that excessive arm movements may lead to the overestimation of physical activity estimates. However, Esliger et al. 2011found that while the levels of accuracy of the waist mounted GENEActiv accelerometer was greatest the estimates using wrist worn devices were closely accurate. In addition it is worth highlighting that estimates from the GENEActiv accelerometer are comparable to other devices placed in the same position (91, 92). While wrist placement has its limitations it is worth noting that this position of wear has been associated with increased compliance compared to hip worn placement in children. Increased compliance improves the quality and quantity of physical behaviour data available for analysis and also increases the number of valid days thus increasing the power of study findings (93).

Accelerometers are costly, data processing is time consuming and not always practicable in large epidemiological studies. Accelerometers cannot accurately measure the added energy expenditure associated with carrying a heavy load, weight-training or walking on an incline. Moreover accelerometers cannot distinguish different types of physical behaviour or characterise the context under which physical behaviour occurs. For example, current Canadian physical behaviour guidelines for children recommend no more than 2 hours of screen time per day (30). This is a low energy expenditure activity. Similarly activities such as reading, drawing, painting and writing are also low energy expenditure activities, however these are not discouraged or time limited. Thus accelerometers will classify these activities as the same intensity type and therefore this information cannot be examined (84). Some accelerometers, such

as the GENEActiv accelerometer, use a single sensor. A limitation of this approach is that no distinction can be made between body postures i.e. no distinction can be made between sitting and standing positions (46). Previous research has suggested that standing may have benefits to health (94-96). Some accelerometers, such as the ActivPAL, use a combined sensor (accelerometer and an inclinometer) which allows for both the measurement of bodily acceleration and posture.

Concluding Paragraph

Subjective and objective measures to assess physical behaviour exist and are widely used in epidemiological studies. Questionnaires have been sufficient to demonstrate basic associations with health outcomes, however uncertainties exist about which dimension of physical behaviour is being assessed and the degree to which it is valid and reliable (58). In addition, the IPAQ-SF was not developed to study aetiological relationships with health outcomes. Thus, comparison of self-reported physical behaviour measures against objective measures is crucial to identify how they differ and whether this matters to study associations with health outcomes. Studies have established that the use of activity monitors such as accelerometers, as oppose to questionnaires, is more likely to result in the detection of significant and meaningful associations with health while other studies have found stronger associations with health outcomes compared to questionnaires (97-100). To date the agreement between the IPAQ-SF and GENEActiv accelerometer-derived MVPA and their associations between a wide range of cardiometabolic and inflammatory markers in middle-aged adults have not been compared.

Role of Physical Behaviour in Health and Disease

Current Physical Activity Guidelines

Public health experts produced physical activity guidelines and recommendations to educate the general population on the optimal amount of physical activity needed to maintain and improve health. The first public health physical activity guidelines were released in 1995 by the American College of Sports and Medicine and the Centres for Disease Control and Prevention (78). These were soon followed by recommendations by the 1996 report of the US Surgeon General (101). These recommendations were similar, they recommended for adults to accumulate 30 minutes of at least moderate intensity activity on most days of the week and that activity should occur in bouts of 10 minutes or more.

In 2007, the American College of Sport Medicine and the American Heart Association proposed new revised guidelines. They proposed 30 minutes of moderate activity on at least 5 days of the week or vigorous-intensity aerobic physical activity for a minimum of 20 minutes on three days each week or an equivalent of both moderate and vigorous activity, and that activity bouts should be 10 minutes or more in duration (102). Similar physical activity guidelines were later adopted by other countries including Ireland and organisations such as the WHO and CDC (4, 103).

Missing from these guidelines are any recommendations on light and sedentary activity. A panel review by the “Physical Activity Guidelines Committee” concluded that since a large body of the evidence to support the relationship between sedentary behaviour and light activity and health outcomes has come from self-reported data and cross-sectional observational studies, current recommendations will not include guidelines on light and sedentary activity (104). As previously discussed self-reported measures of physical activity are subject to bias and may lead to erroneous

conclusions about physical behaviour levels and associations with health outcomes. Self-reported data for physical behaviour are more reliable and valid for MVPA compared to light and sedentary activity (103, 105). Light activity is often poorly reported while it is unclear how well screen time reflects total sedentary activity. Accelerometers now allow the measurement of physical behaviour objectively, removing some of these limitations. In addition, they allow us to examine physical behaviour continuously throughout the day (every second) for long periods of time (up to 30 days). Accelerometers allow us to look at the frequency and variability of physical behaviour throughout the day and week. Information such as this can contribute to the existing evidence that form the basis for physical behaviour guidelines so as to inform whether an optimal daily or weekly pattern of physical behaviour can benefit health. Further longitudinal research should expand on this and examine whether an optimal pattern exits in those who are cardiometabolic healthy compared to unhealthy counterparts. Previous research has demonstrated that increased breaks in sedentary behaviour and reduced bout duration are associated with positive health outcomes. These findings may be partly accounted for by increased physical activity, as time spent in one activity impacts on time available for a different activity or behaviour every break in sedentary behaviour results in an increase in overall physical activity levels. However, the beneficial effects of reduced bout duration or increased breaks in sedentary behaviour may also suggest that patterns of physical behaviour, in terms of how we accumulate physical activity and sedentary behaviour are also important. To test this hypothesis future research involving longitudinal studies focussed on identification of physical activity patterns which predict long term or future cardiometabolic health status is warranted. Such investigations should include a long follow-up period (5-10 years), wherein physical activity patterns and health outcomes

are recorded over multiple time points across this time frame (every 2 years), confounders such as age or other time related issues are accounted for and. Survival analysis used to identify associations between physical activity patterns and cardiometabolic health outcomes. This type of research has the potential to provide answers to a number of current research questions. For example, do those with superlative physical activity patterns throughout the study have positive health outcomes at the end, similarly do those with sub-optimal physical activity patterns have worse outcomes. Furthermore, such longitudinal analysis would allow us to consider changes in either physical activity pattern or health outcome i.e. whether changes in physical activity patterns were associated with transition from one health state to another (e.g from metabolically healthy to metabolically unhealthy or vice versa). While the limitations of observational research in terms of causality have been discussed such investigations may be worthwhile in terms of providing proof of concept, extending the knowledge base and informing subsequent intervention studies to further address causality.

Physical Behaviour and Cardiometabolic Health

Physical activity and sedentary behaviour are inexpensively and easily modifiable behaviours. As already stated, physical activity impacts on both physical and mental health. The physiological mechanisms that occur in response to physical activity have been extensively studied. Physical activity may reduce the risk of CVD by regulating insulin resistance, fasting blood glucose and cholesterol levels, BMI, blood pressure and waist circumference (37, 106-114). More specifically physical activity results in energy expenditure which is positively associated with weight loss and weight management (115, 116). It increases the transportation of glucose and reduces the

production of insulin, in turn preventing or delaying the onset of type 2 diabetes (117, 118). Furthermore increased physical activity levels reduce blood pressure and improve blood lipid profiles (112, 119-121). Research has found total physical activity to be significantly associated with lower prevalence of MetS (122, 123). Sedentary behaviour has emerged as a major concern for the prevention of CVD and diabetes and has been found to be strongly related to metabolic risk (95, 96, 124-126). Since the majority of field-studies are cross-sectional in design one cannot ascertain the true direction of the association, in other words it is unclear whether being sedentary leads to poor health or whether poor health leads to sedentary behaviour. A large body of evidence supports the notion that sedentary behaviour is significantly and negatively associated with morbidity and mortality (127-132). One of the key mechanisms by which physical activity exerts favourable health effects appears to be due to its capacity to influence inflammatory status (133). Cardiometabolic risk factors such as obesity, hypertension, MetS, dyslipidemia and glucose intolerance are known predictors of CHD and diabetes (134).

Most of this research is based on self-reported measures of physical behaviour which have many limitations, as already detailed. A major limitation of self-reported measures of physical behaviour is that daily and day-to-day variation in physical behaviour cannot be examined. To date, most research that has used objective measurements of physical behaviour have examined the relationship between physical behaviour and health using summary estimates across days or averaged estimates for days across all days of measurement or by weekdays and weekend days. However data summed or averaged across entire measurement periods may lead to true associations going unnoticed; for example bouts or patterns accumulated

during a day or across days may be missed when whole day or whole week or whole study period are summed (46, 90).

Current guidelines recommend adults to accumulate 150 minutes of at least moderate-intensity activity per week occurring on most days of the week (29, 51, 52). The rational for recommending activity on most days of the week is attributable to evidence from early intervention studies (135). However, few studies have been able to isolate the effect of physical activity frequency from total-time for all-cause mortality (60, 101). In the past decade, research has reported the emergence of the 'weekend warrior' who accumulates most of their weekly activity into 1-2 days (42, 43, 60, 66). Lee et al. (2004) reported that among low-risk men, this 'weekend warrior' pattern could postpone mortality (60). Metzger et al. (2010) reported the 'weekend warrior' pattern to have higher risk of obesity, low high density lipoprotein cholesterol (HDL-C), and high triglyceride (TAG) levels, but lower risk of high blood pressure and fasting plasma glucose (FPG) when compared to individuals who accumulate similar activity levels over a longer period (43).

Furthermore, exploration of the association between cardiometabolic health status and daily variations in activity patterns has largely used hour-by-hour data. Three studies have examined activity patterns based on hourly data in adults and reported better health profiles associated with greater levels of activity for longer active days (39, 41, 136). Only two studies have examined within-day variation in activity using minute-by-minute data (137, 138). Using minute-by-minute, cumulative physical activity counts Schrack et al. (2014) examined within-day, age-related functional decline in older adults. That study demonstrated that the amount of physical activity in daily life is progressively lower with increased age and follows a different daily pattern in older adults compared with younger adults (137). Steeves et al. (2015) found that

while diabetics had similar daily cumulative activity patterns to non-diabetics, diabetics had lower daily activity levels (138). Thus optimal physical behaviour patterns (i.e. patterns identified in observational studies to be associated with positive health outcomes) may exist.

Previous research has demonstrated that increased breaks in sedentary behaviour and reduced bout duration are associated with health outcomes (3) (22, 36, 122, 136, 137). This would suggest that patterns of physical behaviour, in terms of how we accumulate physical activity and sedentary behaviour are important. However, these analyses do not examine whether accumulating total physical behaviour differently across the day or days of the week affects health status (22, 36, 122, 136, 137). As previously mentioned, the use of accelerometers permits the examination of associations between time-stamped physical behaviour and health outcomes, thereby allowing differences in daily patterns of physical behaviour (morning, afternoon or evening activity) among various population groups to be investigated. Recent research by Schrack et al. (2014) found that older adults had different physical behaviour patterns compared to their younger counterparts (134). We know that increasing age is associated with increased risk of morbidity thus it is plausible that the observed differences in patterns may also contribute to risk of adverse health outcomes. Since most of the studies are cross-sectional in design we cannot ascertain the true direction of the association. While we acknowledge that cross-sectional study designs provide descriptive results, these results cannot infer causation.

Concluding Paragraph

To date physical behaviour research has largely focused on self-reported methods of physical behaviour measurement. As previously discussed, the numerous limitations

associated with such methods impacts on the strength of the evidence and ways to explore the full physical behaviour profile associated with cardiometabolic health. This in turn affects physical behaviour guidelines because certain relationships between physical behaviour and health (breaks and bouts of activity) cannot be examined using self-reported physical behaviour measures. More specifically, time-stamped associations such as time of day and day of the week cannot be associated effectively with health outcomes with self-reported measures.

CHAPTER THREE – METHODS

Introduction

The following chapter outlines the methods of the Mitchelstown Cohort (Phase I) while specific methods are detailed in each result chapters (chapters 4 to 7). The accelerometer study protocol is described in detail at the end of the methods chapter following the structure and evidence from the literature are presented in Appendix 1.

Study Detail

The Department of Epidemiology and Public Health received funding in 2010 from the Health Research Board Centre for Diet and Health Research to recruit a new cohort as part of the Mitchelstown Cohort, Phase I. The current study is a cross-sectional study design and was designed to provide updated information on glucose tolerance status and cardiovascular health and their related factors in an Irish middle-aged population sample.

Ethics, Confidentiality and Security

The Mitchelstown Cohort, and the use of accelerometers in the study, was approved by the Clinical Research Ethics Committee of University College Cork. Written informed consent to participate in the study was requested by the field staff on appointment days. All information gathered was entered in MS-Excel format, downloaded onto password secured laptops and PCs, and was backed-up onto password protected external hard drives. All information gathered were treated with total confidentiality.

Study Subjects

A population representative random sample was recruited from a large primary care centre in Mitchelstown, County Cork, Ireland (139). The primary care centre includes

8 general practitioners and the practice serves a catchment area of approximately 20,000 people with a mix of urban and rural residents. Participants were randomly selected from all registered attending patients in the 50-69 year age group. In total 3,807 potential participants were selected from the practice list. Following exclusion of duplicates, deaths and ineligibles, 3,043 were invited to participate in the study and of these 2,047 (49.2% male) volunteered and completed the questionnaire and physical examination components of the baseline assessment (response rate 67%) during the study period (April 2010 and May 2011). Accelerometers were introduced into the study in January 2011. Of the 745 cohort participants seen between January and May of 2011, 475 (44.6% males; mean aged 59.6±5.5 years) subjects agreed to participate (response rate 64%).

Study Protocol

Prior to Clinic Visit

Once a patient agreed to participate in the study, they were contacted by phone to arrange an appointment. All participants were sent a pack prior to their clinic visit. This pack contained three questionnaires; general health questionnaire (GHQ), food frequency questionnaire (FFQ) and Adverse Childhood Events (ACE) questionnaire, two study consent forms and a urine collection container.

Clinic Visit

The clinic visit consisted of 2 appointments. The first involved the return of three self-completed questionnaires, a urine sample and an 8-hour-fasting blood sample. The second appointment involved a physical assessment in which baseline measurements were taken: height, weight, blood pressure and waist and hip circumference. During

this appointment participants were offered a 24-hour ambulatory blood pressure monitor and GENEActiv accelerometer.

Study Variables

Physical Behaviour Measurements

Self-reported Physical Activity

Subjective physical activity levels were assessed using the self-reported, IPAQ-SF. The IPAQ-SF questions provide information on frequency, duration, and intensity of physical activity. Recommendations on data cleaning and processing were followed (140). Due to logistical issues, self-reported and accelerometer-measured physical activity data were not collected concurrently; self-reported data was collected at the beginning of the week the accelerometer was worn. Due to limited resources, some participants (N=151) wore the accelerometer device a number of weeks after completing the questionnaire, this was due to limited number of devices available for data collection on the day of their physical assessment.

Accelerometer-measured Physical Behaviour

The GENEActiv accelerometer was introduced latter half of the study. Objective physical behaviour levels were assessed using a tri-axial, GENEActiv accelerometer. The accelerometer (ActivInsights Ltd, Kimbolton, Cambridgeshire, United Kingdom) comprised a tri-axial STMicroelectronics accelerometer with a dynamic range of +/-8 g (1 g= 9.81 m/s^2), where *g* represents gravitational unit, and was attached to the participants' preferred wrist with a strap. The technical reliability and validity of this accelerometer has been reported elsewhere (85). Following return of the accelerometer to the co-ordination centre, the data was extracted using GENEActiv software and then collapsed using the following, sum of the vector magnitude,

equation ($\sum |\sqrt{x^2+y^2+z^2} - g|$) (85). This equation was used to calculate the sum (∑) of the signal magnitude vector $\sqrt{x^2+y^2+z^2}$ with gravity subtracted (-g). The sum was calculated for a specific time interval (epoch) e.g. 60 second epoch. Each time interval was categorised based on validated cut-off points (APPENDIX 2). Cut-points were scaled to data measured at a frequency of 100 Hz; cut-points created for APPENDIX 2 were created based on data measured at 30Hz. Wear and non-wear time was identified by the procedure outlined by Van Hees et al. (2011) (141). Four-hundred-and-seventy-five subjects wore the accelerometer, of which 397 have valid data. One-hundred-and-sixty-six participants wore the GENEActiv accelerometer on their non-dominant wrist, 210 wore the device on their dominant hand while 21 did not have this data recorded. Sixteen participants were excluded due to missing data. Choice of wrist was selected by the participant to ensure comfort and wear compliance, this did not influence study findings as the thresholds applied to data were created for dominant and non-dominant hand, thus removing any bias that dominant hand activities would have on physical behaviour estimates..

Biological Analyses

All participants attended a physical examination at the clinic in the morning after an overnight fast, minimum 8 hours. Fasting blood samples were obtained on arrival. Plasma and serum were prepared from fasting blood samples from each subject. FPG, serum total cholesterol, HDL-C, LDL-C, TAG and HbA1c levels were measured by Cork University Hospital Biochemistry Laboratory using fresh blood samples. HbA1c levels were determined based on High Performance Liquid Chromatography on a TOSOH analyser. FPG concentrations were determined using a glucose hexokinase assay and serum lipids were analysed using enzymatic colorimetric tests (Olympus

Life and Material Science Europa Ltd. Lismeehan, Co. Clare, Ireland) on an Olympus 5400 automatic analyser (Olympus Diagnostica Gmbh, Hamburg, Germany). Serum insulin, TNF-α, IL6, ACDC and leptin were determined using a biochip array system (Evidence Investigator; Randox Laboratories, Antrim, UK). Complement c3 (C3) was determined by immunoturbidimetric assay (Rx Daytona; Randox Laboratories, Antrim, UK). Homeostasis model assessment (HOMA), a measure of insulin resistance, was calculated as [(fasting plasma glucose x fasting serum insulin) / 22.5] (142). The quantitative insulin sensitivity check index (QUICKI) measured insulin sensitivity and was calculated as QUICKI=1/[log insulin (μIU/mL)+log glucose(mg/dL)] (143).

Anthropometric Measurements

Anthropometric measurements were recorded with calibrated instruments according to standardised protocol. Height was measured in centimetres to 1 decimal place using a Seca Leicester height gauge (Seca, Birmingham, UK). Body weight was measured in kilograms without shoes, to the nearest 100g, using a Tanita WB100MA weighing scales (Tanita Corporation, IL, USA). BMI was calculated as [weight (kg)/ (height (m)) ^{2}]. Waist circumference (defined as mid-way between lowest rib and iliac crest) was measured in centimetres to 1 decimal place using a Seca 200 measuring tape (Seca, Birmingham, UK). The average of two measures was used for analyses. Blood pressure was measured according to the European Society of Hypertension Guidelines using an Omron M7 Digital blood pressure monitor on the right arm, after a 5 minutes rest in a seated position. The average of the second and third measurements was used for analysis.

Covariate variables

Age, gender and job status were self-reported. Job status was defined based on European Socio-economic classification social class categories (103). Participants were classified into 1 of 10 classifications, for analysis this variable was dichotomised based on employment status (employed/unemployed). Data for season was collected objectively from time-stamped accelerometer data. A dichotomised variable was also created for season; Winter/Spring and Summer/Autumn.

Cardiometabolic outcomes

Obesity and hypertension were defined according to WHO guidelines as BMI>30kg/m^2 and systolic blood pressure ≥140mmHg or diastolic blood pressure as ≥90mmHg. Diabetes was defined by IDF guidelines of FBG >7.0mmol. MetS was defined according to International Diabetes Federation 2006 guidelines; being centrally obese (waist circumference ≥94 cm (males) or ≥80 cm (females) or BMI >30.00kg/m2) plus 2 or more of the following features: FPG >5.6 mmol/l or previous diagnosis of type 2 diabetes, HDL-C <1.03 mmol/l (males) or <1.29 mmol/l (females) or on specific HDL-C treatment, TAG >1.7 mmol/l or on specific TAG treatment, systolic blood pressure >130 mmHg or diastolic blood pressure >85 mmHg or treatment of previously diagnosed hypertension) (222).

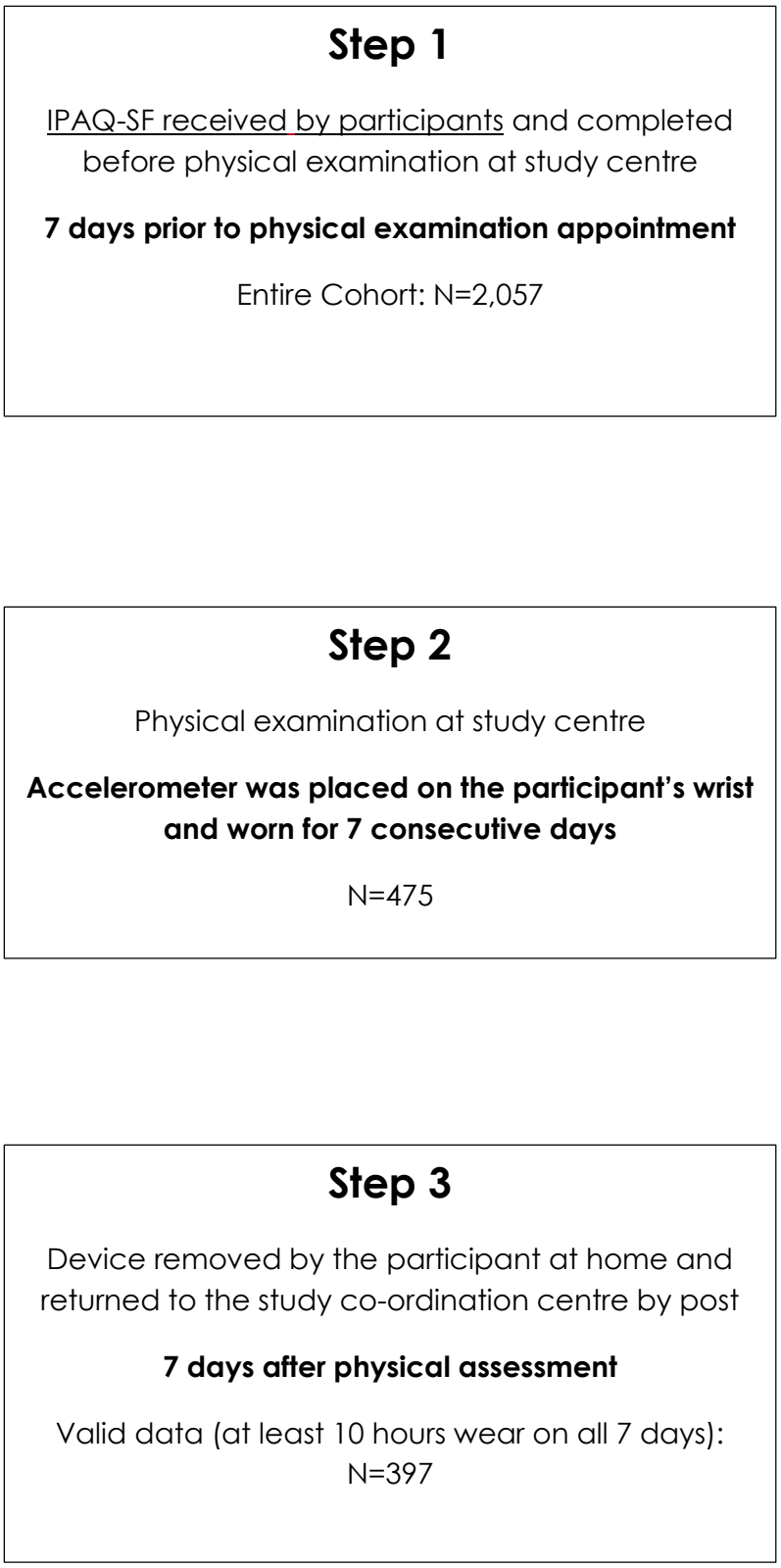


Figure 2: Flow Chart: Illustration of timings of physical behaviour assessments in the study

Data Management and Quality Control

Data management involved the entering, cleaning and organisation of information gathered during the research project. This process took place at the coordination centre (Department of Epidemiology and Public Health, University College Cork, Ireland). The process of data entry took place concurrently with the return of Clinical Report Forms (CRFs), questionnaires, accelerometers, 24-hour ambulatory blood pressure monitors, blood and urine results to the coordination centre. Data from CRFs, GHQ, FFQ and ACE were scanned using Teleform^{TM} and information verified against the hard copy of the questionnaire. Data was subsequently exported to MS-Excel and were checked again for accuracy against the hard copy. On completion of data entry, a 10% random sample was cross-checked for errors. The cleaning, identification and correction of corrupted data and analysis of the data occurred after the conclusion of the study.

To ensure consistency in data collection among the research team, a standard operating procedure manual was formatted. To ensure data quality, all measuring tapes, blood pressure monitors and weight and height scales were calibrated by the research team at regular intervals. The calibration of the blood pressure monitors and weight and height scales took place monthly by the field staff. All results were recorded in the appropriate calibration logs and appropriate action taken. Accelerometers were calibrated in the middle of the data collection, March 2011. A member of the GENEActiv team performed accelerometer calibration. All relevant figures were recorded and stored. These figures were applied to the data retrospectively; data that had already been collected were modified to include these differences in axis movement to ensure all data files captured movement similarly.

Accelerometer Study Protocol

Development of Accelerometer Field Protocol

Standardised accelerometer protocols ensure comparability of study results across studies and with future studies. To date, no other Irish study has reported physical behaviour levels in middle-aged adults with the GENEActiv accelerometer.

Distribution and Collection of Accelerometer

Accelerometers were distributed to participants on a face-to-face basis during their clinic visit. Because of the restricted number of accelerometers, some participants who agreed to wear an accelerometer were contacted at a later date to arrange a fitting at the study centre or, if requested, were sent the device by post. The first group of participants who had devices posted to them were contacted by phone on the day they received the device with instructions on how to use the accelerometer. This procedure proved difficult and time consuming as instructions often had to be repeated, and in a number of cases (n=3), the task of turning the device on was unsuccessful. The second group of participants who were posted the device had a pre-set time delay start. This was a more successful procedure. A prepaid stamped addressed-envelope was provided to return the monitors to the co-ordination centre. Written general instructions were also provided.

Placement of Accelerometer

In this study, the GENEActiv accelerometer was positioned on the participant's wrist. Choice of wrist was selected by the participant to ensure comfort and wear compliance.

Selection of Sampling Frequency

The GENEActiv accelerometer was programmed to gather data at a frequency of 100Hz, i.e. 100 times per second.

Number of Days Monitoring per Week

A review of the literature found a7 day monitoring frame to be the most commonly employed in accelerometer field protocols. Since no previous study examined a suitable monitoring frame for the GENEActiv accelerometer in middle-aged adults, a7 day monitoring frame was employed in this study. Additionally, participants were asked to wear the GENEActiv accelerometer for the full 24-hour day, however for most analyses (except chapter 7) only day-time hours, between 6am-12am, were analysed and interpreted (144).

Accelerometer Data Reduction Protocol

Selection of Sampling Interval

Data was collapsed using sum of the vector magnitude ($\sum |\sqrt{x^2 + y^2 + z^2} - g|$) into 60s epochs (85).

Classification of Non-wear

Wear and non-wear time was identified by the procedure outlined by Van Hees et al. (2011) (145). The estimation of non-wear time was estimated on the basis of the standard deviation and the value range of each accelerometer axis, calculated for consecutive blocks of 30 minutes. A block was classified as non-wear if the standard deviation was less than 3.0 mg for at least two of the three axes, or if the value range for at least two of the three axes was less than 50 mg. These thresholds were based on lab experiments which involved thirty GENEA accelerometers that were left motionless on a flat, stable surface for 30 minutes, showing the standard deviation of an acceleration signal (which has no inherent noise) is 2.6 mg during non-motion. Therefore, the threshold of 3.0 mg allows a maximum increase of 0.4 mg in the standard deviation (141).

Number of Minutes Considered as a Measured Day

A valid measured day was defined as acquiring 600 minutes or more of wear-time, except in chapter 7 where all 24-hours of data was analysed.

Handling of Missing data

It was decided that non-wear/missing data would remain untouched i.e. would not be included in the analysis.

Intensity Cut-off Points

For our data, validated thresholds (unpublished) were used to categorise data into sedentary and non-sedentary activities; light, moderate, vigorous (Appendix 2). These cut-points were scaled to the sampling frequency of 100Hz and are summarised in Table 1.

Table 1: GENEActiv cut-points for dominant and non-dominant wrist scaled to frequency (100Hz)

	GENEActiv Cut points*	
Activity Intensity	**Dominant**	**Non-dominant**
Sedentary	<767	<634
Light	767-1126	634-1046
Moderate	1127-2380	1047-1980
Vigorous	>2380	>1980
*Units expressed as **g·minutes**		

Expressing and Reporting of Data

After all raw data was processed; two datasets were created; a dataset containing summary statistics for each day of the week and another containing minute-by-minute data across all7 days. The following variables were created:

1) Minutes spent in sedentary, light, moderate activity, vigorous activity and MVPA
2) Number of bouts of activity lasting >10 minutes in each activity intensity
3) Average duration of bouts of activity in each activity intensity
4) Cumulative percentage of total day spent in each physical behaviour intensity

Statistical Analysis

Statistical analyses were conducted using Stata (version 12, Stata Corp, College Station, Texas, USA), Mplus software (version 6.12 for Windows), and in the R statistical software version 3.0.3 (http://www.r-project.org). The distribution of all continuous data was assessed and non-normally distributed data log-transformed. Descriptive statistics for non-normally distributed data was presented as median (25th, 75th percentile). An alpha level of 0.05 was set to evaluate significance. Specific statistical analysis will be discussed in more detail in the relevant chapters.

RESULTS

CHAPTER FOUR – COMPARISON OF SELF-REPORT AND OBJECTIVE MEASURES OF MODERATE-TO-VIGOROUS ACTIVITY WITH CARDIOVASCULAR DISEASE RISK FACTORS

Abstract

Introduction

Discrepancies in the measurement of physical activity may lead us to draw improper inferences regards the relationship between physical activity and health. The aims of this study are first to compare the agreement between the International Physical Activity Questionnaire-Short Form (IPAQ-SF) and GENEActiv accelerometer-derived moderate-to-vigorous activity (MVPA) and secondly to compare their associations with a range of cardiometabolic and inflammatory markers in middle-aged adults.

Methods

Data are from a subsample of the Mitchelstown Cohort; 475 (46.1% males; 59.7±5.5years) middle-aged Irish adults. Participants wore the wrist GENEActiv accelerometer for7 consecutive days and completed the IPAQ-SF. Information on cardiometabolic and inflammatory markers; Body Mass Index (BMI), waist circumference, blood pressure, fasting plasma glucose (FPG), serum lipid profile (serum total cholesterol, triglyceride (TAG), high density lipoprotein cholesterol, low density lipoprotein cholesterol), complement c3 (C3), interleukin-6 (IL6), tumor necrosis factor-alpha (TNF-α), leptin, adiponectin (ACDC), insulin resistance (HOMA) and insulin sensitivity (QUICKI), were collected. Physical activity adherence was based on the recommended 150 minutes of weekly MVPA. Kernel-density plots and Cohen's Kappa assessed agreement between self-reported and accelerometer-derived MVPA. Adjusted-linear regression examined the relationship between MVPA and cardiometabolic and inflammatory markers.

Results

Three hundred-and-ninety-seven adults had valid accelerometer data. There was a low level of agreement between the two measures of MVPA in classifying participants

as meeting physical activity guidelines (Cohen's Kappa (κ=0.011)). Accelerometer-derived MVPA variables were inversely associated with waist circumference, BMI, TAG, insulin concentrations, HOMA, C3, IL6, leptin ($P<0.0001$), diastolic blood pressure, FPG and TNF-α (except MVPA bouts) ($P<0.05$) and positively associated with, serum lipid profile (except TAG), QUICKI and ACDC ($P<0.04$). In contrast, self-reported MVPA was not associated with cardiometabolic and inflammatory markers.

Conclusion

GENEActiv accelerometer-derived MVPA appears to be better at detecting relationships with cardiometabolic and inflammatory markers than IPAQ-SF. Thus objective measures of physical activity are important to assess metabolic health to develop more precise physical activity recommendations.

Introduction

Physical activity significantly contributes to overall health and well-being and is associated with decreased inflammatory status, reduced cardiovascular risk and all-cause mortality (106, 107, 133, 146-156). More specifically, moderate and vigorous physical activity has been inversely associated with cardiometabolic markers including BMI, waist circumference, blood pressure, fasting glucose, lipid concentrations, insulin resistance and is positively associated with insulin sensitivity (108-114, 157-159). Furthermore, physical activity may decrease markers of inflammation, such as tumor necrosis factor-alpha (TNF-α), complement c3 (C3), interleukin-6 (IL6), leptin and adiponectin (ACDC) (149, 160-164). There is consensus that a dose-response relationship exists between physical activity and health status. However experts have identified a lack of understanding about the dose-response relationship as a research priority for the field of physical behaviour research (165). Current guidelines recommend adults to accumulate 150 minutes of at least moderate-intensity activity per week in bouts of 10 minutes (29, 47, 51, 52, 78). Only studies where several gradations of physical activity are reported can help address dose-response relationships and most using objective physical behaviour measures are observational. Thus the evidence to support these recommendations has largely come from self-reported physical activity data (166). Furthermore, research has found that self-reported and objective measures have limited agreement in their measurement of physical activity guidelines (72, 166-168). Recent studies using objectively-measured physical activity have suggested that bouts of physical activity with a duration as short as 1 minute may be health enhancing (79). Thus there is some controversy over how moderate-to-vigorous activity (MVPA) should be accumulated.

Self-reported measurements of physical activity have been shown to have poor agreement with objective measures such as accelerometers (168-170). This may be in part because questionnaires, are prone to misclassification error and response bias (74). Moreover, questionnaires are thought to measure different dimensions of physical activity compared to accelerometers, and are most effective at measuring easily recalled, planned, time-structured activities (58). In addition, a major issue in physical activity research is that often terms such as physical activity and exercise are used interchangeably, thus it is hard to say what exactly is being measured in self-reported data (55). Accurately quantifying physical activity is central to epidemiological research for many reasons; the monitoring of physical activity trends, measuring the effects of physical activity interventions, estimating more accurate effect sizes, specifying which aspect of physical activity is important for a particular health outcome and informing public health policies on physical activity guidelines (57, 58). Thus, comparison of self-reported physical activity measures against objective measures is crucial to identify how they differ and whether this matters to study associations with health outcomes.

The International Physical Activity Questionnaire-Short Form (IPAQ-SF) was developed in 1998 to aid in national and international surveillance of physical activity so to facilitate global comparisons and is used extensively in epidemiological studies however it was not developed to study aetiology (32). The IPAQ-SF has been validated in multiple populations against several objective methods, including accelerometers, and overall results have indicated poor validity (31, 32). To date the comparison of the IPAQ-SF against the GENEActiv accelerometer has not been examined nor has the relationships between the IPAQ-SF and GENEActiv accelerometer-derived MVPA variables with cardiometabolic and inflammatory

markers been compared. Furthermore, few studies have compared different methods for measuring MVPA in terms of their impact on health. Such comparative analysis is important regards to determine if various measures of MVPA differ in the relations with health outcomes and thus this analysis is important to compare across studies and different devices

The primary aim of this study is to assess the level of agreement between the IPAQ-SF and GENEActiv accelerometer in achieving the recommended MVPA guidelines and secondly to compare the relationships between self-reported and accelerometer-derived MVPA variables (continuously for each minute of activity and secondly across prolonged 10 minute bouts) with cardiometabolic and inflammatory markers.

Methods

Data are from a subsample of the Mitchelstown Cohort; 475 (46.1% males; 59.7±5.5years) middle-aged Irish adults. Information on anthropometric measures and cardiometabolic and inflammatory markers were collected. Participants wore the wrist GENEActiv accelerometer for 7 consecutive days and completed the IPAQ-SF. Weekly minutes spent in walking, moderate activity, vigorous activity and MVPA was calculated. IPAQ-SF MVPA (minutes per week) was categorised into 3 groups; zero activity, 1-599 minutes and ≥600 minutes. In addition, physical activity was categorised into low, moderate and high levels according to IPAQ-SF guidelines (140). Physical activity adherence was based on the recommended 150 minutes of weekly MVPA. Due to logistical issues, self-reported and accelerometer-measured physical activity data were not collected concurrently; self-reported data was collected at the beginning of the week the accelerometer was worn. Due to limited resources, approximately one third of the study sample (N=151) wore the accelerometer device a number of weeks

after completing the questionnaire, this was due to limited number of devices available for data collection on the day of their physical assessment. Because of seasonal variations in physical behaviour levels, these participants were removed from analysis (171). These methods for this study chapter are described in greater detail in Chapter 3.

Statistical analysis

The distribution of all continuous data was assessed and non-normally distributed data log-transformed. Weekly minutes spent in accelerometer-measured and self-reported physical behaviour intensities were calculated according to gender. Data were presented as median and 25^{th} and 75^{th} percentiles. Kernel-density plots were used to describe the distribution of objectively-measured MVPA in categories defined by IPAQ-SF. Cohen's Kappa was used to test agreement between subjective and objective physical activity adherence groups. Three adjusted linear regression models examined the associations between MVPA variables and cardiometabolic and inflammatory markers, adjusting for the effect of age and sex. All statistical analyses were conducted using Stata (version 12, Stata Corp, College Station, Texas, USA). An alpha level of 0.05 was set to evaluate significance.

Results

Physical activity profiles according to IPAQ-SF and GENEActiv accelerometer

The distribution of subject characteristics and accelerometer-measured physical activity by gender are presented in Table 2. Similar activity levels were recorded in males and females by both the IPAQ-SF and GENEActiv accelerometer. Significant differences were observed between gender by most physical behaviour variables, with the exception of sedentary behaviour and light activity for accelerometer derived MVPA and walking for IPAQ-SF derived MVPA. According to IPAQ-SF categorical data, approximately 49% of participants were categorised as having low levels of physical activity, while 30% and 21% achieved moderate and high levels of physical activity respectively. For IPAQ-SF variables, 22%, 73% and 74% of subjects reported zero-activity for walking, moderate and vigorous activity respectively. For those who reported having any activity, median weekly time spent in walking, moderate and vigorous activity was 210 minutes (3.5 hours), 290 minutes (4.8 hours) and 330 minutes (5.5 hours), respectively.

Validity of the IPAQ-SF and GENEActiv accelerometer for MVPA measurement and physical activity guideline adherence

The distribution of accelerometer-derived MVPA against IPAQ-SF reported MVPA categories is presented in Figure 3. For IPAQ-SF measured MVPA, participants reporting zero minutes (0 min IPAQ-SF MVPA) had similar accelerometer-measured MVPA levels to those reporting any MVPA activity (1-599 min IPAQ-SF MVPA and ± 600 min IPAQ-SF MVPA). Distribution of subjects classified as meeting physical activity guidelines by self-report and accelerometer-measured data is presented in Table 3. Overall 11.6% of subjects were classified as meeting physical activity

guidelines and 44.2% were classified as not meeting physical activity guidelines by both measurement methods. Based on accelerometer data only, 35.1% were classified as meeting physical activity guidelines compared to 32.2% based on IPAQ-SF data only. Cohen's kappa for testing agreement was close to zero (κ = 0.011) thus suggesting discordance between the methods was low. The percentage of participants with perfect agreement between the methods was 55.8%. The specificity of the IPAQ-SF to identify participants who meet physical activity guidelines was 22.9% while the sensitivity of the IPAQ-SF to identify those not meeting physical activity guidelines was 77.5%.

Examination of association between IPAQ-SF self-reported and GENEActiv accelerometer-derived MVPA with cardiometabolic features

Accelerometer-measured MVPA variables, hours per day of MVPA (measured as continuous minutes) and total MVPA accumulated in bouts lasting 10 minutes or more, were significantly related to most cardiometabolic and inflammatory markers with the exception of systolic and diastolic blood pressure. Higher levels in accelerometer-measured MVPA variables were associated with lower waist circumference, BMI, TAG, FPG, insulin concentrations, C3, IL6, TNF-α, leptin, reduced insulin resistance, and higher serum total cholesterol, HDL-C, LDL-C, ACDC and improved insulin sensitivity. Table 4 presents ß coefficients for cardiometabolic and inflammatory markers associated with a 1 hour increase in both accelerometer-measured and self-reported MVPA. No significant relationships between self-reported MVPA and any cardiometabolic and inflammatory markers were observed. Analysis was completed on the full sample (n=397) and similar conclusions were revealed.

Discussion

Our study provides evidence that the IPAQ-SF and GENEActiv accelerometer do not agree in their measurement of weekly MVPA and the proportion of the population who achieved guidelines for MVPA. In addition, our study demonstrated that the IPAQ-SF lacks the characteristics to adequately capture significant relationships between MVPA and cardiometabolic and inflammatory markers in middle-aged adults.

Examination of association between IPAQ-SF self-reported and GENEActiv accelerometer-derived MVPA with cardiometabolic features

There are limited data comparing self-reported and accelerometer-derived MVPA with cardiometabolic and inflammatory markers and results are inconsistent (97, 98). Atienza et al. (2010) found both subjective and objectively-measured MVPA to be significantly related to skinfold thickness, HDL-C and C-reactive protein while systolic blood pressure, BMI, waist circumference, TAG, FBG, insulin concentrations, glycohemoglobin, C-peptide and homocysteine were only significantly related to accelerometer-measured MVPA. (97). Celis-Morales et al. (2012) reported that for some cardiometabolic markers; glucose, insulin concentrations and insulin sensitivity, significant associations were observed with both the IPAQ-SF and accelerometer-measured MVPA. However for other risk factors; TAG, total cholesterol levels, LDL-C, HDL-C, BMI, waist circumference and percentage body fat, significant associations with MVPA were only apparent when activity was captured with accelerometers (98). Our study findings reported that accelerometer-measured MVPA was significantly related to most cardiometabolic and inflammatory markers with the exception of blood pressure and total cholesterol levels, in a representative population of middle-aged Irish adults. Furthermore, MVPA assessed using the IPAQ-SF did not relate with any

cardiometabolic and inflammatory markers. A limitation of the IPAQ-SF in this population was the large proportion of participants who reported no MVPA with approximately 75% of participants reporting no activity. This limits the power of the analyses as sample size decrease when non-normally distributed data is transformed for data analyses. In other populations where self-reported MVPA is low, the IPAQ-SF may be unsuitable for physical activity measurement and to study associations with health outcomes.

Validity of the IPAQ-SF and GENEActiv accelerometer for MVPA measurement and physical activity guideline adherence

The GENEActiv accelerometer has demonstrated excellent criterion validity, using VO_2 as the criterion measure, and concurrent validity compared to the Actigraph and RT3 (85). Accelerometers have been suggested as one of the best measures for the validation of self-reported measurement instruments (172). However, this is highly criticised as accelerometers and questionnaires measure different aspects of activity (173). Thus the observed agreement between the IPAQ-SF and the GENEActiv accelerometer should be interpreted with this in mind. A systematic review of the validity of the IPAQ-SF by Lee et al. (2011) found that evidence to support the use of the IPAQ-SF as an indicator of relative or absolute physical activity is weak (31). Dyrstad et al. (2013) compared absolute values between the IPAQ-SF and the ActiGraph accelerometer (168). Their study demonstrated differences between IPAQ-SF and ActiGraph MVPA to increase with higher activity and intensity level. The results of our study indicate the IPAQ-SF may lack the characteristics to effectively assess MVPA. In contrast to these findings, Román-Viñas et al. (2013) concluded that the IPAQ-SF was valid at measuring total and vigorous physical activity (174).

To the best of our knowledge, only three studies have examined the validity of IPAQ-SF in adequately assessing physical activity guideline adherence and results are conflicting (72, 174, 175). These studies involved relatively small sample numbers and involved broader age groups. Consistent with our findings, Wolin et al. (2008) and Ekelund et al. (2006) suggested the evidence to support the use of the IPAQ-SF for assessing guideline adherence was weak (72, 175). In contrast, Román-Viñas et al. (2013) recommended that the IPAQ-SF can be used to identify adherence to physical activity recommendations (174). It should be noted that the Román-Viñas et al. (2013) study had a small sample size (n=55) of volunteers. Those who agreed to take part in the study might have been healthy volunteers, with different physical activity patterns from those who chose not to participate leading to conflicting findings.

Lee et al. (2011), Ekelund et al. (2006) and Taber et al. (2009) reported the IPAQ-SF to over-estimate physical activity when compared to objective measures (31, 72, 176). Our study revealed that, when compared to the GENEActiv accelerometer as the absolute criterion gold standard, the IPAQ-SF has large measurement error, which both under- and over-estimated activity; with over 66% of participants under-reporting moderate activity while approximately 33% over-reported vigorous activity. The differences in reporting of moderate and vigorous activity on the IPAQ-SF may reflect failure to recall time, poor understanding of physical activity concepts, social desirability bias, inter-individual differences in intensity perception or rounding up of time spent in activities, thus yielding different estimates compared with accelerometer estimates (75, 173). The over-reporting of activity and the large quantity of zero responses in our study could explain the low level of agreement between the IPAQ-SF and GENEActiv accelerometer. Furthermore, self-reported physical activity data was collected a week prior to accelerometer data collection. Physical activity levels in

free-living adults vary seasonally and in response to environmental factors. For these reasons the MVPA levels measured by the IPAQ-SF and GENEActiv accelerometer may not be the same. This could in turn lead to significant differences between the estimates thus increasing the level of disagreement between the measures in relation to guideline adherence and relations with cardiometabolic health markers.

Strengths and limitations

A main strength of our study is the use of a valid and reliable activity monitor which is capable of assessing time spent in sedentary, light, moderate and vigorous activity intensities (85). Furthermore, the high participation rate (64%) and range of metabolic health markers which were determined at a commercial laboratory ensures a high level of reproducibility. Notwithstanding these strengths one limitation of this study is that the sub-sample of the Mitchelstown Cohort for whom accelerometer data was collected, differed by gender in that women were more likely to agree to wear the accelerometer. Nonetheless it should be noted that there were no statistically significant differences in age, education or BMI between those included and excluded in the final analysis. This is a cross-sectional study, therefore cause-effect relations cannot be determined. Additionally, due to logistical issues, approximately one third of the study sample had subjective and objective physical behaviour levels measured at different time-point (weeks apart). For reliability issues and the fact that physical behaviour levels differ significantly between seasons, these data were excluded from analysis. Removing these subjects from analysis decreased the sample size significantly thus reducing the power of the analysis to detect significant association with health outcomes and to measure accuracy in agreement levels between subjects for guideline adherence. However, despite the reduced sample size 95% confidence

intervals were narrow. In addition, findings including all subjects mirrored those obtained in the subset presented in this chapter. Furthermore it should be noted that the GENEActiv accelerometer is not a gold-standard method, thus conclusions about the precise validity of either measure are limited. It should also be highlighted that the arbitrary cut-point for day-time wear may lead to inaccurate estimates of sedentary and non-sedentary activity. For example persons who sleep later than 6am will have inflated sedentary behaviour estimates while those who are active after 12 midnight will have deflated activity estimates. Furthermore, since MVPA levels were measured on different occasions (a week apart) this may affect the results of this study. Activity levels in free-living adults have been reported to vary, seasonally and in response to environmental factors (177-183). IPAQ-SF and accelerometer data were not gathered concurrently. This could be a potential source of bias in our study findings. The IPAQ was developed for surveillance systems and not for aetiological purposes, yet we have used it to examine associations with health outcomes. While caution should be taken in the comparison of the two measures in respect of this, other studies have used the IPAQ-SF for aetiological purposes and thus our results can be compared to these (153, 184-187). In addition, the main aim of this chapter was the IPAQ-SF was being used for comparative purposes i.e. comparing the relationships between subjective and objective measures and cardiometabolic outcomes. Finally, although significant, the co-efficients generated by adjusted regression analysis are small (β: -0.97 to 0.74). Whether a change of this magnitude in a metabolic risk marker will affect cardiometabolic health status is unknown, thus caution should be exercised in relation to the potential clinical significance of these findings. In addition, we need to highlight the existence of random error in the measurement of physical behaviour. Random errors in measurement of a risk factor such as physical behaviour will introduce

downward bias towards the null hypothesis of an estimated association to a disease or a disease marker, regression dilution. Bootstrap techniques in generalized linear models could correct for measurement error. Bootstrapping is a technique that models the inference about a population from sample data by resampling the sample data and performing regression analysis. Thus further research should apply this method.

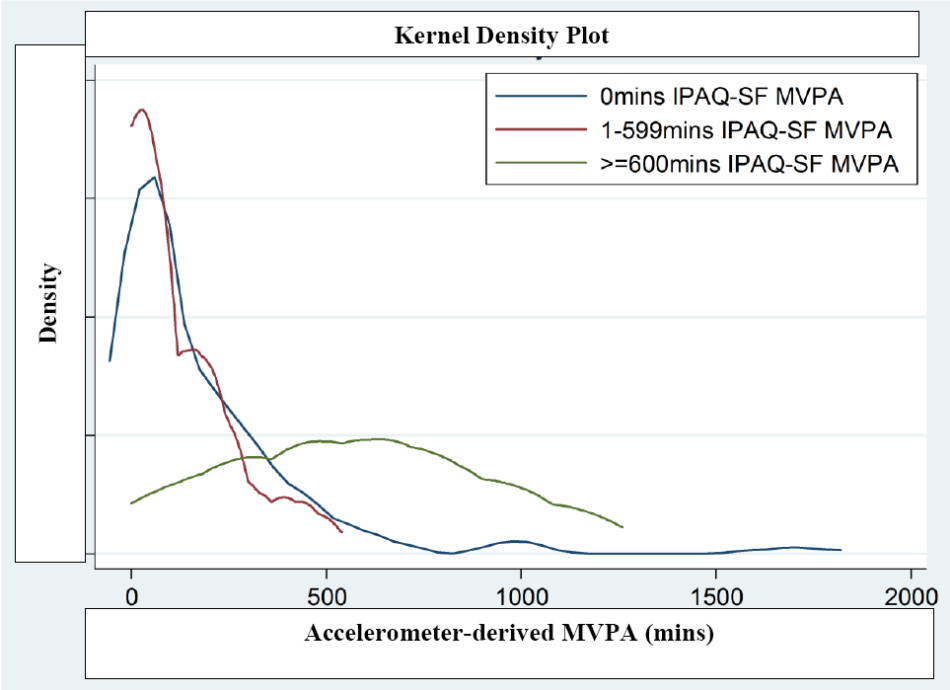
Generalizability of the study

Generalizability of our findings may also be limited. The Mitchelstown Cohort was a random sample of middle-aged adults, 50-69 years of age, in an area which was representative of both urban and rural populations in Ireland. However, previous research suggests that approximately 98% of Irish adults are registered with a general practice (GP) and that although a universal patient registration system is non-existent in Ireland, it is possible to perform a population based epidemiological study that is representative of the general population using GP records (188).

Conclusion

In conclusion, the results of this study, which examines the criterion validity of the IPAQ-SF against the GENEActiv accelerometer, suggests that the IPAQ-SF lacks validity for the assessment of MVPA, guideline adherence and assessing the relationship with cardiometabolic and inflammatory markers.

Figure 3: Kernel-density plot of accelerometer-measured MVPA across categories of IPAQ-SF reported MVPA



For IPAQ-SF measured MVPA, participants reporting zero minutes (0 min IPAQ-SF MVPA) had similar accelerometer-measured MVPA levels to those reporting 1-599 min IPAQ-SF MVPA.

Table 2: Characteristics of participants (N=279)			
	Male (N=147)	**Female (N=132)**	
	Median (25^{th}, 75^{th} percentile)	**Median (25^{th}, 75^{th} percentile)**	**p-values**
Age (years)	59.3 (55.0, 64.3)	60.5 (55.2, 63.6)	0.83
Cardiometabolic Markers			
BMI (kg/m^2)	29.1 (26.7, 31.9)	27.8 (25.0, 30.6)	0.01
Waist circumference (cm)	103.2 (95.1, 110.8)	88.5 (81.3, 96.2)	0.0001
Systolic blood pressure (mm Hg)	128 (120, 140)	124 (116, 140)	0.29
Diastolic blood pressure (mm Hg)	78 (72, 86)	80 (74, 86)	0.25
Cholesterol (mmol/l)	4.9 (4.3, 5.6)	5.5 (4.9, 6.2)	0.0001
HDL-C (mmol/l)	1.24 (1.08, 1.45)	1.60 (1.39, 1.89)	0.0001
LDL-C (mmol/l)	3.1 (2.5, 3.6)	3.2 (2.7, 3.8)	0.05
Triglycerides (mmol/l)*	1.18 (0.92, 1.88)	1.22 (0.84, 1.60)	0.25
Fasting blood glucose (mmol/l)*	5.1 (4.8, 5.6)	4.9 (4.6, 5.3)	0.0004
Insulin (mU/ml)*	10.63 (5.96, 17.04)	8.53 (5.37, 12.89)	0.06
$HOMA_{IR}$	2.42 (1.37, 4.04)	1.88 (1.14, 3.02)	0.03
$QUICKI_{IS}$	0.25 (0.22, 0.29)	0.27 (0.24, 0.31)	0.03
Complement c3 (g/l)	136.6 (123.2, 151.6)	138.3 (122.5, 159.7)	0.27
Interleukin-6 (pg/ml)*	1.93 (1.37, 3.05)	1.72 (1.07, 3.06)	0.12

Tumor necrosis factor-α (pg/ml)*	5.95 (4.92, 7.23)	5.65 (4.54, 7.11)	0.15
Leptin (ng/ml)*	1.71 (0.99, 2.50)	2.11 (1.39, 4.02)	0.0001
Adiponectin (µg/ml)*	3.36 (2.15, 4.87)	6.71 (4.43, 9.67)	0.0001
Accelerometer*			
Sedentary (mins/week)	6226 (5747, 6671)	6225 (5834, 6593)	0.84
Light (mins/week)	710 (478, 950)	737 (540, 899)	0.86
MVPA (mins/week)	489 (292, 764)	375 (192, 646)	0.02
MVPA bouts (mins/week _average duration)	138 (34, 274)	76 (16, 229)	0.03
IPAQ-SF			
Walking (mins/week)	180 (20, 360)	160 (50, 280)	0.52
Moderate (mins/week)	0 (0, 210)	0 (0, 0)	0.0001
Vigorous (mins/week)	0 (0, 180)	0 (0,0)	0.0013
MVPA (mins/week)	0 (0, 380)	0 (0, 30)	0.0001
IPAQ-SF categorical**			
Low	60 (43.5)	66 (53.7)	
Moderate	38 (27.5)	41 (33.3)	
High	40 (29.0)	16 (13.0)	0.007

Accelerometer data are presented as raw, non-scaled data
* Log-transformed variables expressed as exponentiated beta co-efficients
** Data presented as N (%). P-values were generated using non-parametric and chi-squares tests.

Table 3: N (%) of subjects classified as meeting physical activity guidelines according to IPAQ-SF and accelerometer-measured data			
	Accelerometer		
	Yes **N (%)**	**No** **N (%)**	**Total** **N (%)**
IPAQ-SF			
Yes	28 (32.9)	50 (31.9)	78 (32.2)
No	57 (67.1)	107 (68.1)	164 (67.8)
Total N	85 (100)	157 (100)	242 (100)
Pearson chi-square (P 0.862) Level of agreement 55.8% Cohen's κ for test of agreement, K= 0.011 (95% CI; -0.115, -0.137)			

Table 4: Regression coefficients (ß) for relationships between IPAQ-SF self-reported and accelerometer-derived MVPA variables with cardiometabolic markers						
	IPAQ-SF*		**Accelerometer**			
	minutes of MVPA**		**minutes of continuous MVPA****		**total minutes of MVPA in bouts greater than 10 minutes****	
Cardiometabolic Markers	**ß (95%CI)**	**p-value**	**ß (95%CI)**	**p-value**	**ß (95%CI)**	**p-value**
BMI (kg/m²)	-0.27 (-1.10, 0.55)	0.505	-1.52 (-2.12, -0.91)	<0.0001	-0.97 (-1.43, -0.50)	<0.0001
Waist circumference (cm)	-0.62 (-2.58, 1.34)	0.535	-3.64 (-5.19, -2.08)	<0.0001	-2.96 (-4.21, -1.71)	<0.0001
Systolic blood pressure (mm Hg)	0.60 (-1.92, 3.10)	0.642	-0.91 (-3.15, 1.33)	0.426	0.74 (-1.10, 2.56)	0.428
Diastolic blood pressure (mm Hg)	-0.62 (-2.19, 0.94)	0.430	-1.14 (-2.04, 0.14)	0.08	0.16 (-0.89, 1.21)	0.762
Cholesterol (mmol/l)	-0.05 (-0.22, 0.13)	0.598	0.25 (0.12, 0.38)	<0.0001	0.17 (0.05, 0.29)	0.005
HDL-C (mmol/l)	0.03 (-0.02, 0.08)	0.282	0.06 (0.02, 0.11)	0.003	0.04 (0.008, 0.08)	0.016
LDL-C (mmol/l)	-0.04 (-0.20, 0.12)	0.624	0.27 (0.15, 0.39)	<0.0001	0.20 (0.09, 0.31)	<0.0001
Triglycerides** (mmol/l)	-0.03 (-0.08, 0.02)	0.242	-0.06 (-0.10, -0.02)	0.004	-0.06 (-0.09, -0.02)	0.001
Fasting blood glucose** (mmol/l)	0.002 (-0.02, 0.03)	0.879	-0.03 (-0.05, -0.01)	0.006	-0.02 (-0.04, -0.003)	0.025
Insulin** (mU/ml)	-0.01 (-0.14, 0.11)	0.822	-0.27 (-0.36, -0.18)	<0.0001	-0.22 (-0.30, -0.15)	<0.0001

$HOMA_{IR}$**	-0.01 (-0.11, 0.09)	0.849	-0.21 (-0.28, -0.14)	<0.0001	-0.16 (-0.22, -0.10)	<0.0001
$QUICKI_{IS}$	0.0005 (-0.01, 0.01)	0.930	0.02 (0.01, 0.03)	<0.0001	0.02 (0.01, 0.03)	<0.0001
Complement c3 (g/l)	-1.50 (-6.08, 3.10)	0.520	-7.96 (-11.44, -4.47)	<0.0001	-5.59 (-8.46, -2.71)	<0.0001
Interleukin-6 (pg/ml)	-0.11 (-0.21, 0.003)	0.057	-0.25 (-0.33, -0.16)	<0.0001	-0.14 (-0.21, -0.07)	<0.0001
Tumor necrosis factor-α (pg/ml)	0.002 (-0.05, 0.06)	0.949	-0.06 (-0.10, -0.01)	0.008	-0.04 (-0.08, -0.005)	0.026
Leptin (ng/ml)	-0.13 (-0.27, 0.01)	0.074	-0.22 (-0.33, -0.12)	<0.001	-0.15 (-0.25, -0.06)	0.001
Adiponectin (µg/ml)	0.05 (-0.06, 0.16)	0.359	0.11 (0.02, 0.19)	0.011	0.09 (0.02, 0.15)	0.012
N=279 *N=97. **Non-normally distributed variables are log-transformed. Data presented as ß coefficients and 95%CI for change in cardiometabolic marker per 1 hour change in MVPA, adjusted for age, sex and zero/non-zero response (IPAQ-SF model only). P-values are given for ß values for each measurement method variable.						

CHAPTER FIVE – NUMBER OF DAYS REQUIRED TO ESTIMATE HABITUAL ACTIVITY USING GENEACTIV ACCELEROMETER.

Abstract

Introduction

Objective methods like accelerometers are feasible for large studies and may quantify variability in day-to-day physical activity better than self-report. The variability between days suggests that day of the week cannot be ignored in the design and analysis of physical activity studies. The purpose of this paper is to investigate the optimal number of days needed to obtain reliable estimates of weekly habitual physical activity using the GENEActiv accelerometer.

Methods

Data are from a subsample of the Mitchelstown cohort; 475 (44.6% males; mean aged 59.6±5.5 years) middle-aged Irish adults. Participants wore the wrist GENEActiv accelerometer for 7-consecutive days. Data were collected at 100Hz and summarised into a signal magnitude vector using 60s epochs. Each time interval was categorised based on validated cut-offs. Spearman pairwise correlations determined the association between days of the week. Repeated measures ANOVA examined differences in average minutes across days. Intraclass correlations examined the proportion of variability between days, and Spearman-Brown formula estimated intra-class reliability coefficient associated with combinations of 1-7 days.

Results

Three hundred and ninety-seven adults (59.7±5.5yrs) had valid accelerometer data. Overall, men were most sedentary on weekends while women spent more time in sedentary behaviour on Sunday through Tuesday. Post hoc analysis found sedentary behaviour and light activity levels on Sunday to differ to all other days in the week. Analysis revealed greater than 1 day monitoring is necessary to achieve acceptable reliability. Monitoring frame duration for reliable estimates varied across intensity

categories, (sedentary (3 days), light (2 days), moderate (2 days) and vigorous activity (6 days) and MVPA (2 days)).

Conclusion

These findings provide knowledge into the behavioural variability in weekly activity patterns of middle-aged adults. Since Sunday differed from all other days in the week this suggests that day of the week cannot be overlooked in the design and analysis of physical activity studies and thus should be included in the study monitoring frames. Collectively our data suggest that six days monitoring, inclusive of Saturday and Sunday, are needed to reliably capture weekly habitual activity in all activity categories.

Background

Accurately measuring habitual physical activity is crucial to understanding the relationship between frequency, duration, type and amount of physical activity and health. A range of subjective and objective methods to quantify physical activity and sedentary behaviour exist. Objective measures such as accelerometers and pedometers provide information on patterns of physical behaviour within a given day and across several days, are feasible for large studies, are less prone to error and no recall is necessary. Thus in comparison to subjective methods, objective measures provide significantly more reliable data on habitual physical behaviour.

Physical behaviour is influenced by a range of factors including demographic characteristics, emotional influences and behavioural attributes (189). As a result patterns of physical behaviour show substantial intra- and inter-individual variation, the extent of which plays a major role on data quality and reliability (190). Methodological issues such as duration of monitoring-frame, position of wear, accelerometer type and wear-time compliance may also affect data quality. Modern devices are fully waterproof and can be worn on the wrist, resulting in improved wear-time compliance as the device can be worn all day and does not need to be removed for water based activities (191, 192). Minimising the number of days monitoring will likely have important implications on wear-time compliance. Extended monitoring periods can be a burden to participants and financially costly, leading to the removal of the device, reduced wear-time, and subsequently reduced data quality. Thus a current challenge is determining an appropriate monitoring frame for researchers who want to minimise participant burden and maximise wear-time compliance.

Several studies have examined a suitable monitoring frame to accurately measure physical behaviour in adults (53, 193-195). These studies have varied in terms of

statistical analysis, position of wear, type of accelerometer and time-frame of interest, producing variable monitoring frames of 7 days, 5 days, 5-6 days and 3-5 days, respectively (53, 193-195). In addition, some examined the appropriate monitoring frames to reliably estimate habitual physical behaviour intensities individually (193, 194). Matthews et al. (2002) concluded that 3-4 days monitoring were required to correctly measure moderate-to-vigorous physical activity (MVPA), and that 7 days were needed to reliably estimate physical inactivity (193). Findings by Scheers et al. (2012) recommended overall that both Saturday and Sunday in addition to at least 3 weekdays were needed to obtain reliable estimates of habitual physical activity (194). Hart et al. (2011) recommended 5, 3 and 2 days monitoring for sedentary behaviour, light activity, moderate and vigorous activity respectively (53). Such conflicting recommendations highlight the need to determine an appropriate monitoring frame to reliably measure both habitual physical activity and sedentary behaviour for each accelerometer and activity intensity. Importantly no studies to date have sought to determine a suitable monitoring frame to accurately measure physical behaviour using the GENEActiv accelerometer placed on the wrist. The GENEActiv accelerometer is a relatively new device in the field of habitual physical activity research. Unlike many other accelerometers, data is collected and stored as raw acceleration in *g* units (m/s^2) for offline analysis thereby allowing a range of data processing techniques to be applied post data-collection.

Thus the aim of this study is to examine the intra- and inter-individual variability across days, and thus identify an appropriate monitoring frame for capturing weekly habitual physical behaviour in middle-aged adults using the wrist-GENEActiv accelerometer.

Methods

Data are from a subsample of the Mitchelstown Cohort; 475 (46.1% males; 59.7±5.5years) middle-aged Irish adults. Information on anthropometric measures and cardiometabolic and inflammatory markers were collected. Participants wore the wrist GENEActiv accelerometer for 7 consecutive days. Data were collected at 100Hz and summarised into a signal magnitude vector using 60s epochs. Each time interval was categorised based on validated cut-offs. Four-hundred and seventy-five subjects wore the accelerometer. Of these, 397 subjects were eligible for further analysis. The number of participants with various numbers of valid days (days in which the participant recorded >10 hours of wear time data) of data are presented in Table 1. These methods are described in greater detail in Chapter 3.

Statistical analysis

Analysis was performed separately for each intensity category. Individual median and 25th and 75th percentiles for minutes spent in each activity category were calculated for each day for non-normally distributed data. Data are reported as median and 25^{th} and 75^{th} percentiles unless otherwise stated. Kruskal-Wallis p-values assessed whether activity levels varied significantly across days of the week. Spearman pairwise correlations determined the association between days of the week. Number of days required to reliably estimate habitual physical activity was assessed using repeated measures analysis of variance (ANOVA), intra-class correlations (ICC), and modified Spearman-Brown formula (196). Repeated measures ANOVA established whether minutes spent in activity differed across days. In the case of the violation of the assumption of sphericity, the Greenhouse-Geisser adjusted F was interpreted. If an overall significant F level was shown, post hoc tests (Tukey HSD pairwise

comparisons) were used to assess differences between days. Effect size was assessed to determine the amount of variation in the criterion (total weekly minutes) that was accounted for by various days of monitoring. Coefficient of variation ((SD/mean)*100) was calculated to explain intra-individual and inter-individual variability. Intra-individual variability was calculated for each individual using weekly days of data while inter-individual variability was analysed as the group mean and SD for weekly minutes. ICCs were calculated to determine the reliability of using any single day of activity to estimate daily activity using 7 days of data. An ICC of 0.80 is considered standard to designated acceptable reliability (190). A modified version of the Spearman-Brown calculation determined the intraclass reliability coefficient associated with 1, 2, 3, 4, 5, 6, and 7 days of activity (193, 196, 197). The intraclass reliability coefficient was estimated as the proportion of total variance attributable to between-subject variance as follows: *[(between-subject variation)* ^{2} */ ((between-subject variation)* ^{2} *+ ((within-subject variation)* ^{2} */n))]*, where *n* is the number of days monitoring. All statistical analyses were conducted using Stata (version 12, Stata Corp, College Station, Texas, USA), except coefficient of variation and Spearman-Brown formula which were performed by hand. An alpha level of 0.05 was set to evaluate significance.

Results

Descriptive analysis

Median time (minutes) spent in each activity type across days of the week was calculated separately for men and women (Table 2). Overall, differences in median activity levels across days were significant ($P<0.05$), with the exception of vigorous activity ($P>0.05$). Among all subjects time spent in sedentary activity was greatest on

Sunday (946 minutes). Among men, sedentary activity was higher on Sunday (956 minutes) compared to all other weekdays (889-912 minutes), while women were most sedentary on Sunday through Tuesday (930-940 minutes). Both men and women were more physically active on weekdays. Time spent in vigorous activity was similarly low for men and women throughout the week.

Pairwise comparisons

All Spearman pairwise correlations between days of the week were significant (P<0.001). The range of pairwise correlations varied across days of the week and intensity type; sedentary (0.59-0.79), light (0.59-0.77), moderate (0.59-0.77), vigorous (0.37-0.60) and MVPA (0.58-0.78), (Table 17: Appendix 3). The mean pairwise correlations across days of the week were 0.72, 0.68, 0.69 and 0.41 for sedentary, light, moderate and vigorous activity respectively.

Variance analysis

There were significant differences between days for sedentary (P<0.01), light activity (P<0.01), moderate activity (P<0.01) and MVPA (P<0.01), whereas vigorous activity (P=0.15) was not significantly different between days. In relation to sedentary and light activity, Sunday differed from all other days of the week (P<0.05). The differences in mean minutes between days was small; sedentary (0.7%) moderate (0.4%), vigorous (0.2%) and MVPA (0.4%), except for light activity (1.6%). The mean intra-individual variability for each activity type were; sedentary (30.3%), light activity (45.4%), moderate activity (60.8%), vigorous activity (73.7%) and MVPA (61.6%), while inter-individual variability was 1.8-178% of total variance; sedentary (3.3%), light activity (2.3%), moderate activity (1.8%), vigorous activity (107%) and MVPA (178%).

Intra-class reliability coefficients

The ICC for any single day for sedentary, light, moderate activity, vigorous activity and MVPA was calculated, 0.66, 0.69, 0.69, 0.42 and 0.68 respectively. These results demonstrate that between 42-69% variance was accounted for using any single day of data collection to represent 7-day habitual activity. When ICC was calculated by gender, ICC did not alter, with the exception of vigorous activity (32% and 46% for men and women respectively). Spearman-Brown Formula calculated reliability coefficients for combination of days (Figure 4). These results indicate that between 59-82%, 68-87%, 74-90% and 78-92% of the variance was accounted for using 2 days, 3 days, 4 days and 5 days monitoring to represent 7 day habitual activity. The appropriate monitoring frames for each intensity of activity are 3 days, 2 days and 6 days for sedentary behaviour, light and moderate activity and MVPA and vigorous activity respectively. All remaining combinations were higher than 0.80.

Discussion

Our results indicate that the number of monitoring days required to estimate weekly habitual activity vary according to physical behaviour intensity. Based on our findings, we recommend that data collection periods should be based on activity intensity; sedentary (3 days), light activity (2 days), moderate activity (2 days), vigorous activity (6 days) and MVPA (2 days). Because variability between activity intensities across days of the week was small any combination of days appears to be sufficient to acquire a stable weekly estimate of physical activity and sedentary behaviour. Our findings support current guidelines recommending inclusion of both weekend and week days in physical behaviour monitoring frames. Many large studies (e.g. NHANES and Biobank) using similar protocols may apply our findings to reduce monitoring time-frames and increase device turnover in the field. Additionally our result could influence

the analysis of these studies, i.e. if moderate activity is the exposure of interest a minimum wear period of 2 days (inclusive of one weekend day) can be implemented in turn decreasing the number of days and or person excluded from analysis and thus increasing the power to finding significant associations with health outcomes.

While this is the first study to examine the required number of monitoring days needed to accurately measure physical behaviour in adults using the GENEActiv accelerometer, other accelerometers have been examined in this context (53, 193-195). Overall these studies vary in terms of statistical analysis, position of wear, type of accelerometer and time-frame of interest, resulting in variable monitoring frames of 7 days, 5 days, 5-6 days and 3-5 days, respectively (53, 193-195). All studies utilised different accelerometers; Compute Science Applications (CSA) accelerometer (193), SenseWear Armband (194), Caltrac accelerometer (195) and the ActiGraph (53), and positioned the device on multiple body positions; the hip (193), arm (194) and waist (53, 195). Several assessed the appropriate monitoring frames to reliably estimate habitual physical behaviour intensities independently (53, 193, 194). Matthews et al. (2002) determined that 3-4 days monitoring were required to accurately measure MVPA (193). Scheers et al. (2012) suggested that both Saturday and Sunday and at least 3 weekdays were needed to obtain reliable estimates of habitual physical activity, and only 3 days data collection was needed to capture light activity (194). Hart et al. (2011) proposed monitoring frames individually for sedentary behaviour, light activity, moderate and vigorous activity; 5, 3 and 2 days monitoring respectively (53). These inconsistent recommendations emphasise the need to establish an appropriate monitoring frame to reliably capture habitual physical behaviour for each accelerometer, activity intensity and position of wear.

Our results add to the current literature by reporting the number of monitoring days needed to reliably estimate habitual physical behaviour using GENEActiv accelerometers. The number of days needed to reliably estimate habitual physical behaviour vary according to activity intensity and statistical tests used (190). Tudor-Locke et al. (2005) contend that no single statistical test is considered adequate to fully understand the issues underlying the calculation of an appropriate monitoring frame (198). As recommended by Tudor-Locke et al. (2005), which employed a wide range of statistical techniques to determine number of days needed for an appropriate monitoring frame, Spearman-Brown prophecy formula has been used in the majority of studies investigating appropriate monitoring frames (193, 196, 199). Results of Spearman-Brown calculations and ICC for a single day identified consistent monitoring frames for all activity intensities (>1 day monitoring).

In addition, the moderate to high pairwise correlations across days indicated a clear tendency for activity patterns to be consistent across the days, with the exception of vigorous activity where correlations were low suggesting that vigorous activity patterns varied throughout the week, thus explaining the longer monitoring frame. In terms of sedentary and light activity, Sunday had the lowest correlations, suggesting the activity patterns on Sunday are less consistent with other days in the week. Greater between-subject variation and lesser within-subject variation across days results in shorter monitoring frames. Light and moderate intensity activities have the shortest monitoring frames; this could be due to higher levels of between-subject variation and lower levels of within-subject variation across days of the week compared to sedentary and vigorous activity, and thus 2 days of monitoring is sufficient to capture variation in light and moderate intensity activities. In addition, light and moderate intensity activities are more likely to include household activities and activities such as exercise

which tend to be planned, structured and repetitive (45). The same could be said for vigorous activity, however due to the very low levels of vigorous activity measured in this population, variation between- and within-subjects would be hard to capture accurately, thus resulting in a larger monitoring frame. This is supported by the low pairwise correlations across days, which indicate inconsistent activity patterns across the days.

Study strengths and limitations

A main strength of our study is the use of a valid and reliable activity monitor which is capable of assessing time spent in sedentary, light, moderate and vigorous activity categories (85). In addition, this accelerometer collects data as raw acceleration and stores the data as g units for offline analysis thereby allowing for efficient data cleaning, management of spurious data, and the application of various known data processing algorithms post-data collection. Further strengths include the 24-hour study protocol, the high study participation rate and large sample size. Notwithstanding these strengths one limitation of this study is that we only examined the required number of monitoring days needed to reliably estimate weekly habitual activity. Further investigation could be expanded into how many days/weeks of monitoring represent a month, a season, or a year of habitual activity using the GENEActiv accelerometer. Kang et al. (2009) examined a suitable monitoring frame to capture year-round averages of pedometer measured physical activity and found 5 consecutive days and 6 random days to be necessary (200). In addition, many studies have reported seasonal and monthly variations in physical activity leading to recommendations for physical behaviour data collection to occur during certain seasons and specific months of the year (179, 201, 202). Generalizability of our

findings may also be limited. The Mitchelstown cohort was a random sample of middle-aged adults, 50-69 years of age, in an area which was representative of both urban and rural population in Ireland. The sub-sample of the Mitchelstown cohort for whom accelerometer data was collected, differed by gender, in that women were more likely to agree to wear the accelerometer. In addition, participants were recruited from a primary care centre, and therefore could have more health problems or be more health conscious. However it should be noted that there were no statistically significant differences in age, gender, education or BMI between those included and excluded in the final analysis.

The data for this study was collected over 7 consecutive days at a frequency of 100Hz and collapsed into 60s epochs. Under these conditions our results demonstrate the number of monitoring days required to reliably assess weekly habitual activity for each type of intensity. We observed marked differences between weekdays, Saturday and Sundays. If the outcome of interest, for further studies, involves a more detailed examination of patterns of activity both Saturday and Sunday should be included in the monitoring frame. Similarly our gender specific findings, such as comparatively high sedentary activity in women on Monday, should be considered. This consideration may be particularly pertinent when examining overweight and obese adults whose activity on weekend days has been shown to be particularly distinct from normal weight subjects across week days (203, 204).

Conclusion

This study examined the number of monitoring days needed to accurately estimate habitual physical activity and sedentary behaviour from the GENEActiv accelerometer in middle-aged adults. Our data indicates 6 days monitoring are required to reliably

capture weekly activity in all activity categories however a minimum number of 2 days plus Sunday are recommended for sedentary, light and moderate activity intensities. These findings may have important implications in terms of study design and data reduction strategies. Further study protocols employing our recommendations may benefit from reduced number of data collection and processing days and associated reductions in person-time and study cost.

Table 5: Number of participants with valid days (>10 hours of wear time) of data

Number of valid days wear	Number of participants
7 days	397
6 days	27
5 days	12
4 days	4
3 days	3
2 days	4
1 days	6
0 days	6

Table 6: Daily duration (minutes) of sedentary, light, moderate and vigorous activity

	Total (n=397)				
	Sedentary	**Light**	**Moderate**	**Vigorous**	**MVPA**
Monday	926 (833, 984)	94 (64, 140)	50 (24, 93)	1 (0, 5)	56 (25, 100)
Tuesday	921 (837, 981)	98 (64, 135)	48 (24, 91)	1 (0, 6)	52 (25, 101)
Wednesday	911 (829, 976)	100 (68, 143)	55 (25, 95)	1 (0, 5)	59 (27, 100)
Thursday	908 (842, 977)	106 (66, 140)	56 (26, 93)	1 (0, 5)	58 (26, 100)
Friday	903 (826, 977)	106 (68, 148)	57 (25, 100)	1 (0, 5)	62 (25, 106)
Saturday	910 (839, 989)	100 (65, 142)	51 (23, 98)	1 (0, 5)	56 (23, 103)
Sunday	946 (872, 1004)	77 (48, 117)	42 (17, 82)	0 (0, 3)	46 (18, 91)
p-value	<0.001	<0.001	<0.001	0.81	<0.001

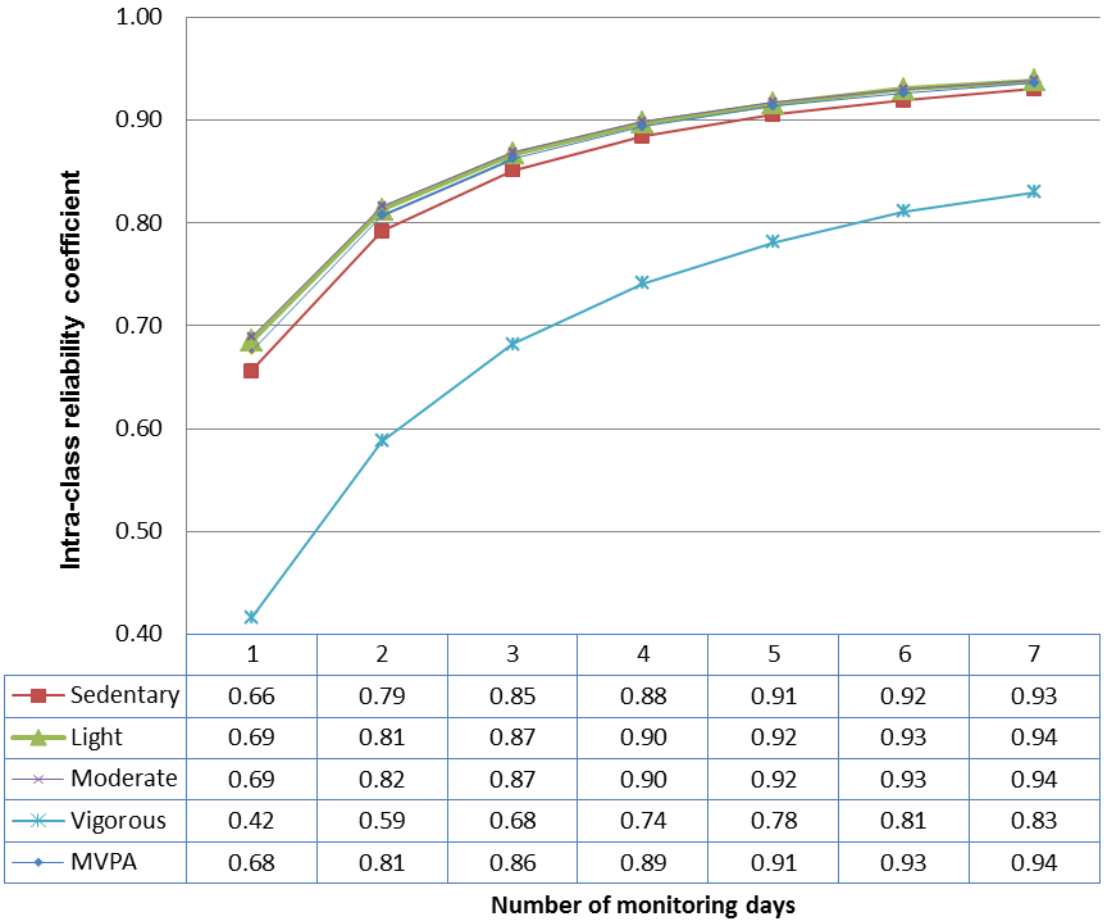
	Men (n=183)				
	Sedentary	**Light**	**Moderate**	**Vigorous**	**MVPA**
Monday	909 (798, 972)	98 (66, 154)	60 (29, 116)	1 (0, 7)	69 (29, 126)
Tuesday	906 (813, 979)	103 (62, 146)	61 (25, 112)	1 (0, 7)	66 (27, 120)
Wednesday	903 (802, 970)	99 (67, 156)	66 (32, 118)	1 (0, 6)	76 (33, 122)
Thursday	901 (815, 978)	104 (66, 143)	66 (31, 107)	1 (0, 5)	71 (31, 116)
Friday	889 (802, 977)	100 (66, 156)	65 (29, 111)	1 (0, 6)	74 (30, 121)
Saturday	912 (840, 987)	99 (65, 135)	58 (25, 99)	1 (0, 6)	64 (25, 103)
Sunday	956 (878, 1009)	70 (43, 108)	45 (18, 85)	1 (0, 4)	47 (19, 85)
p-value	<0.001	<0.001	0.009	0.77	0.01

	Women (n=214)				
	Sedentary	**Light**	**Moderate**	**Vigorous**	**MVPA**
Monday	931 (869, 990)	92 (58, 133)	40 (22, 76)	1 (0, 3)	46 (22, 82)
Tuesday	930 (867, 985)	97 (66, 130)	43 (21, 75)	1 (0, 5)	47 (22, 84)
Wednesday	918 (850, 980)	100 (68, 135)	49 (23, 83)	1 (0, 4)	52 (25, 87)
Thursday	915 (854, 974)	107 (68, 138)	48 (23, 83)	1 (0, 4)	51 (24, 88)
Friday	910 (844, 979)	110 (68, 146)	48 (23, 84)	1 (0, 4)	52 (25, 89)
Saturday	909 (834, 990)	103 (67, 148)	46 (21, 94)	1 (0, 4)	51 (22, 104)
Sunday	940 (862, 1002)	89 (51, 124)	38 (16, 80)	0 (0, 3)	43 (16, 85)
p-value	<0.001	<0.001	<0.001	0.84	<0.001

Data is presented as median (25th, 75th percentile)

P-values presented as Kruskal-Wallis, tests the difference in median activity levels across days of the week.

Figure 4: Reliability coefficients for number of days monitoring based on Spearman-Brown Formula.



	1	2	3	4	5	6	7
Sedentary	0.66	0.79	0.85	0.88	0.91	0.92	0.93
Light	0.69	0.81	0.87	0.90	0.92	0.93	0.94
Moderate	0.69	0.82	0.87	0.90	0.92	0.93	0.94
Vigorous	0.42	0.59	0.68	0.74	0.78	0.81	0.83
MVPA	0.68	0.81	0.86	0.89	0.91	0.93	0.94

Figure 4 illustrates the reliability coefficient associated with different length monitoring frames. The results propose that between 59-82%, 68-87%, 74-90% and 78-92% of variance was explained for by using 2 days, 3 days, 4 days and 5 days monitoring to represent 7 days of habitual activity.

CHAPTER SIX – CROSS-SECTIONAL ANALYSIS OF WEEKLY LEVELS AND PATTERNS OF OBJECTIVELY-MEASURED PHYSICAL BEHAVIOUR WITH CARDIOMETABOLIC HEALTH IN MIDDLE-AGED ADULTS.

Abstract

Introduction

Little is known how combined weekly patterns of physical activity and sedentary behaviour are associated with cardiometabolic health. The objective of this paper is to identify weekly patterns of physical activity and sedentary behaviour and to examine cardiometabolic health status associated with different activity patterns.

Methods

Data are from a subsample of the Mitchelstown Cohort; 475 (59.7±5.5 years) middle-aged adults. Participants wore the wrist GENEActiv accelerometer for7 consecutive days. Data was summarised into 60s epochs and each time interval categorised based on thresholds. LPA defined classes based on observed clustering of sedentary behaviour and physical activity variables while multivariate latent class regression was used to compare cardiometabolic health status across classes.

Results

LPA revealed 4 distinct physical behaviour patterns; Sedentary Group (15.9 %), High Sedentary; Lower Activity Group (28.0%), Lower Sedentary; Higher Activity Group (44.2%) and a Physically Active Group (11.9%). Overall the Sedentary Group had poorer profiles, characterised by high BMI, waist circumference, TAG, FPG, TNF-α, leptin, C3, insulin resistance, IL6 and insulin levels, and low insulin sensitivity, HDL-C, LDL-C, CHOL and adiponectin levels. The remaining classes were characterised by healthier cardiometabolic profiles as sedentary behaviour levels decreased.

Conclusion

The classification of groups of adults with similar physical behaviour patterns offers important information for the identification and tailoring of public health and health

promotion intervention strategies. Future health policy should be directed towards altering patterns of behaviour rather than concentrating on a single type of behaviour.

Introduction

Sedentary behaviour and physical activity have been found to have significant associations with health however their combined association with health have not been extensively studied. Being physically active is a major contributor to both physical and mental health (10, 16, 51, 52, 106, 151, 152). Conversely, sedentary behaviour has been found to be associated with poor health and mortality (12, 23, 25, 205-207). The health benefits of regular physical activity, more specifically moderate-to-vigorous physical activity (MVPA), are well established (10). Current guidelines recommend adults to accumulate 150 minutes of moderate-intensity activity or 75 minutes of vigorous activity or a combination of both per week occurring on most days of the week (29, 51, 52). The rational for recommending activity on most days of the week is attributable to evidence from early intervention studies (135). However, few studies have been able to isolate the effect of physical activity frequency from total-time for all-cause mortality (60, 101). In the past decade, research has reported the emergence of the 'weekend warrior' who accumulates most of their weekly activity into 1-2 days (42, 43, 60, 66). Lee et al. (2004) reported that among low-risk men, this 'weekend warrior' pattern could postpone mortality (60). Metzger et al. (2010) reported the 'weekend warrior' pattern to have higher risk of obesity, low high density lipoprotein cholesterol (HDL-C), and high triglyceride (TAG) levels, but lower risk of high blood pressure and fasting plasma glucose (FPG) when compared to individuals who accumulate similar activity levels over a longer period (43).

Most research examining the relationship between physical behaviour and health has focused on summary estimates of MVPA using self-reported data (99, 100, 208, 209). Self-reported data are prone to various degrees of measurement error and bias (74, 75). Objective physical behaviour measurements offer several advantages including

lower costs, coupled with the rich, accurate, time-stamped data obtained. Furthermore, the time-stamped data offers the potential to examine patterns of physical behaviour across time periods based on frequency, duration and intensity of activity and thus allow more complete physical behaviour profiles to be evaluated. Despite this, most research using objective physical behaviour measurements to identify weekly patterns of activity report summary estimates across days of the week (210-212). There is no doubt that summary estimates have contributed to our understanding of the relationship between physical behaviour and cardiometabolic health. However the application of summary estimates across the entire measurement periods may preclude us from uncovering how weekly patterns or weekly accumulation of physical behaviour intensities differ in their associations with cardiometabolic health outcomes. Thus assessing weekly physical behaviour patterns, using individual specific daily estimates, may highlight relationships not previously observed (46).

Few studies have attempted to identify weekly patterns of physical activity and sedentary behaviour using accelerometry data in middle-aged adults (42, 43). Many have used self-reported data and the majority have been based on children and adolescents populations (213-219). The identification of weekly activity patterns, using LPA, has scarcely been examined in middle-aged adults (42, 43). To date only 2 studies, based on the same study population in the US, have identified weekly patterns of MVPA in adults (42, 43). A major limitation of these studies are that just focusing primarily on MVPA disregards the important contribution of both light and sedentary activity to habitual activity, overlooks the compositional nature of these physical behaviours and thus ignores the association between these interrelated physical behaviours and health. Loprinzi et al. (2014) examined the interrelated association between physical behaviour patterns and health using predefined groups and reported

evidence that individuals who did not meet weekly physical activity recommendations, but who had higher levels of light activity than sedentary activity had more favourable TAG and insulin levels (220). To date, no study has examined the interrelated association between different physical behaviour patterns and health using continuous data, which LPA allows us to assess in a population sample of middle-aged adults. Thus the purpose of this study is to identify and describe unique patterns of physical activity and sedentary behaviour in a population sample of middle-aged adults and to assess whether cardiometabolic health indices differ between profiles of activity patterns.

Methods

Data are from a subsample of the Mitchelstown Cohort; 475 (46.1% males; 59.7±5.5years) middle-aged Irish adults. Information on anthropometric measures and cardiometabolic and inflammatory markers were collected. Participants wore the wrist GENEActiv accelerometer for 7 consecutive days. Daily summaries of time spent (minutes) in sedentary behaviour, light activity and MVPA were calculated. All variables were expressed proportional to individual wear time. These methods are described in greater detail in Chapter 3.

Statistical analysis

Descriptive statistics

Descriptive statistics (number (%) and median (25^{th}, 75^{th} percentile)) were calculated for all study variables and are presented in Table 7.

Latent profile analysis

Firstly, LPA was used to identify coexisting classes of physical behaviour patterns identified by mean time (minutes) spent in sedentary behaviour, light activity and MVPA across each day of the week. These patterns are mutually exclusive classes that maximise between-group variance and minimises within-group variance based on model fit criteria (86). Outcomes of LPA include the number of latent classes, the mean of each indicator variable in each class, and probability of class membership.

Secondly, a multivariate Latent Class Regression (LCR) model examined the association between class memberships and cardiometabolic health status using odds ratios. Latent class regression fits regression equations to coexisting classes of respondents exhibiting similar physical behaviour patterns. Age, gender, season and job status were included as covariates. These covariates were used to help predict class membership. The LCR model identifies a set of classes of a latent variable from a set of observed discrete variables (daily minutes of sedentary behaviour, light activity and MVPA) (104, 105). In contrast to regression models, LCR highlights the set of latent classes identified in the analysis, rather that considering each of the observed indicators separately or all possible combinations of the observed indicators (104).

Selecting the number of classes

In order to select the appropriate number of classes, a series of latent class models, with an increasing number of classes were compared. Determining the number of classes that adequately describe the sample was based on a combination of model fit indices (Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), Sample Size Adjusted SSA-BIC (SSA-BIC), Lo Mendell Rubin (LMR)), theoretical implications and distinctiveness of each latent class profile (entropy). Several models were fit to the data, one through 5 latent profiles. Model parameters were estimated

using Maximum Likelihood Estimator based on the Expectation Maximization algorithm. The AIC (-2 * number of model parameters), BIC (-2 * model log-likelihood + log(*n*) * number of model parameters), and LMR were computed to compare competing models. To ensure maximum likelihood solution was correctly identified within these models, 100 iterations of each model were run using 1,000 random starts. The LPA model included covariates; age, gender, season and job status, to help predict class membership by providing more refined prior probabilities based on the distribution of the socio-demographic characteristics within each class (42). All statistical analyses were conducted using Mplus software (version 6.12 for Windows). An alpha level of 0.05 was set to evaluate significance.

Results

Descriptive information

The distribution of subject characteristics and accelerometer-measured physical activity by gender is presented in Table 7. Similar sedentary behaviour and light activity levels were observed for males and females on most days of the week, with the exception of Monday for sedentary behaviour, where females were significantly more sedentary (P=0.003), and Sunday for light activity (P<0.05) where females had significantly higher light activity levels. In contrast, MVPA levels were similar toward the end of the week and differed significantly Monday through Friday (P<0.03) with males accumulating higher MVPA. The mean age in the sample was 59.7 years (SD 5.5 years) and did not differ between males (46.1%) and females, (P=0.86). Approximately 24.8% of women were unemployed or did home duties while more females wore the accelerometer during Summer/Autumn months (P<0.001). Cardiometabolic variables are presented in Table 8. Statistically significant differences

were observed between males and females (P<0.05), with the exception of systolic blood pressure, C3, IL6 and TNF-α.

Latent profile analysis

During the primary stage of analysis, a LPA model with covariates was fitted to the physical behaviour variables, starting with a 1 class model and progressing to a 5 class model. The Information Criteria, entropy, likelihood ratio tests are presented in Table 9 and class probabilities of each latent class are presented in Appendix 4. AIC and SSA-BIC fit indices decreased as the number of profiles increased while entropy remained high (>0.90) for all models. BIC indices decreased up to a 4 class model where a slight increase was observed. All profiles seem to differ from the smaller ones only by separating out smaller subgroups of participants from the larger profiles. These smaller subgroups were increasingly difficult to interpret theoretically as they showed similar physical behaviour patterns but varied in predictor means. The quality of the resulting classification was also evaluated based on the entropy index. Values range from 0 to 1, and high values (>0.90) indicate that the latent classes are highly discriminative. Allowing for the arguments between model parsimony, statistical fit, and theory, the 4-class model was chosen as best fit model.

Latent class physical behaviour profiles are presented in Figures 5a-5d. The figures illustrate the differences and magnitude of the differences in physical behaviour patterns across the 4 latent classes. Class 1 was characterised by high sedentary behaviour levels and low physical activity levels. In contrast, class 2 was characterised by low sedentary behaviour levels and higher physical activity levels. Class 3 are characterised by high sedentary behaviour and lower physical activity levels while class 4 was highly physically active with low levels of sedentary behaviour. More

specifically, class 1 is characterised as having approximately 2.5hours more sedentary behaviour and 2.5 hours less light activity and MVPA compared to class 2. Additionally, class 3 is characterised as having approximately 4 hours more sedentary behaviour and 3 hours less light activity and MVPA compared to class 4.

LPA and cardiometabolic health status

In relation to cardiometabolic health indices, the four latent classes are characterised as follows: Class 2 (Lower Sedentary; Higher Activity Group) is characterised by high insulin sensitivity and adiponectin levels low FPG and IL6 levels; Class 3 (High Sedentary; Lower Activity Group) is characterised by high insulin resistance, C3, adiponectin and TNF-α and low insulin sensitivity; Class 1 (Sedentary Group) is characterised by high BMI, waist circumference, TAG, FPG, TNF-α, leptin, C3, insulin resistance, IL6 and insulin levels, and low insulin sensitivity, HDL-C, LDL-C,CHOL and adiponectin levels and Class 4 (Physically Active Group) is characterised by high insulin sensitivity and low FPG, insulin, insulin resistance, C3, TNF-α and leptin. Classes 2 through 4 have similar, BMI, waist circumference, HDL-C, LDL-C, CHOL and BP levels. The mean estimates for cardiometabolic predictor variables are presented in Table 10.

Table 11 summarises the associations between cardiometabolic health outcomes (diabetes, obesity and hypertension) and class membership when controlling for the influence of age, gender, season and job occupation on class membership. In relation to class probability, diabetic persons had a 15%, 5%, 10% and 7% probability of being in class 1 through 4 respectively. Obese and hypertensive persons had 49%, 25%, 38%, 24% and 29%, 26%, 67% and 26% probability of being in class 1 thru 4 respectively. Despite these differences, regression analysis only observed significant

differences between classes with respect to obesity and hypertension. Compared to class 1, classes 2 through 4 had significantly higher odds of obesity (OR: 1.59 – 3.17; p<0.023) and hypertension (OR: 1.05 - 1.15; p<0.03), with the exception of class 3 which had lower odds off hypertension 9OR: 0.84; p=0.008). Additionally, classes 3 and 4 had lower odds of obese (OR: 0.533; p=0.004) and hypertensive persons (OR: 0.727-0.908; p<0.02) with the exception of obese persons in class 2 (OR: 1.07; p=0.015). In other words, obese and hypertensive individuals were 1.59 – 3.17 and 1.05-1.15 times more likely to be in classes 2 thru 4 when compared to class 1

Discussion

The primary aim of this study was to identify unique clusters of activity patterns among adults based on their weekly participation in sedentary behaviour, light activity and MVPA. Secondly, to explore differences in cardiometabolic health status between clusters patterns of activity. Our analysis identified four distinct physical behaviour patterns; Sedentary Group, Higher Sedentary; Lower Activity Group, Lower Sedentary; Higher Activity Group and a Physically Active Group. While the sedentary group was characterised as having the worst cardiometabolic profile, no major differences in cardiometabolic markers were observed between the Sedentary Group and the remaining three identified groups (Higher Sedentary; Lower Activity Group, Lower Sedentary; Higher Activity Group and a Physically Active Group). While this is the first study to our knowledge to identify combined, weekly physical activity and sedentary behaviour patterns in a population-sample of middle-aged adults using LPA and accelerometer data, a number of studies have previously identified combined patterns of habitual activities (221, 222). Metzger et al. (2007) identified weekly patterns of MVPA in a population sample of adults. By focusing exclusively on MVPA,

the potential differential effects of light activity compared with sedentary behaviour on health outcomes have been ignored. Buman et al. (2010) reported that both higher intensity-light activity and MVPA are interchangeable with respect to their associations with physical health in older adults; however evidence is lacking in middle-aged adults. Recent studies that have examined the combined, interrelated patterns of physical activity and sedentary behaviour have used newly proposed methods (The ATLAS Index and exposure variation analysis (EVA)) which have yet to be validated in large population samples. Marschollek et al. (2014) proposed a new method 'The ATLAS Index' to derive common measures for distinguishing different characteristic activity phenotypes for accelerometer data while Straker et al. (2014) suggested EVA to capture physical behaviour patterns (221, 222). Straker et al. (2014) reported EVA to be a unique and comprehensive method that is able to capture the time pattern of physical behaviour (221). However, this method needs variables to be categorical thus it does not fully capture the real-time aspects of activity. In addition, this study uses uni-axial or omnidirectional plane for analysis and the sample size is small (n=8). Thus EVA has yet to be validated for use using tri-axial data on a large population sample.

Previous studies examining the relationship between physical behaviour and health have largely focused on averaged or total summary estimates across group. However associations can be overlooked or diluted when the focus is on the group summary estimate and the variation in physical activity and sedentary behaviour patterns throughout the week are ignored. Our results add to the current literature by identifying 4 distinct physical behaviour patterns in middle-aged adults and examining their relationship with numerous cardiometabolic markers. Our data indicate that as physical activity levels increase cardiometabolic health status improves, suggesting

that even modest increases in lower intensity physical activity may have beneficial health effects.

Study strengths and limitations

Strengths of this study include the high participation rate (64%) and the use of objective measurement of physical behaviour and measurement of a wide range of cardiometabolic biomarkers. Compared with self-report, objective measurements are more precise, less biased and reduce the potential for measurement error. The recall and social-desirability biases that accompany self-report measures are well known and may lead to misclassification bias (74). The current study has a number of limitations that should be noted. First, this is a cross-sectional study and therefore cause-effect relations cannot be determined. In addition, different data processing methods could result in different activity classes. Nonetheless, these analyses have shown the merits of LPA for the purpose of identifying and describing groups of adults based on their distinct physical activity and sedentary behaviour patterns throughout the week. Furthermore it should be noted that approximately 24.8% of women were unemployed or did home duties while 0% of males were unemployed. Home duty is very common feature of Irish societies especially in older and middle-aged female adults. In recent decades, more and more women have entered that workplace from all ages. These levels of unemployment in our study population are not representative for the Irish population as unemployment rates for males and females in 2011 were 13.3% and 9.2% respectively. However for this analysis, employment status was used to adjust for differences in physical behaviour patterns between those who have a scheduled work day and those who didn't. The sedentary group was characterised as having the worst cardiometabolic profile however no major differences in

cardiometabolic markers were observed between the groups. LPA analysis found four different physical behaviour patterns in the population, resulting in classes 1 and 4 having small sample sizes (16% and 12% of the study sample respectively). These groups may not have large enough sample sizes for sufficient statistical power to detect accurate association with health outcomes. A study with low statistical power has a reduced chance of detecting true associations and also reduces the probability that a statistically significant finding exposes a true association. Thus further studies using larger sample sizes are required. While outcomes of this study may be considered a consequence of multiple testing, it is worth emphasising that this paper is an exploratory analysis of the association between physical behaviour clusters and cardiometabolic health outcomes. Thus both significant and non-significant associations are presented for transparency.

Generalizability of the study

Generalizability of our findings may also be limited. The Mitchelstown Cohort was a random sample of general practice registered, middle-aged adults, 50-69 years of age, in an area which was representative of both urban and rural population in Ireland. In addition, participants were recruited from a primary care centre, and therefore could have more health problems or be more health conscious.

Conclusion

The classification of groups of adults with similar physical behaviour patterns provides valuable information for the identification and tailoring of specific public health and health promotion messages and intervention strategies. Large prospective studies are needed to assess the relationship between the long-term exposure or impact of

different clustering patterns on inflammatory and cardiometabolic status, as intermediate phenotypes predisposing to risk of developing obesity, cardiovascular disease and overt diabetes.

Table 7: Descriptive characteristics of study participants by gender (N=397)			
	Male (N=183)	**Female (N=214)**	
	Median (25th, 75th percentile)	**Median (25th, 75th percentile)**	**p-values**
Physical activity distal outcomes (minutes)			
Sedentary activity			
Monday	909 (798, 972)	931 (869, 990)	0.003
Tuesday	906 (813, 980)	930 (867, 986)	0.03
Wednesday	903 (802, 970)	918 (850, 980)	0.05
Thursday	901 (815, 978)	916 (855, 974)	0.11
Friday	889 (802, 977)	910 (844, 979)	0.28
Saturday	912 (840, 987)	909 (834, 990)	0.92
Sunday	956 (878, 1010)	940 (862, 1003)	0.29
Light activity			
Monday	98 (66, 154)	92 (58, 133)	0.08
Tuesday	103 (62, 146)	97 (66, 130)	0.28
Wednesday	99 (67, 156)	100 (68, 135)	0.73
Thursday	104 (66, 143)	107 (67, 138)	0.96
Friday	100 (66, 156)	110 (69, 146)	0.71
Saturday	99 (65, 135)	103 (67, 148)	0.31
Sunday	70 (43, 108)	89 (51, 124)	0.007
MVPA			
Monday	68 (29, 126)	46 (22, 82)	0.0003
Tuesday	66 (26, 120)	47 (22, 84)	0.007
Wednesday	76 (33, 122)	52 (25, 87)	0.002
Thursday	71 (31, 116)	51 (24, 88)	0.004
Friday	74 (30, 121)	52 (25, 89)	0.03
Saturday	64 (25, 103)	51 (22, 104)	0.25
Sunday	48 (19, 94)	43 (16, 85)	0.59
Indicator variables			
Age (years)	59.4 (54.9, 64.3)	59.3 (54.8, 64.5)	0.86
Season*			
Winter/Spring	147 (80.8)	131 (61.2)	
Summer/Autumn	35 (19.2)	83 (38.8)	<0.001
Job status*			
Employed	183 (100)	161 (75.2)	
Unemployed	0	53 (24.8)	<0.001
*Data presented as N (%), all other data presented as medians (25th, 75th percentile). P-values were generated using non-parametric and chi-squares tests.			

Table 8: Distribution of cardiometabolic variables by gender (N=397)			
	Male (N=183)	**Female (N=214)**	
	Median (25^{th}, 75^{th} percentile)	**Median (25^{th}, 75^{th} percentile)**	**p-values**
Cardiometabolic distal outcomes			
BMI (kg/m²)	29.1 (26.4, 31.9)	27.8 (25.2, 30.4)	0.004
Systolic blood pressure (mm Hg)	128 (118, 140)	126 (118, 142)	0.97
Diastolic blood pressure (mm Hg)	78.0 (72, 86)	82 (74, 88)	0.03
Cholesterol (mmol/l)	4.9 (4.3, 5.6)	5.5 (4.9, 6.2)	0.0001
HDL-C (mmol/l)	1.25 (1.07, 1.46)	1.62 (1.39, 1.86)	0.0001
LDL-C (mmol/l)	3.1 (2.5, 3.6)	3.3 (2.7, 3.9)	0.02
Triglycerides (mmol/l)	1.25 (0.92, 1.85)	1.12 (0.81, 1.50)	0.01
Fasting blood glucose (mmol/l)	5.1 (4.8, 5.6)	4.9 (4.6, 5.2)	0.0001
Insulin (mU/ml)	10.41 (6.03, 15.84)	8.17 (5.26, 12.58)	0.01
$HOMA_{IR}$	2.40 (1.41, 3.82)	1.78 (1.08, 2.86)	0.0025
$QUICKI_{IS}$	0.25 (0.22, 0.29)	0.27 (0.24, 0.31)	0.0025
Complement c3 (g/l)	134.5 (120.3, 149.4)	137.5 (119.4, 155.0)	0.21
Interleukin-6 (pg/ml)	1.87 (1.33, 3.08)	1.69 (1.09, 2.82)	0.055
Tumor necrosis factor-α (pg/ml)	5.96 (4.92, 7.24)	5.72 (4.56, 7.10)	0.09
Leptin (ng/ml)	1.76	2.20 (1.39, 4.08)	0.0001
Adiponectin (µg/ml)	3.36 (2.24, 4.95)	6.52 (4.37, 9.59)	0.0001
P-values were generated using non-parametric tests.			

Table 9: Latent Profile Analysis; Fit indices for 1-5 class models					
	1 Class	**2 Class**	**3 Class**	**4 Class**	**5 Class**
Log-likelihood	-58661	-60863	-59637	-59058	-58661
AIC	131038	122022	119703	118680	118020
BIC	131384	122612	120559	119803	119410
SSA-BIC	131108	122142	119877	118909	118302
Entropy	-	0.984	0.985	0.974	0.980
LMR test	-	-63512	-60863	-59637	-59209
LMR p-value	-	0.000	0.7602	0.7962	0.777
Variables included in the model: minutes spent in sedentary behaviour , light activity and MVPA					

Figure 5 (a): Class 1: Sedentary Group (15.9%): Weekly Distribution of Physical Behaviour

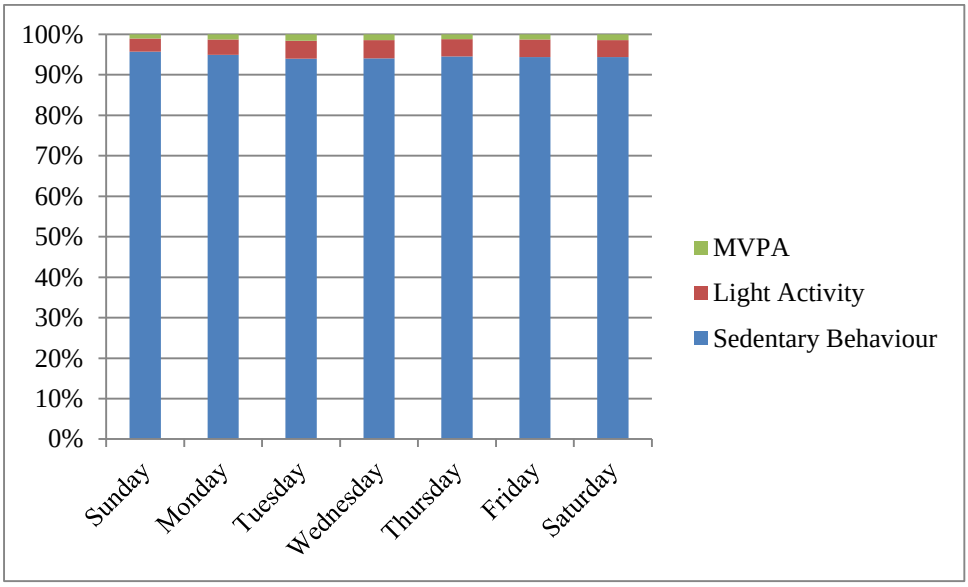


Figure 5 (b): Class 2: Lower Sedentary, Higher Activity Group (44.2%): Weekly Distribution of Physical Behaviour

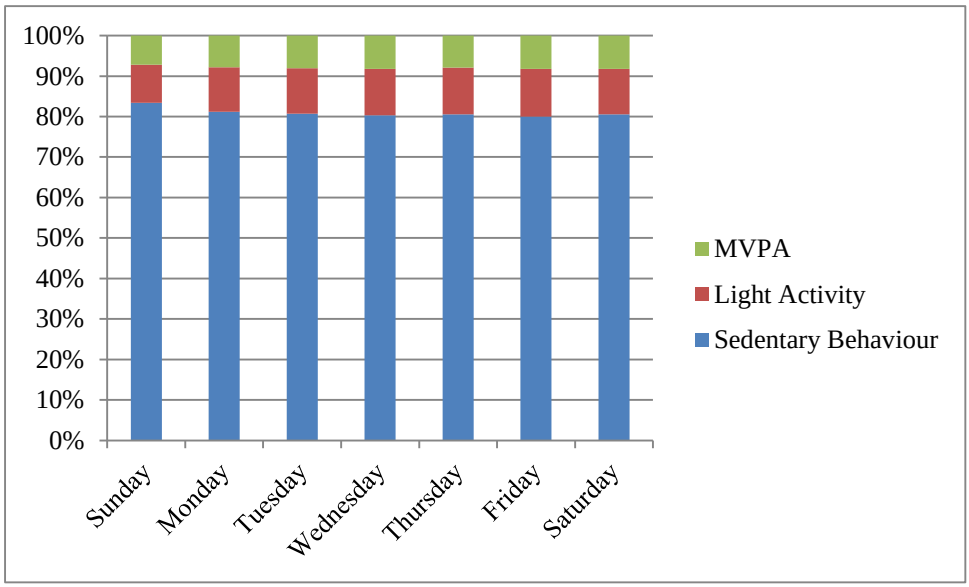


Figure 5 (c): Class 3: Higher Sedentary, Lower Activity Group (28.0%): Weekly Distribution of Physical Behaviour.

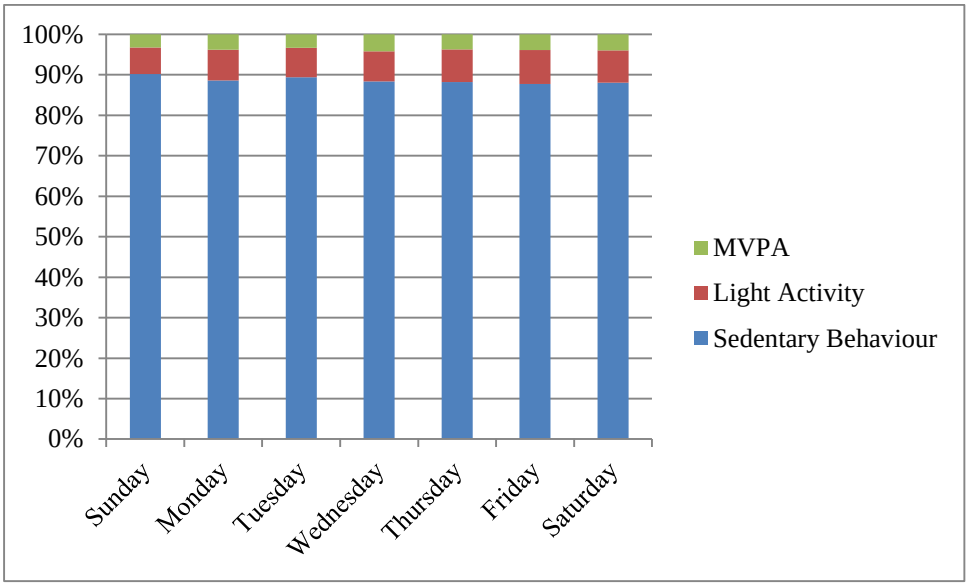


Figure 5 (d): Class 4: Physically Active Group (11.9%): Weekly Distribution of Physical Behaviour

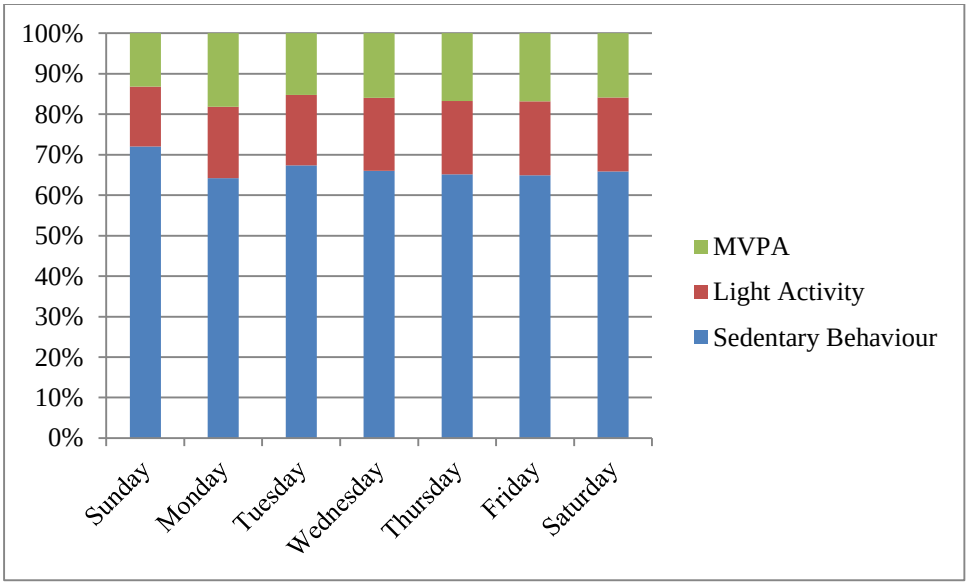


Table 10: Latent class regression; variable means				
	Class 1	**Class 2**	**Class 3**	**Class 4**
Segment size (%)	63 (15.9)	175 (44.2)	111 (28.0)	47 (11.9)
Cardiometabolic markers*				
BMI (Kg/m^2)	31	28	29	28
Waist circumference (cm)	102	95	96	95
Systolic blood pressure (mm Hg)	128	128	132	130
Diastolic blood pressure (mm Hg)	80	80	82	78
Cholesterol (mmol/l)	4.88	5.4	5.38	5.20
HDL-C (mmol/l)	1.38	1.51	1.45	1.48
LDL-C (mmol/l)	2.8	3.3	3.2	3.22
Triglycerides(mmol/l)	1.54	1.28	1.56	1.13
Fasting blood glucose (mmol/l)	5.57	5.11	5.22	5.13
Insulin (mU/ml)	15.89	10.28	14.21	7.43
$HOMA_{IR}$	4.24	2.44	3.6	1.75
$QUICKI_{IS}$	0.24	0.28	0.26	0.299
Complement c3 (g/l)	147.79	135.37	144.51	127.3
Interleukin-6 (pg/ml)	4.31	2.11	2.31	2.59
Tumor necrosis factor-α (pg/ml)	6.52	5.97	6.50	5.88
Leptin (ng/ml)	4.40	2.39	2.84	1.79
Adiponectin (μg/ml)	5.10	5.99	5.83	5.53
*All markers have equal variance				

Table 11: Latent class regression on cardiometabolic factors	
Class comparison	**Odds Ratio (p-value)**
Class 1 compared to class 2	
Diabetes	3.55 (0.059)
Obesity	2.98 (0.004)
Hypertension	1.15 (0.004)
Class 1 compared to class 3	
Diabetes	1.53 (0.057)
Obesity	1.59 (0.015)
Hypertension	0.84 (0.008)
Class 1 compared to class 4	
Diabetes	2.46 (0.170)
Obesity	3.17 (0.03)
Hypertension	1.05 (0.03)
Class 2 compared to class 3	
Diabetes	0.431 (0.05)
Obesity	0.533 (0.004)
Hypertension	0.727 (0.001)
Class 2 compared to class 4	
Diabetes	0.694 (0.166)
Obesity	1.07 (0.015)
Hypertension	0.908 (0.014)
Class 3 compared to class 4	
Diabetes	1.61 (0.168)
Obesity	1.99 (0.03)
Hypertension	1.25 (0.02)

CHAPTER SEVEN - DAILY CUMULATIVE PATTERNS OF OBJECTIVELY-MEASURED PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR BY CARDIOMETABOLIC HEALTH STATUS IN MIDDLE-AGED ADULTS.

Abstract

Background

An understanding of the nature and magnitude of within- and between-day variability in physical behaviour is necessary to translate epidemiological findings into tangible public health recommendations. Metabolic syndrome (MetS) is characterised by the coexistence of obesity, dyslipidemia, hyperglycemia and hypertension and is associated with an increased risk of type 2 diabetes and cardiovascular disease. The aim of this paper is to compare daily cumulative patterns of minute-by-minute accelerometer-measured physical behaviour activity intensities across those with and without MetS.

Methods

Data are from a subsample of the Mitchelstown Cohort; 475 (59.7±5.5 years) middle-aged adults. Participants wore the wrist GENEActiv accelerometer for 7 consecutive days. Data was summarised into 60s epochs and each time interval categorised based on thresholds. MetS was defined according to International Diabetes Federation 2006 guidelines. Cumulative distribution plots were created for weekday and weekend day activity across MetS health profiles.

Results

Individuals with MetS had higher sedentary behaviour and lower light activity and MVPA relative to the subjects without MetS (those with MetS had half the MVPA levels when compared to those without MetS). Overall similar cumulative activity patterns were observed throughout the day regardless of MetS status. However substantial differences were observed for MVPA for both weekday and weekend days; those with MetS started accumulating MVPA later in the day compared to those without MetS and for shorter durations of the day. Individuals with MetS were older, more likely to

be males and were characterised by lower CHOL and LDL concentrations, greater insulin resistance and reduced insulin sensitivity and raised inflammatory status ($p < 0.002$).

Conclusion

This study demonstrates ample within- and between-day variation in physical activity and sedentary behaviour across those with and without MetS to further research. A better understanding of such patterns will aid development of future targeted interventions tailored to an individual's cardiometabolic health status, which may be particularly important for those at increased risk of developing cardiometabolic disease.

Introduction

Physical activity plays a major role in the prevention, management and rehabilitation of many chronic diseases and conditions such as metabolic syndrome (MetS), hypertension, diabetes and obesity (14-16, 26, 77, 223). MetS is characterised by the coexistence of obesity, dyslipidemia, hyperglycemia and hypertension and is associated with an increased risk of type 2 diabetes and cardiovascular disease (CVD) (15, 224). Sedentary behaviour is associated with poor health and mortality (12, 18-21). Recently, a dose-response relationship has been found between sedentary behaviour and MetS (225). Sedentary behaviour and physical activity levels in free-living adults vary throughout the day and from day-to-day (39, 136, 193, 198). An understanding of the nature and magnitude of within- and between-day variability in physical behaviour is necessary to translate epidemiological findings into tangible public health recommendations. Objective physical behaviour measurements, such as accelerometers, are now becoming more popular due to lower costs, coupled with the rich, accurate, time-stamped data obtained. The second-by-second, time-stamped data gives the potential to examine patterns of physical behaviour across minutes based on intensity of activity and thus allows more complete physical behaviour profiles to be evaluated. Understanding the differences in activity levels within days, across days of the week and between different cardiometabolic health profiles allows focussed intervention efforts to be developed, taking into account when people are most sedentary and thus predisposed to efforts to increase activity levels. These interventions could include increasing time spent in light and MVPA intensity activities but also reducing duration of bouts of sedentary behaviour by increasing breaks and time standing especially in with sedentary occupations.

Most studies investigating daily activity levels have focused primarily on summation statistics such as total or mean activity estimates for the week. However, data summed or averaged across entire measurement periods do not have the capacity or potential to detect differences between cardiometabolic risk factor subgroups and daily minute-by-minute physical behaviour patterns. Assessing daily physical behaviour patterns, using participant daily minute-by-minute estimates, may highlight relationships not previously observed (46, 90). Most research that has examined within-day variation in sedentary behaviour and physical activity have averaged data across different time-segments (morning, afternoon and evening) or summarised data across hours (38, 39, 41, 90, 136, 211, 226-232). Furthermore, research that has examined between-day variation have used averaged daily estimates or arbitrary activity counts in analysis (138, 193, 198). Thus there is a paucity of minute-to-minute intensity variability throughout the day, across days of the week from large, cross-sectional sample of middle-aged adults.

The majority of studies examining within-day variation in physical behaviour have been based on children and adolescent populations while few have examined associations with health outcomes (41, 136, 211, 227-232). Lee et al. (2012) determined two characteristic physical activity patterns based on hourly physical activity count data and reported better health profiles associated with those who accumulated greater activity levels for greater amounts of the day (41). Garriguet et al. (2012) reported different MVPA patterns associated with different BMI categories using summarised hourly data (136).

Thus few studies have attempted to identify daily cumulative patterns of physical behaviour using minute-by-minute accelerometry data in middle-aged adults, and no study, to our knowledge, has examined associations between these patterns with

health outcomes (137, 138). Thus the aims of this paper are to explore daily cumulative patterns of minute-by-minute physical activity and sedentary behaviour between those with and without MetS.

Methods

Data are from a subsample of the Mitchelstown Cohort; 475 (46.1% males; 59.7±5.5years) middle-aged Irish adults. Information on anthropometric measures and cardiometabolic and inflammatory markers were collected. Participants wore the wrist GENEActiv accelerometer for 7 consecutive days. Individual daily cumulative percentage of time spent in physical behaviour (sedentary behaviour, light activity and MVPA) were calculated for weekday and weekend days. MetS was defined according to International Diabetes Federation 2006 guidelines. All variables were expressed proportional to individual wear time. These methods are described in greater detail in Chapter 3.

Statistical Analysis

Analysis was performed separately for each intensity category. Individual daily cumulative percentage time spent and hours spent in all physical behaviour intensities were calculated. Data were presented as median and 25th and 75th percentiles. Distribution of cardiometabolic and inflammatory markers across each MetS profile were determined. Daily cumulative percentage of time spent for each weekday in all physical behaviour intensities were calculated. Daily cumulative distribution plots, using median values, were created for weekday and weekend days across MetS profile. All statistical analyses were conducted using Stata (version 12, Stata Corp,

College Station, Texas, USA) and R statistical software version 3.0 (http://www.r-project.org). An alpha level of 0.05 was set to evaluate significance.

Results

Descriptive Characteristics

Participant's characteristics by MetS status are detailed in Tables 12 and 13. The prevalence of MetS in the study sample was 29.1%. Participant's physical behaviour levels by weekday and weekend day are presented in Table 12. Significant differences in weekday and weekend day physical behaviour across all physical behaviour intensities were observed between those with and without MetS (p<0.006). Individuals with MetS had higher sedentary behaviour and lower light activity and MVPA on both weekdays and weekend days. Moreover, those with MetS had half the MVPA levels when compared to those without MetS on weekdays (3 and 12 minutes) and weekend days (15 and 39 minutes) respectively. Individuals with MetS were older and more likely to be males (Table 13).

Daily Cumulative Distribution of Physical Activity and Sedentary Behaviour

Next we examined daily cumulative patterns of each physical behaviour intensity across week and weekend days. Overall similar cumulative activity patterns were observed throughout the day for sedentary behaviour and light activity between those with and without MetS (Figures 6a-d). Substantial differences were observed for MVPA during both weekday and weekend days (Figures 6e - 6f). Differences were observed regards how MVPA was accumulated for both weekday and weekend day. Those with MetS started cumulating MVPA later in the day compared to those with MetS. Furthermore, those with MetS accumulated MVPA for shorter durations of the

day, thus finished accumulating MVPA earlier in the day when compared to those without MetS. The most pronounced differences in daily cumulative activity between groups can be observed in weekday MVPA (Figure (e)).

Discussion

The results of this study suggest those with MetS had higher sedentary behaviour and lower light activity and MVPA when compared to those without MetS. Moreover, those with MetS had half the MVPA levels when compared to those without MetS. Overall similar cumulative activity patterns were observed throughout the day regardless of MetS status. However substantial differences were observed for MVPA for both weekday and weekend days; those without MetS started accumulating MVPA earlier in the day compared to those with MetS and for longer durations of the day.

Our findings confirm previous findings in that those with MetS have lower physical activity levels when compared to those without MetS (233, 234). The findings also highlight differences in daily cumulative patterns of physical behaviour across weekdays and weekend days among those with and without MetS. Our results suggest that in the context of physical behaviour both time of day and also day of week may play a role in cardiometabolic health status. More specifically, our results highlight significant differences in weekday and weekend day MVPA whereby those without MetS start accumulating MVPA earlier in the day and for a longer period. Our results provide a better understanding of adults' physical behaviour patterns throughout the day across weekdays and highlight some key issues pertinent (time of day and weekday may be associated with cardiometabolic health status) to the development of future interventions for high cardiometabolic risk middle-aged adults.

A number of previous studies have shown a prospective inverse association between PA and MetS (233, 235-238).This inverse association between PA and MetS highlights the importance of physical activity in the reduction of MetS risk Previous evidence suggest that participation in activities of greater intensity result in greater health benefits (78, 239-241). Thus participation in MVPA has the potential to positively impact on cardiometabolic health. This may explain why significant differences were observed in the current work when stratified by MetS status.

Earlier research exploring the association between cardiometabolic health status and within-day variations in activity patterns has largely used hour-by-hour data. These studies reported better health profiles associated with greater levels of activity for longer active days (39, 41, 136). Only two studies to date have examined within-day variation in activity using minute-by-minute data (137, 138). Schrack et al. (2014) demonstrated that the amount of physical activity is progressively lower with increasing age and follows a different daily pattern in older adults compared with younger adults (137). Steeves et al. (2015) found that despite having similar activity patterns, diabetics had significantly lower total activity counts compared to non-diabetics (138). These findings highlight the use of minute-by-minute data to fill gaps in understanding activity patterns and trends in subgroups of the population (137, 138). However data was summarised over the entire measurement period (7 days) which loses detail on between-day variation in physical behaviour patterns. In addition, while the use of activity count data in older adults whose activity primarily consists of sedentary behaviour is acceptable, count data lacks descriptive detail of the intensity of activity which is relevant to physical activity guidelines for younger populations i.e. physical activity guidelines for middle-aged adults recommend 150 minutes of moderate activity or 75 minutes of vigorous activity or a combination of both for health.

The results of our study demonstrate differences in daily cumulative patterns of each intensity of physical behaviour across time of day and weekday between those with and without MetS.

A main strength of our study is the use of a valid and reliable activity monitor which is capable of assessing time spent in sedentary, light, moderate and vigorous activity categories (85). In addition, this accelerometer collects data as raw acceleration and stores the data as g units for offline analysis thereby allowing for efficient data cleaning, management of spurious data and the application of various known data processing algorithms post-data collection. Furthermore, the high participation rate (64%) and range of metabolic health markers which were determined at a commercial laboratory ensures a high level of reproducibility. Notwithstanding these strengths some limitations can be identified. The cross-sectional design of our study prevents causal relations from being determined. In addition, the application of different thresholds could result in different activity patterns. Those with Mets were more likely to be males and older. However due to small sample sizes these differences could not be adjusted for in the current analysis. Thus results should be interpreted with this in mind. The sample sizes of subgroup analysis were small thus reducing statistical power of study findings. A study with low statistical power has a reduced chance of detecting a true effect, and also reduces the probability that a statistically significant finding exposes a true effect. Thus these groups may not have sufficient power to detect true association with health outcomes. Potential confounding factors were considered in the analysis to ensure that the study findings are true or whether they are due to another factor that is distorting the true association. Due to the exploratory nature of the statistical analysis techniques applied to the data possible confounders could not be adjusted for. Stratification would further decrease study power. Thus the

difference in physical behaviour patterns may be due to a confounding factor and not due the MetS status. Furthermore, participants were recruited from a primary care centre, and therefore could have more health problems or be more health conscious. Although the Mitchelstown Cohort was a random sample of middle-aged adults, 50-69 years of age, in an area which was representative of both urban and rural population in Ireland, generalizability of our findings may also be limited.

Conclusion

In conclusion, those with MetS had higher sedentary behaviour and lower physical activity levels. In particular, weekend day physical activity levels were lower among those with MetS while similar cumulative activity patterns were observed throughout the weekdays among those with and without MetS. Examination of physical activity intensity revealed differences in cumulative MVPA levels across weekday and weekend days; those with MetS appeared to start accumulating MVPA later in the day and finish accumulating MVPA earlier in the day relative to those without MetS. These findings suggest that those who are more physically active have better cardiometabolic health, thus recommendations of sit less and move more should be suggested.

Table 12: Physical Behaviour Levels by Metabolic Syndrome Subgroups						
	Metabolic Syndrome		**No Metabolic Syndrome**		**p-value**	
	Weekday	**Weekend day**	**Weekday**	**Weekend day**	**Weekday**	**Weekend day**
Sedentary behaviour (mins)	1356 (1253-1418)	1329 (1263-1390)	1306 (1182-1388)	1278 (1169-1362)	0.006	0.0002
Light activity (mins)	75 (19-152)	88 (40-139)	100 (42-192)	105 (55-182)	0.004	0.008
MVPA (mins)	3 (0-19)	15 (3-41)	12 (1-53)	39 (8-85)	0.0001	0.0001
Figures presented as average figures (95% Confidence Intervals) across weekdays (Monday-Friday) and weekend days (Saturday-Sunday).						

Table 13: Subject Characteristics of Study Sample by Metabolic Syndrome Subgroups				
	Full	**Metabolic Syndrome**	**No Metabolic Syndrome**	**p-value**
Male	183 (46.1)	59 (54.6)	109 (41.4)	0.02
Age (years)	59.3 (55.0, 63.8)	61.2 (56.5, 65.1)	58.5 (54.6, 63.4)	0.01
BMI (kg/m²)	28.3 (26.0, 31.1)	30.8 (27.8, 34.0)	27.6 (24.8, 29.6)	0.0001
Waist circumference (cm)	95.1 (87.1, 105.5)	103.9 (96.8, 112.8)	91.6 (84.7, 99.9)	0.0001
Systolic blood pressure (mm Hg)	128 (118, 140)	136 (126, 146)	126 (116, 136)	0.0001
Diastolic blood pressure (mm Hg)	80 (74, 86)	82 (76, 86)	78 (72, 86)	0.0001
Cholesterol (mmol/l)	5.3 (4.6, 6.0)	5.1 (4.6, 5.6)	5.4 (4.7, 6.1)	0.006
HDL-C (mmol/l)	1.43 (1.19, 1.68)	1.2 (1.05, 1.49)	1.51 (1.32, 1.77)	0.0001
LDL-C (mmol /l)	3.1 (2.6, 3.8)	2.9 (2.4, 3.4)	3.3 (2.7, 3.9)	0.0001
Triglycerides* (mmol/l)	1.16 (0.86, 1.62)	1.84 (1.30, 2.35)	1.02 (0.79, 1.41)	0.0001
Fasting Blood Glucose (mmol/l)	5.0 (4.7, 5.4)	5.65 (5.1, 6.5)	4.9 (4.6, 5.2)	0.0001
Insulin* (mU/ml)	9.11 (5.48, 14.46)	15.24 (9.23, 24.96)	7.31 (4.71, 11.7)	0.0001
$HOMA_{IR}$*	2.03 (1.19, 3.26)	3.61 (2.27, 6.83)	1.60 (0.94, 2.60)	0.0001
$QUICKI_{IS}$	0.26 (0.23, 0.31)	0.23 (0.19, 0.25)	0.28 (0.25, 0.33)	0.0001
Complement c3 (g/l)	136.5(120.3, 152.01)	148.4 (132.9, 166.9)	131.6 (116.7, 147.8)	0.0001
Interleukin-6 (pg/ml)	1.78 (1.19, 2.98)	2.52 (1.59, 3.63)	1.53 (1.06, 2.50)	0.0001
Tumor necrosis factor-α (pg/ml)	5.86 (4.74, 7.16)	6.51 (5.29, 8.23)	5.56 (4.59, 6.82)	0.0001
Leptin (ng/ml)	2.03 (1.25, 3.16)	2.39 (1.32, 4.05)	1.89 (1.14, 2.85)	0.002
Adiponectin (µg/ml)	4.87 (2.86, 7.54)	3.43 (2.37, 5.10)	5.59 (3.56, 8.24)	0.0001

Figure 6 (a): Metabolic Syndrome: Daily Cumulative Percentage Time Spent in Sedentary Behaviour across Time of Day (minutes since midnight) - Weekday

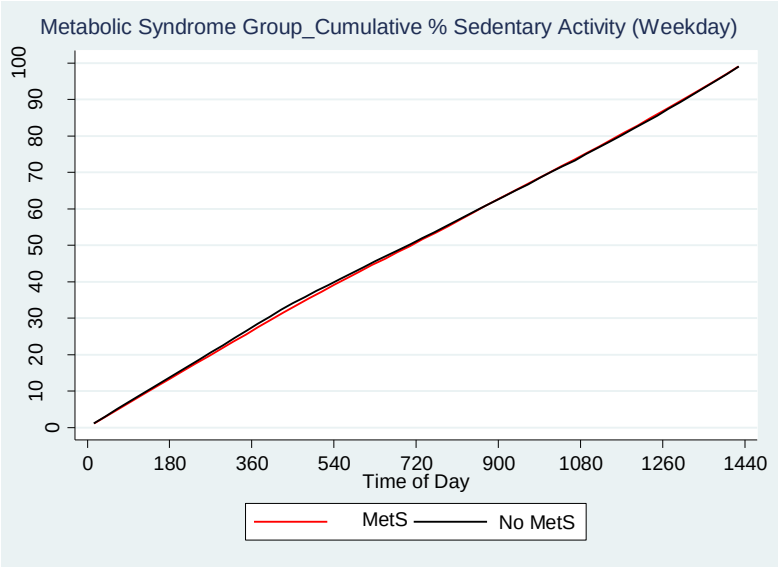


Figure 6 (b): Metabolic Syndrome: Daily Cumulative Percentage Time Spent in Sedentary Behaviour across Time of Day (minutes since midnight) – Weekend day

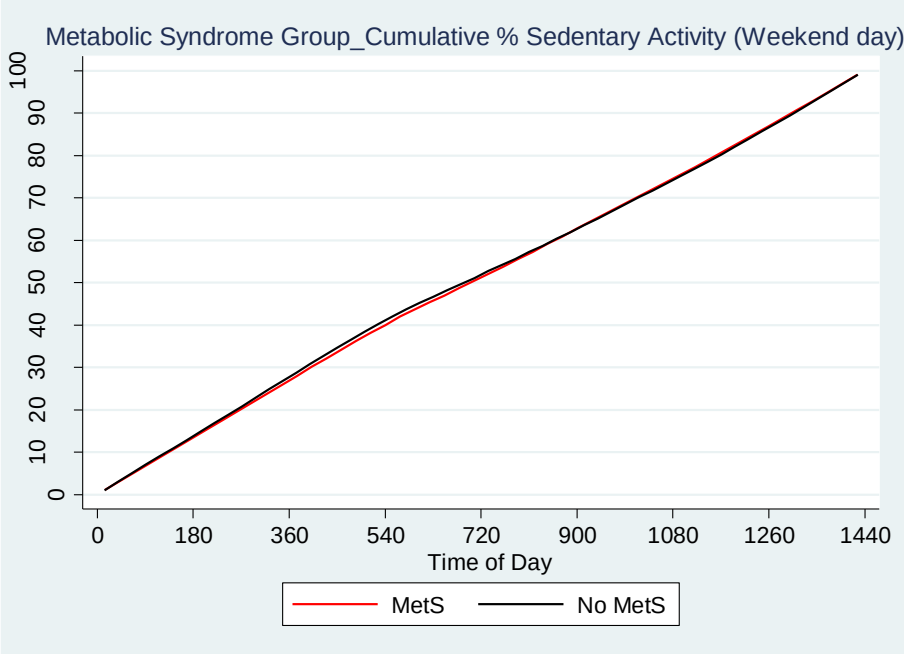


Figure 6 (c): Metabolic Syndrome: Daily Cumulative Percentage Time Spent in Light Activity across Time of Day (minutes since midnight) – Week day

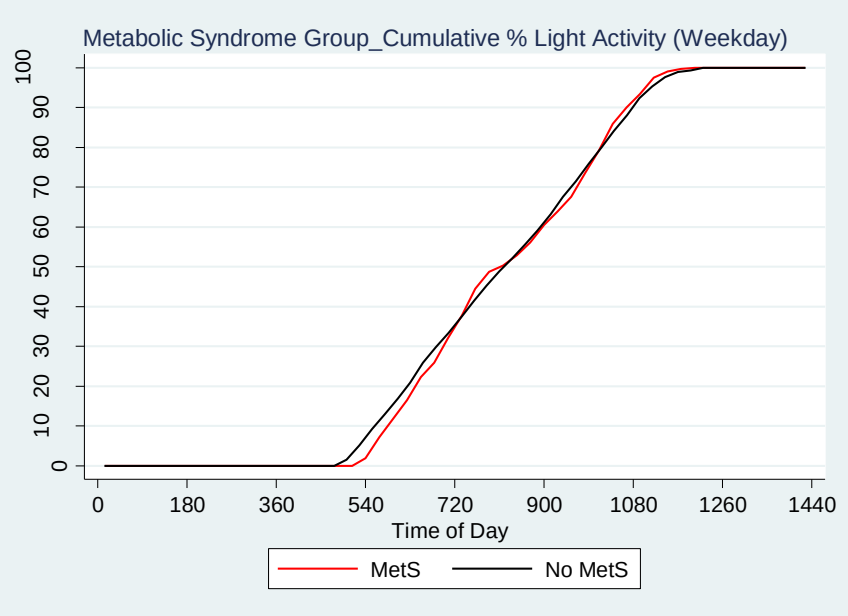


Figure 6 (d): Metabolic Syndrome: Daily Cumulative Percentage Time Spent in Light Activity across Time of Day (minutes since midnight) – Weekend day

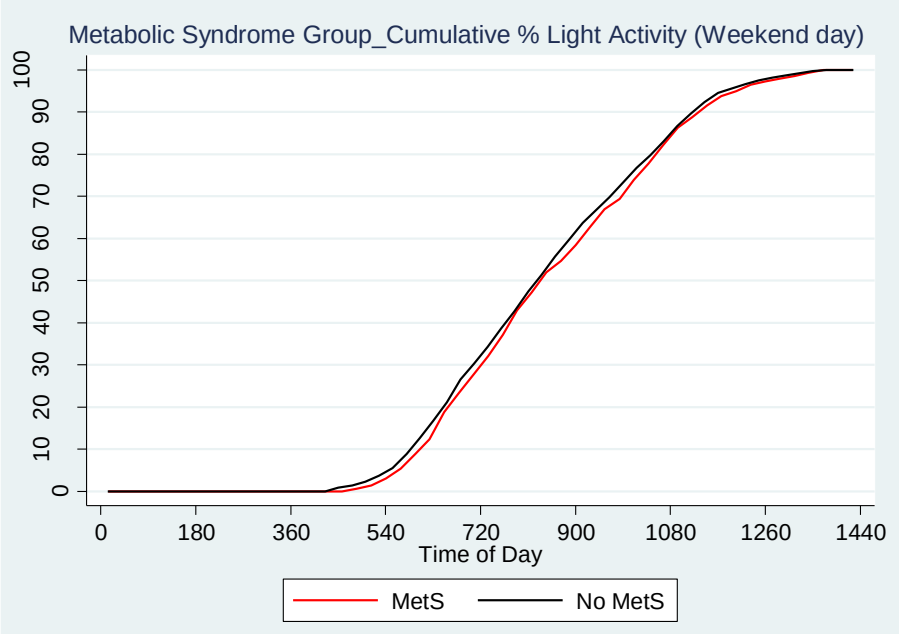


Figure 6 (e): Metabolic Syndrome: Daily Cumulative Percentage Time Spent in MVPA across Time of Day (minutes since midnight) – Week day

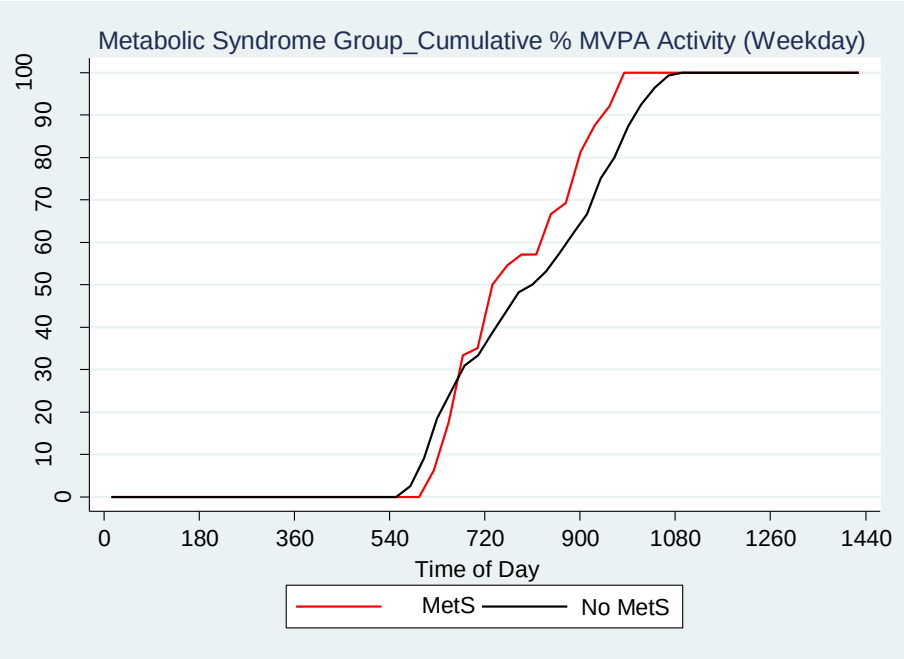
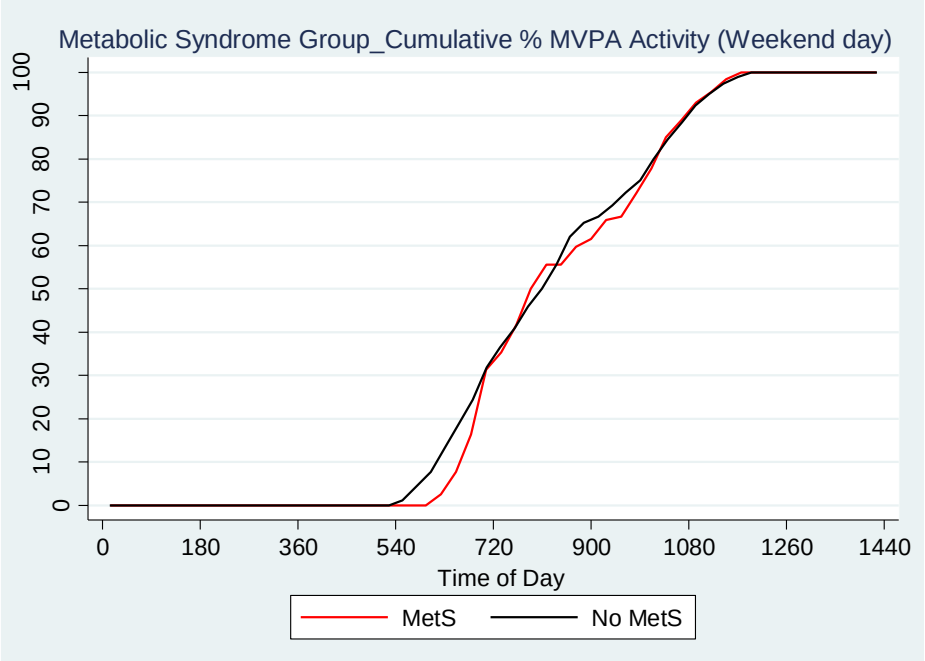


Figure 6 (f): Metabolic Syndrome: Daily Cumulative Percentage Time Spent in MVPA across Time of Day (minutes since midnight) – Weekend day



CHAPTER EIGHT - DISCUSSION

Introduction

This thesis explored the relationship between daily and weekly patterns of physical behaviour and cardiometabolic health in a cohort of middle-aged Irish men and women. To reiterate, the specific objectives of this thesis are:

1) Compare the associations between subjective and objective accelerometer-derived MVPA activity in relation to physical activity guideline adherence and cardiometabolic and inflammatory health

2) Determine a suitable monitoring frame to reliably capture weekly, accelerometer-measured, habitual activity

3) Identify groups of participants who accumulate similar weekly patterns of physical behaviour and determine differences in cardiometabolic profiles existing among these groups

4) Explore the daily patterns of physical behaviour amongst different cardiometabolic health profiles

In addition, important areas of further research in the area of physical behaviour pattern analysis and its impact on health outcomes are outlined, the strengths and limitations of the research carried out will be discussed and finally, the conclusion of this discussion will be presented.

Study Findings

The first results chapter of this thesis compared the agreement between GENEActiv accelerometer- and IPAQ-SF-derived MVPA and secondly compared associations with a range of cardiometabolic and inflammatory markers. The results suggest that the IPAQ-SF lacks sensitivity for the assessment of MVPA, guideline adherence and the relationship with cardiometabolic and inflammatory markers. These findings may

have important public health implications as they highlight the range in differences between methods with regard to associations between MVPA and cardiometabolic and inflammatory health markers. The second results chapter investigated the optimal number of days needed to obtain reliable estimates of weekly habitual activity, using the GENEActiv accelerometer, by examining variation in day-to-day physical behaviour between- and within-subjects. The main finding suggests that six days monitoring, four weekdays plus Saturday and Sunday, are needed to reliably estimate weekly habitual activity in all activity intensities. Earlier research highlights the important role of between- and within-subject variation in examining physical behaviour patterns and in determining the optimal number of days of data collection to accurately capture weekly habitual activity. Furthermore, an important secondary finding of the present study was that Sunday differed from all other days of the week for sedentary and light activity. This suggests that physical behaviour patterns vary between days of the week and that day of the week cannot be ignored in accelerometer data collection monitoring frames. These findings suggest that both weekday and weekend days need to be included in monitoring frames and that physical behaviour patterns across weekdays could play a role in health status. In addition, these findings may have important implications in terms of study design and data reduction strategies as they highlight that a shorter time frame of 3 days (inclusive of Sunday) is required in the study design to capture weekly variation in sedentary behaviour, light and moderate activity. In terms of data reduction this shorter time frame implies that all participants with 3 full days of physical behaviour data can be included in data analysis thus increasing sample size and power to detect statistically significant associations.. Further study protocols employing these recommendations

may benefit from reduced number of data collection and processing days and associated reductions in person-time and study cost.

The third results chapter identified weekly, interrelated patterns of physical behaviour and to examine the cardiometabolic health status associated with these different behaviour patterns. LPA revealed four distinct physical behaviour patterns; Sedentary Group (16.6%), Sedentary; Lower Activity Group (27.5%), Sedentary; Higher Activity Group (43.1%) and a Physically Active Group (12.8%). Overall the Sedentary Group had poorer profiles, characterised by unfavourable lipid profiles, hyperglycaemia, pro-inflammatory profiles, greater insulin resistance and reduced insulin sensitivity. The remaining classes were characterised by healthier cardiometabolic profiles as sedentary behaviour decreased. Study findings from Chapter 6 highlight the important contribution of the inter-relatedness of physical behaviour activity intensities for physical behaviour guidelines. Chapter 6 identified four different physical behaviour patterns in the population and although we did not detect any significant differences in cardiometabolic and inflammatory markers between the extreme groups (the Sedentary and Physically Active Groups) this may be partly accounted for by the sample size. Therefore larger studies may have the necessary statistical power to detect associations between various clusters of individuals with similar physical behaviour patterns and cardiometabolic and inflammatory health outcomes. Thus our analysis highlights the potential for the examination of the specific effects of the inclusion of sedentary behaviour and light activity in public health guidelines. In addition, these data confirm previous findings; variations in physical behaviour across days exist and may play a role in cardiometabolic health.

The fourth results chapter compared daily cumulative patterns of minute-by-minute physical behaviour activity intensities across those with and without MetS. MetS is

associated with an increased risk of CVD and is characterised by the co-existence of cardiometabolic abnormalities. The role of physical activity in the treatment of cardiometabolic disease is well acknowledged and is an inexpensive treatment option for cardiometabolic health. The findings from the second and third results chapters revealed differences between weekday and weekend days with regard to sedentary behaviour, light activity and MVPA patterns. Thus average weekday and weekend day estimates were examined in fourth results chapter. Results highlight significant differences in weekday and weekend day MVPA between those with and without MetS. Those with MetS started accumulating MVPA later in the day and for a shorter day period, both on weekdays and weekend days. The results highlight differences in physical behaviour patterns both within and across weekdays, supporting previous observations in the second and third results chapters.

Strengths and Limitations

This study has many strengths:

- The use of an objective measure of physical behaviour which is capable of assessing time spent in sedentary, light, moderate and vigorous activity intensities. Compared with self-report, objective measurements are more precise, less biased and reduce the potential for measurement error. The recall and social-desirability biases that accompany self-report measures are well known and may lead to higher misclassification bias.
- The use of an accelerometer which collects data as raw acceleration and stores the data as g units for offline analysis thereby allowing for efficient data cleaning, management of spurious data, and the application of various known data processing algorithms post-data collection. Previous thresholds by Esliger

et al. (2011) estimated very high levels of MVPA for the study population. Thus the ability of this device to store data for offline analysis allows the data to be reprocessed with new thresholds to give alternative estimates and in the future when algorithms are available for specific activities to revisit datasets and assess in more detail the types of activities that may be being undertaken.

- The application of dominant and non-dominant wrist wear thresholds prevents the over-estimation of physical activity levels from devices placed on the dominant wrist. In this study the participants were asked which wrist they preferred to wear the GENEActiv accelerometer. This protocol was to ensure high compliance to the 24 hours wear procedure, thus increasing the sample size for analysis (7 days valid data was required), quality of the data and thus statistical power of study findings. An additional limitation of the study is that the accelerometer device was not placed on the non-dominant wrist for data collection. Recommended protocol states that wrist worn devices should be worn on the non-dominant hand to avoid the over-estimation of physical activity due to the increase use of the dominant hand in everyday activities.
- The high participation rate (64%) limits the possibility of sampling bias thus producing high quality data which is not influenced by sampling bias or missing data.
- Measurement of a wide range of cardiometabolic health markers which were determined at a commercial laboratory ensures a high level of reproducibility.

The current study also has a number of limitations that should be noted:

- First, this is a cross-sectional study design. This type of study design implies that all measurements are taken at the same point in time, thus cause-effect relations cannot be determined. Intervention and prospective longitudinal

studies would be needed to confirm causality of the observed associations found between physical behaviour and cardiometabolic and inflammatory health markers.

- The sub-sample of the Mitchelstown Cohort, for whom accelerometer data was collected, differed by gender in that women were more likely to agree to wear the accelerometer. Nonetheless it should be noted that there were no statistically significant differences in age, education or BMI between those included and excluded in the final analysis in both males and females. Thus results appear to be generalizable to both Irish males and females.
- Furthermore, due to logistical issues subjective and objective physical activity data were not collected in the same week. Since MVPA levels were measured on different occasions (a week apart) this may affect the outcomes of results Chapter four. Activity levels in free-living adults have been reported to vary from day-to-day, seasonally and in response to environmental factors. Thus, this could be a potential source of bias in our study findings. More specifically, this could lead to significant differences between the estimates thus increasing the level of disagreement between the measures in relation to guideline adherence and relations with cardiometabolic health markers. However, weekly variation has not yet been examined. Furthermore, it should be noted that the GENEActiv accelerometer is not a gold-standard measure of physical behaviour, thus conclusions about the precise validity of either measure are limited.
- It should also be highlighted that the arbitrary cut-point to classify day-time wear may lead to inaccurate estimates of sedentary activity. For example persons who sleep later than 6am will have inflated sedentary behaviour estimates while

those who are active before 6am or after 12 midnight will have deflated activity estimates.

- In addition, different data processing methods could result in a data point being classified in different activity classes and thus different conclusions could be drawn on physical behaviour patterns. Currently there is no consensus on one set of thresholds in the research field for the GENEActiv accelerometers however the thresholds applied to the study have been derived in an Irish adult population so therefore are appropriate to apply to this study population. Nonetheless, these analyses have shown the merits of LPA and daily minute-by-minute cumulative plots of physical behaviour for the purpose of identifying and describing groups of adults based on their distinct physical behaviour patterns throughout the week and identify segments of the day when activity levels differ between groups. More specifically, the application of different thresholds could result in different activity patterns. The GENEActiv accelerometer is a new tri-axial accelerometer device. New thresholds may be refined in the future which could alter current findings. Consequently, the present findings may change if different thresholds to define each physical behaviour intensity are applied to the data.
- A possible limitation to the analysis is that the thresholds applied to this data were scaled to 100HZ and 60s epoch (threshold study measured data at 80Hz and at 15s epochs). While the issue of scaling thresholds to suit study epoch and sampling frequencies is warranted it is worth highlighting that this procedure is encouraged and recommended by accelerometer companies. Further research in this area is needed. It is debatable whether it is feasible or even necessary to create specific thresholds for each set of possible epochs

and sampling frequencies. Thus a possible alternative that has come to my attention are thresholds which are based on the ENMO metric (242). The metric is independent of sampling frequency and epoch as it uses the average acceleration over an epoch rather than the sum (242).

- In Chapter 4 approximately one third of the study sample had subjective and objective physical behaviour levels measured at different time-point (weeks apart). For reliability issues these data were excluded from analysis. Removing these data from analysis decreased the sample size significantly thus reducing the power of the analysis to detect significant associations with health outcomes and to measure accuracy in agreement levels between subjects for guideline adherence.
- In relation to the findings of results Chapter 6, the sample sizes of comparable groups for analysis were small. In these cases one cannot ignore the influence of the lack of power on study findings. A study with low statistical power has a reduced chance of detecting a true effect, and also reduces the probability that a statistically significant finding exposes a true effect. The consequences of low statistical power include overestimates of effect size, low chance of detecting true relations between exposure and outcomes, and low reproducibility of results. In Chapter 6, LPA analysis found four different physical behaviour patterns in the population, resulting in classes 1 and 4 having small sample sizes (16% and 12% of the study sample respectively). Thus these groups may not have large enough sample sizes for sufficient statistical power to detect accurate association with health outcomes. It should be noted that this study was powered to initially examine the prevalence of diabetes and CVD in this population. This study was not powered for the current analysis. While some

researchers would expect a back calculation of power current recommendations however advise against this practice (243, 244).

- Throughout the results section potential confounding factors were considered in the analysis to ensure that the study findings are true or whether they are due to another factor that is distorting the true association. Confounding factors distort the true relationship between an exposure and outcome. In Chapters 4 and 6 the analysis were adjusted for possible confounders i.e. age, gender, employment status, BMI. In Chapter 5 this was not necessary as analysis was not aetiologically focused however in the final results chapter (Chapter 7) possible confounders could not be adjusted for. This is mainly due to the descriptive nature of the statistical analysis techniques used and the further decrease in study power associated with stratifying analysis this type of analysis. Thus the difference in physical behaviour patterns seen in Chapter 7 may be due to a confounding factor and not due the METs status. In addition, it may be possible that not all confounders could be adjusted for in this analysis despite the large quantity of health variables measured
- The study findings may also be influenced by chance. It is well known that chance can never be eliminated completely for research findings but it can be reduced through large sample sizes. As previously mentioned, analysis of Chapters 4, 6 and 7 may be influenced by low statistical power due to small samples sizes across comparable groups. While overall study sample were high (n=397) these sizes were reduced considerably during subgroup statistical analysis. For all statistical analysis 95% confidence intervals were calculated. Wide 95% confidence intervals indicate a high probability of chance affecting

study findings. Random error can be reduced in this study by averaging out the large number of observations

- Finally, participants were recruited from a primary care centre and therefore could have more health problems or be more health conscious. In addition, the primary care setting may omit certain subgroups of the population such as the homeless, transient workers and religious groups. Thus generalizability of these findings could be limited.

Future Research

The purpose of the research carried out as part of this PhD thesis is to contribute to important research gaps related to the understanding of the relationship between cumulative daily and weekly interrelated patterns of physical behaviour and cardiometabolic health status, and consequently provide evidence that will be useful in refining public health physical behaviour recommendations for middle-aged adults. The findings of this novel research add to the limited body of literature examining the association between daily and weekly patterns of physical behaviour using objective physical behaviour measures and cardiometabolic health. Result chapters six and seven are the first studies to evaluate the relationship between weekly interrelated and daily cumulative patterns of physical behaviour and cardiometabolic health. Further research to determine if causal relations exist between these physical behaviour patterns and cardiometabolic health is warranted. Experimental, longitudinal designs are required to confirm causality of the associations, and to be able to determine the biological mechanism involved. Additional research is needed to determine whether the associations change when dietary, socio-demographic and lifestyle factors are taken into account.

This thesis has addressed several aspects of research that are now allowed by time-stamped accelerometer data. However, it is pertinent to acknowledge that there remain many important research questions relating to physical behaviour patterns and cardiometabolic health that must be addressed. Some of these include the following:

- The further examination of associations between the interrelated patterns of physical behaviour and health in all ages using different statistical methods, such as structural equation modelling, compositional data analysis and substitution analysis. This is necessary to strengthen existing physical behaviour and cardiometabolic health findings and to provide evidence which will aid in the development of existing physical behaviour guidelines. More specifically, these methods may better account for the variability of other factors and better assess factors that are highly correlated such as light activity and MVPA.
- To develop a valid and reliable algorithm to identify sleep start and finish is crucial to the future use of the GENEActiv accelerometer in order to accurately determine the true association between physical behaviour intensities and health. Without such development, researchers will continue to use arbitrary cut-points to exclude sleep, leading to the over- or under-estimation of sedentary behaviour levels and the misinterpretation of relations with cardiometabolic health particularly as inadequate levels of sleep has been identified as an independent risk factor for cardiometabolic risk. If sleep time is under-estimated this results in the over-estimation of sedentary behaviour levels. Over-estimated or higher levels of sedentary behaviour would lead to stronger associations with cardiometabolic risk factors. Furthermore, it may lead to a positive association between sedentary behaviour and

cardiometabolic health as the misclassification of sleep, which in adequate levels has a positive effect on health, as sedentary behaviour would lead to positive and inaccurate conclusions.

- Future physical behaviour intervention studies should be more targeted to examine the impact of adapting different physical behaviour patterns, similar to those identified in Chapter 6, on cardiometabolic health status. Physical behaviour guidelines recommend at least 30 minutes of MVPA on most days of the week. However, for the majority of adults, especially those who are predisposed to adverse cardiometabolic health, MVPA is difficult to achieve. Thus further research involving longitudinal and intervention studies, should examine the role of light intensity activity and sedentary behaviour on health as these behaviours may be easier to change than MVPA.
- In addition, further analysis should examine the long-term effects of substituting sedentary behaviour with light activity on cardiometabolic health. Promoting a reduction in sedentary behaviour rather than increasing MVPA should also be explored further.
- Accelerometer-derived physical behaviour data appears to be more sensitive at revealing relationships with cardiometabolic and inflammatory health markers. Thus we recommend the use of objective measurement of habitual activity in the context of examining the relationship between habitual activity and health. Particularly as the technology is feasible in large-scale studies and use in free-living conditions is more practical, i.e. water-proofed devices that are easier to wear. Improved understanding of the different characteristics of habitual activity that are captured by accelerometers may have important public health implications regards identification of suitable patterns and levels of

activity for optimal health and more defined future physical behaviour guidelines.

- Since physical activity and sedentary behaviour patterns are complex and interrelated, future policy development and intervention studies aiming to increase adult physical activity should be directed towards altering patterns of behaviour rather than concentrating on altering a single type of physical behaviour.
- Further research in the application of physical behaviour measures in the primary care setting is needed. Nurse practitioners in the primary care setting are in an ideal position to promote health by encouraging appropriate levels of each physical behaviour intensity. Increased knowledge and use of physical behaviour measurement instruments in the clinical setting would allow nurse practitioners to identify and address sedentary behaviours in their patients, especially those with adverse cardiometabolic health.
- Large prospective studies assessing the relationship between the long-term exposure of different clustering patterns to the development of obesity, CVD and change in inflammatory and cardiometabolic status would be useful. The current 5-year follow-up of the Mitchelstown study will make this possible.
- Differences in cumulative patterns of physical activity and sedentary behaviour between cardiometabolically healthy and unhealthy groups highlight patterns of behaviour which could be adapted by those at greatest cardiometabolic risk with a view to improving cardiometabolic health status. The classification of groups of adults with similar physical behaviour patterns provides valuable information for the identification and tailoring of specific public health and health promotion messages and intervention strategies. Therefore future interventions

tailored to an individual's cardiometabolic health status would be worthwhile to explore.

Concluding Paragraph

The role of physical activity in the prevention and treatment of many chronic diseases has been recognised for some time but improved methods of capturing physical behaviour are now allowing us to refine our knowledge. With new technological advancements in the area of physical behaviour measurement, complex associations between physical behaviour and health status can now be examined.

This research examines the relationship between daily, minute-by-minute cumulative and weekly patterns of physical behaviour in relation to cardiometabolic health in middle-aged adults. Findings from the current research have revealed associations between cardiometabolic health and both daily and weekly patterns of physical behaviour. Since physical activity and sedentary behaviour are complex interrelated behaviours, public health guidelines on physical behaviour should focus on encouraging changing entire physical behaviour patterns opposed to just a single behaviour.

Thus public health policy should focus on suggesting a broader range of physical behaviours that fit into everyday life rather than emphasising MVPA activity which is more strenuous and relatively harder to achieve among individuals predisposed to adverse cardiometabolic health.

APPENDICES

APPENDIX ONE

Guidelines for Accelerometry Usage – Building a Protocol

In order to better understand accelerometry-based physical behaviour monitoring, we need to understand the basic concepts of the physical behaviour movement, the technology of these physical behaviour monitoring sensors and the processes involved in the collection, processing and analysing of data (83). There are many methodological issues to consider when processing this type of data and these will now be discussed further. Accelerometer usage involves both the field use of accelerometers "Accelerometer Field Protocol" to collect data and the processing of the collected data "Accelerometer Data Reduction Protocol" to produce interpretable units of information.

Accelerometer Field Protocol

Distribution and Collection of Accelerometer

The distribution and collection of accelerometers in a study is largely dependent on study design. For larger epidemiological and intervention studies, some distribution and collection methods, for example face-to-face based methods, may not be feasible, particularly if the project has limited funding. In these circumstances, a common approach to accelerometer distribution and collection has been through post. In smaller, field-based studies the most common method of distributing and collecting accelerometers is on face-to-face bases. Some studies have distributed accelerometers to participants on a face-to-face basis and provided a prepaid envelope to return the monitors by post. This approach ensures participants are adequately briefed about the maintenance and use of the accelerometer and avoids

the need for a return visit to the health centre by participants and researchers for data recovery (245).

Placement of Accelerometer

Accelerometer placement is largely dependent on the manufactures specifications. Research has reported that accelerometers should be attached as close to the body's centre of mass as possible i.e. the waist (245). However, it was found that this position of wear lead to reduce wear-compliance. Validation studies comparing the level of agreement between different wear positions of an accelerometer have found wrist-worn accelerometry data to be in high agreement with waist-worn accelerometry data (85). The feasibility and subject burden of accelerometer placement should be carefully considered when planning an accelerometer study protocol to ensure both high quality data and wear compliance (245).

Selection of Sampling Frequency

The rate of data acquisition is determined by the sampling frequency of the accelerometer device. To ensure that the full range of human movement is captured, the sampling frequency should fulfil the Nyquist criterion (83, 246). Nyquist criterion specifies that the sampling frequency must be at least twice the frequency of movement. If this criterion is not met, measurements of rapid movements (movements occurring at a higher frequency domain) will be distorted.

Number of Minutes Considered as a Measured Day

When using accelerometers to measure physical behaviour, researchers need to determine whether subjects have worn the device for a sufficient period to be considered a representative full day of physical behaviour. Physical activity and sedentary behaviour levels vary throughout the day thus it is necessary to determine

the minimum daily wear time required to reliably estimate habitual physical behaviour. If the estimated monitoring time in a day is below the designated thresholds (i.e. 10 hours), accelerometer data for that day are considered invalid. Thus the valid day threshold directly affects data loss (247). In general, days with less than 600 minutes of data recorded have been criteria for elimination (248-250), while other studies have used 800 minutes as elimination criteria (251).

Number of Days Monitoring per Week

The minimum number of days monitoring in order to reliably capture habitual behaviour has important implications for wear compliance, accelerometer turnover and overall study costs. The primary goal for researchers is to record activity for a sufficient period of time so that the resulting estimates reflect usual habitual behaviour levels (84). Physical behaviour is influenced by a range of factors including demographic characteristics, emotional influences and behavioural attributes (189). As a result, patterns of physical activity show substantial intra- and inter-individual variation, the extent of which plays a major role on data quality and reliability (190). Intra- and inter-individual variation is accelerometer dependent therefore monitoring frames are dependent on accelerometer type.

Prior to this thesis, no study had examined the required number of monitoring days needed to accurately measure physical behaviour in adults using the GENEActiv accelerometer, however other accelerometers have been examined in this context (197, 199). These studies reported variable monitoring frames 3-5 days, 3 days, 7 days and 4-5 days, respectively (53, 197-200). In addition, other studies have examined the appropriate monitoring frames to reliably estimate habitual physical behaviour categories separately (193, 194). Matthews et al. (2002) concluded that 3-4 days monitoring were required to accurately measure physical activity, and that 7

days were needed to reliably estimate physical inactivity (193), while Scheers et al. (2012) recommended both Saturday and Sunday, and at least 3 weekdays were needed to obtain reliable estimates of habitual physical activity (194). Such conflicting recommendations highlight the need to determine the number of monitoring days required to reliably measure both habitual physical activity and sedentary behaviour for each accelerometer type and population under study.

Accelerometer Data Reduction Protocol

Selection of Sampling Interval

The acceleration signal from an accelerometer monitor is sampled at a certain frequency and, depending on type of accelerometer, is stored for offline analysis. The first stage in the data reduction of accelerometry data is to collapse these data signals into a user-defined time interval. This time interval is commonly referred to as an epoch and choice of epoch can be crucial in the planning process of an accelerometer data reduction protocol and for data interpretation (83). Epoch lengths can vary from 1 second to 1 minute. For longer epoch lengths, the process of data smoothing can potentially affect the validity of estimates of time spent in activity intensity (252, 253). Smoothing occurs when the epoch length is longer than the actual bout of activity or when the activity is split between epochs, and within each both sedentary behaviour and non-sedentary behaviour is considered together to determine physical behaviour intensity for the user-defined epoch length (254). Previous research has indicated the adults and children physical behaviour patterns differ in that children have shorter, more frequent bouts of movement (255-257). This suggests shorter epoch lengths are more suitable to capture children physical behaviour levels. This issue of epoch length has not been systematically studied in adults. A study by Gabriel et al. (2010)

examined the role of epoch length on physical activity estimates in post-menopausal women. Differences in physical activity estimates presented as 10 seconds and 60 second epochs were evaluated. This study suggested that shorter time sampling intervals would reduce misclassification error of physical behaviour estimates however association with health outcomes did not yield strikingly different results (258).

Classification of Non-wear

One main disadvantage of accelerometers is that subjects may remove them periodically. Accelerometers, such as the GENEActiv accelerometer, are waterproof. Thus there is no need for participants to remove the device at any stage during the monitoring time frame. Despite this, participants can remove the device. Researchers need to identify these time periods of non-wear to ensure activity is classified accordingly. Non-wear time definitions vary. In general, studies define non-wear as prolonged blocks of non-movement. Duration of these "prolonged blocks" can vary from ≥10 minutes to ≥60 minutes of non-movement (42, 43, 259-264) and some allow for brief interruptions, 1-2 minutes of movement counts (166, 249, 259, 265). The definition of non-movement varies by type of accelerometer (266). For some accelerometer, such as the ActiGraph, non-movement is recorded as zero values, under the rationale that accelerometer sensitivity to even small movements will result in the accumulation of a count value >0 if the monitor is worn correctly. However some studies, using different accelerometers, have applied different definitions for non-movement. For example, Van Hees et al. (2011) applied a non-movement threshold estimated on the basis of the standard deviation and the value range of each accelerometer axis. A block was classified as non-movement if the standard deviation was less than 3.0 mg for at least two of the three axes or if the value range, for at least two of the three axes, was less than 50 mg. This threshold was based on lab

experiments in which thirty GENEA accelerometers were left motionless on a flat, stable surface for 30 minutes, showing that the standard deviation of an acceleration signal, which has some characteristic noise, is 2.6 mg during non-motion.

Handling of Missing Data

When periods of non-wear have been identified a decision has to be made as to how the missing data is to be handled, should it be imputed or should it be left as missing. The later will potentially reduce the number of valid minutes of data and can result in the exclusion of the day or person from the dataset. Exclusion of subject data or even subjects can reduce sample size and can increase the chances of sampling-bias influencing study outcomes (267).

Imputation is a statistical procedure which reduces biases caused by missing data (268, 269). Various means of data imputation have been proposed. The fundamental idea of imputation is to use observed values to assist in predicting missing values. To determine how missing data should be handled, we need to determine why data is missing. Reasons for missing data are commonly classified as: missing completely at random, missing at random, and missing not at random. When missing data does not occur at random the imputation cannot give an unbiased estimate at population level. Thus missing data is a major issue when it is non-random. Unfortunately it is not possible to objectively test whether data are missing in a random pattern in real data-collection situations (270, 271).

Intensity Cut-off Points

The GENEActiv accelerometer measures and stores physical behaviour data as raw acceleration. Raw accelerometry counts are unitless and dimensionless and thus they require calibration in order to be translated and reported in ways that are biologically meaningful. Definitions of activity intensity are derived from calibration of a device with

a gold standard technique, e.g. Doubly Labelled Water technique for energy expenditure comparisons or direction observation and maximal oxygen consumption for intensity comparisons, which provides a cut-off threshold that is identified by specific values (85).

Expressing and Reporting of Data

Since physical behaviour data is measured in acceleration units a decision needs to be made on how physical activity and sedentary behaviour activities are to be quantified and expressed. Output data and summary statistics will depend firstly on what outcomes are of interest and secondly of which will be most interpretable (84). According to Ward et al. (2005) and Matthews et al. (2005), time spent in activity intensities, and number and average duration of bouts of activity intensities should be reported (272, 273).

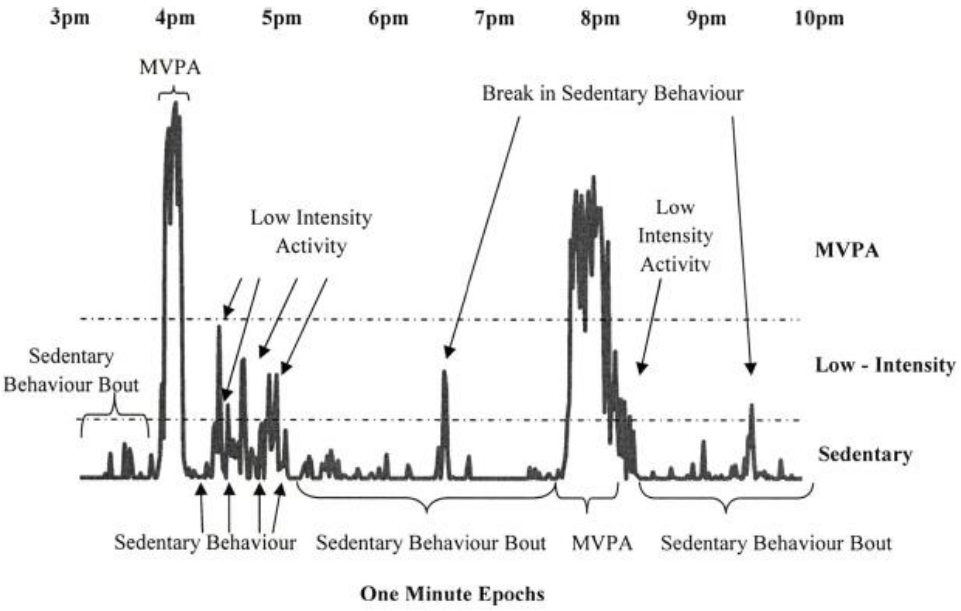


Figure 7: Examples of physical activity and sedentary behaviour variables derived from accelerometer data (274).

APPENDIX TWO

Criterion validity and calibration of the GENEActiv accelerometer in middle-aged adults

Abstract

Introduction

Previous thresholds applied to GENEActiv accelerometer data are based on left- and right-wrist wear. Ideally, due to greater use of the dominant hand in everyday activities, cut-points should be created for dominant and non-dominant wrist. The greater use of the dominant hand in everyday activities may lead to the overestimation of thresholds for physical activity intensities. The objective of this paper is to validate the GENEActiv accelerometer against energy expenditure measured by expired gas to complete a value calibration to develop thresholds for sedentary, light, moderate and vigorous activity for wrist-worn placement in adults and to perform a cross-validation for these thresholds.

Methods

The GENEActiv accelerometer was used to measure sedentary behaviour and physical activity during 7 structured activities in 56 adults (35 developmental, 21 cross-validation) aged 18-65 years. VO_2 and resting metabolic rate were measured using a portable metabolic unit (Cosmed K^4B^2, Rome, Italy). Data were extracted and collapsed into 15-second epochs. The mean value of the final 2 minutes of each activity was used for data analysis. Receiver operating characteristic analysis and Youden's Index were used to develop intensity thresholds across activity intensities.

Results

Intensity thresholds (sum of the vector magnitude counts) were created for dominant and non-dominant wrist wear (Table 16). Sensitivity and specificity were 69-98% for the developed intensity thresholds. Area under the curve (AUC) analysis were between 70-99% for sedentary, moderate and vigorous activity.

Conclusion

This is the first study to develop accelerometer cut-points for dominant and non-dominant wrist GENEActiv accelerometer data that reflect sedentary, light, moderate and vigorous activity. Data suggests that the developed intensity thresholds for GENEActiv data are valid at determining physical behaviour intensity, but are slightly poorer but acceptable at estimating moderate activity in adults aged 18-65 years.

Introduction

The relationship between physical behaviour and health has been studied extensively (5, 6, 275, 276) (2) (3) (4) (4, 7-11). Understanding the determinants of physical behaviour and health outcomes is essential to the design and implementation of intervention studies which aim to prevent morbidity and subsequent mortality. Questionnaires and accelerometers are widely used to assess physical behaviour in epidemiological studies. Self-reported questionnaires are commonly used as they are the most cost-effective and feasible method in large populations. However collection of accurate self-report physical behaviour data is difficult as measures largely depend on the recall abilities of participants. Objective methods are increasingly being used to measure physical behaviour and are now being recommended over self-reported measures. Accelerometers can record activity objectively reducing the effects of subjective limitations. They can provide detailed information on various aspects of physical behaviour such as intensity of activity, minutes spent in activity, breaks in activity transition, duration of bouts of activity between activity transitions and time of day when activity occurred. Accelerometers measure physical behaviour as raw acceleration and in order to be interpretable for public health recommendations have threshold values applied to them. Threshold cut-offs can be limited in that they may misclassify intensity levels. Some studies have dealt with this limitation by using raw acceleration data (137). However these results are hard to interpret and, more importantly, are harder to translate into physical behaviour guidelines for population health. Thus value calibration and validation of accelerometer devices are vital to obtaining accurate, interpretable physical behaviour data to quantify relationships with health outcomes.

The technical reliability and validity of the GENEA accelerometer and threshold values for middle-aged adults have been reported (85). However these thresholds were developed for left- and right-hand wear and thus did not take hand dominance into account. Ideally, due to greater use of the dominant wrist in everyday activities, cut-points should have been created for dominant and non-dominant hand wear (277). The greater use of the dominant hand in everyday activities may lead to the overestimation of cut-points for moderate-to-vigorous activity (MVPA), 88% of validation study participants were right-handed (85). In the Esliger paper, participants were asked to complete a number of tasks ranging from static, posture, positions to lifestyle and ambulatory movements. Hand dominance is not an issue in posture

positions or ambulatory movements such as walking and running. However, lifestyle activities such as window washing is generally a dominant hand activity, which leads to an increase in recorded acceleration signals and in turn an increase in intensity defining cut-points. Furthermore, not all activities carried out by participants in Esliger et al. (2011) were categorised into the same intensity category by both the left- and right-hand cut-points. According to left-hand cut-points, seated computer work was classified as light activity when placed on the right wrist compared to sedentary activity when place on the left-wrist or when right-wrist cut-points were applied. In addition, window washing, according to left-wrist cut-points, was classified as light when placed on the left wrist and moderate (close to vigorous activity) when placed on the right wrist and according to right-hand cut-points, is classified as moderate activity on both wrists. This is further evidence that hand dominance should have been accounted for in the current intensity thresholds for the GENEActiv accelerometer. Furthermore, these threshold values were based on a previous version of the GENEActiv accelerometer, GENEA (Unilever Discover, Colworth, UK), which had slight technological differences.

The specific aims of this paper are to validate the GENEActiv accelerometer against energy expenditure measured by oxygen consumption and to perform a cross-validated, value calibration of the GENEActiv accelerometer to develop thresholds for sedentary, light, moderate and vigorous activity in middle-aged adults.

Methods

Participants

Participant recruitment was initiated in December 2014 in an effort to obtain a convenience sample of 56 volunteers aged between 18 and 65 years, free from injury and in good health from the University of Limerick and its surrounding area. The recruitment method involved an email to employees of the University of Limerick, Limerick, Ireland. A health and fitness report was offered as an incentive to participate. Data collection was undertaken between February and July 2015 after which 70 adults completed the study protocol. Each participant was allocated a number, and a randomization table was used to assign each participant to either an equation development group or a cross-validation group. Written informed consent was

obtained from each participant. The study was approved by the Faculty of Education and Health Sciences Research Ethics Committee at the University of Limerick.

Physical Behaviour Measurement Devices

The GENEActiv accelerometer (ActivInsights Ltd, Kimbolton, Cambridgeshire, UK) comprised a tri-axial STMicroelectronics accelerometer with a dynamic range of +/-8 g (1 g= 9.81 m/s^2), where 'g' represents 'gravitational unit', and was attached to both participants wrists with straps. Information on hand dominance was also recorded. The same two GENEActiv accelerometers were used on all study participants throughout the study. Data was sampled at a frequency of 30Hz and collapsed into 15-second epochs for data analysis.

Metabolic Unit

Oxygen consumption (VO^2) was measured breath-by-breath, minute-by- minute, using a portable metabolic unit (Cosmed K4B^2, Rome, Italy) with the exception of the measurement of resting metabolic rate (RMR) where VO^2 was measured in 30-second blocks. The Cosmed K4B^2 is a lightweight system with a heart rate receiver and has been deemed an appropriate criterion measure for minute-by-minute energy expenditure (278). Before each testing session, the device was calibrated, according to manufacturer standard procedures, using known gas concentrations, and flow sensor calibrations and environmental conditions were updated.

Testing Protocol

Participants arrived at the testing facility having fasted and refrained from consuming nicotine, caffeine and completing any exercise for at least 3 hours. Anthropometric measurements were recorded with calibrated instruments according to standardised protocol. Height (to the nearest 0.25 cm) and weight (to the nearest 0.1 kg) was measured without shoes and socks using Seca stadiometer (model 214, Seca Ltd. Birmingham, UK) and electronic scales (model 770, Seca Ltd. Birmingham, UK), respectively. Body Mass Index (BMI) was calculated as [weight (kg)/ (height (m^2))]. The GENEActiv accelerometers and Cosmed K4B^2 metabolic unit were conclusively fitted. The accelerometer was attached to both participant's wrists and was initialised prior to the participant's arrival and clock synchronised with the main investigator

computer and metabolic unit. The metabolic unit was placed over the participants shoulders and a mask fitted over their face. Subsequently, participants were introduced to the protocol of activities. Activities were completed in ascending intensity. Participants were instructed when to start and finish each activity by a single instructor. The activity category, the exact start and finish times of each activity were recorded by the observer. Resting VO^2 was measured for 15 minutes, prior to which the participant lay on a bed in a darkened, quiet room for 10 minutes to ensure the participants were provided with an adequate amount of time to achieve resting state. During the sitting activity, participants were asked not to speak or take part in any other activities, sit looking straightforward, feet flat on the floor and hands in resting position. For the standing activity, participants followed similar protocol with feet shoulder width apart and hands held by their side. During both activities, participants were unaided. Participants were asked to complete each activity at a pace that was comfortable to them, but within each speed range: slow walking (2.5–4.5 km/hour), brisk walking (4.5–6.5 km/hour) and light jogging (6.5–8.5 km/hour). Prior to the study beginning, the upper and lower time limits required to complete each section of the track during each speed category were calculated. The time taken to complete each section of the track was then used to estimate the speed of each participant. This procedure is outlined in more detail elsewhere (279).

Calibration Activities

The activities in the protocol included resting VO^2, sitting on a chair, standing upright unaided, washing dishes, sweeping the floor, slow walking (2.5-4.5km/hour), brisk walking (4.5-6.0km/hour) and jogging (6.5-8.5km/hour). All ambulatory activities included a resting period where the participant was allowed to prepare for the next activity and heart rate was allowed to return below 100 beats per minute. For sitting, standing activities, washing dishes and floor sweeping, data was collected for 5 minutes, while 7 minutes data was collected for all remaining ambulatory activities.

Data Processing

The data was extracted using GENEActiv software in comma separated files (.csv) and then collapsed into 15-second epochs using the following, sum of the vector magnitude, equation

($\sum |\sqrt{x^2+y^2+z^2} - g|$) (85). Using Cosmed K4B^2 software, the VO^2 information was averaged for every 15-second period. The breath-by-breath VO^2 data from the Cosmed K4B^2 and the resulting epoch-by-epoch GENEActiv accelerometer data were imported into customised spreadsheets and collated, ensuring start and finish times of each activity was synchronised for both devices. The mean value of the final 2 minutes of each activity (excluding resting VO2) was used for data analysis, these durations were selected as VO^2 remains stable (at a steady rate) after 3 minutes for light activity and after 3-5 minutes for more intense activities (280). All data was exported and analysed in Stata (version 12, Stata Corp, College Station, Texas, USA) (281).

Analysis Variable Definitions

Participant's individual RMR were used to calculate their resting metabolism equivalent task (MET) values, with energy cost during activity being expressed in calculated METS (MET score = Activity VO^2 mL·kg^{-1} min^{-1} / Resting VO^2 mL kg^{-1} min^{-1}). The VO^2 data were converted to METS using the standard conversion of 1 MET = 3.5 mL·kg^{-1}·min^{-1} and then coded into one of four absolute-intensity categories: sedentary (<1.5 METS), light (1.5–2.99 METS), moderate (3.00–5.99 METS), or vigorous (6+ METS) activity. Subsequently, accelerometer data were recoded to create binary indicator variables (0 or 1) to facilitate the receiver operating characteristic (ROC) curve analyses. For sedentary behaviour, this related to sedentary activities versus more than sedentary activities. For moderate activity, this related to less than moderate activities versus moderate to vigorous activities. For vigorous activity, this related to vigorous activities versus less than vigorous activities.

Statistical Analysis

Descriptive characteristics of study participants are presented in Table 1. Table 2 presents average intensity (METS) and average dominant and non-dominant wrist positioned GENEActiv output (SVMgs (g.minutes)) across the study sample. ROC curve analysis and Youden's Index (j=sensitivity+specificity-1) were used to access area under the curve (AUC) and define thresholds which optimize sensitivity (correctly identified points at or above the activity intensity threshold) and specificity (correctly excluded activities below the activity intensity thresholds) (282). Various threshold

values were tested regarding sensitivity and specificity, for each intensity of activity. Youden's index was used to determine optimal cut-off values (reference). The sedentary and moderate thresholds provided the boundaries for the light intensity category. Thresholds were cross-validated using ROC analysis on an independent group.

Results

Descriptive analysis

Fifty-six adults (27 males: 40.5±11.6years) had valid data for all 7 activities for both dominant and non-dominant wrist wear. Descriptive characteristics of study participants by developmental and cross-validation group are presented in Table 14. Overall the prevalence of obesity is 9.1% and overweight is 33.4%. Of those who were tested, 8% were left-handed.

Value calibration

Table 15 compares average METS and wrist specific GENEActiv output results by study group. Thresholds for dominant and non-dominant wrist wear were similar. Each activity had a suitable METS score to its relative intensity of physical activity with the exception of sweeping and slow walking. Sweeping and slow walking, which were deemed light intensity activities, resulted in an average 3.55/3.53 and 3.21/3.98 METS for developmental/cross-validation group respectively. Intensity thresholds (sum of the vector magnitude counts) were created for dominant and non-dominant wrist wear (Table 16). Across dominant and non-dominant wrist wear, discrimination of sedentary behaviour and vigorous activity was high, with AUC ranging from 0.97-0.99. On account of reduced sensitivity and specificity, the discrimination of moderate activity was less precise, with sensitivity and specificity scores ranging 78-6-80.4% (AUC from 0.70-0.72). The Youden Index approach identified the point on the ROC curve that was furthest from chance of discrimination. The optimal thresholds identified by Youden's Index for sedentary, moderate and vigorous activity are presented in Table 16.

Cross-Validation of Developed Thresholds

Thresholds were cross-validated with an independent group using ROC analysis. Each threshold demonstrated high levels of sensitivity and specificity when cross-validated. As the AUC for all intensity thresholds were the same the threshold with the highest value was selected as the optimal threshold (Table 16). An optimal threshold of 338/314 and 714/594 was identified for dominant/non-dominant wrist wear for moderate and vigorous intensity activity, while an optimal threshold of 230/190 was identified for sedentary behaviour.

Discussion

This is the first study to develop accelerometer cut-points for dominant and non-dominant wrist GENEActiv accelerometer data that reflect sedentary, light, moderate and vigorous activity. The value calibration of raw accelerometer data provides an overall indicator of bodily movement which subsequently can be used to calculate time spent in specific activity intensities. This data can in turn be used to study the association between physical behaviour and health outcomes. In addition, being able to identify the amount of time spent in a range of intensity categories is useful to identify international physical activity guideline recommendations to achieve optimal health.

In the present study the thresholds established for the GENEActiv accelerometer demonstrated excellent accuracy for classifying physical behaviour intensity across the activity spectrum, specifically sedentary behaviour and vigorous activity. The discrimination of moderate intensity activity was acceptable (AUC 0.67-0.71), but not as precise as sedentary and vigorous activity. Only one other study has determined thresholds for GENEActiv accelerometer data (85). However the cut-points presented by Esliger et al. (2011) were created for left- and right-wrist wear (277). The greater use of the dominant hand in everyday activities could lead to the overestimation of cut-points for physical activity intensities. Hand dominance is not an issue in posture positions and most movements. However, lifestyle activities such as window washing is generally a dominant hand activity, which leads to an increase in recorded acceleration signals and in turn an increase in intensity defining cut-points. Other studies have created thresholds for the GENEActiv accelerometer however these have been in different populations and across intensity domains (reference Zhang

and Phillips). Phillips et al. 2012 demonstrated the GENEActiv accelerometer to have excellent (AUC 0.94-0.99) accuracy at discriminating between physical behaviour activity intensities with both wrist and hip mounted devices in children. While Zhang et al. 2012 successfully developed an algorithm to classify physical activity into walking, running, household and sedentary activities. A study by Welch et al. 2013 tested the accuracy of previously published left-hand GENEActiv accelerometer thresholds for predicting intensity categories during structured bouts. Although sensitivity and specificity was lower than those previously reported by Esliger et al., they were within similar range.

This study has a number of strengths. The GENEActiv accelerometer collects data as raw acceleration and stores the data as g units for offline analysis thereby allowing for efficient data cleaning and the application of various data processing algorithms post-data collection. ROC analysis was used to identify optimal thresholds to discriminate sedentary, light, moderate and vigorous activity. This statistical method is known to be superior to previous value calibration methods which have used linear regression approaches. In addition, the choice of cut-points were determined using Youden index which ensures optimality of cut-points. Thresholds were cross-validated which further guarantees the optimisation of the chosen threshold values. The study protocol was developed on a non-treadmill-based validation approach to mimic free-living activities by accelerometer and energy expenditure measurements. Free-living activities were assessed using a portable CosMed K4B^2 device which objectively measures energy expenditure. Finally, we used individualised RMR to normalise energy cost between participants for each activity opposed to using a standardised RMR for the entire study population (reference see 36 of Kieran paper)

Notwithstanding these strengths, a number of limitations of the study have been identified. The study population varied in age, gender and BMI status however due to the large variation between subject characteristics and small sample size (n=56) these thresholds may be non-representative thus further research using larger sample sizes are necessary. In addition, only 7 activities were used in this study protocol. These activities may not be representative of habitual activities of all middle-aged adults nor habitual activities across different cultures thus generalizability of results should be warranted.

Conclusion

The GENEActiv accelerometer was found to have excellent accuracy for classifying physical behaviour intensity across the activity spectrum. This is the first study to develop accelerometer cut-points for dominant and non-dominant wrist wear GENEActiv accelerometer data that reflect sedentary, light, moderate and vigorous activity. Data suggests that the developed intensity thresholds for GENEActiv data are valid at determining physical behaviour intensity, but are slightly poorer but acceptable at estimating moderate activity in adults aged 18-65 years.

Table 14: Descriptive characteristics of study participants										
	Sample size		**Age**		**Left-Handed**		**Right-Handed**		**BMI (kg/m2)**	
	Development	Cross-validation	Development	Cross-validation	Development	Cross-validation	Development	Cross-validation	Development	Cross-validation
Male	18	9	37.3 (12.6)	38.8 (9.1)	4	1	14	8	24.7 (3.5)	24.6 (3.1)
Female	17	12	41.7 (12.4)	43.4 (10.1)	2	0	15	12	25.8 (4.2)	23.9 (4.0)
Total	35	21	39.5 (12.5)	41.4 (10.0)	6	1	29	20	25.2 (3.8)	24.2 (3.5)

Table 15: Average intensity (METS), average dominant and non-dominant wrist positioned GENEActiv output (SVMgs (15sec epoch) at 30 Hz)								
			METS		**Dominant Wrist**		**Non-dominant wrist**	
Activity	**Grouping**	**N**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Development group								
Sitting	Posture	35	1.04	0.21	4.74	1.74	4.82	2.21
Standing		35	1.12	0.19	3.62	1.26	3.45	1.37
Washing dishes	Ambulatory	35	1.55	0.29	64.42	29.27	52.71	19.54
Floor sweeping		335	3.50	0.99	132.34	48.73	102.68	44.47
Slow walking		35	3.21	0.44	70.1	13.35	74.42	17.18
Fast walking		35	4.17	0.85	110.66	33.54	118.36	64.16
Jogging		35	9.48	1.58	394.7	83.39	374.9	71.81
Cross-validation group								
Sitting	Posture	21	1.00	0.15	4.36	1.05	3.44	0.91
Standing		21	0.95	0.13	3.53	1.02	2.88	0.88
Washing dishes	Ambulatory	21	2.14	0.60	59.6	31.0	51.2	23.1
Floor sweeping		21	3.53	0.90	122.2	54.9	95.5	50.7
Slow walking		21	3.98	0.64	72.8	21.1	74.2	23.3
Fast walking		21	4.93	0.65	127.7	49.4	129.4	53.3
Jogging		21	8.74	0.95	441.4	134.2	378.5	110.3

Table 16: Sensitivity, specificity, AUC and GENEActiv cut-points based on 3 and 6 METS					
Intensity	**Sensitivity**	**Specificity**	**Area under the curve (95%CI)**	**GENEActiv cut-points (SVMgs (15s epoch))**	
Dominant wrist				**30Hz**	**100Hz**
Sedentary	91.6	92.4	0.97	<57.5	<191.8
Light	NA	NA	NA	57.5-84.3	191.8-281.5
Moderate	67.9	67.9	0.694	84.4-178.4	281.6-595
Vigorous	97.1	97.0	0.994	>178.4	>595
Non-dominant wrist					
Sedentary	92.9	92.4	0.98	<47.5	<158.5
Light	NA	NA	NA	47.5-78.3	158.5-261.8
Moderate	70.5	68.6	0.716	78.4-148.5	261.9-495
Vigorous	97.1	97.0	0.992	>148.5	>495
* sedentary (<1.5 METS), light (1.5-2.99 METS), moderate (3.00-5.99 METS), vigorous (>6 METS)					
NA; not applicable as sedentary and moderate intensity cut-points provide the margins for light intensity					

APPENDIX THREE

SUPPLEMENTARY TABLE FOR CHAPTER 4

Supplement Table 17: Spearman pairwise correlation coefficient of physical activity intensity by days of week							
	Sunday	**Monday**	**Tuesday**	**Wednesday**	**Thursday**	**Friday**	**Saturday**
Sedentary behaviour							
Sunday	**1.00**						
Monday	0.59	**1.00**					
Tuesday	0.63	0.73	**1.00**				
Wednesday	0.64	0.74	0.73	**1.00**			
Thursday	0.63	0.72	0.75	0.77	**1.00**		
Friday	0.68	0.72	0.73	0.75	0.79	**1.00**	
Saturday	0.71	0.67	0.66	0.69	0.71	0.71	**1.00**
Light activity							
Sunday	**1.00**						
Monday	0.59	**1.00**					
Tuesday	0.62	0.70	**1.00**				
Wednesday	0.65	0.71	0.77	**1.00**			
Thursday	0.60	0.67	0.71	0.74	**1.00**		
Friday	0.64	0.66	0.70	0.74	0.74	**1.00**	
Saturday	0.68	0.67	0.66	0.70	0.69	0.72	**1.00**
Moderate activity							
Sunday	**1.00**						
Monday	0.59	**1.00**					
Tuesday	0.59	0.69	**1.00**				
Wednesday	0.63	0.71	0.69	**1.00**			
Thursday	0.64	0.73	0.75	0.76	**1.00**		
Friday	0.68	0.72	0.71	0.72	0.77	**1.00**	
Saturday	0.70	0.67	0.64	0.64	0.67	0.68	**1.00**
Vigorous activity							
Sunday	**1.00**						
Monday	0.46	**1.00**					
Tuesday	0.45	0.60	**1.00**				
Wednesday	0.37	0.50	0.55	**1.00**			
Thursday	0.43	0.52	0.47	0.53	**1.00**		
Friday	0.52	0.53	0.51	0.50	0.53	**1.00**	
Saturday	0.48	0.49	0.40	0.43	0.47	0.48	**1.00**
MVPA							
Sunday	**1.00**						
Monday	0.58	**1.00**					
Tuesday	0.60	0.70	**1.00**				

Wednesday	0.62	0.73	0.68	**1.00**			
Thursday	0.65	0.74	0.75	0.76	**1.00**		
Friday	0.68	0.72	0.72	0.72	0.78	**1.00**	
Saturday	0.69	0.67	0.64	0.64	0.68	0.68	**1.00**
**All values have a significance <0.001*							

APPENDIX FOUR

SUPPLEMENTARY TABLE FOR CHAPTER 6

Table 18: Latent Profile Analysis; Model class probabilities					
Two-class-model	***1***	***2***			
1, *n* = 243 (61.4%)	0.996	0.004			
2, *n* = 153 (38.6%)	0.002	0.998			
Three-class-model	***1***	***2***	***3***		
1, *n* = 125 (31.6%)	0.997	0.003	0.000		
2, *n* = 214 (54.0%)	0.003	0.995	0.002		
3, *n* = 57 (14.4%)	0.000	0.012	0.988		
Four-class-model	***1***	***2***	***3***	***4***	***5***
1, *n* = 114 (28.8%)	0.976	0.021	0.003	0.000	
2, *n* = 169 (42.7%)	0.004	0.992	0.009	0.004	
3, *n* = 66 (16.6%)	0.006	0.000	0.994	0.000	
4, *n* = 47 (11.9%)	0.000	0.008	0.000	0.992	
Five-class-model					
1, *n* = 62 (15.7%)	0.990	0.010	0.000	0.000	0.000
2, *n* = 102 (25.7%)	0.002	0.982	0.013	0.000	0.002
3, *n* = 161 (40.6%)	0.000	0.006	0.989	0.005	0.000
4, *n* = 47 (11.9%)	0.000	0.000	0.005	0.995	0.000
5, n= 24 (6.1%)	0.000	0.007	0.006	0.000	0.987

APPENDIX FIVE

RESEARCH OUTPUTS, DISSEMINATION AND TRAINING

Table 19: Peer-reviewed publications during PhD			
Published			
	Year	**Peer-reviewed journals**	**Citation**
Journals			
	2016	PLOS ONE	**Dillon C.B**, Fitzgerald A.P, Kearney P.M, Perry I.J, Rennie K.L, Kozarski R, Phillips C.M. Number of days required to estimate habitual activity using GENEActiv accelerometer: A cross-sectional study.
	2015	Journal of aging and physical activity. (epub ahead of print)	McCullagh, R., Brady, N.M., **Dillon, C**., Horgan, N.F. and Timmons, S..A Review of the Accuracy and Utility of Motion Sensors to Measure Physical Activity of Frail Older Hospitalised Patients
	2013	PLOS ONE. 2013 Oct 17; 8 (10).	Phillips C.M, **Dillon C.B,** Harrington J,

			McCarthy V.J.C, Kearney P.M, Fitzgerald A.P, Perry I.J. Defining metabolically healthy obesity: role of dietary and lifestyle factors.
Abstracts			
	2015	Journal of Epidemiology and Community Health	**Dillon C.B**, Dahly D, Donnelly A.E, Kearney P.M, Perry I.J, Rennie K.L, Phillips C.M. Cross-sectional analysis of weekly levels and patterns of objectively-measured physical behaviour with cardiometabolic health in middle-aged adults.
	2015	Journal of Epidemiology and Community Health	**Dillon C.B**, Dahly D, Donnelly A.E, Kearney P.M, Perry I.J, Rennie K.L, Phillips C.M. Daily Cumulative Patterns of Objectively-measured Physical Behaviour by Metabolic

			Syndrome Health Profiles in Middle-aged Adults.
	2012	Journal of Science and Medicine in Sport 12/2012; 15:S161-S162	**Dillon C.B**, Kearney P.M, Perry I.J. McCarthy V.J.C. Metabolic health in the overweight and obese, what is the role of physical activity?
Under review			
	2015	PLOS ONE	**Dillon C.B**, Fitzgerald A.P, Donnelly A.E, Kearney P.M, Perry I.J, Rennie K.L, Kozarski R, Phillips C.M. Comparison of self-report and objective measures of moderate-to-vigorous activity with cardiovascular disease risk factors in a population-based cross-sectional study

Table 20: Other research outputs during PhD
Detail
Papers (in preparation)
McCullagh R, **Dillon C.B,** Horgan F, Timmons S. Accuracy of the Stepwatch Activity Monitor and ActivPAL3 in frail hospitalised patients.
Phillips C.M, **Dillon C.B**, Otvos J.D, Perry I.J. Reducing sedentary time and increasing moderate physical activity modulates atherogenic dyslipidaemia in middle-aged adults.
Phillips C.M, **Dillon C.B**, Perry I.J. Does physical activity duration or intensity counteract obesity and insulin resistance associated low-grade inflammation in middle-aged adults?
Dillon C.B, Fitzgerald A.P, Donnelly A.E, Perry I.J, Rennie K.L, Li X, , Phillips C.M. Daily cumulative patterns of objectively-measured physical activity and sedentary behaviour by cardiometabolic health status in middle-aged adults; A cross-sectional analysis.
Dillon C.B, Fitzgerald A.P, Donnelly A.E, Perry I.J, Rennie K.L, Li X, , Phillips C.M. Cross-sectional analysis of weekly levels and patterns of objectively-measured physical behaviour with cardiometabolic health in middle-aged adults.

Table 21: Conference presentations during PhD			
Poster presentations			
Year	**Title**	**Authors**	**Conference**
2015	**Daily Cumulative Patterns of Objectively-measured Physical Behaviour by Metabolic Syndrome Health Profiles in Middle-aged Adults.**	**Dillon C.B**, Dahly D, Donnelly A.E, Kearney P.M, Perry I.J, Rennie K.L, Phillips C.M.	**Society for Social Medicine Conference,** Dublin, Ireland 3rd-5th September
2015	**Cross-sectional analysis of weekly levels and patterns of objectively-measured physical behaviour with cardiometabolic health in middle-aged adults**	**Dillon C.B**, Dahly D, Donnelly A.E, Kearney P.M, Perry I.J, Rennie K.L, Phillips C.M.	**Society for Social Medicine Conference,** Dublin, Ireland 3rd-5th September
2015	**Criterion validity and calibration of the GENEActiv accelerometer in adults.**	**Dillon C.B**, Powell C, Dowd K, Carson B, Donnelly A.E,	**International Conference on Ambulatory Monitoring of Physical Activity and Movement. University of Limerick,** Limerick, Ireland 10th-11th June
2015	**Cross-sectional analysis of**	**Dillon C.B**, Dahly D,	**International Conference on Ambulatory Monitoring of**

	weekly levels and patterns of objectively-measured physical behaviour with cardiometabolic health in middle-aged adults	Donnelly A.E, Kearney P.M, Perry I.J, Rennie K.L, Phillips C.M.	**Physical Activity and Movement. University of Limerick,** Limerick, Ireland 10th-11th June
2013	**Validation of the International Physical Activity Questionnaire-Short Form against the GENEActiv accelerometer**	**Dillon C.B**, Fitzgerald A.P, Kearney P.M, Perry I.J, Rennie K.L, Kozarski R, Phillips C.M	**HRB Centre for Health and Diet Research Conference.** Cork, Ireland. October 2013.
2013	**Validation of the International Physical Activity Questionnaire-Short Form against the GENEActiv accelerometer**	**Dillon C.B**, Fitzgerald A.P, Kearney P.M, Perry I.J, Rennie K.L, Kozarski R, Phillips C.M	**HRB Clinical Research Facility Conference.** Cork, Ireland. June 2013.
2013	**Number of days required to estimate habitual physical activity using GENEActiv accelerometer.**	**Dillon C.B**, Fitzgerald A.P, Kearney P.M, Perry I.J, Rennie K.L, Kozarski R,	**International Conference on Ambulatory Monitoring of Physical Activity and Movement.** UMASS, Amherst, Boston, US. 17th-19th June 2013.

		Madden J.M, Phillips C.M	
2012	**Metabolic Health in the Overweight and Obese, What is the Role of Physical Activity?**	**Dillon C.B**, McCarthy V.J.C, Perry I.J, Kearney P.M	**4th International Congress on Physical Activity and Public Health,** Sydney, Australia 31st Oct - 3rd Nov 2012.
2012	**Metabolic Health in the Overweight and Obese, What is the Role of Physical Activity?**	**Dillon C.B,** McCarthy V.J.C, Perry I.J, Kearney P.M	**The European Congress of Epidemiology** in Porto, Portugal 5th-8th Sept 2012.
2012	**Number of days required to estimate habitual physical activity using GENEActiv accelerometer.**	**Dillon C.B**, Fitzgerald A.P, Kearney P.M, Perry I.J, Rennie K.L, Kozarski R, Madden J.M, Phillips C.M	**The Food Health Choice and Change conference**. Cork, Ireland. June 2012
2012	**Number of days required to estimate habitual physical activity using GENEActiv accelerometer.**	**Dillon C.B**, Fitzgerald A.P, Kearney P.M, Perry I.J, Rennie K.L, Kozarski R, Madden J.M, Phillips C.M	**UCC Doctoral Showcase**, semi-final. Cork, Ireland. April 2012

Table 22: Training and workshops attended during PhD	
Year	**Course**
UCC post graduate modules	
Sept 2012-May 2013	**Scholarly Approaches to Teaching and Learning** in Higher Education, University College Cork
Jan 2012-Jun 2012	**Teaching and Learning** Module for Graduate Studies, University College Cork
Apr 2011-Jun 2011	**Systematic Reviews** for the Health Sciences, University College Cork
Feb-May 2011	**Graduate Information Literacy Skills,** University College Cork
Oct 2010	**Scientific Training for Enhanced Postgraduate Studies,** University College Cork
Training outside of UCC	
Nov 2012-Jan 2015	**Management** Diploma, Pitman Training, Cork
Sept 2012 (24^{th}-28^{th})	MRC **Physical Activity Measurement** Seminar, Cambridge Institute of Public Health, MRC Epidemiology Unit, UK
Sept 2008-Dec 2008	**Managing People effectively at work**, College of Commerce, Cork
Other workshops, seminars and training attended	
Sept 2015	**Forging a career in research:** a survival kit, ECR Committee, Trinity College, Dublin
Nov 2014	**Editing and Proofreading for Professionals and Editing and Proofreading for Academic Purposes,** University College Cork
Oct 2014	**Managing your career,** University College Cork
Sept 2013	**Time management** workshop**,** University College Cork

Oct 2012	**Seven secrets of highly successful PhD students** with Hugh Kearnes**,** University College Cork
Oct 2012	**Turbocharge your writing** with Hugh Kearnes**,** University College Cork

Table 23: Awards and funding		
Institution	**Year**	**Detail**
Health Research Board	**2010-2015**	PhD Scholarship 2010-2015. Awarded full PhD funding from the Health Research Board Ireland, tenable for 5 years at €18,000 per year plus fees.
College of Medicine and Health Doctoral Student Bursaries	**2012**	Awarded a travel bursary to attend the 5th ICPAPH conference in Sydney, Australia.

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