

Life-Course Health Impact of Childhood Physical Activity Interventions

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Abstract

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Non-communicable diseases comprise an increasing burden on national health provision and budget, and low physical activity levels constitute a risk factor for non-communicable diseases. Analysis of the 2012 and 2015 Health Survey for England revealed few systematic differences in childhood physical activity levels, except that boys become increasingly more active than girls with age due to imbalances in formal sport participation. However, meta-analysis of 14 controlled studies revealed minimal effects of intervention in childhood, showing a mean difference of only 1.47 (95% CI's: -1.88, 4.82) minutes a day of moderate-to-vigorous physical activity at six months post-intervention.

A proportional multi-state life table was constructed to quantify effects of intervention on childhood physical activity levels and subsequent health outcomes within the life course of a simulated closed cohort. All scenarios produced negligible effects on life expectancy. A scenario based on The Daily Mile produced a reduction of 13748 (95% CI's: 20188, 7601) years of life in disability per 100,000 population, while a Mind, Exercise, Nutrition, Do it! scenario showed a reduction of 23494 (95% CI's: 32234, 15405) years, largely due to reductions in type 2 diabetes prevalence.

Overall, contemporary interventions in childhood show negligible sustained effects on physical activity levels, with minimal subsequent impact on adult disease outcomes, and caution is recommended in claims and expectations to the contrary. Observed health benefits were largely accrued by targeting the least active within the population, and future research should focus on the relative effectiveness of 'treatment' versus 'population' approaches to intervention.

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List of Abbreviations

LPA	Light Physical Activity
MPA	Moderate Physical Activity
VPA	Vigorous Physical Activity
MVPA	Moderate-to-Vigorous Physical Activity
MET(s)	Metabolic Equivalent(s)
BMR	Basal Metabolic Rate
IPAQ	International Physical Activity Questionnaire
GPAQ	Global Physical Activity Questionnaire
PASBAQ	Physical Activity and Sedentary Behaviour Assessment Questionnaire
BMI	Body Mass Index
HDL-C	High Density Lipoprotein Cholesterol
UK	United Kingdom
HSE	Health Survey for England
QIMD	Quintile of Index of Multiple Deprivation
UCL	University College, London
NHS	National Health Service
ANOVA	Analysis of Variance
ACE	Assessing Cost Effectiveness

DALY	Disability-Adjusted Living Years
ICD-10	International Classification of Diseases – 10th Edition
ONS	Office for National Statistics
DisMod II	Disease Modeller – Version Two
CHD	Coronary Heart Disease
CVD	Cardiovascular Disease
MI	Myocardial Infarction
NHANES	National Health and Nutrition Examination Survey
HR	Hazard Ratio
NCRAS	National Cancer Registration and Analysis Service
PHE	Public Health England
TTM	Trans-Theoretical Model of Change
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
NICE	National Institute for Health and Clinical Excellence
USA	United States of America

Publications and presentations arising from this thesis

An adapted version of the systematic review and meta-analysis presented in Chapter Five was published in PLoS One in July 2015:

- Sims, J., Scarborough, P., & Foster, C. (2015). The effectiveness of interventions on sustained childhood physical activity: A systematic review and meta-analysis of controlled studies. *PLoS One, 10*(7), e0132935.

This paper was also orally presented at the annual conference for the International Society of Behavioural Nutrition and Physical Activity, Edinburgh, 2015.

Further publications arising from the content of this thesis are planned for submission over the next 12 – 24 months:

- An analysis of childrens physical activity from the 2012 and 2015 Health Survey for England. Drawing on the content from Chapter Two. Target journals: Preventative Medicine, Preventative Medicine Reports, International Journal of Physical Activity and Health, International Journal of Behavioural Nutrition and Physical Activity.

- Modelling the life-span benefits of child physical activity interventions in a simulated English cohort. Drawing on the content from Chapters Three, Four, Six, and Seven. Target Journals: International Journal of Physical Activity and Health, International Journal of Behavioural Nutrition and Physical Activity, PLoS One.

- Cost-effectiveness of interventions to increase childhood physical activity interventions. Drawing on the content of Chapters Three, Four, Seven, and Eight, along with collaborations. Target journals: Population Health Metrics, PLoS One, Health Economics.

Chapter 1 - Introduction

1.1. Chapter Overview

This opening chapter seeks to lay the conceptual foundation for the subsequent thesis. With the more detailed methodological information presented in subsequent chapters, this chapter defines the context from which the research question originated and identifies the commonly accepted component parts that comprise the subject area of physical activity. In particular, a summary of the hypothesised health consequences and burden of disease from inadequate levels of physical activity is presented as a justification for continued research in this area.

1.2. Thesis Context

Epidemiological transition theory outlines three initial phases of epidemiological development within the Anthropocene era (McKeown, 2009; Omran, 1971, 2005): firstly, a lengthy initial period in which infectious diseases and malnutrition largely accounted for mortality rates; secondly, a period of receding pandemics in which increasing wealth resulted in the availability of sufficient nutrition; thirdly, while improved public health and water treatment progressively increased life expectancy and reduced infectious disease and malnutrition, a period of degenerative and man-made issues such as smoking and reduced physical activity resulted in increased prevalence of cardiovascular disease and cancer. This framework was subsequently extended to include a fourth stage, in which technological advances and a focus on preventative strategies delayed the effect of degenerative and man-made issues with consequential gains in life expectancy (Olshansky & Ault, 1986; Rogers & Hackenberg, 1987). More recently, suggestions have been made regarding transition to a fifth phase of epidemiological focus (Gaziano, 2010). This contemporary period displays rising prevalence of obesity and physical inactivity which threatens to at least partially reverse the gains in risk factor prevention and, for the first time, potentially observes reduced life-expectancy of future generations compared to their parents (Olshansky et al., 2005).

There exists growing and corroborative evidence that populations within developed countries are leading increasingly sedentary lifestyles with long-term adverse consequences both for population health (e.g. Department of Health, 2011; Guthold, Stevens, Riley, & Bull, 2018; Ozemek, Lavie, & Rognmo, 2019) and governmental health budgets (Barquera, Pedroza-Tobias, & Medina, 2016; Lightwood et al., 2009; Stein & Colditz, 2004). While the wider body of literature focusses more on the causal role of obesity on mortality (e.g. Flegal, Kit, Orpana, & Graubard, 2013; Ng et al., 2014), physical inactivity constitutes an independent risk factor both for all-cause mortality and specific non-communicable diseases (Lee et al., 2012; World Health Organization, 2010). Indeed, the global burden of disease due to physical inactivity has been estimated as being broadly equivalent both to smoking and to obesity (Lee et al., 2012), although a more recent report from the Australian Institute of Health and Welfare (2017) more conservatively estimated that the burden of physical inactivity and obesity combined is the equivalent of smoking. The World Health Organization (2009b) suggested six percent of global deaths are attributable to physical inactivity, a reduction of 25% in which would prevent 1.3 million deaths per year (Lee et al., 2012), with the most recent Global Burden of Disease report (Gakidou et al., 2017) suggesting nearly 1.4 million deaths were attributable low levels of physical activity in 2016.

1.3. Economic Burden of Disease

An inevitable consequence of ill health is the financial burden associated with the healthcare costs to service the population (Kohl et al., 2012). An estimation of the global burden of physical inactivity was completed by Lee et al. (2012), suggesting it causes 6% of the burden of coronary heart disease, 7% of type 2 diabetes and 10% of breast and colon cancer. Scarborough et al. (2011) suggested that the direct costs to the NHS for physical inactivity approximates £0.9 billion annually, which with indirect costs potentially exceeds £2 billion. Globally, costs are estimated to be $53.8 billion (Ding et al., 2016). These costs are a primary motivation for governments to promote cost-effective interventions to reduce the future burden of disease (Cecchini et al., 2010; Cobiac, Vos, & Barendregt, 2009).

1.4. Definitions

'Physical activity', as distinct from 'exercise', is defined as "any bodily movement produced by skeletal muscles that results in energy expenditure" (Caspersen, Powell, & Christenson, 1985, p. 126). Exercise is a sub-category of physical activity, and is defined as "physical activity that is planned, structured, repetitive, and purposive in the sense that improvement or maintenance of one or more components of physical fitness is an objective" (Caspersen et al., 1985, p. 128). Lastly, 'physical fitness' is defined as "a set of attributes that people have or achieve that relates to the ability to perform physical activity" (Caspersen et al., 1985, p. 129). In addition to the activity-specific definitions, the term 'sedentary behaviour' is "any waking behavior characterised by an energy expenditure ≤1.5 metabolic equivalents (METs), while in a sitting, reclining or lying posture" (Tremblay et al., 2017), with sedentary behaviours including TV viewing, video game playing, computer use (collectively termed "screen time"), driving automobiles, or reading.

1.5. Intensity, Frequency, and Duration

Physical activity inevitably occurs across constantly changing levels of intensity but is typically qualitatively classified into four types: physical inactivity, light physical activity (LPA), moderate physical activity (MPA), and vigorous physical activity (VPA). Moderate-to-vigorous physical activity (MVPA) is often combined for the purposes of analysis as this level of activity is considered to be 'health enhancing'. The relative level of intensity of each episode of physical activity can be measured and described according to its metabolic equivalent (MET). A MET value represents a unit of measurement of the amount of energy expended to maintain a specific activity relative to a basal metabolic rate (BMR) of 1 MET (Ainsworth et al., 2000), but therefore does not provide a measure of absolute activity. For the purposes of standardisation, 1 MET is calculated as 3.5 ml of O_2 per kg per hour for a 70 kg 40 year old male sitting quietly (Byrne, Hills, Hunter, Weinsier, & Schutz, 2005) and estimated MET codes for specific activities are available for a large number of human behaviours (Ainsworth et al., 2011), although while two-thirds of MET estimates are derived from referenced measurement, the remainder are based on expert opinion (Butte et al., 2018). In reality, and

potentially problematically, while each individual's BMR may be benchmarked at 1 MET, physiological, environmental, and temporal differences dynamically determine BMR, and therefore relative energy expenditure, in any given episode of physical activity (Speakman & Selman, 2003).

Relative to BMR, LPA is considered to be time spent in any activity that requires between 1 and 3 METs (e.g. cooking and food preparation = 2.5 METs), MPA to be time spent in any activity that requires between 3 and 6 METs (e.g. walking for pleasure = 3.5 METs), and VPA to be any activity requiring greater than 6 METs (e.g. competitive singles tennis = 8 METs) (Ainsworth et al., 2011), although more recent research has suggested higher thresholds by which to categorise relative intensity (de Almeida Mendes et al., 2018). While sedentary behaviour is conceptualised as behaviourally distinct from physical inactivity (Ford & Caspersen, 2012; Tremblay, Colley, Saunders, Healy, & Owen, 2010) the two can be considered functionally equivalent in terms of metabolic expenditure and are typically assigned a value of 1.5 METs (Owen, Healy, Matthews, & Dunstan, 2010).

Children, however, have a higher BMR relative to their weight, which gradually reduces to adult rates through the childhood years (McMurray et al., 2015); furthermore, organ maturation, laying down of muscle mass, and relative adiposity contribute to additional differences between adults and children (Butte et al., 2018), as a result of which the use of adult-derived figures underestimate child BMR. In addition, children acquire skill in certain movements with developing refinement resulting in reduced energy expenditure, with submaximal activity expenditure decreasing with age relative to body mass. These shortfalls were formally addressed by Ridley, Ainsworth, and Olds (2008) who produced an updated compendium which included child specific MET equivalences. However, limitations in sample size, included child activities, published sources, and restriction to a single MET value for children aged five to seventeen years, reduced the sensitivity and utility of estimates for specific age groups within the childhood years (Butte et al., 2018). Lastly, and in common with the adult compendium, there was insufficient recognition of activities within which it was possible to perform at considerably different intensities.

A subsequent review of 137 publications on observation of child-specific energy expenditure led to the provision of an extended and expanded compendium of youth MET equivalences for 196 activities across four childhood age groups. In exploring a range of activities, Butte et al. (2018) discovered that age held little effect on sedentary activities, such as computer games or schoolwork, but was positively correlated with MET estimates for sub-maximal moderate-to-vigorous activities. In addition, Butte et al. (2018) provided estimates at different intensity levels for a larger number of generic activities, such as walking, cycling, running, and swimming, over the age groups to allow a more nuanced estimation of group-level intensities across childhood age-groups.

Frequency of physical activity refers to the number of occasions within a specific time frame, typically a week, in which individuals engage in meaningful physical activity. UK government guidelines acknowledge the importance of frequency by suggesting that although at least 150 minutes of moderate physical activity is the weekly minimum for adults, this should be optimally achieved through five 30-minute episodes across any given week (Department of Health and Social Care, 2011, 2019). Duration refers to the length of time an individual can be described as meaningfully engaged in physical activity in a given episode. UK government guidelines acknowledge the importance of duration, suggesting that episodes should be at least ten minutes long, and ideally 30 minutes or longer (Department of Health and Social Care, 2011, 2019).

1.6. Domains

In addition to stratification by intensity, physical activity can be categorised according to the context within which it largely occurs. These categories are: occupational, domestic, leisure, and travel time (Bauman et al., 2012; Craig et al., 2003). Briefly, occupational physical activity involves all energy expenditure that occurs within an individual's employment, and also typically includes educational curriculum time; domestic physical activity includes expenditure while completing routine household and gardening tasks; leisure time physical activity includes volitional pursuits taken outside of domestic and occupational time; travel typically describes the method by which an individual moves

from domestic to employment locations, with walking and cycling time considered to be 'active transport' (Dishman, Heath, & Lee, 2004; Jones et al., 2019).

1.7. Measurement

The study of physical activity behaviour is dependent on the quality of available data and therefore both reliability and validity are of high importance as measurement error may lead to incorrect inferences (Ainsworth et al., 2012a). Commonly used methods for measuring physical activity fall under two broad categories: 'self-report' and 'objective' measures. Self-report measurement is reliant upon an individual, or a parent, reporting amounts of time spent in particular activities throughout a specified time period. These reports are typically gathered through the completion of a questionnaire or survey. A common approach, such as that used by the International Physical Activity Questionnaire (IPAQ) (Craig et al., 2003) or the Global Physical Activity Questionnaire (GPAQ) (Bull, Maslin, & Armstrong, 2009), is to collect the estimated amount of time respondents spend in each domain of physical activity. The respondent specifies which activity they were primarily engaged in during specified episodes of time, typically, but not inevitably, in blocks of fifteen minutes. Energy expenditure can then be calculated by multiplying the number of minutes by the MET value allocated to each activity.

The alternative approach, 'objective' measurement, most commonly uses devices to collect information about physical activity, although other methods are available such as direct observation (McKenzie, 2002) and measures of variability in oxygen consumption (see Bassett, 2000). Where used, devices are typically either motion sensors, such as pedometers and accelerometers, or heart-rate monitors. Pedometers measure steps taken, but capture no sense of the effort placed into each step due to load, incline, or intensity, and therefore have limited application outside assessing walking or sedentary behaviour (Rush et al., 2012). Accelerometers capture implied energy expenditure over time through detecting three-dimensional motion, with devices usually attached either to the arm,

hip, or calf. Heart-rate monitors capture changes in pulse frequency which, when compared to an individual's basal heart rate, permits an estimation of activity intensity.

The key benefit of self-report lies in the simplicity of implementation and low relative cost, making this approach a pragmatic choice for large-scale projects. Additional relative benefits are that self-report measurement has less 'mere-measurement effect' on participant behaviour (Morwitz & Fitzsimons, 2004) and that behaviour type can be captured to a meaningful level of specificity, i.e. domain and activity can be identified (Scholes et al., 2014a). The disadvantages of self-report include the reliance on human recall over time (Mindell, Coombs, & Stamatakis, 2014; Shephard, 2003) and susceptibility to social desirability bias (Adams et al., 2005; Celis-Morales et al., 2012). The more costly objective measures offer a precise method of capturing motion, although the subsequent interpretation of raw data from devices involves a series of generalisations and interpretations, inevitably leading to some loss of precision (Dishman et al., 2004; Kelly, Fitzsimons, & Baker, 2016). The presence alone of a measurement device has been shown to change physical activity behaviour, introducing potential systematic bias into measurement (Bravata et al., 2007).

Due to the comparative expense of objective measurement and inherent difficulties with compliance, the majority of large-scale surveys and intervention studies rely on self-report measurement as a primary source of data. Objective measures are often employed as a confirmatory exercise, comparing the self-report data with objective measurements among a sub-sample (Hagströmer, Oja, & Sjöström, 2006; Terwee et al., 2010). For example, the 2008 Health Survey for England (HSE) data indicated Spearman's correlation coefficients of 0.20 in men and 0.30 in women for total physical activity, and of 0.32 in men and 0.41 in women for metabolic expenditure, representing only moderate correlation between the rankings of individuals on physical activity levels as measured by the Physical Activity and Sedentary Behaviour Assessment Questionnaire (PASBAQ) and accelerometry (Scholes et al., 2014a).

When attempting to measure physical activity in children there are several additional issues that must also be taken into consideration (Mindell et al., 2014; Sirard & Pate, 2001). While small-scale or highly

specific studies can use direct observation, this is not practical in larger samples (Fairclough et al., 2019; McKenzie, 2002). With self-report measurement, younger children do not inevitably possess the necessary cognitive development to accurately report activities over non-immediate time-frames (Mindell et al., 2014; Sallis, Buono, Roby, Micale, & Nelson, 1993). In addition, children's activity patterns are typically more varied than adults, particularly in periods of active play, and therefore a loss of measurement precision in activity type intensity and duration is common (Saint-Maurice & Welk, 2015; Welk, Corbin, & Dale, 2000). These issues can be partially addressed with objective measurement, and while child compliance with device usage presents additional difficulties (Rowlands, 2007), wrist worn devices have shown improved compliance (Fairclough et al., 2016; Rowlands et al., 2014).

In summary, an awareness of the limitations of physical activity measurement is important when considering epidemiological and intervention evidence (Kelly et al., 2016). Precision can be improved with careful attention to the outcome that is required from measurement and the context within which data are to be gathered, however researchers must be realistic about the utility and precision of selected measurement approaches (Kelly et al., 2016). Finally, it is important to distinguish between the measurement of physical activity per se, as opposed to sedentary time, as evidence has shown them to be independent behaviours with a small but statistically significant negative association, indicating that these two broad behaviour categories do not inevitably displace each other (Pearson, Braithwaite, Biddle, Sluijs, & Atkin, 2014).

1.8. Childhood Origins of Non-Communicable Disease

Non-communicable disease, sometimes termed chronic illness, refers to a group of diseases that typically involve a lengthy duration of both causation and realisation, including cardiovascular disease, cancer, chronic pulmonary disease, and diabetes, and grouped together represent the largest cause of premature death globally (Vandenberghe & Albrecht, 2020; World Health Organization, 2013). While a significant majority of non-communicable disease symptoms, and therefore any consequence

of insufficient physical activity, only become evident in adulthood, it has been argued that the seeds of such health outcomes are sown in childhood. Boreham and Riddoch (2001), in an extension of the work of Blair, Clark, Cureton, and Powell (1989), provide a useful framework within which to consider the effects of childhood physical activity levels, suggesting these can be meaningfully grouped into:

- Immediate effects on child health
- Biological (direct) legacy effects into adult health
- Behavioural (indirect) legacy effects into adult health

1.8.1. Immediate Effects on Child Health

Non-communicable diseases tend to possess lengthy causal mechanisms and therefore the onset of chronic disease symptoms in childhood is rarely observed (Reiner, Niermann, Jekauc, & Woll, 2013). In addition, physical inactivity typically clusters with a number of other environmental, sociological and behavioural risk factors (Myers, Kokkinos, & Nyelin, 2019; Sallis, Prochaska, & Taylor, 2000; Van der Horst, Paw, Twisk, & Van Mechelen, 2007) that may also contribute towards non-communicable disease incidence and therefore the isolation of the unique effect of physical inactivity on child health outcomes is difficult to calculate. A risk factor is considered to be "a factor that raises the probability of adverse health outcomes" (World Health Organization, 2009a). Furthermore, given the numerous behavioural and environmental factors that potentially influence the development of subsequent disease outcomes in adulthood, the association between childhood physical activity is not directly compared with disease outcome but instead with the relative presence of known or suspected physiological risk factors for specific non-communicable diseases, e.g. increased Body Mass Index (BMI) or atherosclerosis (Väistö et al., 2014). Typically then, it is only possible to measure associations between childhood physical activity levels and risk factors (Ekelund et al., 2012), and although early associations remain weak (Andersen et al., 2006; Eisenmann, 2004), more recent research has

discovered significant associations between metabolic syndrome and objectively measured childhood MVPA (Renninger et al., 2020).

Physical inactivity tends to cluster with overweight and obesity, which itself possesses independent associations with key risk factors of poor health (Leech, McNaughton, & Timperio, 2014). Obesity is the result of a positive energy imbalance between the intake of energy through consumption of food and drink, and the energy expended by BMR and physical activity (Brownson, Chriqui, Burgeson, Fisher, & Ness, 2010). In younger children, growth and development also add to expenditure of energy. Increased adiposity compounds the potential for physiological detriment, but also potentially raises psychological issues such as low self-esteem, social exclusion, and depression (Pulgarón, 2013). Systematic reviews by Flegal et al. (2013) and by Camacho-Minano, LaVoi, and Barr-Anderson (2011) found significant negative associations between objectively measured physical activity and weight status, with stronger associations for MVPA rather than for total physical activity. Corresponding associations were found between cardiovascular fitness and weight status (Janssen & LeBlanc, 2010). It is possible that some reverse causality is occurring, or a 'vicious cycle' of weight gain and physical inactivity, although it remains difficult to show an effect for physical activity on adiposity in childhood (Richmond et al., 2014).

Childhood physical activity is suggestive of protection against obesity although the causations are complex and certainly not definitive (Hills, Andersen, & Byrne, 2011). Intuitively, and following the energy balance principle, physical activity is seen as logically beneficial, although the extent to which modifiable calorific expenditure is responsible for weight control is questionable (Harris, Kuramoto, Schulzer, & Retallack, 2009; Sahoo et al., 2015). Childhood obesity is problematic because it tends to track into adulthood (Simmonds, Llewellyn, Owen, & Woolacott, 2016) where it constitutes a major risk factor for type 2 diabetes (Pulgaron & Delamater, 2014), cardiovascular disease (McCrindle, 2015), and cancer (Stewart & Wild, 2017) incidence and mortality. These factors combine with indirect consequences that also arise from childhood obesity, including psychological, social, and economic

issues, to compound negative health impacts (Chu et al., 2019; Kelsey, Zaepfel, Bjornstad, & Nadeau, 2014; Reilly et al., 2003).

More recently, the concept of 'metabolic syndrome' has been proposed, serving as an umbrella term for the cluster of symptoms that indicate future risk of cardiovascular disease and type 2 diabetes (Alberti, Zimmet, & Shaw, 2005; De Ferranti & Osganian, 2007; Kaur, 2014). Risk factors include general and visceral adiposity, hypertension, hypertriglyceridaemia, depressed high density lipoprotein cholesterol (HDL-C), and glucose intolerance or hyperinsulinaemia, which when considered together typically show a more robust relationship with physical activity (Chaput et al., 2013; Jiménez-Pavón et al., 2013; Renninger et al., 2020) following a dose-response relationship both in conjunction with and independent from cardio-respiratory fitness (Janssen & LeBlanc, 2010). Within overweight or obese children, moderate associations exist between sedentary time and HDL-C but not lipids, broadly suggesting that reducing sedentary time, rather than increasing MVPA is indicated (Cliff et al., 2013) although Ekelund et al. (2012) and Jiménez-Pavón et al. (2013) found all risk factors to be associated with MVPA time. While the literature is to some extent compromised by a lack of agreed cut-off points for what constitutes childhood metabolic syndrome (van Vliet et al., 2011) the evidence suggests those with a higher metabolic syndrome profile are at an increased risk of later disease outcome and death (Gami et al., 2007; Mottillo et al., 2010).

Some evidence indicates a direct impact of physical activity in childhood with bone health, important in the prevention of osteoporosis in later adulthood (Janz et al., 2010). More active young children exhibit higher bone density in adolescence (Bailey, McKay, Mirwald, Crocker, & Faulkner, 1999; Janz et al., 2010), possibly indicating a specific window of opportunity in the early teenage years which should be exploited by involving weight bearing exercise in early years (Welten et al., 1994). Poitras et al. (2016) also found evidence for an association between physical activity levels and bone health in a broader systematic review of several potential health outcomes. A strong skeleton is a protective factor against osteoporosis in later life and remains a benefit of child weight-bearing physical activity

irrespective of other variables, although evidence of a dose-response relationship remains weak (Department of Health, 2004; Vuori, 2001).

With regard to psychosocial consequences, there is evidence for a beneficial effect of higher physical activity levels on child self-esteem (Ekeland, Heian, Hagen, & Coren, 2005) and depression (Camacho-Minano et al., 2011), although findings are limited to small and immediate effects of physical activity interventions (Dale, Vanderloo, Moore, & Faulkner, 2019). The association between physical activity and academic performance has received some support, although an early review by Biddle and Asare (2011) suggested that the evidence shows only small or inconsistent effects and that the quality of studies is low. Since this, further work suggests a positive association (Rasberry et al., 2011; Singh, Uijtdewilligen, Twisk, Van Mechelen, & Chinapaw, 2012; Wassenaar et al., 2020), and most particularly in younger children (Norris, van Steen, Direito, & Stamatakis, 2020).

In summary, the focus of investigations into childhood benefits from physical activity tends to surround initial changes in physiological risk factors rather than chronic disease onset, which is typically not observed until mid-to-late adulthood (Ekelund et al., 2012). The combined effect of physical inactivity and overweight status appears to result in increased prevalence of risk factors for future chronic disease incidence, both physiological and psychological (Janssen & LeBlanc, 2010). In particular, the avoidance of physical inactivity appears to be indicated when summarising associations with risk factors (Biddle & Asare, 2011). However, associations do not confer causation, and it appears that the most consistent conclusion is that low levels of physical activity cluster with cardio-metabolic risk factors (Janssen & LeBlanc, 2010) and metabolic syndrome (Strasser, 2013). In addition, numerous potential environmental and social confounders exist when seeking to quantify the effect of physical activity on risk factors (Sallis et al., 2000).

1.8.2. Biological (direct) Legacy Effects into Adult Health

Insufficient levels of physical activity have been implicated in the aetiology of several chronic illnesses (Australian Institute of Health and Welfare, 2017; Lee et al., 2012), including some forms of cancer (Li

et al., 2016), cardiovascular disease (Li & Siegrist, 2012; Nocon et al., 2008; Wendel-Vos et al., 2004), type 2 diabetes (Bassuk & Manson, 2005; Colberg et al., 2010; Lao et al., 2019), dementia (Hamer & Chida, 2009; Kivimäki et al., 2019), mental health (Dale et al., 2019; Mammen & Faulkner, 2013), and bone health (Kohrt, Bloomfield, Little, Nelson, & Yingling, 2004), which along with insufficient muscular strength constitute a risk factor against falls and fractures in later life (Feskanich, Flint, & Willett, 2014; Gregg, Pereira, & Caspersen, 2000). With the possible exception of bone health for which evidence remains inconclusive, a consistent finding within systematic reviews and meta-analyses is the emergence of a non-linear inverse dose-response relationship between levels of physical activity and non-communicable disease mortality (Kyu et al., 2016; Lee & Skerrett, 2001; Wahid et al., 2016) indicating a diminishing returns benefit for increased levels of physical activity with the greatest potential health benefit observed in the least active (Janssen & LeBlanc, 2010).

Additional direct effects are observed in all-cause mortality (Kyu et al., 2016; Wahid et al., 2016) which demonstrates an inverse linear relationship with physical activity, although the relative contribution of intensity, duration, and frequency was not conclusively shown. Adult physical inactivity tends to cluster with overweight and obesity, which constitute an independent risk factor for all-cause mortality (Flegal & Graubard, 2009; Flegal et al., 2013) and numerous additional disease outcomes (Flegal, Graubard, Williamson, & Gail, 2007; Solomon & Manson, 1997), although over longer periods of time the association is weak. Although a biologically plausible role for physical activity in the prevention or reduction of obesity is clear (Dishman, Heath, & Lee, 2012) the evidence is not supportive of a causal relationship.

1.8.3. Behavioural (indirect) Legacy Effects into Adult Health

In addition to the measurable physiological effects of childhood physical activity, much interest has been given to the formation of unhealthy behavioural patterns, or habits, that commence in childhood and potentially carry over to adulthood (Boreham & Riddoch, 2001). Such behaviour patterns may be explicit, i.e. participation in formal sport or exercise classes or active pursuits, but also implicit, such

as attitudes and motivation towards physical activity (Dimmock & Banting, 2009). Given the largely psychological or behavioural, rather than biological, pathways in this field the evidence is less compelling, dealing with complex interactions and potential reverse causalities, e.g. obesity may result in lowered physical activity but conversely low levels of physical inactivity may result in obesity (Ekelund, Brage, Besson, Sharp, & Wareham, 2008). As well as psychological variables, competency and social networks play a role in adult physical activity participation, e.g. if a child has friends in sport they are more likely to participate in the future (Allender, Cowburn, & Foster, 2006). Levels of physical literacy developed as a consequence of involvement with physical activity in childhood may also play a part in participation and physical activity decisions in adulthood (Bauman et al., 2012; Dudley, Cairney, & Goodway, 2019).

In the absence of a formal model of indirect effects of the consequences of childhood physical activity across the lifespan, the persistence over time of physical activity behaviour can be estimated by 'tracking' studies, which measure the extent to which an individual's rank order within a population is maintained (Malina, 2001). The term has also been used more broadly to refer to the level of predictability of an outcome or outcomes from specified initial conditions, in this case physical activity behaviour (Telama et al., 2013). Tracking studies have been conducted both on cardio-respiratory fitness (Malina, 1996; Ortega et al., 2015) and on obesity (Lloyd, Langley-Evans, & McMullen, 2012; Singh, Mulder, Twisk, van Mechelen, & Chinapaw, 2008), finding that such traits typically persist over time.

Telama et al. (2013) examined tracking from early childhood through adolescence and into early adulthood. They followed a cohort (n = 3596) for 27 years taking self-reported physical activity measurements every three years. They found a moderate ranked correlation (r = 0.25-0.45) across measurement points, indicating the presence of moderate stability within the cohort, with males showing a stronger correlation than females. Interestingly, it appears that inactivity tracks with more stability than activity, potentially suggesting that while active individuals vary the amount of activity

they perform over time, inactive individuals tend to show an intransigent pattern (Hayes, Dowd, MacDonncha, & Donnelly, 2019; Telama et al., 2013).

A major drawback of tracking studies is the over-reliance on self-report data, which has been shown to possess a wide standard error (Ainsworth, Cahalin, Buman, & Ross, 2015). Studies typically capture data from one day, or at most one week, and are therefore highly susceptible to inaccuracy due to short-term variation in behaviour (Telama, 2009). Although correlations from tracking studies are weak, this is not necessarily a surprise as physical activity represents a behaviour and is therefore far more exposed to temporal perturbation from the environment than a physiological marker, such as bone density, obesity, or physical fitness which persist with greater reliability (Malina, 1996), especially through times of key transition in life (Hayes et al., 2019; Telama et al., 2013).

1.9. Physical Activity Guidelines

These findings and consequences have increasingly formed the basis of government-level recommendations on appropriate levels of physical activity (Kohl et al., 2012). Government guidelines are largely predicated on the concept of a dose-response relationship between physical activity and various health outcomes (Warburton, Charlesworth, Ivey, Nettlefold, & Bredin, 2010) which are then presented to the public in an understandable and achievable manner. The greatest benefit of increased physical activity is observed at the lowest level of the continuum, with health outcomes improving more quickly for the least active (Camacho-Minano et al., 2011; Department of Health, 2011). Relative improvement then follows a principle of diminishing returns with progression up the physical activity continuum, with little observable health gain for the most active individuals.

Physical activity can include all forms of activity, such as everyday walking, cycling, active play, work-related activity, active recreation, dancing, gardening, as well as organised or competitive sport (Department of Health, 2011). The UK Chief Medical Officers suggest that adults should attempt to be active daily but should achieve 150 minutes of at least moderate activity per week in bouts of ten minutes or more. Children are recommended to achieve at least 60 minutes of MVPA daily. These

guidelines match those of the American College of Sports Medicine who recommend that adults engage in moderate intensity aerobic physical activity for 30 minutes at least five days per week, or vigorous intensity aerobic physical activity for 20 minutes three days per week, or a viable combination of the two that totals at least 150 minutes of weekly MVPA (Kohl et al., 2012), while recommending children should engage in 60 minutes of MVPA per day (Centers for Disease Control, 2018). Recent data suggest that only 66% of men and 56% of women (Health and Social Care Information Centre, 2013), and 23% of boys and 20% of girls (NatCen, 2017), in England report meeting these guidelines. The publication of more recent guidelines suggests that children continue to engage in at least 60 minutes of MVPA per day across the week, and that this should be completed at different intensities and durations, while also limiting sedentary time by replacing inactivity with at least light activity (Department of Health and Social Care, 2019). Adults are recommended to complete 150 minutes of MVPA, or 75 minutes of VPA, or a viable combination of the two, potentially including short episodes of very vigorous activity. Adults are also encouraged to complete at least two episodes per week of activity leading to relative strengthening of muscles, while also braking up periods of inactivity with at least light activity bursts (Department of Health and Social Care, 2019).

1.10. Physical Activity Intervention

Studies investigating the extent to which levels of physical activity track from childhood into adulthood provide a logical justification for attempting to intervene in childhood (Hayes et al., 2019; Malina, 2001; Telama et al., 2013) as part of policy for reducing non-communicable disease mortality and morbidity in later life (Department of Health, 2011) and subsequent economic burden. Interventions broadly focus either at a population level, with the intention of shifting the distribution of physical activity incrementally towards the more active end of the continuum, or a treatment level, in which a specific section of the continuum is targeted, most typically the least active.

The treatment approach, or 'high risk strategy' (Rose, 1985; Rose, Khaw, & Marmot, 2008), is conceptualised as the effort to identify and then treat individuals with a relatively high propensity

towards disease, with the advantage that treatment is targeted to the individual and therefore confers 'patient' motivation, but the disadvantages of a reliance on appropriate screening of the population and a focus on relief of symptoms rather than of prevention. The population approach is described as an attempt to favourably shift the distribution of risk, typically using environmental or societal interventions. The advantages of the population approach are that it attempts to prospectively reduce incidence of disease, rather than treat incidences, and offers the potential to shift societal norms towards a context of reduced population prevalence, but also carries the disadvantages that there is little perceived advantage to any one individual and therefore motivation is more difficult to maintain (Rose, 1985).

In order to frame physical activity interventions, government organisations such as the Centres for Disease Control (CDC) have drawn on the social-ecological model (Sallis, Owen, & Fisher, 2015), which typically presents five levels of societal organisation: individual, which considers personal, including psychological and biological, and demographic factors; interpersonal, most typically referring to immediate support network for an individual, such as a family; organisational, which includes those delivery systems around an individual; environmental, referring to the physical context, such as transportation systems and availability of relevant facilities; and population, referring to societal-level changes or promotions, including government policy and public health campaigns (Sallis et al., 2015).

Population-type interventions broadly include all forms of intervention that do not systematically discriminate between potential participants as a consequence of their existing level of physical activity, often aiming to prospectively reduce a key risk factor or factors in an entire population irrespective of existing individual risk level (Foster et al., 2018). While the vast majority of interventions necessarily focus on a particular group, for example by specific age, ethnic minority or geographical region, there are no explicit exclusion criteria within the population of interest. For intervention in childhood, such strategies may involve environmental or policy level interventions (see

Sallis, Bauman, & Pratt, 1998), school level interventions (see Kriemler et al., 2011) or community-based interventions (see Foster et al., 2018; Kahn et al., 2002; van Sluijs, McMinn, & Griffin, 2008).

Treatment-type interventions tend to work retrospectively, and include those aimed at a specific individuals, families, or a section of society to remediate low levels of physical activity or more typically an associated correlate, such as high levels of adiposity or sedentary behaviours (Oude Luttikhuis et al., 2009; Reilly & McDowell, 2003). These interventions necessarily possess criteria for inclusion, and often recruit via formal individual referral from statutory services. Such strategies are typically time-limited and seek to directly address directly the lowest end of the continuum. Examples include the community-based Mind, Exercise, Nutrition, Do it! (MEND) intervention (Robertson, 2013) which specifically recruited overweight children referred via schools or a residential summer camp for overweight children (e.g. Gately, Cooke, Butterly, Mackreth, & Carroll, 2000).

The majority of systematic reviews focussed on childhood physical activity have explored the effect of intervention on adiposity, measured by BMI, concluding that intervention has limited utility in the reduction of body mass relative to a non-intervention control group (Gonzalez-Suarez, Worley, Grimmer-Somers, & Dones, 2009; Harris et al., 2009; Ho et al., 2012; Kamath et al., 2008b; Stice, Shaw, & Marti, 2006), although more recent reviews have focused on increases in physical activity behaviour (e.g. Beets, Beighle, Erwin, & Huberty, 2009; Dobbins, Husson, DeCorby, & LaRocca, 2013). However, recent reviews by van Sluijs et al. (2008) and Metcalf, Henley, and Wilkin (2012) and Sims, Scarborough, and Foster (2015) show that at post-intervention follow-up there was no clinically significant gain on measured physical activity behaviour, although there have been comparatively few intervention studies that include a meaningful follow-up measurement period and therefore evidence remains limited.

1.11. Chapter Summary

The role of physical activity in children has been hypothesised as being important in the development, and therefore potential prevention, of non-communicable diseases across the life-span. While

measurement issues persist across the literature, evidence suggests that inactivity in childhood both directly and indirectly increases the likelihood of the development of risk factors known to be associated with adult disease outcomes. The burden of disease, and associated economic cost, are significant concerns for governments globally, and therefore an interest in increasing childhood physical activity levels is justified.

Interventions largely follow either a prevention approach, in which recruitment is indiscriminate and targeted at positively influencing a population, or a treatment approach, in which a higher risk group is identified and specifically targeted. Across both approaches there have been numerous and heterogeneous efforts at increasing childhood physical activity levels, ranging across various behavioural domains, age groups, and delivery mechanisms. To date the evidence for the efficacy of these interventions remains inconclusive and, although positive examples do exist, there appears to be no strong indication of a specific form of delivery that will achieve sustained change, including whether to concentrate on a prevention or treatment approach.

1.12. Thesis Overview

The chapter above presents the context of childhood physical activity in England and the potential future health burden associated with low levels of physical activity in childhood. Also presented are the issues associated with intervention and measurement in childhood physical activity.

The broad questions addressed within this thesis are:

- What are the population benefits of intervention in childhood physical activity?
- Are both a prevention or treatment approach efficacious in addressing low childhood physical activity levels?

These questions will be addressed by this thesis within the following structure: Chapter 2 will present and explore the childhood physical activity measurements from the Health Survey for England 2012

dataset to clarify the 'real world' baseline scenario in England; Chapter 3 will present the justification and specification of the method, including data sources, derivation of input parameters, and the overall modelling approach; Chapter 4 will present the baseline structure of the core model along with key outputs and associated uncertainty; Chapter 5 will present a systematic review of intervention studies and draw a comparison of modelled intervention between prevention and treatment approaches; Chapter 6 will present the modelling of the outputs from the meta-analysis, one prevention and one treatment approach, with analyses; Chapter 7 will present the modelling of two specific interventions, one prevention and one treatment, with analyses; Chapter 8 will specify a hypothetical physical activity increase, using both a prevention and a treatment approach; finally, Chapter 9 will discuss the pertinent outcomes from the modelling analysis, discuss the strengths and limitations of the thesis, and draw conclusions from the body of work.

Chapter 2 - Analysis of Physical Activity in England

2.1. Chapter Overview

This chapter builds on the concepts introduced in Chapter 1 with an exploration and presentation of patterns of physical activity within the English population. A critical review of published studies on population physical activity levels is provided, before a more specific investigation of available information of the levels and nature of physical activity reported for children. In particular, limitations within the literature are identified and a case is made for further investigation of child physical activity patterns.

A strategy for the analysis of child physical activity data from the 2012 and 2015 iterations of the Health Survey for England (HSE) is specified below. The objectives of these analyses are to characterise the quantity and context of the physical activity within the population of interest and present relevant details from the primary data set. The results from these analyses are then presented in a systematic manner. The chapter concludes with a discussion of the key issues emerging from these analyses in terms of population-level patterns.

2.2. Introduction

2.2.1. The Health Survey for England

The HSE is an annual survey of a nationally-representative cross-section of the population of England. The survey uses the Royal Mail's Postcode Address File database to conduct a multi-stage stratified probability sample on private houses within England. The survey is conducted throughout the year to control for seasonality in responses. Each survey iteration contains standard areas of investigation within the broader questionnaire, but also includes specific modules on a regular basis. A module on physical activity has periodically been included within the wider survey, including 2004, 2008 and 2012. Respondents include both adults and children within households in England, with children's responses either verified or completed on their behalf by a parent. In the 2015 iteration of the HSE a

boost sample of children aged two to fifteen was recruited to provide additional data points on child-specific survey items.

2.2.2. Measurement of Physical Activity

The HSE uses the Physical Activity and Sedentary Behaviour Assessment Questionnaire (PASBAQ) to collect self-reported physical activity behaviour over the four weeks immediately preceding the interview. The PASBAQ collects the duration and frequency of participation in specific forms of physical activity across occupational, walking, domestic, sport and leisure, and 'do-it-yourself' domains. A broad estimation of intensity is also gathered for each episode of physical activity participation (Lee, Macfarlane, Lam, & Stewart, 2011; Scholes et al., 2014b). Episodes of participation in specific periods of at least ten minutes or more over the preceding four weeks are recorded and summed to provide domain-specific estimates. The domain specific estimates are in turn summed to produce a total for minutes of physical activity. These specific activities can then be referenced against compendiums of metabolic equivalents (METs) (e.g. Ainsworth et al., 2011; Butte et al., 2018) to allow an estimation of minutes spent at each level of physical activity: "light" physical activity, below three METs (e.g. slow walking or housework); "moderate" physical activity, between three and six METs (e.g. swimming or garden digging); and "vigorous" physical activity, above six METs (e.g. competitive sport or circuit training). This grouping is relevant as most health gains are thought to accrue following Moderate-to-Vigorous Physical Activity (MVPA) and therefore it is important to identify activities belonging to each group within any surveillance of physical activity behaviour. Total estimates can then by divided by four to produce average exertion in MET minutes per week within each domain of physical activity.

Common to all self-report questionnaires, the inherent weakness of the PASBAQ remains a reliance on human memory and subjective estimate, with a consequential risk of social desirability bias and measurement error (Scholes et al., 2014b). Systematic review of reliability and validity studies of self-report physical activity questionnaires suggests that test-retest validity possessed "acceptable

reliability, the validity is moderate at best" (Helmerhorst, Brage, Warren, Besson, & Ekelund, 2012). However, the key advantage of data collection through questionnaire is the ability to distinguish between domains and contexts (Kelly et al., 2016).

Scholes et al. (2014b) assessed the concurrent validity of the PASBAQ in a sufficiently large sample to stratify by age, sex, and Body Mass Index (BMI). A random sub-sample (*n* = 2,175) of respondents on the 2008 iteration of the HSE (*n* = 15,054) were recruited to wear accelerometers for one week, excluding swimming and bathing. Results indicated an overall correlation of 0.30 which, while weak, was broadly concordant with investigations of alternative questionnaires. Correlations were slightly stronger for women than men, with men more likely to over-estimate physical activity via self-report, and stronger for younger adults than older. Overall, Scholes et al. (2014b) concluded that the PASBAQ was a "useful and valid instrument for ranking individuals according to levels of physical activity". However, validation periods were not concurrent, as the self-report period occurred in the four weeks prior to the completion of the questionnaire, while accelerometers were worn for the week subsequent to the questionnaire. In addition, the validation was restricted to an adult sub-sample and therefore remains silent on the specific utility of the PASBAQ with children.

More recently, the PASBAQ was directly compared to the short form of the International Physical Activity Questionnaire (IPAQ), probably the most frequently used self-report tool for collecting physical activity data (Hagstromer et al., 2008). The IPAQ has been the subject of numerous validation studies, including against accelerometers (Craig et al., 2003) and against objectively measured fitness (Fogelholm et al., 2006) although in the latter study the sample was exclusively males. Both questionnaires were administered in the 2012 iteration, in a sub-sample of 1252 adults, finding acceptable correlations between the measures, although the IPAQ estimated that a lower numbers of respondents achieving government guidelines and engaged in higher amounts of sedentary behaviour (Scholes, Bridges, Ng Fat, & Mindell, 2016), which represents a worrying finding given the tendency of the IPAQ to over-report physical activity (Hagstromer et al., 2008).

2.2.3. Interim Critique of Measurement Within the HSE

While the methods of physical activity data collection are described above, along with a discussion of the efforts to ensure representativeness and accuracy within those data, a brief discussion is required to more critically examine these methods and alternative approaches to maximise accuracy of physical activity data from young participants. As such, there follows a summary of the evidence for the effectiveness and limitations of the self-report approach forming the primary method of data collection for the HSE to date. A discussion of alternative approaches is then provided reflecting the potential to improve the accuracy of survey-level data collection of physical activity behaviour, and child and youth behaviour in particular.

The advantages of self-report questionnaires are clear; they are cheap to administer and highly scalable, hence their usage in larger surveys such as the HSE. Furthermore, self-report, in contrast to accelerometry or other device-based measurement, provides information on context and setting in addition to an estimate of bodily motion, and as such retains relevance in behavioural research (Fairclough et al., 2019). This reflects the priorities of larger surveys in comparison to interventions studies, with the former focuses on comparatively crude group-level aggregated data in order to identify broad trends, while the former necessitates precision at the individual level in order to detect effects. Larger, non-clinical, surveys are also pragmatically constrained to the use of self-report as the primary method of gathering physical activity data as the financial and time investment of the equipment and data processing required when using objective measures is typically prohibitive; indeed, even longer self-report questionnaires are seen as constituting an excessive time burden (Scholes et al., 2016). However, this 'accuracy-practicality' trade off is more pertinent when seeking to capture physical activity behaviours in children as measurement is less accurate with this group (Welk et al., 2000), with self-report underestimating MVPA in young children, and overestimating MVPA in older children (Fairclough et al., 2019).

Perhaps the most important limitation for self-report questionnaires is that recall is inevitably inaccurate, especially as social desirability bias produces more positive and fewer negative reported behaviours (Mindell et al., 2014). Questions seeking to discover habitual physical activity tend to report most active weeks rather than typical weeks. Additionally, it is very difficult to accurately capture light physical activity data from self-report, as this is typically irregular, unrecognised, and incidental. Furthermore, accurately measuring physical activity in children is more difficult given the necessity to assess frequency, duration, and intensity that vary considerably (Mindell et al., 2014). Large-scale surveys to some extent address the difficulty of random error, i.e. the variability around the mean, with large sample sizes and standardised procedures. By contrast systematic error, and associated questions of validity, remains problematic (Ainsworth et al., 2012b).

A systematic review of 54 publications, totalling 61 self-report physical activity questionnaires, was conducted by Chinapaw, Mokkink, van Poppel, van Mechelen, and Terwee (2010), finding no instrument possessed both strong positive reliability and validity, with convergent validity measured as correlation to accelerometry. These weaknesses were confirmed more recently by a further systematic review, including 89 questionnaires, by Hidding, Chinapaw, van Poppel, Mokkink, and Altenburg (2018), although allowing that low methodological quality of papers compromised the review. The authors concluded that while a number of surveys possess acceptable test-retest reliability, potentially allowing the meaningful identification of change over time, very few questionnaires possessed adequate validity, with construct validity judged especially weak for the majority of instruments.

Biddle, Gorely, Pearson, and Bull (2011) also highlight the increased difficulty with measuring physical activity in young people using self-report questionnaires. However, they concede that while the pragmatic utility of objective measures will increase, there was likely be key role for self-report instruments in large scale surveys for many years, and therefore there remained an interest in the identification and improvement of reliable questionnaires. The authors reviewed 89 self-report

questionnaires specifically targeted at capturing children and youth physical activity data. An expert panel agreed that with three exceptions, self-report questionnaires either possessed insufficient reliability, insufficient validity, or were not appropriate for surveillance. Biddle et al. (2011) concluded that given its high validity, moderate reliability, and broad feasibility, the Physical Activity Questionnaire for Older Children (PAQ-C) (Crocker, Bailey, Faulkner, Kowalski, & McGrath, 1997), and variant Physical Activity Questionnaire for Adolescents (PAQ-A) (Bailey, 1997), represent the most promising self-report instrument for use in large surveys.

In response to the limitations summarised above with the use of self-report questionnaires, and in an effort to increase accuracy of physical activity data collection in children and youth respondents, Saint-Maurice, Welk, Beyler, Bartee, and Heelan (2014) presented a method of calibrating self-report physical activity responses against objectively measured data. Saint-Maurice et al. (2014) described and provisionally calibrated recall accuracy using the PAQ with direct reference to accelerometry data over the same seven days. The calibration model estimates were highly correlated ($r = 0.63$) against independent accelerometry data for percentage of time in MVPA, constituting a significant improvement when compared to values between self-report and accelerometry on the HSE which are nearer 0.40 (see Scholes et al., 2014b).

Building on the promising, but provisional, findings of Saint-Maurice et al. (2014) and in attempt to address some of the limitations of the PAQ, Saint-Maurice and Welk (2015) developed a new self-report instrument called the Youth Activity Profile (YAP). The YAP includes information from pre-school and commuting time, distinguishes between weekend days, and removes potential overlap between items in order to improve accuracy. Estimates from a calibration model were strongly correlated against accelerometry data for items measuring sedentary behaviour, moderately correlated for in-school physical activity, but not correlated for out-of-school activity either during the week or at weekends. The authors conclude that although, further refinement was needed, the YAP represented a promising approach to gathering physical activity data through self-report with

improved accuracy. A further calibration of the YAP with accelerometry largely reinforced these conclusions (Saint-Maurice et al., 2017).

A further calibration study, this time recruiting a cohort of 402 English school children, was completed by Fairclough et al. (2019) in order to assess the applicability of existing calibration algorithms, and potentially refine these algorithms for an English sample. A similar protocol was used, in that self-report and accelerometry measured the same seven-day episode. The authors found that the calibration model estimates from the original participants in the United States showed poor agreement, both at individual and group level; a finding that reinforces Saint-Maurice and Welk (2015) recommendation to calibrate within the specific measurement context rather than using norms referenced from groups from other populations (Fairclough et al., 2019). In line with previous findings from studies correlating self-report with more robust measures (e.g. Kelly et al., 2012), correlation remained poor at individual level even when using modelled estimates derived from the English participants, but at group level estimates were either of similar or superior levels of agreement to previous calibration studies.

The developments above describe an approach with the potential to improve the accuracy and utility of self-report questionnaires within large-scale surveys of physical activity behaviour. In particular, the method of using regression models to calibrate self-report estimates appears to convey a clear advantage in accuracy at group level for children and youth physical activity. To date, a subsample of survey participants is used to assess validity against self-report data, and typically identifies acceptable reliability but moderate convergent reliability at best. The adoption of the YAP, or a similar calibration-based measurement approach, holds the potential to use accelerometry subsample data to increase validity. Given increased accuracy at group level, the inclusion of this approach within the HSE holds the likelihood that important summary estimates, for instance the percentage of children meeting physical activity guidelines (Strain, Milton, Dall, Standage, & Mutrie, 2019), are more accurately reported.

2.2.4. Adult Physical Activity

Several studies investigating trends in physical activity have used the HSE as a primary data source, the majority of which have focussed on the adult population, particularly regarding the nature and quantity of those achieving the government physical activity guidelines. Stamatakis, Ekelund, and Wareham (2007) investigated temporal trends in walking, sports, leisure, and occupational physical activity from nine iterations of the HSE between 1991 and 2004. Regression models, adjusted for age and socio-economic status, identified a reduction in occupational physical activity over time, but an increase in sport participation, with an incrementally greater number of adults meeting government guidelines. However, alterations in survey questions limited the accuracy of the overall temporal trends through the period of analysis.

Using data from the HSE 2008, Bélanger, Townsend, and Foster (2011) explored the physical activity profile specifically of those adults meeting the government guidelines (*n* = 4,750). Of those adults achieving at least 30 minutes of MVPA on at least five days per week, they found that younger adults accumulated their physical activity time primarily from leisure-based sport and exercise while older adults gained proportionally more time from domestic activities. Walking was revealed to be an important contributor to meeting guidelines across all ages. Bélanger et al. (2011) suggested that physical activity interventions need to be tailored to the target age-group as activity profiles change with age, although these recommendations are based only on observations of individuals already achieving guidelines.

Roberts, Townsend, and Foster (2016) expanded and updated this research with an analysis of the complete adult sample from the HSE 2012. In a profile of adult physical activity, total and domain-specific minutes of physical activity were presented, stratified by region, academic qualification, social-economic status, age, and gender. Results indicated that 61.1% of adults reported meeting the government physical activity guidelines of at least 150 minutes of MVPA per week. In terms of meeting the guidelines, men were more likely to report doing so than females, while younger adults were more

likely than older adults. In addition, those living in the South were more likely to report meeting the guidelines than those in the North, while those of a higher socio-economic status were more likely than lower status adults (Roberts et al., 2016).

Figure 2.1 shows the relative contribution from each domain of physical activity towards total activity, by age and sex, for those respondents not meeting government guidelines. To contrast, Figure 2.2 shows the contributions for those 'active' adults who reported meeting the government physical activity guidelines. Roberts et al. (2016) suggest the major differences between active and inactive adults are that inactive adults are less likely to accrue weekly minutes from occupational physical activity, while active adults gather relatively fewer minutes from domestic activity.

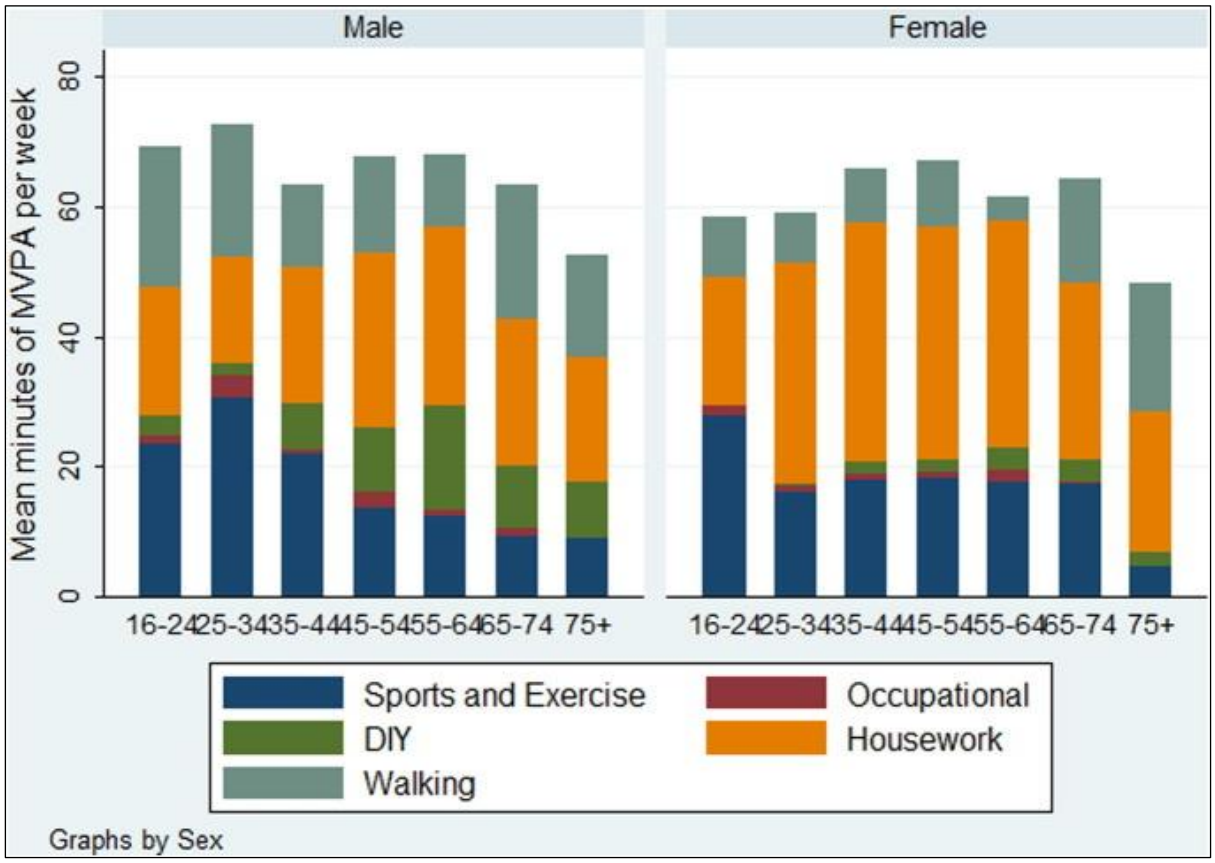


Figure 2.1 - Stacked column graph showing the domain-specific mean weekly minutes of MVPA for insufficiently active adults in England 2012, by age band and sex (n = 1826) (Reprinted from Roberts et al., 2016, p. 55)

Further stratification of these data revealed significant differences within age and sex bands according to other variables, representing high levels of inequality with regard to meeting guidelines across socio-economic status, age, region, and gender. Socio-economic status was highly predictive of odds

of achieving guideline levels of physical activity, and people with higher socio-economic status more likely to participate in sports and leisure time activities, while those of lower status were more likely to accrue minutes from occupational and domestic activity (Roberts et al., 2016). The authors caution against uniform application of total figures given the inherent socio-demographic inequalities within the aggregate figures.

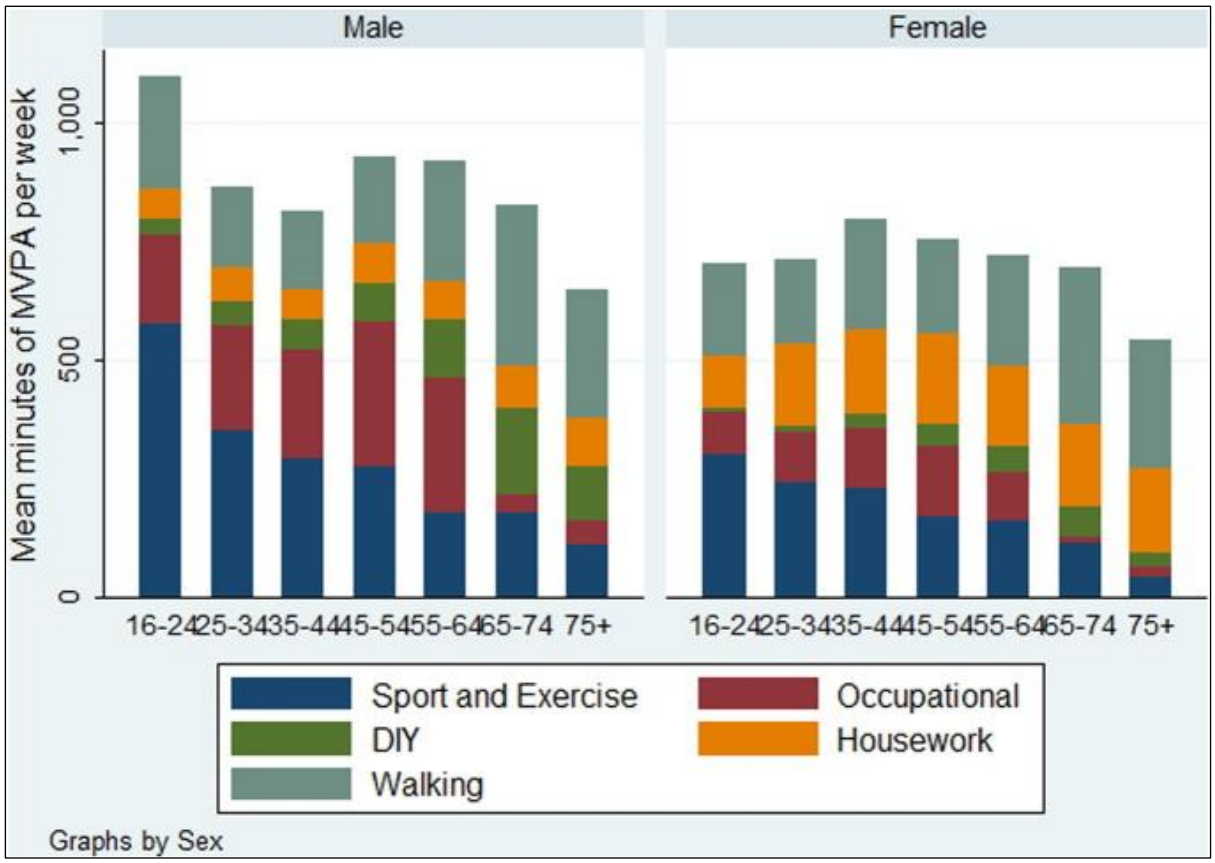


Figure 2.2 – Stacked column graph showing the domain-specific mean weekly minutes of MVPA for active adults in England 2012, by age band and sex (n = 4785) (Reprinted from Roberts et al., 2016, p. 58)

2.2.5. Child Physical Activity

An analysis of the nature specifically of child physical activity, again restricted to the subset of children whom met childhood physical activity guidelines, was completed by Payne, Townsend, and Foster (2013). The authors found numerous variations in the contributions of domain specific physical activity to total activity across gender, age, and socioeconomic status. In particular, Payne et al. (2013) identified that active play was the largest contributor to total childhood physical activity for both genders, although this decreased with age to be partially replaced by formal sport participation, see

Figure 2.3. Although walking was the second largest contributor for both genders, the overall contribution from active travel was minimal. Formal sport was more popular among boys than girls at all age-groups but reduced in popularity as socioeconomic status declined.

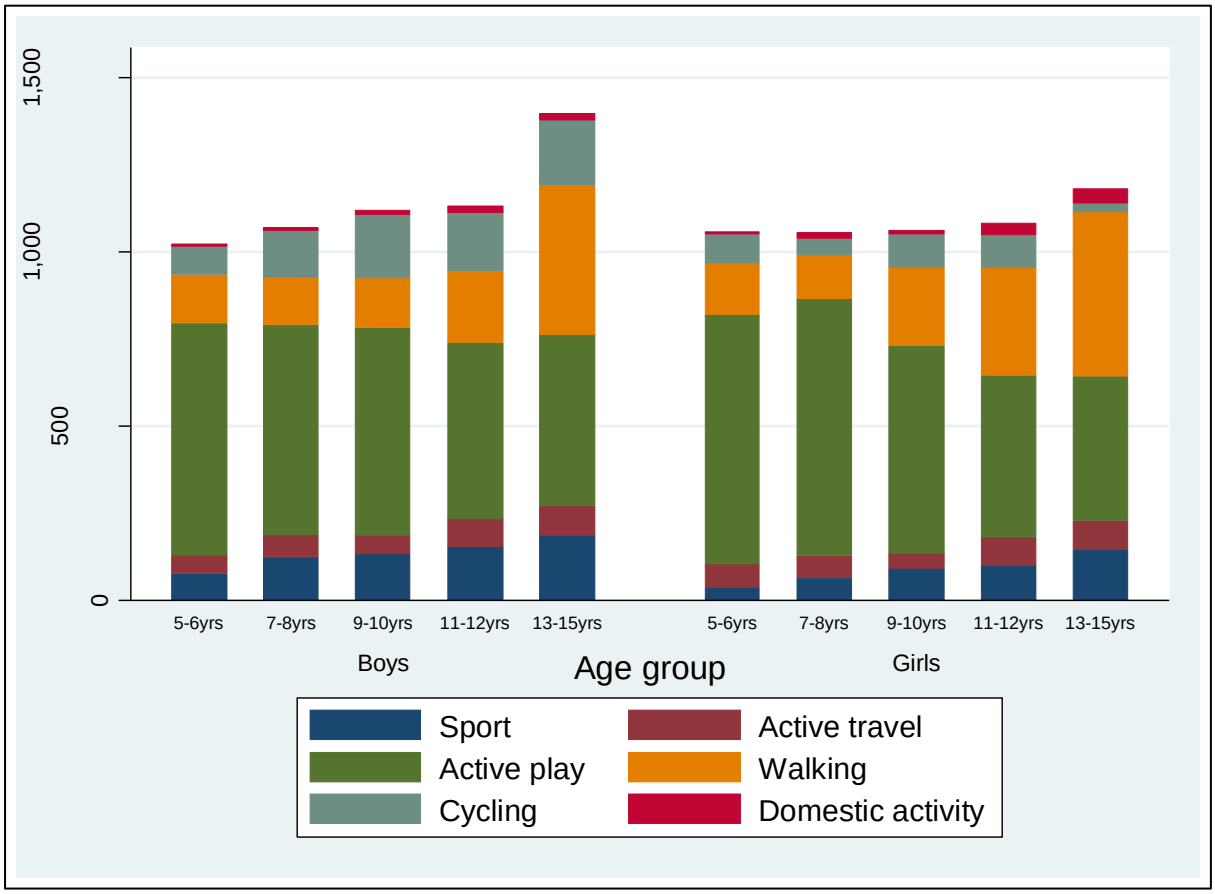


Figure 2.3 – Stacked column graph showing the relative contribution of mean minutes of physical activity for 'active' children, by age band and sex (n = 1110) (Reprinted from Payne et al., 2013, pp., p. 4)

However, as this analysis was restricted to 'active' children it does not provide a comprehensive picture of childhood physical activity in England. For the purposes of a more complete analysis it is necessary to explore the complete sample of child respondents. In addition, while Payne et al. (2013) provide a focussed analysis of the active strata of the physical activity distribution, their claim to inform future intervention policy is somewhat unwarranted given the greater requirement to target interventions at those children not meeting guidelines and therefore at a higher risk of consequential health detriment.

A limiting factor within data from previous iterations of the HSE was that they did not collect information on curriculum time physical activity. This omission potentially unbalances the data set as occupational physical activity is routinely collected for adults and therefore it becomes difficult to hypothetically project forwards from child to adult. For children between two and fifteen, this deficit was addressed in the 2015 iteration of the HSE with the inclusion of a single item estimating the number of minutes spent performing physical activity in the previous week.

2.3. Aims

The following analysis explores the types of activity that contribute to total physical activity levels in children aged from two to fifteen. Variations in physical activity patterns are explored for gender and age within the whole distribution of physical activity. Where power permits, geographical location, Quintile of Index of Multiple Deprivation (QIMD), identified ethnic origin, and weight status are included as stratification variables. A comparison of the child physical activity data between the 2012 and 2015 iterations of the HSE is presented in order to both explore the stability of the relationships and to examine the additional contribution of curricular physical activity. Lastly, relative contributions from domain-specific activity are explored by stratifying the population by levels of total activity in order to ascertain whether physical activity differs by type as well as by overall quantity at progressive levels of total activity.

2.4. Methods

2.4.6. Sources of Data

The physical activity data for the HSE were collected through the administration of the PASBAQ, included in the HSE 2012 iteration. Children aged above twelve years were interviewed directly, while for younger children the questionnaire was completed with both a parent and the target child present. Data on a maximum of two children per household were collected. Information was collected via recall concerning the seven days prior to the interview but did not include school curriculum time physical activity. The PASBAQ asks the number of episodes children spent in specific activities across the

domains of active travel, formal sport, informal activity and play, and domestic activities. For each episode the interviewer asked on which days this occurred, the duration, and whether each episode involved strenuous activity. On the HSE 2015 iteration, a single item requesting an estimate of school-based physical activity in minutes over the past week was included. The raw data for both HSE iterations is made available for download by UCL Data Unit/NHS Digital and as a result no consent or ethics procedures were required for this study.

2.4.7. Treatment of Data

The raw data were downloaded for all respondents from the HSE 2012 (*n* = 10,333) and 2015 (*n* = 13,748) into the Stata 15 statistics package (StataCorp, 2017). Additional demographic and social data were retained for analysis, including age, sex, geographical region of residence, identified ethnic group, index of multiple deprivation, rurality of residence, and BMI status. Index of multiple deprivation is a composite score of the locality based on weighted estimates of: income deprivation; employment deprivation; education, skills and training deprivation; health deprivation and disability; crime; barriers to housing and services; and, living environment deprivation (Department for Communities and Local Government, 2015). Scores are typically reported as quintiles within each survey, meaning that scores cannot be compared directly between survey years as quintile bands vary.

All respondents aged above fifteen were excluded (8,290 from HSE 2012 and 8,034 from HSE 2015) along with those under two years of age (311 from HSE 2012 and 278 from HSE 2015). Both surveys incorporated weighting to address sampling bias due to oversampling of households from sparsely populated areas, dwelling and household unit selection, and non-response calibration. The HSE 2015 also included a weighting specifically for child respondents to address potential under-selection from households with more than two children (NatCen Social Research & UCL, 2016).

For each recorded type of physical activity, across all domains, MET estimates were referenced from compendiums of physical activity equivalences (Ainsworth et al., 2011; Butte et al., 2018; Ridley et al., 2008). Estimates of MET minutes per week were then generated by multiplying the number of minutes

per week by the associated MET estimate for the specific activity. Relevant activity estimates were then summed to provide an estimate of MET minutes per week for each domain of physical activity, active transport (walking or cycling to school), formal physical activity (structured extra-curricular sport and exercise such as rugby or swimming), informal physical activity (unstructured activities such as play, skipping or dancing), non-specified physical activity (other forms of physical activity not covered by pre-defined domain-specific questions) and, for the HSE 2015 only, school physical activity (all activity occurring within the school curriculum including break and lunch times). These domain-specific estimates were then summed to provide a total amount of weekly exertion through physical activity.

2.4.8. Statistical Analysis

For both data sets, total minutes of reported physical activity and mean contributions of physical activity domains towards total activity were calculated for each domain, by age and sex. Descriptive investigation was conducted for total and domain-specific mean physical activity, stratified by demographic and social factors. A series of linear regressions were conducted to examine the effects of ordinal demographic factors on mean total MET minutes per week, as well as domain specific means, within both survey samples. For ethnicity and geographical region, one-way ANOVA's were conducted on total and domain specific estimates. Weighted estimates were used throughout the analyses. Within each survey year, total weekly physical exertion was divided into quintiles, providing stratification by physical activity level. Informal activity typically constituted a large component of total activity, and therefore was explored descriptively. The contribution of school physical activity to overall activity was specifically explored within the HSE 2015 data. A series of t-tests were run to explore differences between 2012 and 2015 datasets.

2.5. Results

For the HSE 2012 a household response rate of 64% was achieved, with 8,291 adults and 2,043 children interviewed. A sample of 1,732 unique individuals were included in the present analysis, of which 50%

were female. Table 1 presents means of total and domain-specific MET mins per week by individual factors for the HSE 2012, with additional demographic analysis available in Appendix 1. For the HSE 2015 a household response rate of 60% was achieved, with 8,034 adults and 5,714 children (3,591 within the boost sample), of which 49% were female. Table 2 presents means of total and domain-specific MET mins per week by individual factors for the HSE 2015, with additional demographic analysis available in Appendix 2. The data are presented in separate tables as, while the means and standard deviations broadly correspond across datasets, the inclusion of school physical activity within HSE 2015 renders the estimates not directly comparable. A brief summary of comparisons between HSE 2012 and 2015 data is provided in Appendix 3, finding that although occasional differences are observed between isolated subgroups, no systematic differences occur between survey iterations by variables presented below.

2.5.9. Gender

For the HSE 2012, boys reported higher total levels of physical activity than girls (t_{1732} = 4.86, p <0.001). However, although boys reported higher levels of activity than girls in each age group, differences between boys and girls were only statistically significant for 8- to 10-year olds (t_{366} = 2.39, p = 0.017) and 13- to 15-year olds (t_{298} = 4.39, p <0.001). There were only minor differences between boys and girls on totals for active travel and non-specific physical activity, with no specific differences emerging when stratified by age group. Boys recruited a higher percentage of physical activity from formal sports than girls (t_{1674} = 5.47, p <0.001), while girls conversely recruited a higher percentage of physical activity from informal activities than boys (t_{1674} = -2.83, p = 0.005) although boys still reported higher absolute values of informal physical activity (t_{1730} = 3.15, p = 0.005). When stratified by age group, informal activity only differed statistically significantly between the 13- to 15-year-old groups, but formal activity showed large differences in all school-age groups, with males consistently achieving more informal activity and total physical activity than females.

A similar pattern was observed within the relative values for the HSE 2015, with boys reporting statistically significantly higher physical activity than girls on total MET mins per week excluding (t_{5436} = 7.19, p <0.001) and including (t_{5436} = 7.29, p <0.001) school physical activity. The differences between boys and girls largely persisted when stratified by age, although differences were not significant on either variable for the 8- to 10-year old age group. Boys again recruited a higher percentage of total physical activity than girls from formal activity (t_{5122} = 10.30, p <0.001), with girls reporting a higher but non-significant percentage from informal activity (t_{5122} = -1.61, p = 0.107), although once again boys reported higher absolute amounts within both domains. The difference between girls and boys on reported formal activity remained highly significant within all age groups, while the difference on informal activities was only significant within the 11- to 12-year and 13- to 15-year age group. The remaining domains of active transport, non-specific, and school physical activity showed little variation between males and females.

2.5.10. Age

Within the HSE 2012, age predicted outcomes on total MET minutes per week, as well as all domain specific physical activity, on linear regressions controlling for sex. Overall, age was positively correlated with active travel, non-specific, and formal physical activity, but negatively with total and informal physical activity. Summary results from these regressions are presented in Appendix 4, while the domain-specific contributions from each domain to total MET minutes per week are presented in

Figure 2.4. Further regressions were run stratifying for age, finding age a significant predictor of domain-specific outcomes. However, while age was a predictor of total MET minutes per week for females (B = -236.78, p < 0.001) it was not for males (B = -5.06, p = 0.949).

Category	*n*	Total Mean (SD)	Active Transport Mean (SD)	%	Non-Specific Mean (SD)	%	Formal Mean (SD)	%	Informal Mean (SD)	%
Cohort	1732	3326.3 (3054.4)	183.2 (275.4)	5.5	112.5 (494.3)	3.4	470.4 (934.7)	14.1	2560.3 (2840.0)	79.7
Gender										
Male	862	3682.6 (3297.6)	189.0 (288.5)	5.4	106.1 (430.0)	3.1	611.6 (1086.9)	18.8	2775.8 (2571.9)	72.7
Female	870	2973.4 (2749.5)	177.5 (261.8)	6.0	118.8 (550.9)	4.0	330.4 (728.4)	11.9	2346.8 (2173.8)	78.1
Effect of Gender		t = 4.86 **	t = 0.87		t = -0.53		t = 6.33 **		t = 3.15 **	
Age Group										
2-4	428	3636.0 (3725.2)	93.2 (160.7)	2.6	16.0 (97.8)	0.4	200.6 (616.4)	5.5	3326.2 (3643.4)	91.5
5-7	376	3139.2 (2511.6)	160.7 (183.1)	5.1	78.0 (292.8)	2.5	372.3 (586.0)	11.9	2528.3 (2497.8)	80.5
8-10	368	3355.8 (2717.5)	169.4 (210.0)	5.0	136.5 (387.4)	4.1	606.0 (1009.2)	18.1	2444.0 (2481.2)	72.8
11-12	260	3561.9 (3205.3)	289.2 (385.5)	8.1	206.1 (815.0)	5.8	710.7 (1190.9)	20.0	2355.9 (2676.7)	66.1
13-15	300	2878.6 (3054.4)	264.9 (385.1)	9.2	182.8 (711.2)	6.4	603.5 (1183.4)	21.0	1827.4 (2308.6)	63.5
Effect of Age		*B* = -119.32 **	*B* = 45.11 **		*B* = 45.44 **		*B* = 115.45 **		*B* = -325.31 **	
Weight Status										
Normal	947	3254.1 (2961.2)	186.7 (274.0)	5.7	127.5 (503.7)	3.9	500.9 (963.2)	15.4	2439.0 (2742.6)	75.0
Overweight	190	3566.9 (3345.6)	213.7 (311.7)	6.0	174.0 (812.4)	4.9	534.6 (1080.9)	15.0	2644.5 (3017.5)	74.1
Obese	184	3452.3 (3074.7)	195.4 (287.0)	5.7	64.7 (215.3)	1.9	603.9 (1130.1)	17.5	2588.3 (2667.2)	75.0
Effect of Weight Status		*B* = 122.26	*B* = -3.89		*B* = -29.77		*B* = 18.69		*B* = 137.25	

Table 1 – Means and standard deviations for total and domain-specific MET minutes per week, and percentage contributions by domain to total MET minutes per week, stratified by gender, age, weight status, from HSE 2012 data
*** p < 0.05*

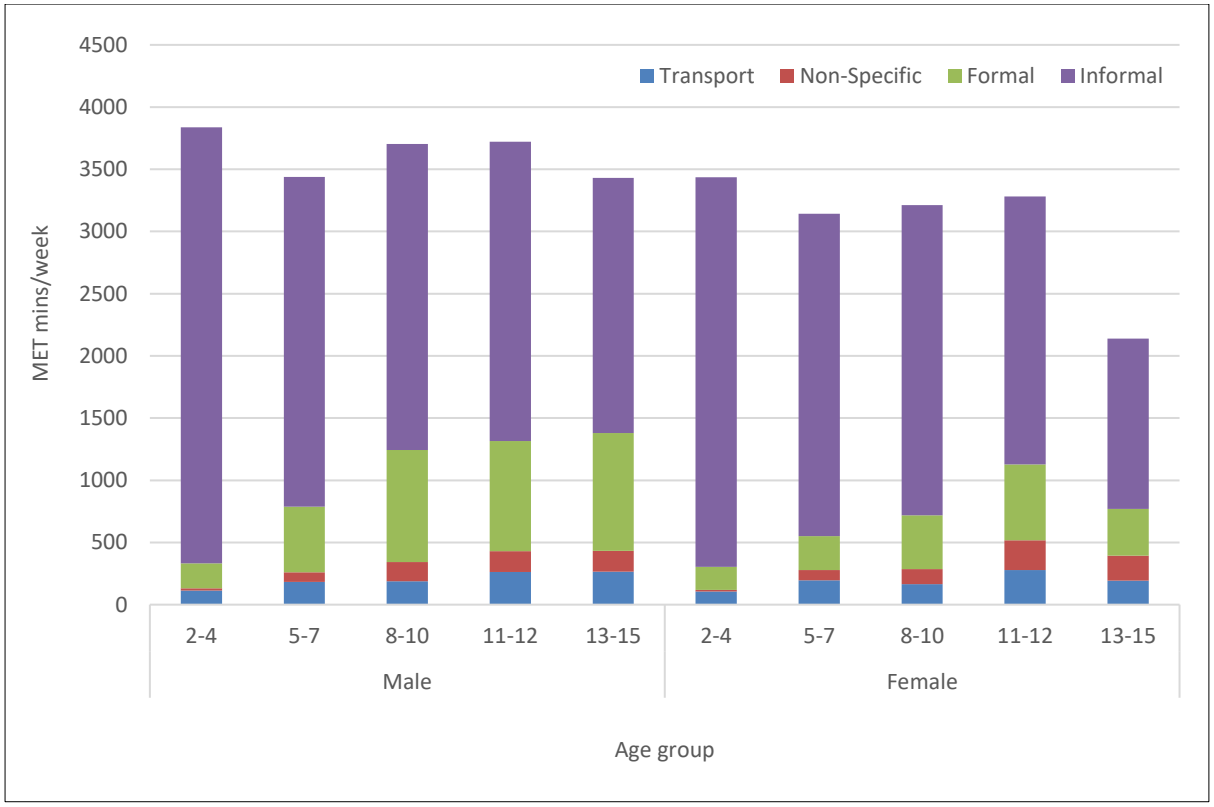


Figure 2.4 – Stacked column graph showing the relative domain-specific contributions towards total mean MET minutes per week from HSE 2012, by age and sex

For the HSE 2015 data, age again predicted outcomes on total MET minutes per week, both including and excluding school physical activity. Age also predicted all domains of physical activity. Age was once more positively correlated with totals for active travel, non-specific physical activity, formal activity, and also for school-based activity, and was negatively correlated with informal activity and total MET minutes per week both including and excluding the contribution from school time. The summary results are presented in Appendix 5, with the domain-specific contribution to total MET minutes per week presented in Figure 2.5. Age remained a statistically significant predictor for all outcomes when stratifying for sex, with the exception of total MET minutes per week including school activity, which showed a significant effect for girls (B = -198.83, $p < 0.001$) but not for boys (B = -7.71, p = 0.876).

2.5.11. Deprivation

Within the HSE 2012, QIMD did not predict levels of total MET minutes per week, although when stratifying by sex, this effect approached significance within females (B = -124.41, p = 0.054) but not males (B = -42.96, p = 0.583). There were no significant effects for QIMD across domain-specific totals

with the exception of formal physical activity, for which increasing QIMD was a highly significant predictor (B = -58.84, p < 0.001) of reduced activity, an effect which persists when stratified by sex. Details on domain-specific regression coefficients are presented in Appendix 4, with relative contributions from each sex displayed in Appendix 6.

For HSE 2015, QIMD did not predict total MET minutes per week for the amount including (B = 19.10, p = 0.554) or excluding (B = 26.67, p = 0.407) school activity. Increasing QIMD negatively predicted non-specific, formal, and school activity levels, but positively predicted levels of informal activity, presented in Appendix 5. Stratification by sex revealed no differences between gender on specific outcomes with the exception of school activity, which showed a significant effect for females (B = -14.93, p = 0.001) but not for males (B = -1.00, p = 0.823). The relative contributions from specific domains to total MET minutes per week are presented in Appendix 7.

Category	n	Total Mean (SD)	Active Transport Mean (SD)	%	Non-Specific Mean (SD)	%	Formal Mean (SD)	%	Informal Mean (SD)	%	School Mean (SD)	%
Cohort	5436	3792.0 (3418.8)	160.0 (263.5)	4.2	75.5 (344.2)	2.0	535.4 (1220.3)	14.1	2795.6 (3096.6)	73.7	225.7 (337.1)	6.0
Gender												
Male	2698	4131.1 (3616.3)	156.7† (255.3)	3.8	74.9† (358.3)	1.8	697.9 (1360.9)	16.9	2970.7 (3208.7)	71.9	230.8 (343.4)	5.6
Female	2738	3457.8 (3338.8)	162.8 (271.5)	4.7	76.1† (329.8)	2.2	375.2 (1039.5)	10.9	2623.1 (2511.7)	75.9	220.7 (330.8)	6.4
Effect of Gender		t = 7.29 **	t = -0.85		t = -0.13		t = 9.84 **		t = 4.15 **		t = 1.10	
Age Group												
2-4	1281	3926.5 (3785.1)	88.7 (154.6)	2.3	26.2 (175.5)	0.7	206.4 (552.9)	5.3	3605.1 (3712.9)	91.8	22.4 (135.6)	0.6
5-7	1265	3531.1 (3119.3)	125.0† (184.4)	3.5	56.1 (231.0)	1.6	421.9 (1034.4)	11.9	2927.8† (2875.0)	82.9	164.7 (239.7)	4.7
8-10	1171	3848.8 (3591.3)	125.3† (186.8)	3.3	103.5 (361.7)	2.7	690.2 (1478.9)	17.9	2929.7† (3091.7)	76.1	197.4 (282.2)	5.1
11-12	730	3470.4 (3166.9)	252.3 (353.9)	7.2	102.0† (393.2)	2.9	799.2 (1491.9)	23.0	2316.9 (2596.8)	66.8	274.4 (392.8)	7.9
13-15	989	2880.8 (3124.7)	268.7 (382.3)	9.3	111.4 (517.8)	3.9	728.3 (1386.1)	25.3	1772.4 (2430.9)	61.5	266.3 (415.9)	9.2
Effect of Age		*B* = -102.08 **	*B* = 47.18 **		*B* = 23.73 **		*B* = 147.06 **		*B* = -401.97 **		*B* = 81.91 **	
Weight Status												
Normal	3148	3665.2† (3447.8)	157.9† (260.9)	4.3	86.8† (378.7)	2.4	563.8 (1300.8)	15.4	2856.6 (3099.0)	77.9	182.2 (314.8)	5.0
Overweight	644	3505.2 (3192.7)	167.7† (260.0)	4.8	68.6† (290.8)	2.0	577.7 (1031.1)	16.5	2691.2† (3025.7)	76.8	177.5 (296.6)	5.1
Obese	639	3219.9 (3188.8)	184.7 (271.0)	5.7	77.8 (378.2)	2.4	563.7 (1269.7)	17.5	2393.7 (2713.2)	74.3	210.3 (374.6)	6.5
Effect of Weight Status		B = -222.65 **	B = 4.09		B = -0.80		B = -50.94		B = -174.95 **		B = -0.05	

Table 2 - Means and standard deviations for total and domain-specific MET minutes per week, and percentage contributions by domain to total MET minutes per week, stratified by gender, age, and weight status, from the HSE 2015.

*** p < 0.05* *† Significant difference (p < 0.05) between 2012 and 2015 data*

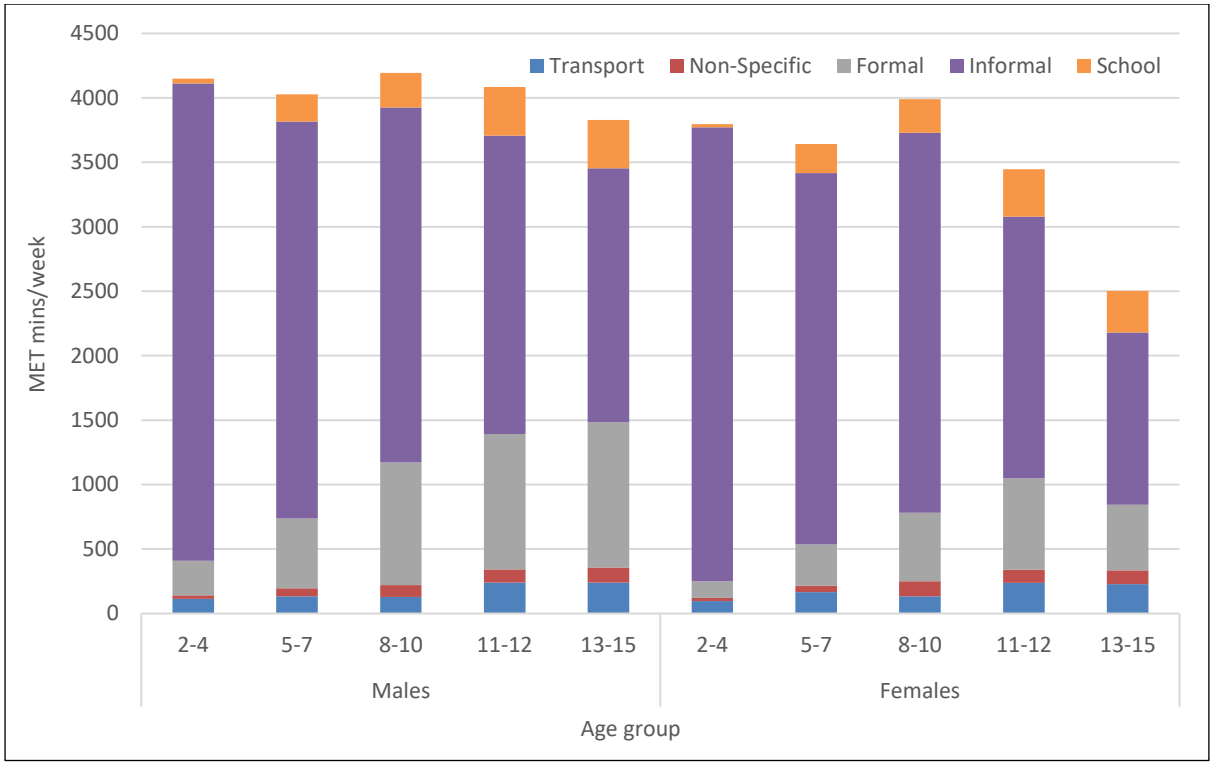


Figure 2.5 – Stacked column graph showing the relative domain-specific contributions towards total mean MET minutes per week from HSE 2015, by age and sex

2.5.12. Weight Status

For the HSE 2012 data, weight status did not predict either total MET minutes per week (*B* = 122.26, *p* = 0.296) nor any domain-specific total, nor did any significant effects emerge when stratifying by sex. On the HSE 2015, weight status significantly predicted total MET minutes per week both including (*B* = -222.65, *p* = 0.002) and excluding (*B* = -222.60, *p* = 0.002) school activity, and persisted when stratifying by sex. As shown in Appendix 4, increasing weight status also predicted reductions in informal activity (*B* = -174.95, *p* = 0.005) and approached significance in predicting formal activity (*B* = -50.94, *p* = 0.053). When stratifying by sex, boys retained a significant effect for formal (*B* = -81.04, *p* = 0.045) but not informal (*B* = -112.49, *p* = 0.202) activity, while girls retained a significant effect for informal (*B* = -249.21, *p* = 0.004) but not formal (*B* = -15.95, *p* = 0.626) activity, with full effects by weight status presented in Appendix 4 and Appendix 5. Relative contributions from each domain, stratified by weight status and sex, are shown for HSE 2012 and 2015 in Appendix 8 and Appendix 9 respectively.

2.5.13. Ethnicity

Within the HSE 2012, participants from different identified ethnicities showed a significant variation on total MET minutes per week (F_4 = 6.02, p < 0.001) when controlling for age and sex. At domain level, there were no significant differences on active travel or non-specific activity levels but there were effects on formal (F_4 = 5.83, p < 0.001) and informal (F_4 = 4.54, p = 0.001) activity, presented in Appendix 10. Appendix 11 displays the relative contribution from domains to total MET minutes per week by ethnicity and sex for the 2012 HSE and shows clear disparities within gender groups between identified ethnic groups. All significant effects persisted when stratified by sex.

For the HSE 2015, participants from different identified ethnicities showed a significant variation on total MET minutes per week both when excluding (F_4 = 28.12, p < 0.001) and including (F_4 = 28.97, p < 0.001) school activity, when controlling for age and sex, presented in Appendix 12. There were significant effects for all domain-specific totals. Appendix 13 displays the relative contribution from domains to total MET minutes per week by ethnicity and sex for the 2015 HSE. All significant effects persisted when stratified by sex with the exception of boy's active travel (F_4 = 0.79, p = 0.533) and school activity (F_4 = 0.59, p = 0.667).

2.5.14. Geographical Region

Within the HSE 2012, total MET minutes per week did not vary significantly between region of residence (F_8 = 1.07, p = 0.380) when controlling for age and sex. With the exception of formal activity (F_8 = 1.96, p = 0.049), no regional variations were noted on domain-specific totals and no significant variation was noted in any outcome when stratifying for sex. The relative contributions from domains to total activity are presented in Appendix 14. Within the HSE 2015, total MET minutes per week significantly varied across region of residence when including (F_8 = 5.88, p < 0.001) and excluding (F_8 = 6.41, p < 0.001) school activity, as well as for all domain-specific totals with the exception of active travel. Contributions from specific domains to total activity levels for each region are presented in Appendix 15, stratified by sex. When stratifying by sex, effects remained significant for girls but not

for boys on total MET minutes per week both including and excluding school activity, a pattern that also held for non-specific activity. Effects remained significant for both boys and girls on formal and informal activity. Detailed results of the statistical analyses for HSE 2012 and 2015 are presented in Appendix 10 and Appendix 12 respectively.

2.5.15. Informal Physical Activity

The difference in totals of informal activity between HSE 2012 and 2012 was not statistically significant, although both boys and girls reported higher levels in 2015. Within this domain the same activities are included on each year of the survey. The contribution from each activity to the total for the informal activity domain is displayed in Figure 2.6. The major contributor to informal activity was playing, followed by walking, cycling, and dancing. On HSE 2012 all activities showed significant distances between gender, with the exception of housework and gardening and hopscotch, while on HSE 2015 there were significant differences on all activities. Boys obtained greater relative contribution from cycling and skating, while girls obtained greater relative contribution from walking, housework and gardening, hopscotch, trampolining, dancing, and skipping (see Appendix 16). In 2012, boys accrued greater relative contribution from skating than girls, but in 2015 the reverse was reported. There were significant differences between survey years in all activities contributing to the informal activity domain total with the exception of housework and gardening and trampolining, differences.

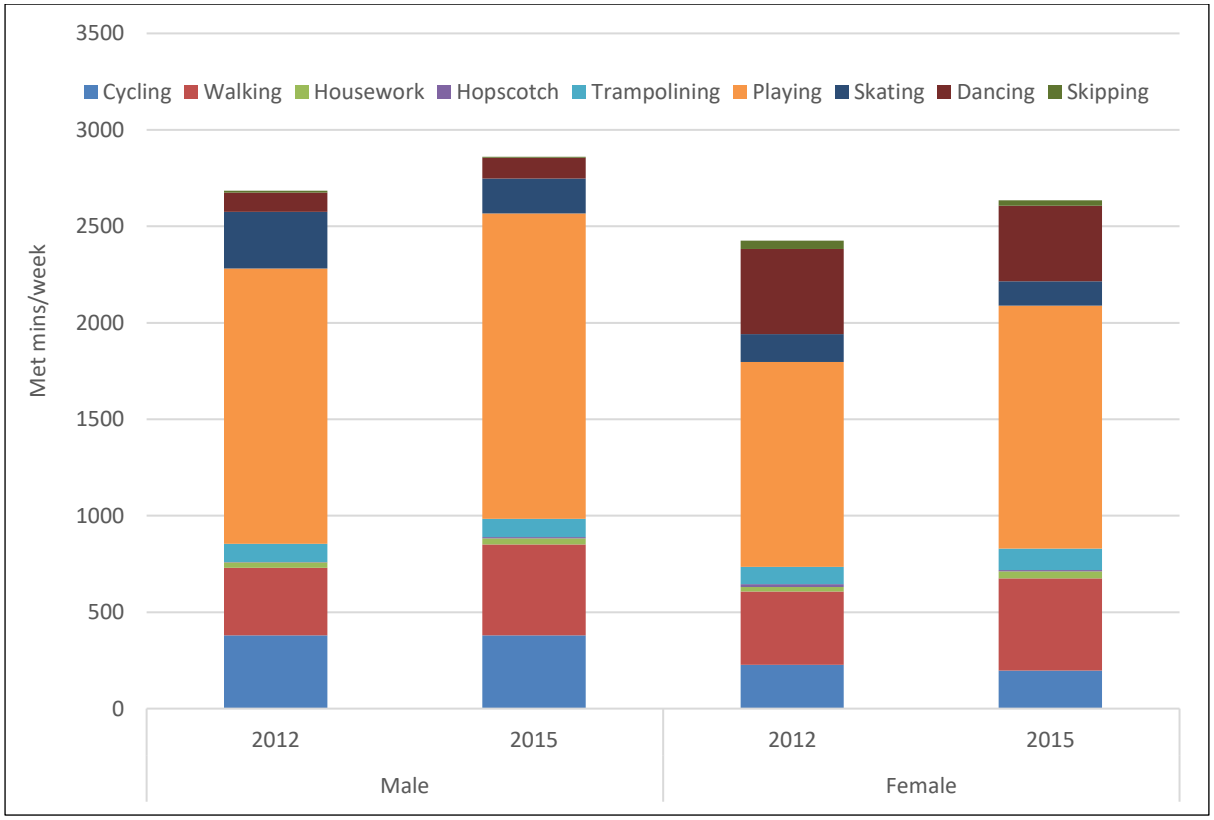


Figure 2.6 – Stacked column graph comparing HSE 2012 and 2015 activities contribution to informal activity, by sex

2.5.16. School-based Physical Activity

The HSE 2015 included a measure of physical activity within curriculum time, the first time this had been included in any HSE iteration. The relative contributions of school activity are shown in Figure 2.8, stratified by age and sex, and more explicitly in Appendix 17. Once of school age, there are significant increases in school physical activity levels for both genders, with age predicting an increase in school-based MET minutes per week for both boys ($B = 87.69$, $p < 0.001$) and girls ($B = 74.67$, $p < 0.001$).

2.5.17. Levels of Physical Activity

Stratifying the HSE 2012 cohort by levels of physical activity reveals the relative contributions from each domain of physical activity to total MET minutes per week for activity-based quintiles of the population. The results of linear regressions for each domain by physical activity quintile are presented in Appendix 18 and show highly significant effects for each domain. All effects persisted when stratified by sex with the sole exception of active travel within the HSE 2012 dataset for both boys (*B*

= 11.85, p = 0.082) and girls (B = 10.72, p = 0.088) which showed a statistically non-significant effect. For the HSE 2015 data, all domain-specific contributions showed significant regression effects by physical activity quintile when controlling for age and sex, effects which persisted when stratifying by sex. There were no statistically significant differences between survey years on comparable domains, although considerable variation appears when represented graphically. The percentage contributions across both HSE 2012 and HSE 2015 from comparable domains are presented in Figure 2.7, with further data specifically including school activity from HSE 2015, presented in Figure 2.8.

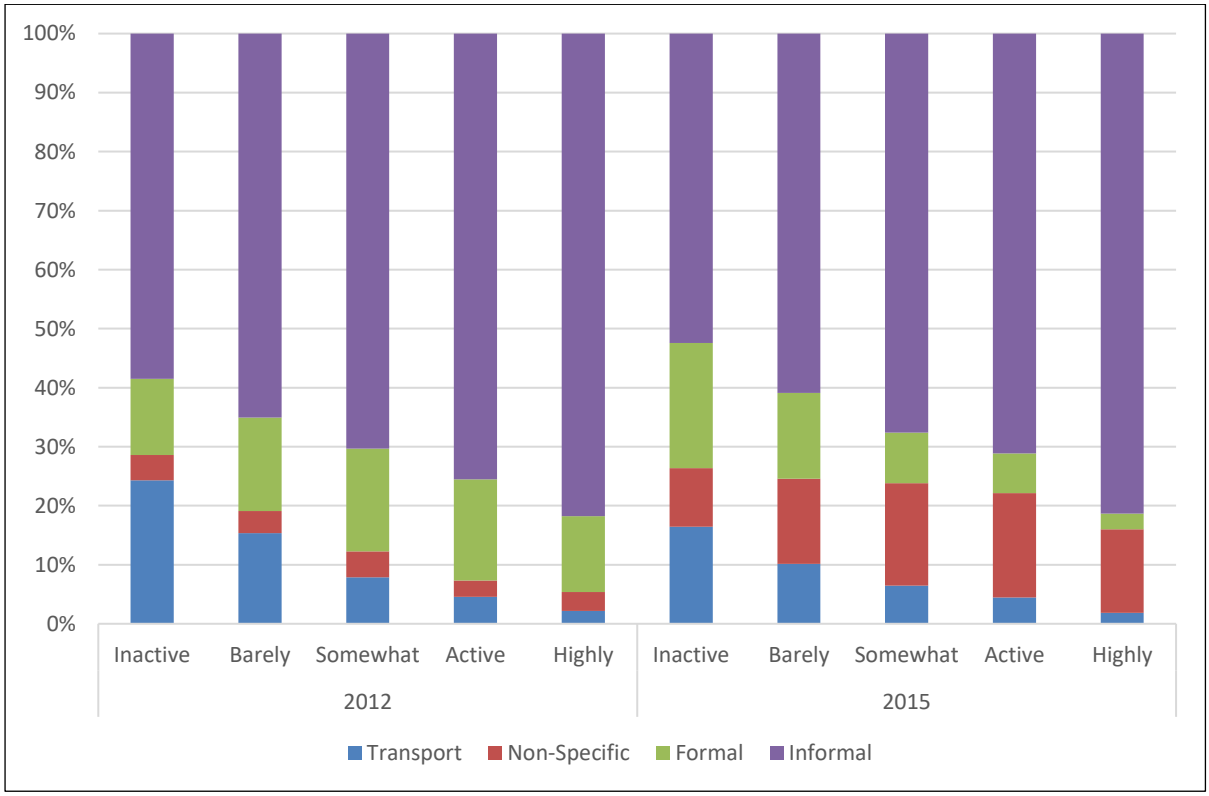


Figure 2.7 – 100% stacked column graph showing relative contribution from domain-specific activity to total MET minutes per week for HSE 2012 and HSE 2015, by physical activity strata

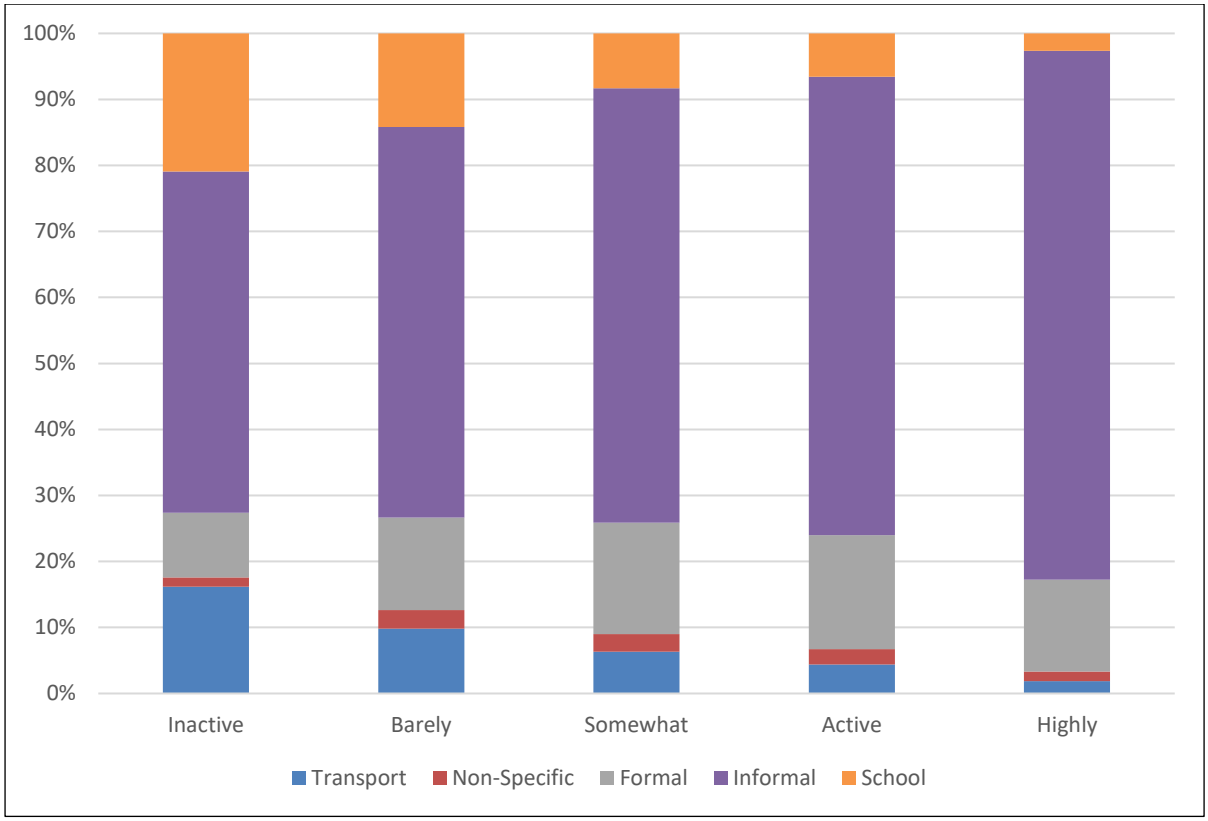


Figure 2.8 – 100% stacked column graph showing relative contribution from domain-specific activity to MET minutes per week for HSE 2015, by physical activity strata

2.6. Discussion

Analysis of both surveys revealed that boys engage in higher levels of physical activity than girls, both in terms of simple time spent in activity and in relative energy expenditure expressed in MET minutes per week, broadly matching the majority of findings from tracking studies (Hayes et al., 2019; Malina, 2001; Metcalf, Hosking, Jeffery, Henley, & Wilkin, 2015; Nader, Bradley, Houts, McRitchie, & O'Brien, 2008; Telama et al., 2013). Boys reported significantly larger absolute counts of MET minutes per week on the majority of domains of activity, with the exception of active transport. In terms of the relative contribution from specific domains, the most marked difference between genders was participation in formal sport. This difference was previously reported by Payne et al. (2013) although their analysis was limited to data for the most active children; this more recent and more comprehensive analysis confirms this difference persists over time and throughout the sample.

When stratified by age and sex, a consistent pattern of physical activity within the population appears across both 2012 and 2015. While active travel and non-specific activity remain comparatively stable,

there is a steady decline in informal activity throughout childhood, and most dramatically in females as they reach their mid-teens. In contrast, an increase in boy's participation in formal activity appears to counteract the reduction in informal activity, with participation rates appearing to consolidate by nine to ten years of age, but no such increase was apparent in girls. This reinforces earlier work suggesting this declining pattern is evident in girls (Ekelund et al., 2012; Hallal et al., 2012; Telford, Telford, Olive, Cochrane, & Davey, 2016), and that there is a potential role for sports participation in addressing later decline (Pate, Dowda, O'Neill, & Ward, 2007; Vella, Cliff, & Okely, 2014).

There were few differences when stratifying physical activity by QIMD, in line with other research on this subject (Carroll-Scott et al., 2013; Metcalf, Hosking, et al., 2015). Overall, a slight pattern of declining physical activity levels was observed as relative deprivation increased across all domains although mean levels of physical activity due to active travel, comprising walking or cycling to and from school, were largely robust to the influences of deprivation. Previous research (e.g. Kinra, Nelder, & Lewendon, 2000; Twaits & Alwan, 2020) indicates weight status is correlated with deprivation, although not necessarily with physical inactivity (Noonan & Fairclough, 2018), confirmed by analysis of previous HSE iterations by Stamatakis, Wardle, and Cole (2010) and with significant post hoc correlations between weight status and QIMD in both the 2012 and 2015 iterations.

A pattern of relative stability was observed for levels of activity across geographical region. While some variations were noted, particularly within the totals on the HSE 2015, these statistically significant differences are unlikely to represent clinically meaningful or policy-relevant variation between specific regions. Perhaps surprisingly, although there was a mild trend of lower levels of physical activity with rising weight status, more evident in the larger 2015 sample, these differences were comparatively mild compared to what might be expected if weight status and physical activity levels were strongly associated. In some domains, and most particularly on the 2012 dataset, reported physical activity increased as weight status increased. This is in broad contrast to some, (e.g. Ness et

al., 2007), but not all (e.g. Noonan & Fairclough, 2018), published research and potentially suggests physical activity does not directly moderate weight status in children.

There were notable differences in reported physical activity when responses were stratified by identified ethnicity. White children consistently reported higher levels of physical activity across all domains than other broad minority ethnic groups. In addition, there were significant increases in physical activity observed between 2012 and 2015 within the white child sample, while no increases were noted in other ethnic groups. Across majority-Caucasian nations there is considerable agreement that white children are more active than children from minority ethnic groups (Bryan, Tremblay, Pérez, Ardern, & Katzmarzyk, 2006; Gordon-Larsen, McMurray, & Popkin, 1999; Smith, Aggio, & Hamer, 2018; Van, Paw, Twisk, & Van, 2007), although there are likely to be interactions with QIMD and weight status (Love, Adams, Atkin, & Van Sluijs, 2019).

Between the two iterations of the HSE, there were few differences in the amount and nature of physical activity by QIMD, by region of residence, or by reported weight status. Comparison between survey years by sex revealed few statistically significant differences, suggesting a relatively stable pattern of physical activity by gender. A larger number of small but statistically significant differences were identified on the 2015 dataset but this is likely to be due to the larger sample size; 2015 was a boost child sample as the inclusion of school physical activity was included for the first time.

Given the age-based reduction in contribution of informal activity to total levels of physical activity, a closer investigation of this domain revealed that the major contributor within this domain is active play. When stratifying the activities comprising informal activity by age and sex, the reduction in active play appeared to account for the majority of this reduction in informal physical activity. Contributions from other activities included within this domain remained broadly consistent with advancing age.

As can be expected, school physical activity remained largely consistent in the mean values across both age and sex, in the same way that active travel was a small but consistent contributor to overall

levels of physical activity. School physical activity, within the 2015 dataset, and active travel, across both datasets, appeared largely robust to change across any variable. When stratifying the sample by levels of physical activity into quintiles the role of school activity and active transport played a far higher role in contributing to overall physical activity for the least active children. The major reductions were noted in formal and informal activity as people became less active.

2.7. Chapter Summary

The above analysis provides a detailed exploration of the childhood physical activity data from the 2012 and 2015 iterations of the HSE, the last two iterations including a survey module on children's physical activity. Overall, it appears that school curriculum-time activity, and active travel to and from school, provide a small but consistent contribution to weekly physical activity levels irrespective of age and sex, with this contribution becoming greater and more important for the least active children. Informal physical activity, largely consisting of play, but also including walking, cycling and (for girls) dancing, shows a pattern of steady decline through the childhood years. In boys, an increase in formal physical activity (i.e. sport) participation to some extent compensates for the decline in informal physical activity, but this compensation is not sufficient to maintain overall physical activity in older girls.

The disadvantages of self-report and the volitivity of youth physical activity notwithstanding, the above analysis suggests no significant systematic differences between HSE 2012 and 2015 in the absolute energy expenditure between the two survey iterations that cannot be explained in terms of the inclusion of school data. In addition, there are few significant differences either within the relative contribution from domain-specific physical activity or by social and demographic factors. As such the integrity of the summary means of MET minutes per week appear intact and therefore provide a sound representation of the dataset once stratified by age and sex.

Chapter 3 - Methods

3.1. Chapter Overview

This chapter presents a description and justification of the central method of analysis taken within this thesis, along with an account of the key methodological decisions taken within the project. The description begins with a discussion on the purposes of modelling within epidemiological research and the selection of the approach specifically taken within this investigation. This is followed by an overview of modelling in population health and a justification for the selected modelling strategy. The sources of data for the model are presented, followed by a description of how these were encoded within the 'back end' of the model, which constitutes the core epidemiological model of the simulated cohort. The 'front ends' of the model constitute the counterfactual physical activity scenarios applied to this back end, and analyses of these are presented in subsequent chapters.

3.2. Methodological Approach

Modelling is a methodological approach that is common across many research disciplines and serves a wide variety of purposes (Epstein, 2008). Within population health research, and more specifically the study of non-communicable disease epidemiology, modelling is a viable method of analysis or evaluation for situations in which formal experimentation, such as a randomised controlled trial, is not possible. Such trials may be unethical, such as the withholding of a suspected beneficial intervention or imposition of unhealthy conditions, or may be implausible, usually due to issues of cost or time, such as a time-bound investigation into lifelong health outcomes due to childhood exposures (Briggs, Scarborough, & Smith, 2016; Metcalf, Edmunds, & Lessler, 2015).

In simple terms, a model is a simplified and focused analogue of reality that facilitates the exploration and analysis of a specific issue or problem (Webber et al., 2014). The specification of a formal model provides an account of how the model was conceptualised and developed, as well as an explicit description of all data and assumptions involved. While this process necessarily involves an abstraction from reality, the formal description allows assumptions and estimates to be explicitly presented and

justified, as well as an assessment of the likely impacts these assumptions will make. In addition, the effects of these assumptions can often be formally presented and assessed through the process of uncertainty and sensitivity analysis (Epstein, 2008).

The key benefit of modelling studies within population health is the ability to conduct concurrent analyses of a series of hypothetical 'what if' scenarios that are not feasible to conduct in a live population. Modelling studies typically specify a baseline, usually a 'do nothing' or 'business as usual' scenario, that closely matches the real world before applying plausible counter-factual scenarios to explore their effects within the simulated cohort (Cobiac et al., 2012). In epidemiological terms, a model allows the independent or concurrent manipulation of one or more exposures and then observation of the outcomes presented as outputs as they differ between the baseline and counterfactual scenarios (Webber et al., 2014).

Within the current thesis, and specifically within the case of physical activity, the construction of an appropriately parameterised model allows the application of specific 'interventions' within a simulated cohort and the observation of outcomes of interest that occur as a result. This would not be affordable or ethical within the real population, nor would estimates regarding the effects of intervention be available to inform public health policy for several decades (Briggs, Scarborough, et al., 2016). As such, a modelling approach is warranted for the present project in order to provide an estimate regarding the potential for time-limited interventions to affect health outcomes over the life-course, as well as to permit physical activity interventions to be compared to alternative approaches to population health.

3.3. Selection of Modelling Strategy

There exist a number of formal modelling approaches within the health-related context, all of which to a greater or lesser extent serve as a means of simplifying the complexity of the world in order to formalise, simplify, and evaluate a particular question (Briggs, Scarborough, et al., 2016). However, across the various modelling approaches there are methods which are more applicable to specific

situations or research questions. Each modelling strategy possesses relative strengths and weaknesses within each given context, with the selection of the most appropriate strategy requiring explanation and justification.

A taxonomy of modelling approaches is provided by Briggs, Wolstenholme, Blakely, and Scarborough (2016) in an attempt to assist population health researchers in the selection of an appropriate strategy for evaluation of interventions to reduce non-communicable diseases. The selection of an appropriate modelling method is informed by several requirements and there is often more than one way of modelling a particular scenario. However, the choice of model is typically informed by three areas: a) what level of interaction is required within the model (i.e. no interaction, the relevance of spatial variables, or interaction between heterogeneous entities); b) the role that time plays within the model (i.e. no time requirement, discreet time events, or continuous/simultaneous time events); and, c) the level of complexity within the model (i.e. few simple states/decisions, numerous states, or large numbers of possible states/entity-specific states) (Briggs, Wolstenholme, et al., 2016).

The requirements of the present study necessitated an approach capable of evaluating population-level changes in a limited number of life-course health outcomes due to hypothetical changes in a single variable (i.e. levels of physical activity). There was no requirement for individual interaction within this population approach. There was a clear requirement for a time component in order to monitor changes over the lifespan, but discrete time steps were sufficient for this purpose. No interaction between entity and environment was required beyond exposure and outcome estimates, however some interaction between specific outcomes would be advantageous for accurate modelling.

3.4. The Multi-State Life Table Approach

A life table approach enables the probability of incidence and mortality to be calculated by age and sex. These estimations are typically made for discreet periods, rather than on a continuous basis. Although not inevitable these periods, or cycles, are typically yearly allowing the simulation of a population cohort as it ages (Hinde, 2014). The multi-state life table is an extension to this method,

allowing the specification of more than one outcome. For example, while a simple life table specifies estimates of mortality within a population by age, a multi-state life table would permit the specification of incidence and mortality for several disease outcomes (Hinde, 2014) and the monitoring of these outcomes within a simulated cohort over time (Briggs, Wolstenholme, et al., 2016). The model can then be re-run for different scenarios to compare the effects of each of these over the life course of the simulated cohort (Briggs, Wolstenholme, et al., 2016).

There are limitations to the multi-state life table in line with the underlying structural assumptions. Firstly, this method almost inherently involves group estimation and possesses no method of characterising individuals within a population. The model therefore provides only cohort, or sub-cohort, averages. As a further consequence, multi-state life tables do not allow for any 'memory' between cycles. For example, it is not possible to say whether an individual had become incident with myocardial infarction one year or twenty years prior to death.

Secondly, a standard multi-state life table does not allow an individual to be present in more than one state. In the case of modelling several health outcomes this has the consequence that an individual who has become incident with bowel cancer cannot then become incident with additional disease outcomes, such as type 2 diabetes. This can be addressed with the specification of additional states to provide the possibility of comorbidity, e.g. a state for incident bowel cancer *and* type 2 diabetes, but the complexity of the model would then increase almost exponentially with each additional outcome of interest. While this issue is less relevant for infectious disease modelling, typically featuring brief morbidity periods and high case-fatality rates, it becomes an increasingly important limitation when modelling non-communicable diseases which involve longer morbidity periods, limited remission, and an increased probability and relevance for comorbidity (Barendregt, Van Oortmarssen, Van Hout, Van Den Bosch, & Bonneux, 1998).

Thirdly, due to the discreet conceptualisation of time and health-states it is not possible for an individual to experience two 'life events' in the same cycle. All life events are represented as

transitions from one state to another, with the possibility of this transition occurring determined by an age-specific probability. All transitions take effect at the cycle boundary, conceptually as individuals age by one year, and therefore only one transition can occur each year. As a consequence, for example, a person becoming incident with type 2 diabetes cannot then either become incident with another disease or die in that same year. Furthermore, it is not possible for an individual to experience the same outcome twice as once they have transitioned from 'well' to 'incident stroke' they cannot recover and then re-transition.

The use of proportional multi-state life tables partially addresses the limitations described above, allowing comorbidity to be estimated without a corresponding increase in structural complexity. Rather than describing the prevalence of a specific disease outcome in absolute figures, a proportional multi-state life table represents this prevalence in terms of a proportion of the live cohort for each age. Each disease outcome then possesses a specific incidence proportion and levels of comorbidity can be derived from the product of their respective rates (Barendregt et al., 1998). The absolute prevalence figures can then be calculated by multiplying the disease-specific proportions by the number of living individuals in the simulated cohort. However, although this approach provides a method by which to estimate comorbidity prevalence, it retains the assumption that disease incidences and morbidities are independent.

3.5. Previous Studies Using This Approach

Modelling of physical activity and non-communicable diseases has been conducted in Australia, as part of the Assessing Cost Effectiveness (ACE) - Obesity programme. Cobiac et al. (2009) conducted a modelling study to assess the cost-effectiveness of six physical activity interventions, including counselling, media campaigns, general practitioner referral, and internet resource provision. They used a proportional life-table approach to assess change in disease incidence and mortality due to projected increased physical activity relative to a baseline population modelled from national survey data. Cobiac et al. (2009) concluded that the package of physical activity interventions represented a

cost-effective investment for reducing obesity in Australia but cautioned that the scenarios were largely based on poor quality data.

Further intervention evaluations were conducted using the ACE methodological approach, including assessments of walking bus programmes (Moodie, Haby, Galvin, Swinburn, & Carter, 2009), school active transport plans (Moodie, Haby, Swinburn, & Carter, 2011), and active after-school programmes (Moodie et al., 2013). The former two studies explored the effects of intervention scenarios that, while based on real-world programmes, were derived almost entirely from assumptions rather than measurement data, both concluding that interventions were not cost-effective. However, the latter study used survey physical activity and anthropomorphic data from an longitudinal evaluation of the Be Active – Eat Well programme (Sanigorski, Bell, Kremer, Cuttler, & Swinburn, 2008) to parametrise the intervention scenario. Moodie et al. (2013) concluded that the intervention was a cost-effective investment in the reduction of childhood obesity, although a more conservative estimate regarding participant maintenance of the intervention may reduce this effectiveness.

A modelling study was completed by the Centers for Disease Control in order to assess the cost-effectiveness of seven community-based physical activity interventions, including healthy living information campaigns, community walking programmes, and enhanced access to healthy environments (Roux et al., 2008). This model used a state-transition approach that permitted transition between one of four strata of physical activity: inactive, irregularly active, meets guidelines, and highly active. Roux et al. (2008) found all seven interventions to be cost-effective, even after sensitivity analysis, and recommended them for implementation, most especially those interventions that specifically targeted high-risk populations. Once again, the authors cautioned against over-interpretation of the findings, particularly with regard to the uncertainty surrounding intervention effect legacy, but do suggest that overall results were more sensitive to intervention effects than legacy scenario.

3.6. Formal Model Overview

A discreet-time, proportional multi-state life table was constructed to conduct a single closed simulated cohort study. The model was constructed in Microsoft Excel (Microsoft, 2013), using additional statistical and epidemiological software to manipulate data. The model was constructed according to the specifications outlined by Barendregt et al. (1998). A separate life table was constructed for each sex, and within sex for five strata of physical activity, producing ten tables for the baseline and for each counterfactual. The cohort boundaries were from five years of age to 100 years of age. Cycles were equivalent to one year of age.

Figure 3.1 provides a simplified conceptualisation of the model, describing the exclusive states that the cohort must inhabit, as well as the transition probabilities that define the proportion of the cohort that will move from one state to another each cycle. Additional complexity would not produce significantly more accuracy when weighed against the fidelity of the input data and the implicit constraints around time and computational power.

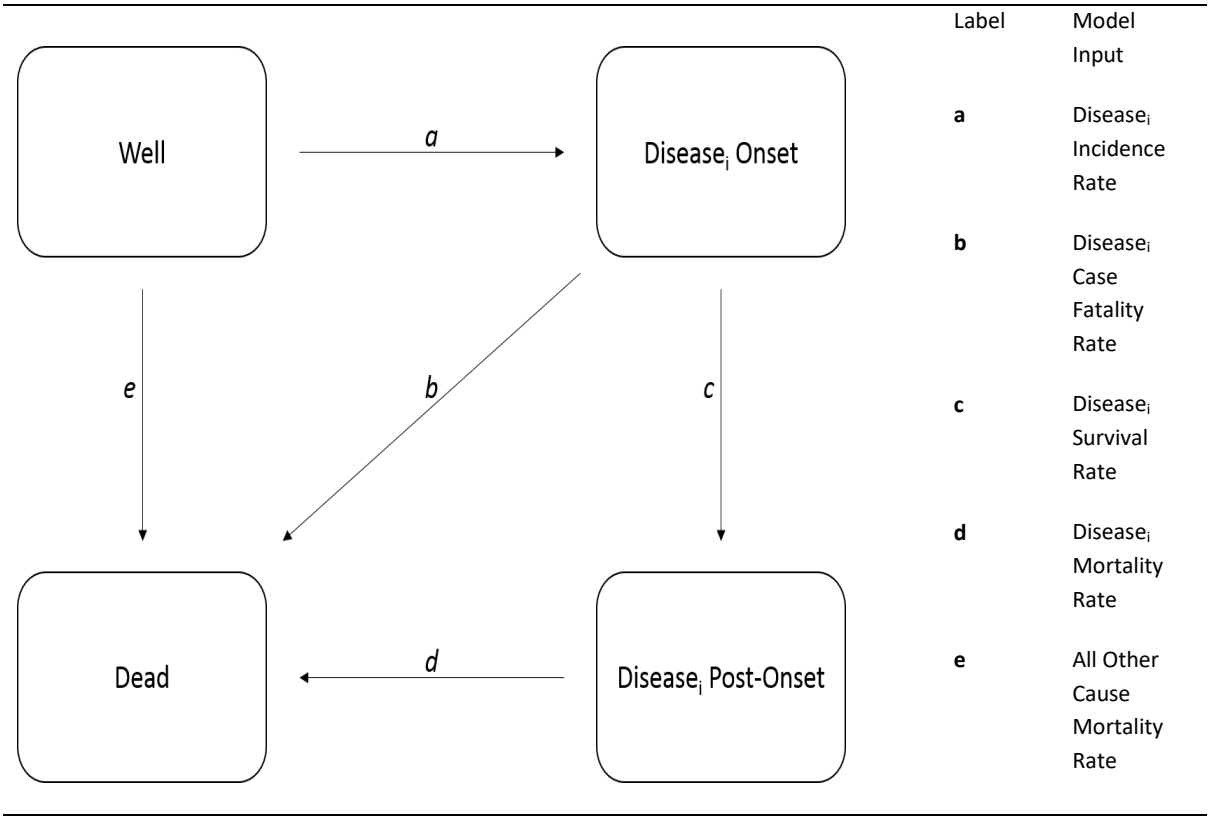


Figure 3.1 - Presentation of the formal model, transition probabilities, and data requirements of the model

All parameters were taken for the year 2012 where available. While these statistics vary with age, and some trends evidence a reduction or increase in prevalence, these data are not intended for forecast and no discount was applied.

3.7. Model Outputs

The model specified above permitted a comparison between baseline estimates, in which no intervention was applied, and counter-factual estimates for a variety of hypothetical physical activity interventions. The primary outcomes for comparison were life expectancy and years of life in disability. Secondary outputs generated from the model were years of life lost, individual disease prevalence by age and sex, and changes in lifetime physical activity levels.

- Life expectancy was calculated for each life-table and then averaged to provide sex-specific and whole population estimates. The estimates for life expectancy are attained by summing

the number of person years remaining above age *x*, divided by the number of people left alive at age *x*.

- Years of life in disability is the sum of all years spent alive but prevalent with disease, i.e. the proportion of the population that has become incident but not yet died. Years of life in disability was calculated for each life-table, as well as aggregated for sex-specific or population-level estimates. This is distinct from Disability-Adjusted Living Years (DALY's), which is a measure of disease burden.

- Years of life lost was calculated within each life-table by subtracting the total years spent alive in each counter-factual scenario from the total years spent alive in the baseline scenario. These figures are negative if an intervention is effective at extending life expectancy. This is distinct from years of life lost due to premature mortality, which is a calculation used within a single life table.

- Prevalence figures for specific diseases can be generated for each year of life within each life-table. Prevalence is an estimate of the fraction of live cases of morbidity within a given population in each given year. The prevalent proportion estimates were generated for each disease within each life-table at 65 years of age for the purposes of comparison across scenarios.

3.8. Sources of Data

3.8.1. Physical Activity - England and Wales 2012

Physical activity data for the cohort population were taken from the Health Survey for England (HSE) 2012 dataset, described in detail in Chapter 2. Briefly, the HSE is a national representative annual household survey that has since 1991 collected core and supplementary health information such as smoking, blood pressure, and other general health details (Mindell et al., 2012). The data are cross-sectional, with no explicit link between years, hence no age- or time-related change can be directly

assumed. The HSE has been used for numerous cross-sectional and demographic research (Scholes et al., 2016).

Although the HSE 2015 provides a more recent dataset, the use of the 2012 dataset is warranted within the core model given the absence of systematic differences between two survey years, as presented in Chapter 2. While the 2015 dataset possesses the advantage of both the inclusion of the school physical activity times and a larger sample size, the advantages of the use of the HSE 2012 are clear, in that data for both children and adults are available for a single dataset, including a detailed analysis of both child and family physical activity. In addition, and most significantly for more accurate modelling, the 2012 dataset permits parameterisation in annual cycles, which is not possible with the 2015 data due to the use of broader age-banding.

Following the analysis of the HSE 2012 and 2015 physical activity data, presented in Chapter 2, there is sufficient detail to allow a specification of a simulated cohort stratified by age and sex, and also to permit population stratification by quintile of physical activity level. Although some variation was noted in geographical location, quintile of index of multiple deprivation, weight status, and ethnicity, there exists no published data that would permit discreet modelling of disease incidence and mortality for the sub-groups within these variables (e.g. Attwood, van Sluijs, & Sutton, 2016).

In terms of consequences for modelling, this indicates that the stratification of the population according to self-report data is likely to be sound but brings into question the accuracy of the point estimates for each stratum, potentially resulting in an underestimate of the physical activity of the population and therefore the benefits within the model. In contrast, the self-reported data over-estimated the amount of time spent in MVPA, potentially due to the division of time into ten minute blocks within the survey, while actual episodes of MVPA are typically shorter (Scholes et al., 2014b).

3.8.2. All-Cause Mortality

Rates for all-cause mortality were taken from the Office for National Statistics (ONS) 2012 data set (Office for National Statistics, 2013a). The ONS registers all deaths in the UK by cause of death, age, sex, and area of residence. Also provided are rates of death for each single year of life for the English population. Information is collated from legally required certification and registration of all deaths in the UK and are compiled for each calendar year. Included within these statistics are all those deaths occurring within England in the year, irrespective of the normal country of residence of the deceased. All deaths are coded according to the International Classification of Diseases – 10th Edition (ICD-10) (World Health Organization, 1993), including primary and any secondary causes of death. The sources of data for all-cause mortality and specific disease outcomes are presented in Table 3.

Health Outcome	**Source Publication Reference**
All-Cause Mortality	(Office for National Statistics, 2013b)
Myocardial Infarction	
Incidence	Smolina, Wright, Rayner, and Goldacre (2012b)
Mortality	Smolina, Wright, Rayner, and Goldacre (2012a)
Prevalence	Townsend et al. (2012)
Case-Fatality	Smolina et al. (2012b)
Stroke	
Incidence	Scarborough et al. (2009)
Mortality	Scarborough et al. (2009)
Prevalence	Townsend et al. (2012)
Case Fatality	Rothwell et al. (2004)
Type 2 Diabetes	
Incidence	Holden et al. (2013)
Mortality	n/a
Prevalence	NHS England (2013)
Case-Fatality	n/a
Bowel Cancer	

Incidence	Office for National Statistics (2013a)
Mortality	Office for National Statistics (2013a)
Prevalence	Office for National Statistics (2013a)
Breast Cancer	
Incidence	Office for National Statistics (2013a)
Mortality	Office for National Statistics (2013a)
Prevalence	Office for National Statistics (2013a)
Uterine Cancer	
Incidence	Office for National Statistics (2013a)
Mortality	Office for National Statistics (2013a)
Prevalence	Office for National Statistics (2013a)
Increase in Risk of MI or CVA for Prevalent Type 2 Diabetes	Tancredi et al. (2015)

Table 3 – Epidemiological parameters for specific disease outcomes and sources of data

3.8.3. Myocardial Infarction (ICD 121 - 122)

Myocardial infarction is a type of coronary heart disease (CHD) in which the blood flow is interrupted and causes damage to the heart muscles; events are usually acute episodes secondary to atherosclerosis, which is a build-up and hardening of plaques in the coronary arteries (Mendis et al., 2010). The atherosclerotic process is accelerated by high blood pressure, higher levels of low-density lipoprotein cholesterol, and lower levels of high-density lipoprotein, all of which are subject to beneficial effects from increased physical activity levels (Dishman et al., 2012). In 2010, CHD was the cause of approximately 80,000 deaths in the UK, although deaths due to both CHD and myocardial infarction have been declining (Townsend et al., 2012). CHD was estimated to cost the UK economy approximately £6.7 billion per year in 2012 (Townsend et al., 2012). In a review of the effects of modifiable risk factors for incidence of myocardial infarction, Yusuf et al. (2004) suggested that lack of regular physical activity produced a total population attributable risk of 12.2%. In a more recent study estimating the global burden of non-communicable disease as a result of physical activity, Lee et al. (2012) suggested an unadjusted population attributable fraction of 10.4% for all CHD.

In order to meaningfully incorporate any relative risk into the model, it is necessary to ascertain a dose-response estimate. A dose-response relationship can be defined as the relationship between changes in outcome with reference to changes in exposure (Dishman et al., 2012); in this case the dose-response relationship refers to the changes in relative risk of myocardial infarction incidence and mortality in any associated changes in physical activity levels. Where reliable dose-response data are available, it is possible to determine the changes in relative risk across the five strata of physical activity within the model provided that the relationship is stratified by age and ideally by sex, with the precision of modelling dependent on the specificity within the source paper.

Previous studies had produced estimates that were either limited to specific forms of physical activity, such as only leisure time physical activity (e.g. Sattelmair et al., 2011) or only light physical activity (e.g. Woodcock, Franco, Orsini, & Roberts, 2010), or studies only reported outcome differences between categories of physical activity, such as 'less than 30 minutes', 'between 30 and 60 minutes', or 'more than one hour' of walking per day (e.g. Fujita et al., 2004), or 'meets national physical activity guidelines' versus 'no activity' (e.g. Lee et al., 2012).

Wahid et al. (2016) extended the literature by conducting a systematic review and meta-analysis on the relationship between whole-day physical activity and several disease outcomes, including cardiovascular diseases and type 2 diabetes. Pooled data from 36 studies were analysed to produce a continuous estimate of association between physical activity (MET hours per day) and disease incidence and mortality (relative risk), showing that increases in physical activity levels were associated with reductions in risks for all outcomes. While only two studies (Patel et al., 2013; Petersen et al., 2012) contributed to the relative risk estimate of 0.75 (95% CI's: 0.62, 0.89) for myocardial infarction used within the model, when reviewing the individual diagnoses contributing to the group estimate for CVD, Wahid et al. (2016) found that each component was very similar to the total figure. The authors concluded that the greatest benefit in terms of reducing risk of CVD and type 2 diabetes is observed with movement between inactivity and low-levels of physical activity. In a similar but

independent study, Kyu et al. (2016) reviewed 174 studies to inform the Global Burden of Disease study 2013, to identify the continuous relative risk profile for breast cancer, colon cancer, type 2 diabetes, ischemic heart disease, and ischaemic stroke by levels of physical activity. Relative risk profiles on common disease outcomes were broadly similar to Wahid et al. (2016) for common outcomes.

3.8.4. Stroke (ICD 160 – 169)

A stroke is a cerebro-vascular event that interrupts cerebral function for longer than 24 hours but is not attributable to alternative causes (e.g. head injury) (Feigin, Lawes, Bennett, Barker-Collo, & Parag, 2009). The interruption of blood supply causes damage or death to corresponding areas of the brain, and in serious cases permanent loss of brain function (Allen & Bayraktutan, 2008). Similar to myocardial infarction, atherosclerosis is implicated in stroke risk, as well as thrombosis within the cerebral blood vessels, both of which are reduced in people reporting higher levels of physical activity (Lee, Folsom, & Blair, 2003). Feigin et al. (2016) suggested that over 90% of the global burden of stroke was attributable to modifiable behaviour risk factors, such as smoking, poor diet, and physical activity, as well as environmental risk factors such as air pollution. The authors further suggested that a low level of physical activity was accountable for 7.7% of the global risk of stroke, rising to 11.2% for high income countries (Feigin et al., 2016).

Stroke incidence and mortality rates were taken from Scarborough et al. (2009), itself drawing on figures produced by the OxVasc study (Oxford Vascular Study) (Rothwell et al., 2004; Rothwell et al., 2005). Case-fatality rates were taken directly from the source OxVasc publications (Rothwell et al., 2004; Rothwell et al., 2005). Prevalence rates for stroke in England was taken from Townsend et al. (2012). The relative risk estimate was taken from the meta-analysis by Wahid et al. (2016) mentioned above, providing an estimate of 0.78 (95% CI's: 0.69, 0.88) for those achieving current physical activity recommendations of 11.5 MET hours per week compared to inactive individuals. This estimate differs somewhat from that provided by the Kyu et al. (2016) of 0.74, (95% CI's: 0.66, 0.81) for those achieving

above 8000 MET minutes per week compare to those achieving below 600 MET minutes per week, however, these authors included an additional estimate for higher quality papers of 0.80 (95% CI's: 0.70, 0.90) which is very close to the estimate selected for inclusion within the model.

3.8.5. Type 2 Diabetes (ICD E11)

Type 2 diabetes is a chronic condition in which insulin production is deficient or the body is unable to transport glucose, resulting in a toxic level of glucose in the blood (Dishman et al., 2004). In contrast to type 1 diabetes, which is present from birth, type 2 diabetes is acquired. The 2010 Global Burden of Disease study showed that diabetes-related mortality had doubled to nearly 1.3 million worldwide since 1990 (Lozano et al., 2013), although due to under-diagnosis and lack of specificity on death certificate completion it is suggested that this likely represents an underestimate (Alberti & Zimmet, 2013). In the UK, diabetes was suggested to have cost £23.7 billion in direct and indirect costs in 2010/2011, with approximately 90% of this burden due to type 2 diabetes (Hex, Bartlett, Wright, Taylor, & Varley, 2012).

Risk factors for type 2 diabetes may be brought forward through physiological vulnerabilities and lifestyle choices (Reinehr, 2013), forming a 'prediabetes' pattern consisting of impaired fasting glucose and impaired glucose tolerance (Abraham & Fox, 2013). In a systematic review of 42 studies, Berman, Weigensberg, and Spruijt-Metz (2012) found that insulin sensitivity was associated with lower levels of physical activity in children. Cross-sectional evidence from the National Health and Nutrition Examination Survey (NHANES) study suggests that while weight status and CHD risk factors largely remained unchanged between 1999 and 2008, the prevalence of type 2 diabetes and prediabetes increased by 14% in 12 to 19 year olds (May, Kuklina, & Yoon, 2012), with prevalence forecasted to increase by approximately 25% by 2050 (Boyle, Thompson, Gregg, Barker, & Williamson, 2010).

Incidence figures were acquired from a study by Holden et al. (2013), who explored changes in rates of diagnoses of new cases of type 2 diabetes between 1991 and 2010, concluding that incidence was increasing, especially for people under 40 years of age. Prevalence figures were taken from The

Diabetes Society's annual figures. No mortality figures were available for type 2 diabetes as in the vast majority of cases it constitutes a secondary cause of death. No information was available for case-fatality or remission, and within the model these were assumed to be zero.

The relative risk for diabetes incidence was taken from the study by Wahid et al. (2016) (see Table 4) who provided an estimate of 0.74 (95% CI's: 0.72, 0.77) for those achieving guidelines compared to inactive individuals, although only three studies contributed to this figure. However, this estimate is broadly comparable to those from other publications; for example, Kyu et al. (2016) provided a relative risk of 0.75 (95 CI's: 0.70, 0.81) for those achieving over 8000 MET minutes per week compared to those achieving under 600 MET minutes per week, while Jeon, Lokken, Hu, and Van Dam (2007) provided an estimate of 0.69 95% CI's: 0.58, 0.83) for those participating in regular weekly moderate physical activity compared to those reporting sedentary lifestyles. Finally, an estimate for the rate of excess mortality was taken from Tancredi et al. (2015) who conducted a controlled prospective cohort study with people diagnosed with type 2 diabetes, finding an elevated risk of cardiovascular disease of 1.14 (95% CI's: 1.13, 1.15) in mortality relative to controls without type 2 diabetes.

3.8.6. Bowel Cancer (ICD C18-20)

Cancer is a group of diseases involving abnormally dividing cells, typically at an accelerated rate, which in advanced stages may spread to other parts of the body (Dishman et al., 2012). Bowel cancer is a categorisation of cancers first occurring in the large bowel, consisting of the colon and rectum, also referred to as colorectal cancer (Jensen, 2018). In the majority of cases bowel cancer evolves from pre-cancerous polyps which form on the lining of the large bowel (Bowel Cancer UK, 2017). It is the fourth most common cancer diagnosis in the United Kingdom, predominantly occurring in people aged over 50, although mortality rates have been steadily reducing for both England and the UK (Marshall et al., 2016).

There exist biologically plausible mechanisms by which physical activity levels can influence cancer development, although there is significant interplay between these mechanisms (World Cancer

Research Fund/American Institute for Cancer Research, 2007). These mechanisms include a reduction in insulin resistance, through both contribution to cell damage and inhibition of repair, as well as promoting chronic inflammation, leading to cancer initiation and proliferation (Orgel & Mittelman, 2013; Stojsavljević, Jukić, Kralj, & Duvnjak, 2016). Bowel cancer incidence is associated with higher levels of overweight or obesity, potentially due to the effects of increased levels of adipocytokines which are largely produced in fat cells and have been implicated in the development and transportation of cancer cells (Okabayashi et al., 2012). In particular, visceral or abdominal fat appears to confer a higher risk than subcutaneous fat, partially accounting for comparatively higher incidence of the effects of adiposity on incidence within males (Bardou, Barkun, & Martel, 2013). Physical activity, along with a healthy diet, contributed to reduced transit time of faeces within the colon, while increased transit time potentially increases the harmful activity of colonic bacteria (Louis, Hold, & Flint, 2014). Finally, physical activity appears to affect immune system function, although the nature of relationship is currently not well understood (Leitzmann et al., 2015).

Within a comprehensive review of behavioural and environmental risk factors for cancer the World Cancer Research Fund/American Institute for Cancer Research (2007) conducted a series of meta-analyses investigating the association of physical activity levels and specific cancer risk. The report concluded that there was 'convincing' evidence for a protective effect of higher levels of physical activity on colorectal cancer, which remained true for specific analyses of levels of walking, recreational, occupational, and total physical activity. An update to this report (World Cancer Research Fund/American Institute for Cancer Research, 2018) included additional data but did not revise any conclusions regarding the association between physical activity and colorectal cancer. Most studies reviewed in the report combined colon and rectal cancer into a single category, but differentiated analysis was possible where a greater level of evidence was found for a protective effect against colon cancer, independent of other risk factors. More recently, Moore et al. (2016) conducted a systematic review and meta-analysis of prospective cohort studies investigating the association between leisure

time physical activity and cancer. They found that hazard ratios (HR's) for both colon (*n* = 12, HR 0.84) and rectal (*n* = 12, HR 0.87) cancer were associated with low levels of leisure time physical activity.

Baseline cancer incidence, prevalence, and mortality rates were taken from the ONS 2012 release. All cancers are registered by the National Cancer Registration and Analysis Service (NCRAS), part of Public Health England, and then submitted to the ONS for dissemination. Some registrations can take up to five years to appear in the statistics and as a result tables are updated retrospectively year on year, with survival outcomes added to tables from previous years. Only melanoma cancers appear in the statistics, and all are classified by age and sex according to ICD-10 codes. The ONS typically report five-year survival rather than 30-day case-fatality rates for cancers and therefore case-fatality was not incorporated into the epidemiological consistency modelling for bowel, breast, or endometrial cancer.

A relative risk estimate of 0.87 (95% CI's: 0.80, 0.95) for increased cancer incidence and mortality was taken from additional research by Wahid et al. (2016), although the data on bowel cancer was not published as part of their systematic review. While alternative sources for parameters were available within the literature, the unpublished data Wahid et al. (2016) were completed as part of the same analysis and were the only such estimates to have been derived using a single continuous comparable index of physical activity. The provided estimate closely approximates other systematic reviews investigating this area. Kyu et al. (2016) provided a relative risk estimate specifically for colon cancer of 0.79 (95% CI's: 0.74, 0.85) for 'highly active' individuals achieving 8000 MET minutes per week when compared to an 'insufficiently active' category achieving under 600 MET minutes per week. Previously, Harriss et al. (2009) had investigated the dose-response relationship between leisure time physical activity levels and colorectal cancer risk, with meta-analysis providing a relative risk estimate of 0.80 (95% CI's: 0.67, 0.96) and 0.86 (95% CI's: 0.76, 0.98), for men and women respectively, comparing uppermost to lowermost categories of leisure time physical activity.

3.8.7. Breast Cancer (ICD C50)

Breast cancer is a categorisation of cancers first occurring in the breast. The most common type is invasive breast cancer (no special type) in which cancer cells originating in the lining of the lobules or ducts have permeated the surrounding fat tissue, constituting approximately 70% of diagnoses (Dishman et al., 2012). In contrast, *in situ* breast cancers have not permeated the surrounding tissue and remain localised in either the ducts or lobules. Together, breast cancers are the most common category in the UK, accounting for approximately 15% or all cancer diagnoses (Maddams, Utley, & Møller, 2012). While breast cancer also occurs in males, it accounts for less than one percent of all cancer incidence in males, and for one percent of breast cancer prevalence, and as a consequence the epidemiology is limited (İğci, Tükenmez, & Özkurt, 2016) and has therefore not been included in this thesis.

The World Cancer Research Fund/American Institute for Cancer Research (2007) expert review suggested that there was a 'probable' link between physical activity levels and post-menopausal breast cancer incidence following systematic reviews of total, recreational, and occupational physical activity. The report concluded that the association between physical activity and pre-menopausal breast cancer was limited and inconsistent, but that a link was 'suggestive'. In addition to the general benefits on cancer risk described above, including reduced adiposity and insulin sensitivity, increased physical activity is negatively associated with oestrogen levels which are implicated in the development and proliferation of cancer cells, although there is a strong interaction with overweight and obesity (Lynch, Neilson, & Friedenreich, 2010).

Baseline cancer incidence, prevalence, and mortality rates were taken from the ONS 2012 release. A relative risk estimate of 0.93 (95% CI's: 0.91, 0.95) for increased cancer incidence and mortality was taken from additional research by Wahid et al. (2016), although the data on breast cancer was not published as part of their systematic review. The estimate provided closely approximates other systematic reviews investigating this area. Kyu et al. (2016) reviewed 35 articles to provide a relative

risk estimate specifically for breast cancer of 0.86 (95% CI's: 0.83, 0.90) for highly active individuals achieving above 8000 MET minutes per week when compared to an insufficiently active category achieving under 600 MET minutes per week, while Moore et al. (2016) reviewed ten studies, finding a hazard ratio of 0.90 (95% CI's: 0.87, 0.93) for high versus low percentile physical activity in leisure time.

3.8.8. Endometrial Cancer (ICD C54)

Also referred to as uterine or womb cancer, endometrial cancer is a categorisation of cancers originating in the upper female reproductive apparatus. While occasionally used interchangeably with endometrial cancer, uterine cancer includes an additional category of uterine sarcoma which originates in the uterine muscle wall (D'Angelo & Prat, 2010). Endometrial cancer includes: endometrial adenocarcinoma, the most common sub-type, which originates in the endometrial glands; adenosquamous carcinoma, typically more aggressive, which originates in the linings of organs and glands; and papillary serous carcinoma, typically rare but highly malignant, almost entirely affecting post-menopausal women, originating in the lining of the uterus (Burke et al., 2014). Endometrial cancer is the fourth most common type in females in the UK (Crosbie & Morrison, 2014).

The World Cancer Research Fund/American Institute for Cancer Research (2007) report suggested that the association was 'suggestive' that total, occupational, and leisure time physical activity played a protective role in the development of endometrial cancer. Endometrial cancer shares implicated mechanisms with breast cancer, including adiposity, elevated oestrogen, and reduced immune system response (Burke et al., 2014), although a more detailed investigation found convincing associations with insulin resistance (Hernandez et al., 2015). Once again, while there is a suggestion that each proposed mechanism may independently contribute to the risk of incidence, there are insufficient data to disentangle these mechanisms (Crosbie & Morrison, 2014). The updated report from World Cancer Research Fund/American Institute for Cancer Research (2018) included additional data but did not alter any conclusions.

Baseline cancer incidence, prevalence, and mortality rates were taken from the ONS 2012 release. A relative risk estimate for increased cancer incidence and mortality was taken from Moore et al. (2016). The other disease outcomes incorporated into the model recruited relative risk estimates from Wahid et al. (2016). While the relative risk estimates produced from this study remain a comparison between 'inactive' and 'active' groups, in this case the 'inactive' was defined as achieving 1.5 METs and 'active' as an increase of 11.5 MET hours per week, this estimate is provided with reference to a continuous dose-response curve. The establishment of a dose-response relationship permits the derivation of estimates for each physical activity strata within the model.

In the case of uterine cancer, the relative risk estimate was drawn from Moore et al. (2016), in which the comparison was made between the 10th ("inactive") and 90th ("active") percentiles of the physical activity distribution assuming a linear dose-response relationship. Other papers have taken a slightly different approach to formulating this comparison, for example Gierach et al. (2009) compared an inactive group who reported completing no VPA in a typical week to an active group who reported completing over five episodes of VPA per week, while Voskuil, Monninkhof, Elias, Vlems, and van Leeuwen (2007) compared the least active group with the most active group as defined in the ten constituent studies, with Schmid et al. (2015) following a similar approach in their meta-analysis of 19 studies. These studies reported relative risk estimates of 0.77 (95% CI's 0.63 – 0.95), 0.77 (95% CI's 0.70 – 0.85), and 0.80 (95% CI's 0.75 – 0.85) respectively, indicating that the estimate is robust to methodological heterogeneity, the relative risk point estimate from Moore et al. (2016) of 0.79 (95% CI's 0.68 – 0.92) is concordant with other studies, and that there is considerable overlap in the confidence intervals. Furthermore, while Wahid et al. (2016) did not include uterine cancer, their unpublished estimates for bowel (0.87, 95% CI's 0.80 – 0.95) and breast cancer (0.93, 95% CI's 0.91 – 0.95) are comparable to those reported within Moore et al. (2016), of 0.84 (95% CI's 0.77 – 0.91) and 0.90 (95% CI's 0.87 – 0.93) respectively, further indicating equivalence between continuously and categorically derived estimates, and suggesting that minor

changes in the point along this curve at which the estimate is specified is unlikely to result in substantial changes in the risk estimate.

While concordance exists between categorically-derived estimates, the absence of a specific dose-response relationship necessitates that the differential estimates across the physical activity strata must be assumption driven. Although Moore et al. (2016) assumed a linear relationship across all cancers in their published analyses, they completed an initial examination of the shape of associations between leisure-time physical activity and each cancer type using cubic splines and likelihood ratio tests. Supplementary material from Moore et al. (2016) suggests that uterine cancer follows a dose-response curve at least broadly consistent with the transformed curve used in the other disease outcomes in the model, featuring a rapid reduction in relative risk when progressing from inactive to slightly active with subsequent increases in physical activity conferring diminishing benefit. Therefore, given the notable alignment of estimates, their apparent robustness to methodological heterogeneity, and the tentative indication of a dose-response curve concordant with the risk profile specified for other disease outcomes, the relative risk estimate from Moore et al. (2016) was encoded within the model in the same manner as for the other disease outcome as described in Section 3.9.3., assuming the same transformed curve by which to derive the strata-specific estimates applied within the model.

3.9. Treatment of Data

3.9.1. Parameterisation of Proportional Multi-State Life Tables

In order to provide the required parameters for the specification of a proportional multi-state life table, estimates for all-cause mortality, incidence rates, and mortality rates were identified for each disease state of interest. In addition, these parameters were required for each year of age and by sex. Furthermore, given that input parameters are necessarily drawn from heterogeneous populations, a process of standardisation was needed in order to produce a set of internally consistent parameters.

The general section of the proportional multi-state life table. Legends: δ^o stands for 'all other causes' mortality rate; δ^d for a disease specific mortality rate; δ for total mortality rate. Other notation follows standard life table convention

δ^o_a	δ_a	q_a	l_a	d_a	L_a	T_a	e_a
δ^o_0	$\delta^o_0 + \sum_d \delta^d_0$	$1 - e^{-\delta_0}$	100 000	$l_0 q_0$	$0.5(l_0 + l_1)$	$\sum_{a=0}^{95} L_a$	$\frac{T_0}{l_0}$
δ^o_1	$\delta^o_1 + \sum_d \delta^d_1$	$1 - e^{-\delta_1}$	$l_0 - d_0$	$l_1 q_1$	$0.5(l_1 + l_2)$	$\sum_{a=1}^{95} L_a$	$\frac{T_1}{l_1}$

Figure 3.2 - Formal definition of the general section of a proportional multi-state life table from Barendregt et al. (1998)

A disease specific section of the proportional multi-state life table. Legends: γ is incidence rate; δ the disease specific mortality rate; i the incidence probability; m the disease specific mortality probability; and n the disease prevalence

γ_a	δ_a	i_a	m_a	n_a
γ_0	δ_0	$1 - e^{-\gamma_0}$	$1 - e^{-\delta_0}$	0
γ_1	δ_1	$1 - e^{-\gamma_1}$	$1 - e^{-\delta_1}$	$\frac{n_0 - m_0 + (1 - n_0) i_0}{1 - m_0}$

Figure 3.3 - Formal definition of the disease specific section of a proportional multi-state life table from Barendregt et al. (1998)

The general section of the proportional multi-state life table is presented in notational form in Figure 3.2, into which the specific disease mortality rates are incorporated. All disease-specific mortality rates are then summed along with 'all other cause' mortality to produce total mortality rate, from which the transition probabilities are calculated. All transition probabilities are assumed to be equal across each cycle, in this case specified as years. The number of people dying in each year can then be calculated by multiplying the live population by the mortality transition rate, with each year of annual death numbers being summed to provide a cumulative death total for the cohort. Mid-year estimates are preferred in order to provide a point estimate that represents the whole cycle, given that all transition probabilities are applied at the beginning of the cycle, and these are calculated by averaging the number alive in the cohort across two years. These mid-year estimates of the cohort alive at each year can be summed to provide a total estimate of 'remaining person years' within the cohort at any given cycle, which in turn can be divided by number of people alive to provide individual life expectancy.

The disease specific table is presented in Figure 3.3, in which the prevalence proportion for disease of interest is calculated from the incidence and mortality parameters. Each disease of interest requires a separate disease-specific table, as independence of incidence and mortality is required within the model. The incidence and mortality rates are transformed into transition probabilities from which a prevalent proportion is calculated. By multiplying these prevalent proportions by the number of people left alive within each cycle it is possible to calculate the prevalence percentages for each disease within the cohort, which then sum to provide an overall estimate of years of life in disability. In addition, an estimate of comorbidity for two specific diseases can be calculated by simply multiplying the cycle-specific incidence probabilities together before applying this probability to the live population.

3.9.2. Epidemiological Consistency

In order to provide a complete and internally consistent set of transition probabilities for each age and sex and for each health outcome, the use of additional software was required. Versions of Disease Modeller – 2nd Edition (DisMod II) (Barendregt, Van Oortmarssen, Vos, & Murray, 2003) have been used in several projects both to calculate missing data and to impose internal consistency on input estimations within a cohort (Cobiac et al., 2009; Kruijshaar, Barendregt, & Hoeymans, 2002; Murray et al., 2013) and most particularly those publications arising from the Global Burden of Disease studies. The software assumes zero population disease trends by default and therefore permits the specification of quasi-longitudinal cohort rates from age-specific cross-sectional estimates. The functionality provided by this software is particularly useful for integrating epidemiological data from a range of diseases and characterising an epidemiological profile for a disease or set of diseases within a modelled cohort where insufficient data are available (Barendregt et al., 2003).

As estimates for incidence and mortality were largely available from population-relevant research papers or formal statistics releases from the ONS (see Table 3), DisMod II was used primarily as a means of ensuring internal consistency. A 50% weighting was applied to incidence estimates within

this process, reflecting greater confidence in these input data. For type 2 diabetes, age specific relative risks of excess mortality were included in the disease estimates. While the epidemiological data were entered into DisMod II in accordance with the age-categorisation specified in the source publications, the smoothing functionality then permitted the specification of a consistent age categories across for incidence and mortality rates for each health outcome, allowing a finer granularity than was possible from the original data. Estimates were specified in five year bands as there exist some concerns regarding the accuracy of age-specific estimates of some modelled diseases (Scarborough, Smolina, Mizdrak, Cobiac, & Briggs, 2016); the full input and output figures from DisMod II are presented in Appendix 19 to Appendix 28. The output estimates from DisMod II are shown against the input point estimates for incidence and mortality in Figure 3.4 and Figure 3.5 respectively. The concordance between these curves constitute evidence of acceptable structural integrity of the process.

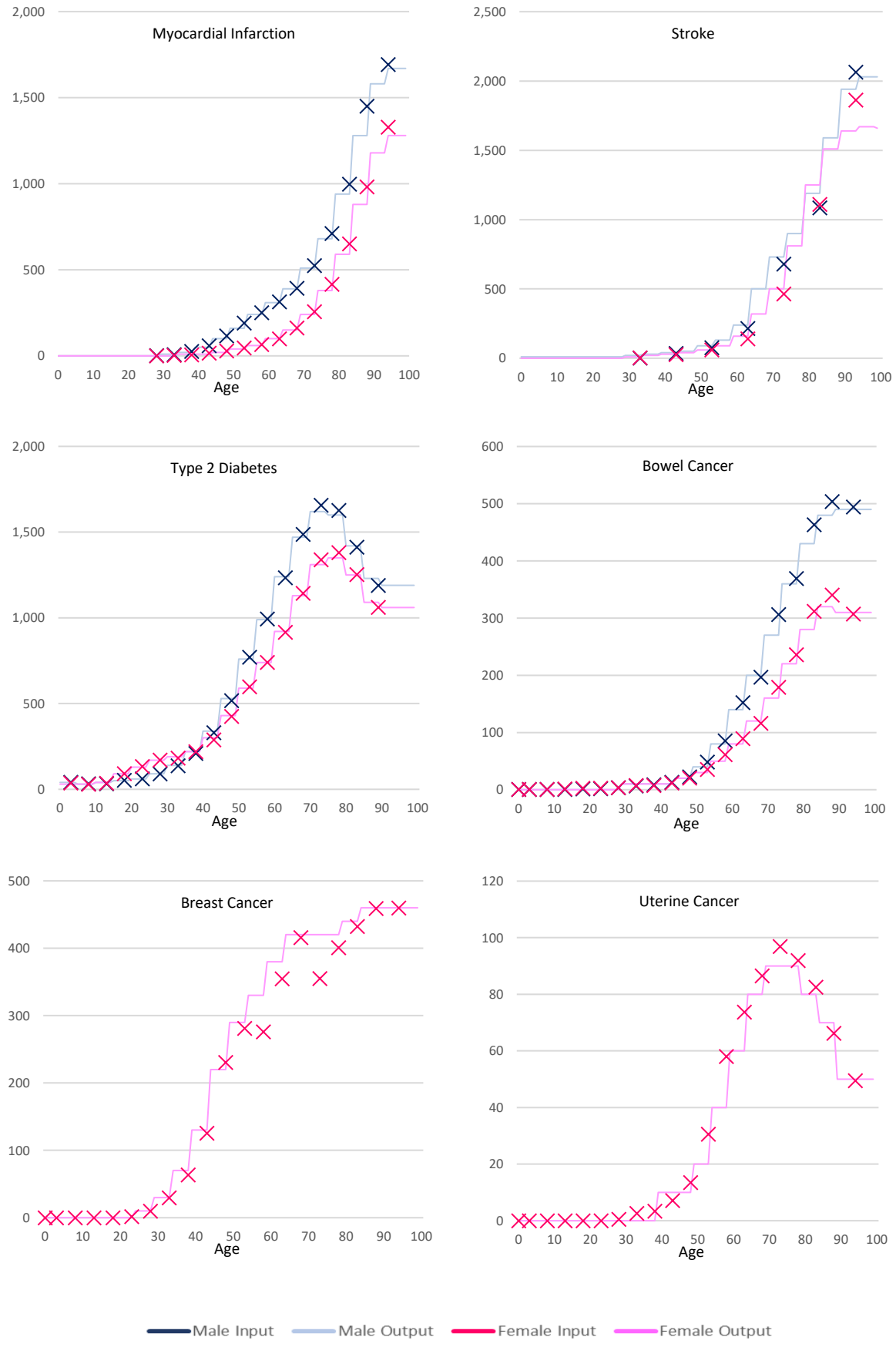


Figure 3.4 - Series of line graphs showing concordance between input and output incidence estimates for specific disease outcomes per 100,000 population from DISMOD II by age (note varying y axis scales)

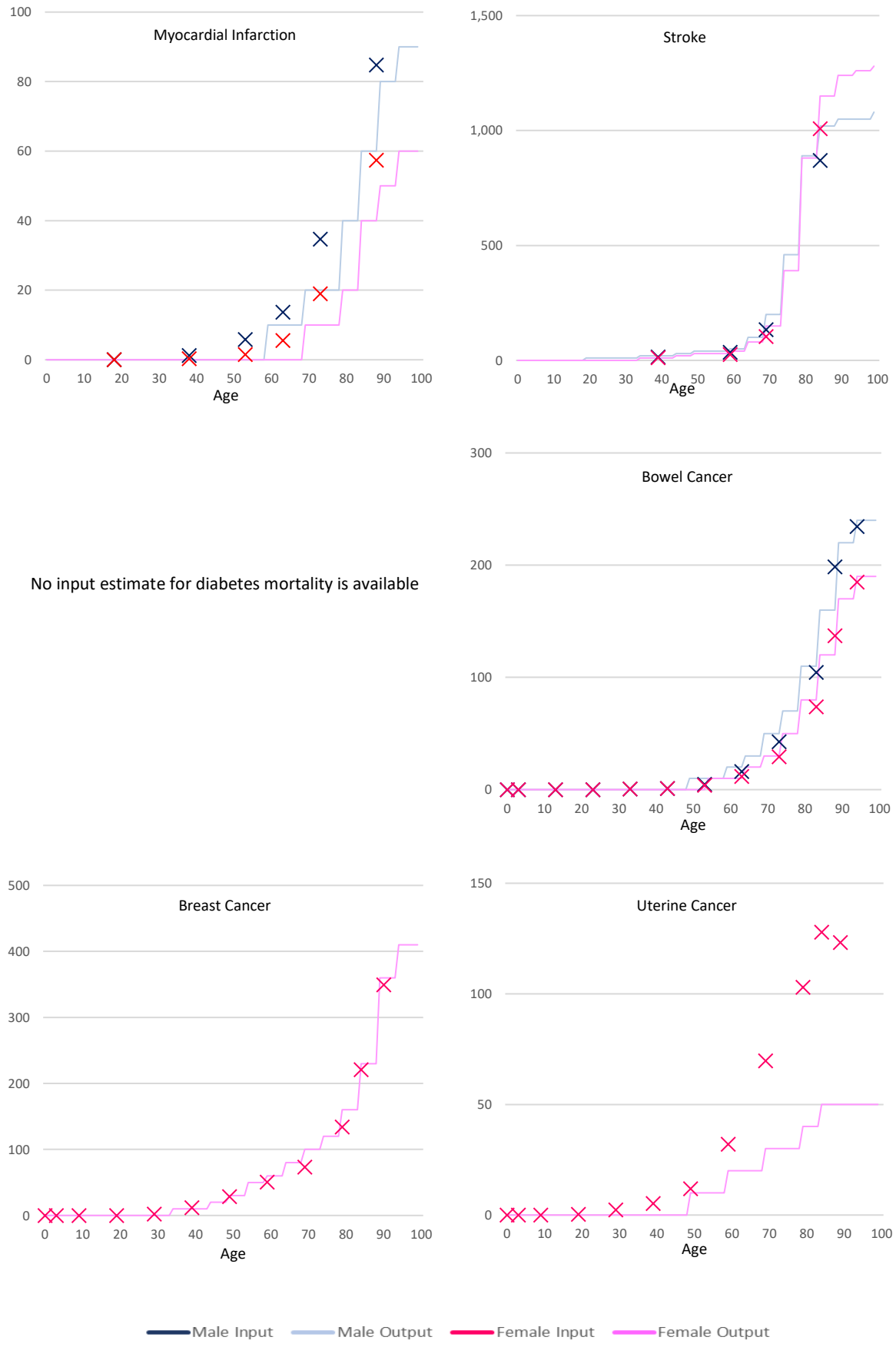


Figure 3.5 - Series of line graphs showing concordance between input and output mortality estimates for specific disease outcomes per 100,000 population from DISMOD II by age (note varying y axis scales)

3.9.3. Relative Effects of Physical Activity

Following the establishment of age- and gender-specific disease risks within the English population, the extent to which these risks are moderated by physical activity level was modelled. While a number of studies have explored changes in disease risk associated with levels of physical activity, the majority of these studies focus specifically on one outcome, typically using a limited or single domain of physical activity, for example Sattelmair et al. (2011) looked only at leisure time physical activity and coronary heart disease, or do not adjust for adiposity and thereby fail to calculate the independent effects of physical activity. Furthermore, the majority of studies provide only categorical estimates, such as low, moderate, and vigorous physical activity, or more commonly by comparing a sedentary group with an active group meeting the national guidelines, with the consequence that any dose-response relationship is obscured.

Wahid et al. (2016) conducted a meta-analysis of qualifying papers to a continuous metric for numerous disease outcomes. By synthesising outputs from 36 published papers, both the shape and location of relative risk curves for specific outcomes were produced. Replicating and expanding the process specified by Sattelmair et al. (2011), Wahid et al. (2016) proposed that a 0.25 power transformation most accurately characterises the dose-response relationship between levels of physical activity and disease risk, or more specifically the reduction in disease risk associated with additional physical activity. As notionally represented in Figure 3.6, individuals engaging in no physical activity experience the full risk of disease and, therefore, with a known intercept and curve trajectory, only one further point is required in order to parameterise a continuous dose response curve. Wahid et al. (2016) completed a meta-analysis on the reduction in disease risk associated with an increase of 11.25 MET hours per week, or 1.61 MET hours per day, itself the equivalent of progressing from an entirely sedentary mode to meeting typical national guidelines. Meta-analysis then produced a point estimate and confidence intervals around a relative risk, a beta, for each specific disease outcome at 1.61 MET hours per day, thereby parameterising continuous dose-

response curves for each disease. With these disease-specific curves now available, the betas were specified using the following equation:

$$\beta = (RR - 1)/(1.61^{0.25})$$

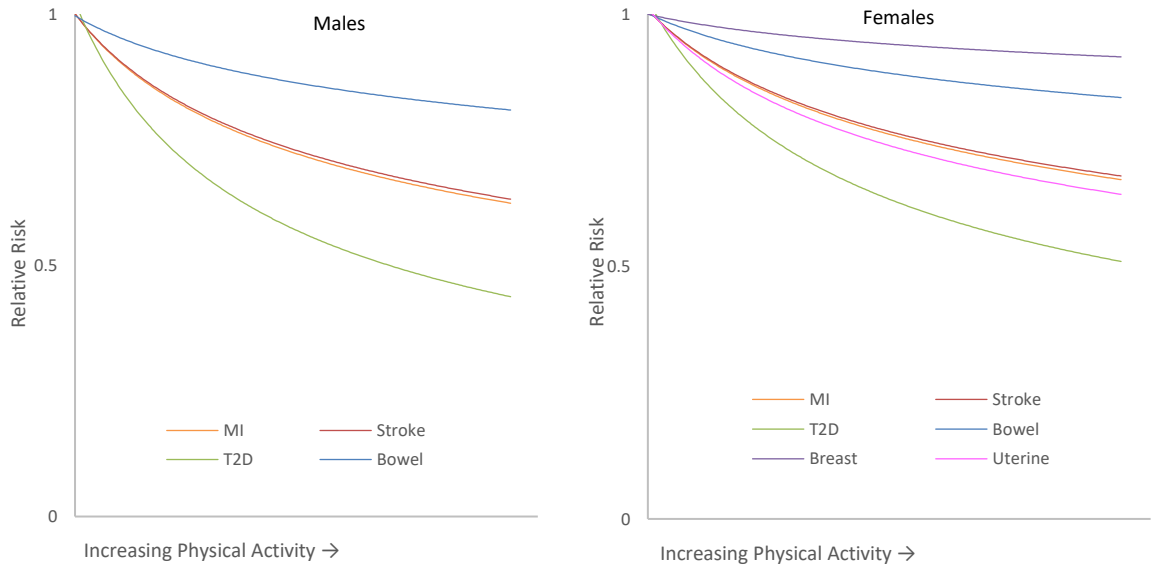


Figure 3.6 - Line graphs showing the notional relative risk curves for specific diseases for increasing levels of physical activity, by sex.

3.9.4. Adapting Type 2 Diabetes Estimates

Type 2 diabetes behaves differently to the other health outcomes in the model due to the absence of a direct mortality attributable to the disease. Incident cases with type 2 diabetes are, however, at an increased risk of mortality of other causes (Lind et al., 2013; Read et al., 2016; Tancredi et al., 2015), most specifically CVD (Booth, Kapral, Fung, & Tu, 2006), and as such type 2 diabetes behaves as both an outcome and a risk factor. In order to accommodate the unique behaviour of type 2 diabetes within the model, the disease was initially specified by encoding the available data within DisMod II following the processes described above. In the case of type 2 diabetes, only incidence rate and prevalence were available for the target population. Incidence rates were taken from a study by Holden et al. (2013) following a review of diagnostic statistics collected by the Clinical Practice Research Datalink, a system which routinely gathers information from primary care services across the UK. Prevalence data are

provided by NHS England (2013). Consistent with the modelling approach taken above, remission, case fatality and mortality rates were initially assumed to be zero.

These initial outputs were provisionally entered into the Excel spreadsheet (Microsoft, 2013) hosting the core model following the process described by Barendregt et al. (1998). This provided a complete and internally consistent model that met the requirements specified above, but did not take sufficient account for the behaviour of type 2 diabetes. Therefore, the elevated risk experienced by type 2 diabetes cases for both myocardial infarction and stroke incidence was derived from figures provided within a review by Tancredi et al. (2015). The elevated risk estimate was used to calculate the additional proportion of deaths from myocardial infarction and stroke that were due to type 2 diabetes. These deaths were then removed from the mortality rates for myocardial infarction and stroke and reallocated to type 2 diabetes using the process outlined below.

The rate for the total population is a product of the prevalence of type 2 diabetes multiplied by the rate for cases with type 2 diabetes, plus one minus the prevalence of type 2 diabetes multiplied by the rate for the population without type 2 diabetes:

$$Rate_T = (p)Rate_D + (1 - p)Rate_{ND}$$

Where T is Total Population, *p* is prevalence of type 2 diabetes (by age and sex), D is prevalent type 2 diabetes cases, ND is non-diabetic cases and RR is the relative risk of myocardial infarction or stroke for prevalent diabetics.

The relative risk for diabetic cases can be calculated from the following:

$$RR = \frac{Rate_D}{Rate_{ND}}$$

Rearranged to:

$$Rate_D = RR.Rate_{ND}$$

Therefore:

$$Rate_T = p.RR.Rate_{ND} + (1-p)Rate_{ND}$$

Rearranged to:

$$Rate_T = Rate_{ND}(p.RR + (1-p))$$

The residual rates for myocardial infarction and stroke were then calculated using:

$$Rate_{ND} = \frac{Rate_T}{p.RR + (1-p)}$$

These residual rates were then used as the input variables for myocardial infarction and stroke prior to modelling and therefore avoided double counting.

The diabetes-specific mortalities for myocardial infarction and stroke were then calculated:

$$Rate_D = RR.Rate_{ND}$$

3.9.5. Addition of Physical Activity Data

Physical activity data were recruited from the 2012 iteration of the HSE and imported into Stata 15 (StataCorp, 2017). The broad treatment of these data is presented in Chapter 2, but is further extrapolated here for the purposes of modelling transparency. Other than sex and age, all variables not relating to physical activity were dropped, along with data pertaining to individuals aged under five or over 100 years. In contrast to the data preparation presented in Chapter 2 no domain-specific totals were derived; the outputs were simply total physical activity levels by age and sex. For each type of self-reported physical activity, across all domains, MET estimates were obtained from the compendium of physical activity equivalences (Ainsworth et al., 2011). Estimates of MET minutes per week were then generated by multiplying the number of minutes per week by the associated MET estimate for the specific activity. These activity specific estimates were then summed to produce an estimate for total MET minutes per week for the cohort.

The total cohort estimate for MET minutes per week was divided into quintiles, with each being allocated a label based on level of physical activity, “Inactive”, “Barely Active”, “Somewhat Active”,

"Active", and "Highly Active". This process was performed independently for each sex. A median point estimate was then derived for each quintile for each year of age. A conceptual model for the strata within the model is presented in Figure 3.7.

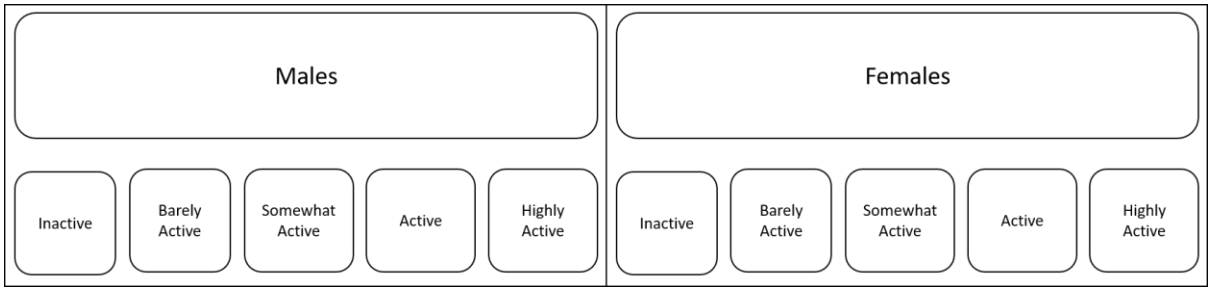


Figure 3.7 – Diagram depicting the division of the simulated population into representative strata by sex and physical activity level

A separate proportional multi-state life table model was constructed for each of the ten sub-components specified above, which together modelled the baseline state of the simulated cohort. This disaggregation of the cohort allowed stratification of the cohort by level of physical activity and therefore the ability to explore and evaluate the impact of interventions on specific portions of the population. The point estimates, by age, sex, and physical activity strata, were exported from Stata into Excel and constituted the raw baseline for the model. These raw scores are presented in Appendix 29. As can be seen in this raw dataset, while the broad trends between the strata-specific estimates, i.e. that the 'barely active' strata report a higher level of physical activity than the 'inactive' strata and so on up to 'highly active', there are some year on year fluctuations within each stratum that likely reflect sampling variation within the specific survey year.

As discussed in Chapter Two, the 2012 iteration of the HSE did not measure physical activity occurring within school hours. This was completed within the 2015 iteration of the survey. In order to address this absence, the percentage of the total weekly physical activity accounted for within school hours was calculated for each age, sex, and strata. The total physical activity estimates from the 2012 survey were then multiplied by these percentages to provide a more comprehensive estimate within the model. These new data points are presented in Appendix 30 for the ages of five to fifteen only.

In order to resolve the within-strata fluctuations for incorporation into the baseline models, the data were interpolated into a curve function. To ascertain the most appropriate curve to describe the data accurately, curves up to and including a quintic polynomial equation for each stratum were compared to the raw data points. Two examples of this process are presented in Figure 3.8 and Figure 3.9, while curves for all strata are presented from Appendix 31 to Appendix 38. Across the ten strata the cubic polynomial most consistently represented the data and was therefore selected for use in the core model.

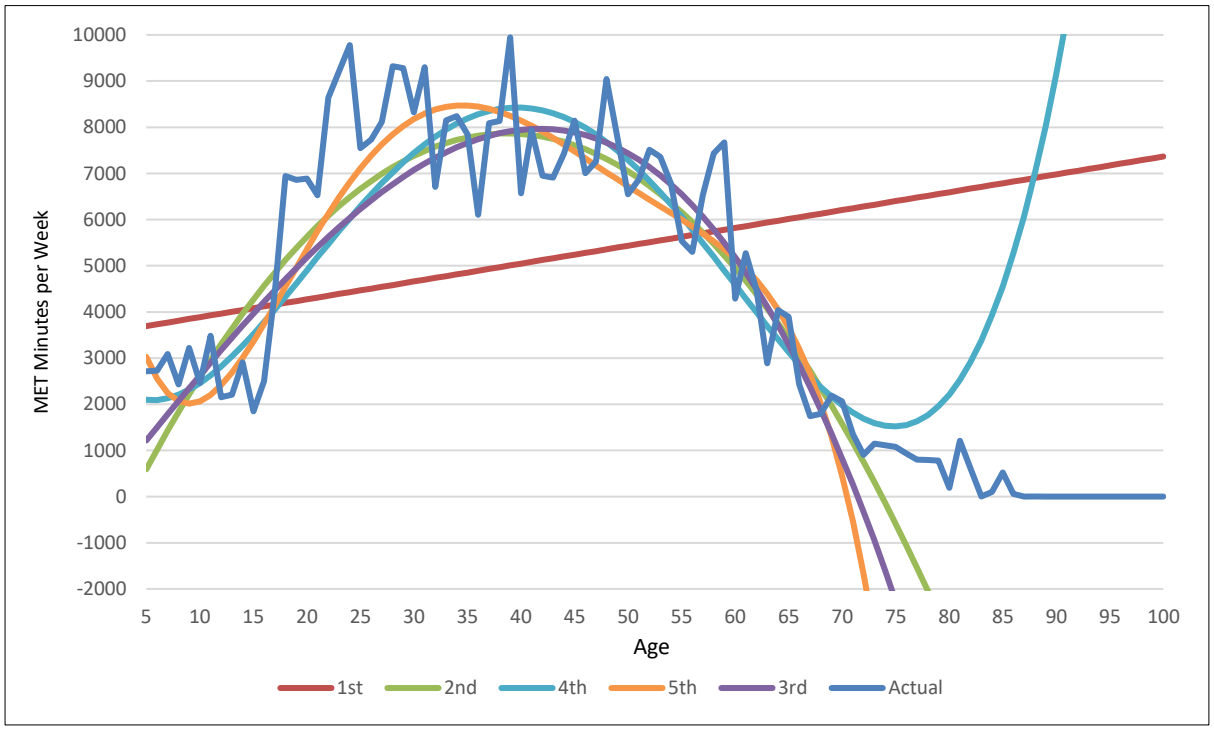


Figure 3.8 - Line graph showing the relative fit of degrees of polynomial compared to raw data for the Male Active stratum

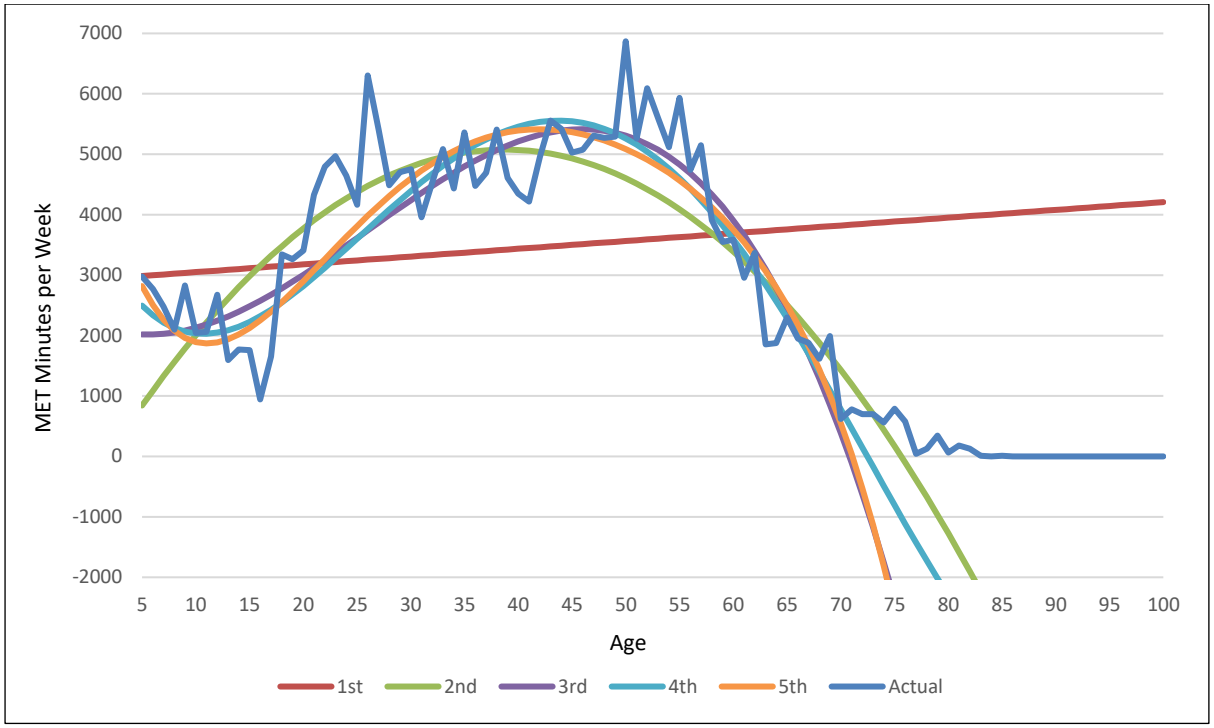


Figure 3.9 - Line graph showing the relative fit of degrees of polynomial compared to raw data for the Female Active stratum

The curve fitting process revealed a consistent issue with all polynomials with the exception of the linear function, in that there was a substantial loss of fidelity once the curve approached 70 years of age. The curves either continued down below zero, which is an impossibility, or an overfit of the data would steer the curve into an exponential increase, which is again not credible. As a result, the curve was adapted to introduce a forced exponential decay at 65 years of age in order to more accurately represent the data, again with examples shown in Figure 3.10 and Figure 3.11 and the full series of graphs presented in Appendix 39 to Appendix 46. These adapted cubic polynomials were then applied across all strata in order to ascertain physical activity levels by age, sex, and physical activity strata.

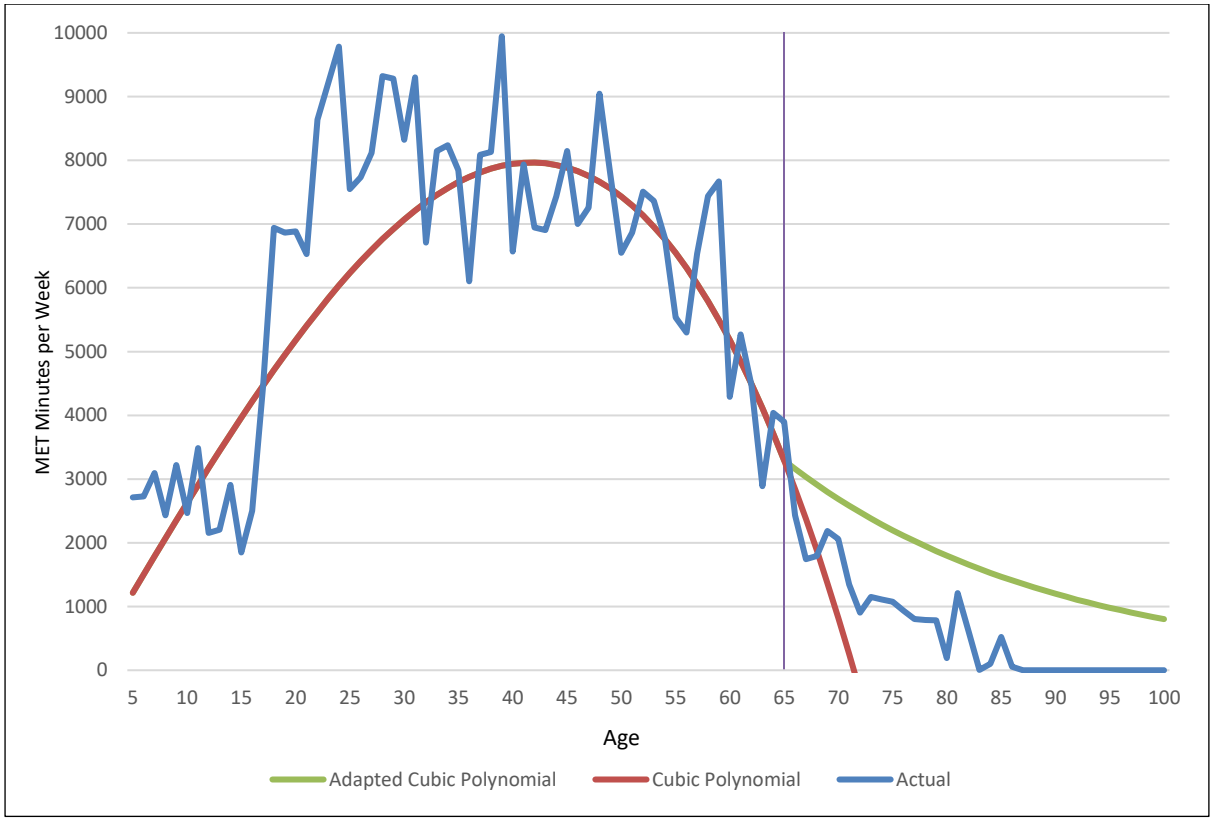


Figure 3.10 - Line graph showing actual data, cubic polynomial, and cubic polynomial with forced exponential decay after 65 years for Male Active stratum.

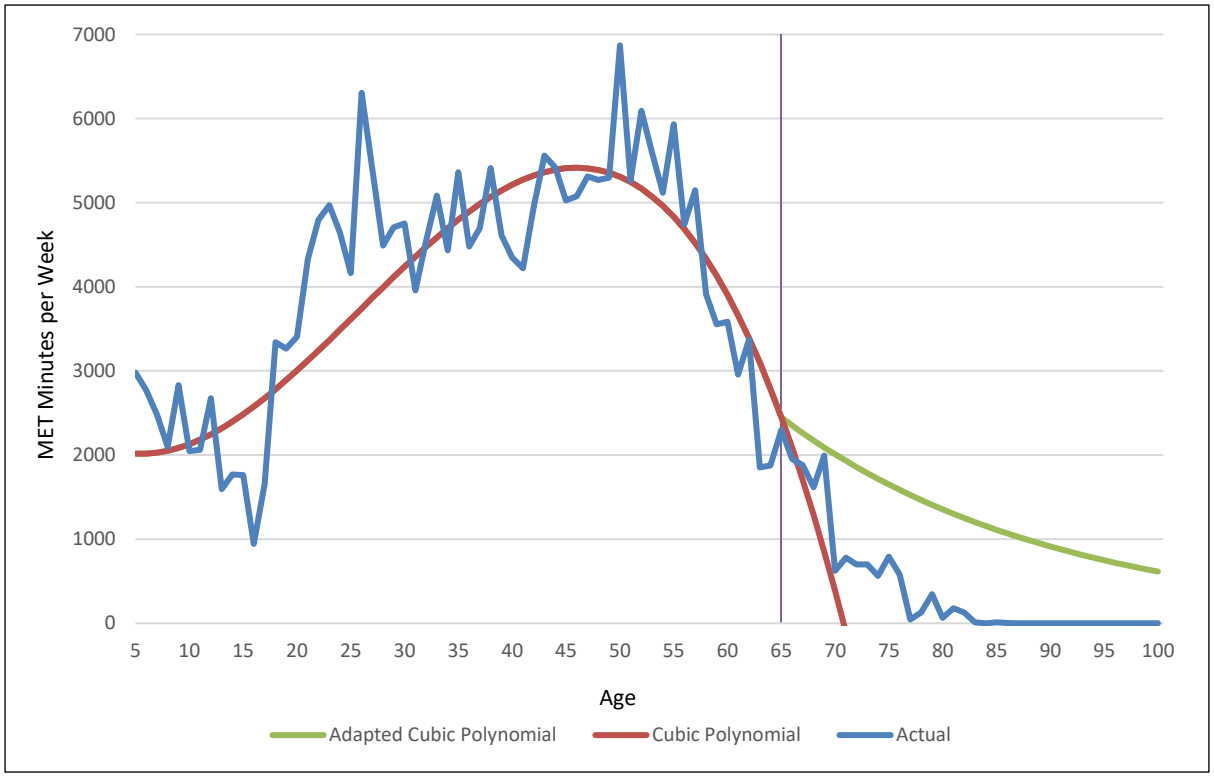


Figure 3.11 - Line graph showing actual data, cubic polynomial, and cubic polynomial with forced exponential decay after 65 years for Female Active stratum.

3.9.6. Relative Risks by Physical Activity Level

In order to apply differentiated relative risks to each disease state within each physical activity strata, these relative risks were adjusted by level of physical activity within each of the ten strata. This process was completed by calculating independent raw population impact fractions (PIF's) for each disease outcome, by age, sex, and physical activity strata, by applying the relevant physical activity level within the formula:

$$PIF_i = 1 + \beta_i \times a^{0.25}$$

Where β represents the beta for each risk curve trajectory and a represents a point estimate of physical activity in MET hours/day for age and sex. All PIF's were then divided by the PIF for the Inactive strata in order to standardise the estimates against this comparator, providing a disease risk by level of physical activity relative to inactivity. For the remaining additional strata, involving comparatively higher point estimates of physical activity levels, incidence and mortality, the risks are consequentially reduced according to the disease specific trajectories and completes the specification of the baseline model upon which hypothetical interventions are applied.

3.9.7. Application of Intervention Scenarios

With the epidemiological data, the physical activity data, and the relative risk estimates complete, the baseline model was fully parameterised. This then permitted the alteration, or perturbation, of physical activity trajectories in order to simulate the effects of specific intervention strategies on the baseline data and determine their effect on the key outcomes identified above. For each scenario a new set of proportional multi-state life tables were specified, one for each of the planned intervention scenarios in addition to the baseline models for each of the ten strata. Specifying all the models to operate in parallel in this manner allowed their outputs to be analysed and compared directly. For each scenario, the physical activity levels were altered in accordance with the modelled 'front ends' derived either from evidence from systematic review (Chapter 6) or individual intervention studies (Chapter 7), or were specified by hypothetical outcome scenario (Chapter 8).

3.10. Uncertainty and Sensitivity Analysis

Briggs, Sculpher, and Buxton (1994) specify four types of uncertainty in economic evaluation of clinical data, taken to broadly reflect the modelling of such data to outcome-based analyses. These comprise: variability in sample data, which essentially represents the specificity of the pooled differences between the intervention and control groups from individual trials within a meta-analysis, including sample group heterogeneity; generalisability of results, including the external validity of the imposed treatments; extrapolation of data, including any assumptions, smoothing and function fitting employed in the modelling process; and, selection of analytical methods, which largely addresses how the choice of analytical method may systematically influence the outcome estimates, but also to some extent concerns any disagreement on the most appropriate method by which a particular problem context should be modelled, also termed 'structural' uncertainty (Barendregt, 2009).

The addressing of uncertainty within the model followed a framework by Briggs et al. (1994), who proposed four types of sensitivity analysis. Firstly, simple sensitivity analysis was conducted on single parameters, allowing them to vary in a deterministic manner. Where source data allow, this variation occurred from a point estimate and deviation along a known distribution. Where parameters are independent, variation in single inputs produce informative data on the sensitivity of the outcomes to specific parameters or assumptions. To complete the analysis, the model is run numerous times, allowing the specific parameter to vary in each iteration and storing the outcomes of interest. The results from this analysis are reported in a tornado plot, depicting the variation in outcome measure according to uncertainty in the input estimates.

Secondly, threshold analysis is a means by which to determine the point of variation within the parameters that leads to a change in the overall conclusion within a study (Briggs et al., 1994). In the case of threshold assessment against a continuous outcome, such as physical activity, care must be taken to assign and justify a specific and meaningful cut-off. Thirdly, analysis of extremes utilises the best- and worst-case scenarios, most often in cost analysis, in order to provide confidence in

treatment effectiveness. This approach is particularly useful when parameters are assumption-driven, rather than data-driven, and allow the examination of 'optimistic', 'realistic' and 'pessimistic' scenarios, although there is no concept of how likely these scenarios are to occur.

Lastly, probabilistic sensitivity analysis addresses this weakness by permitting the assignment of distributions and ranges to each parameter. An analysis is then run over numerous iterations in which a random point estimate is selected from the determined ranges and the permutations in outcomes of interest for a given scenario are recorded. This form of cumulative iterative analysis, or Monte Carlo analysis, provides a mean point estimate with confidence intervals.

3.10.8. Addressing Uncertainty

Uncertainty of outcomes is inevitable in any modelling study, and there is a requirement to address this inevitability in a systematic and transparent manner (Epstein, 2008). For the core model used within the present thesis, variability within the sampling data, or parametric uncertainty, was addressed through both simple and probabilistic sensitivity analysis. Within simple sensitivity analysis, individual parameters were inspected for variability on outcomes of interest, with the input-output ratios quantified and presented in graphical format, using the Ersatz (Barendregt, 2009) software package in conjunction with the core Excel model. This software also permits a stochastic sensitivity analysis to be completed on the input parameters against the outcome estimates, thereby quantifying the extent of variation around the deterministic point estimate for each outcome.

Estimate	Point Estimate (95% CI's)	Applied to	Source	Adjusted for	Distribution
Myocardial Infarction	0.75 (0.62, 0.89)	Incidence, Mortality	Wahid et al. (2016) meta-analysis of	Age, sex, adiposity	Lognormal
Stroke	0.76 (0.66, 0.86)	Incidence, Mortality	Wahid et al. (2016)	Age, sex, adiposity	Lognormal
Type 2 Diabetes	0.64 (0.57, 0.73)	Incidence	Holden et al. (2013) retrospective cohort study	Age, sex	Lognormal
Bowel Cancer	0.87 (0.80, 0.95)	Incidence, Mortality	Wahid et al. (2016)*	Age, sex, adiposity	Lognormal
Breast Cancer	0.93 (0.91, 0.95)	Incidence, Mortality	Wahid et al. (2016)*	Age, sex, adiposity	Lognormal
Uterine Cancer	0.73 (0.58, 0.93)	Incidence, Mortality	Moore et al. (2016) meta-analysis of 9 prospective cohort studies (5346 cases)	Age, sex, smoking status, education, ethnicity	Lognormal

Table 4 - Table showing the specific disease estimates used to parameterise the model, including confidence intervals, etc plus uncertainty analysis

**Unpublished additional analyses conducted within the Wahid et al. (2016) study*

Specific to the present model, the input parameters under investigation within the uncertainty analysis are presented both in Table 4, which lists the disease-specific relative risk estimates used to parameterise the back-end of the model, and in Table 5, which lists the hypothesised increases in physical activity applied within the counterfactual scenarios. Simple sensitivity analysis was conducted by allowing each relative risk estimate in turn to vary stochastically along the parameterised distribution, over multiple iterations in order to produce confidence intervals for the output estimate.

The psychical activity estimates were allowed to vary at the same time, as the estimates inform sub-models that run independently within the model. A cumulative stochastic sensitivity analysis was then conducted by allowing all parameters to vary within the same analysis, again for multiple iterations.

Physical Activity Scenario	Point estimate in MET mins/week (CI's)	Source	Adjusted	Distribution
Meta-analysis				
Population	5.27 (-12.99, 23.51)	Sims et al. (2015) meta-analysis of 10 controlled studies (3011 cases)		Normal
Treatment	22.85 (-4.14, 49.89)	Sims et al. (2015) meta-analysis of 2 controlled studies (201 cases)		Normal
Daily Mile				
4-9 Years	332.48 (232.79, 432.16)	Morris, Daly-Smith, Archbold, Wilkins, and McKenna (2019)		Normal
10-11 Years	368.28 (257.86, 478.70)	Morris et al. (2019)		Normal
MEND				
5-7 Years	889.46 (368.05, 1441.54)	Sacher, Wolman, Chadwick, and Swain (2008) RCT		Normal
8-16 Years	1226.84 (582.75, 1840.26)	Sacher et al. (2010)		Normal

Table 5 - Model parameter estimates for physical activity inputs, sources, distributions, etc

The external validity of the model is partially addressed by an explicit and transparent construction of the core model and the front-end counterfactuals that represent the simulated interventions. In addition, graphical comparisons between sample and modelled data are provided as evidence for the accuracy of the structure of the model (see Figure 3.4). In any model, whether a formal statistical

model or the dedicated model used in the current project, levels of abstraction away from both the sample estimates and the underlying 'reality' of the population of interest are inevitable in order to focus on the specific research question, to create a manageable project, and to produce a comprehensive data set. It is normal modelling practice to both smooth the raw data and to fit the data to a curve. However, while this represents a further step of abstraction, the modelled outcomes can be compared against known data sets or even other models in an attempt to demonstrate external validity, and these triangulation comparisons were completed in the intervention-specific chapters to follow.

3.11. Chapter Summary

This chapter set out the process by which the model, comprising the core methodological component of the thesis, is selected and constructed. The selection and adaptation of a multi-state life table, a robust and established model format, is described and justified along with reference to a selection of major projects and subsequent publications that have utilised a similar approach. The epidemiological parameters are presented for each health outcome of interest, with the estimates for physical activity levels and subsequent relative risks, along with a description of how these were encoded within the model. Finally, a description of how uncertainly was handled within the model was presented. The process of construction and adaptations produced the current model, which represents a globally unique model for the analysis of physical activity. In conclusion, the methodological approach taken within this thesis is one familiar to large population health studies in the past and, although some modifications were required, the strengths and weaknesses of the approach are well-documented.

Chapter 4 - Baseline Model Outputs

4.1. Chapter Overview

The present chapter serves two purposes. Firstly, an analysis of the model structure is presented as a justification for the methodological decisions and associated rigour within the modelling process. Secondly, an interim evaluation of the baseline outputs of the core model is presented, including triangulation with existing datasets. Overall, the objective for this chapter is to assess the strengths and limitations of the core model prior to the application of the counterfactual scenarios as described in the subsequent chapters.

4.2. Baseline Physical Activity Estimates

The process for the derivation of the physical activity estimates, by strata, age, and sex, is described in Chapter 3. However, a closer scrutiny of these estimates across the lifespan is required in order to fully evaluate the accuracy of the model. This evaluation allows both the extent to which the model accurately represents the wider reality within the English population, and the identification of any specific areas of reduced fidelity within the model by which to inform a more precise evaluation of the findings.

A series of graphs within Chapter 3 present details on the specific functions that were derived to represent each stratum of physical activity for each sex. The physical activity levels of the two sexes are therefore disaggregated into ten distinct strata which form the basis of the core model. Chapter 3 also described the adaptation of the selected cubic polynomial curves to more accurately represent the physical activity profiles in older age groups. Figure 4.1 and Figure 4.2 present the strata-disaggregated physical activity profiles over the life span for males and females respectively.

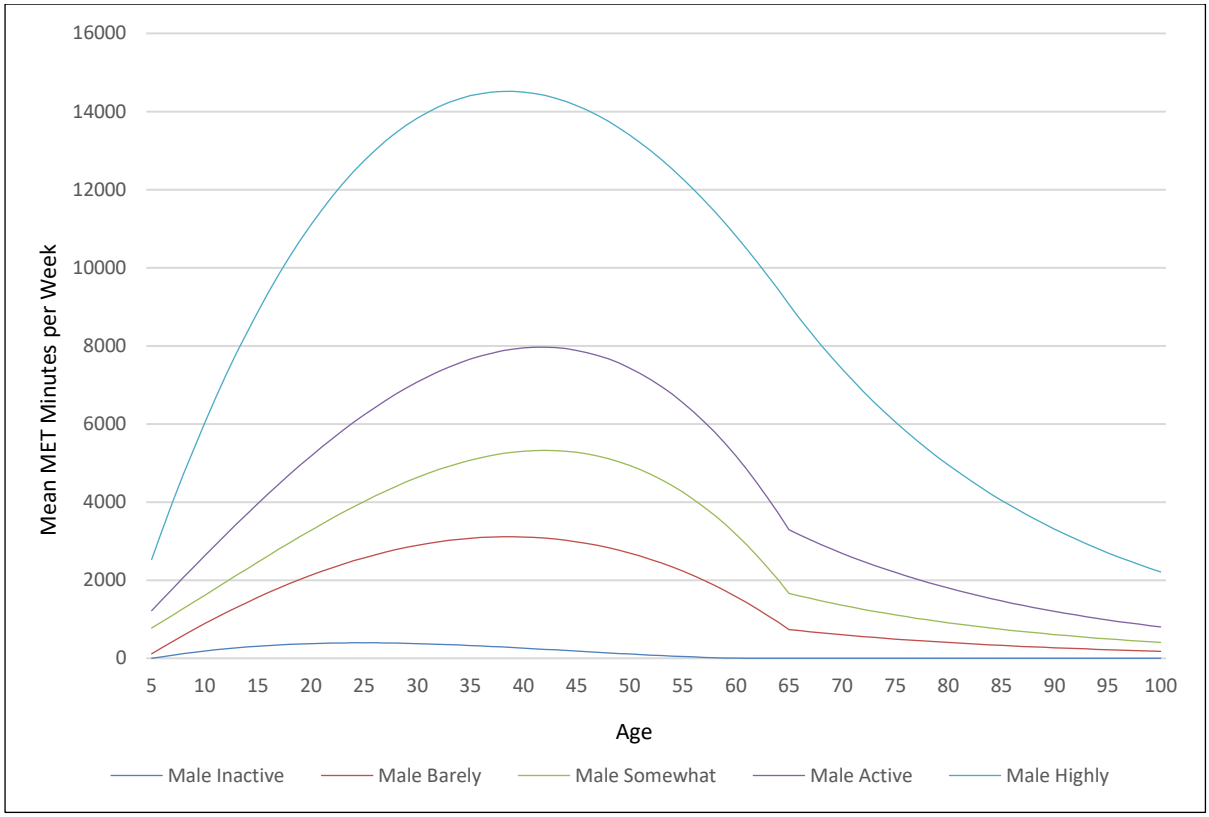


Figure 4.1 - Line graph showing physical activity level trajectories for male strata through the life course

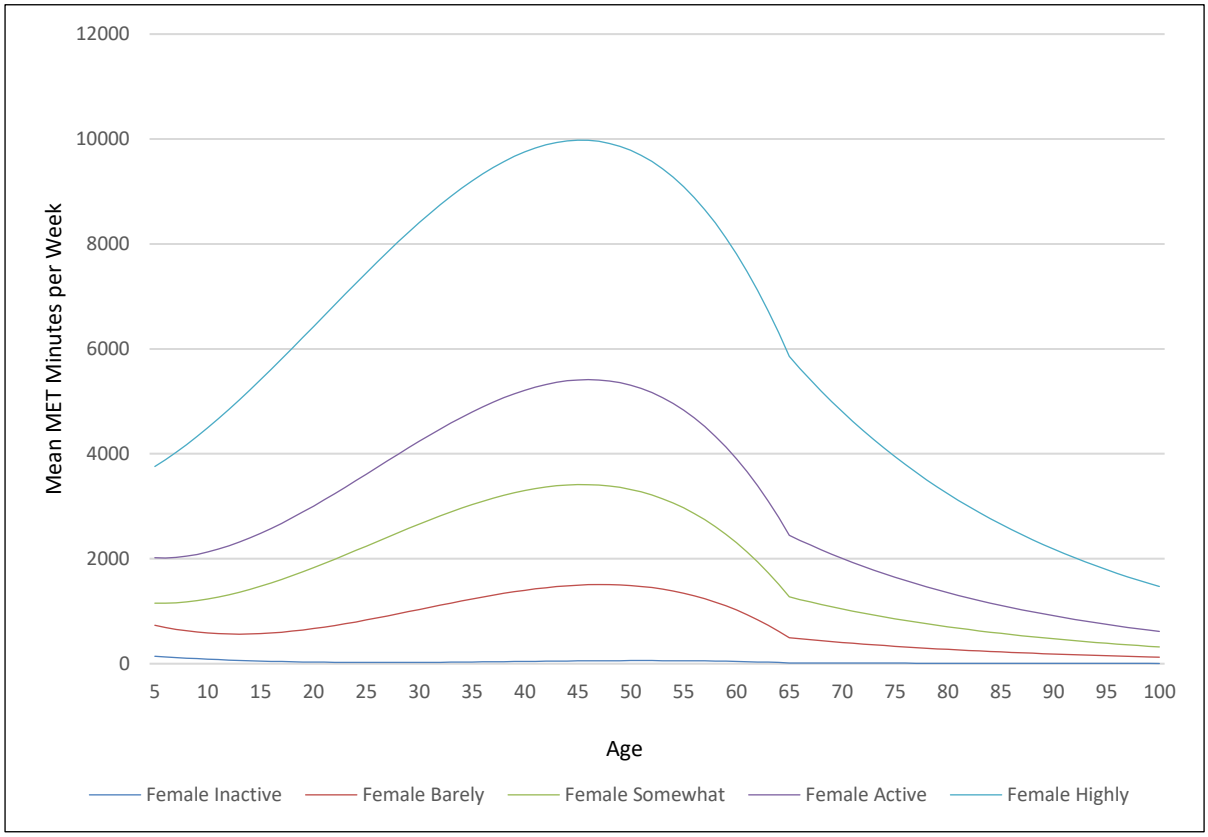


Figure 4.2 - Line graph showing physical activity level trajectories for female strata through the life course

In terms of an initial assessment of plausibility these trajectories appear intuitively valid, for instance an inspection of the extremes the highest single example of physical activity expenditure within the dataset is 14516 MET minutes per week, specifically for 39-year-old males. This figure, assuming the activity is evenly dispersed across the seven days of the week, constitutes an average of 2.88 MET minutes across twelve hours of the day, an energy expenditure broadly equivalent to slow walking (Ainsworth et al., 2011), while the lowest values approach zero. Furthermore, the trajectories do not intersect or overlap at any point. The baseline physical activity profiles therefore possess face validity and it is appropriate to proceed with additional complexity within the model.

4.3. Baseline Outcome Estimates

The specification of the model structure and disease-specific inputs which determine the health outcomes are presented in Chapter 3, along with a description of the process by which the age, sex, and physical activity specific estimates were derived and applied to the core proportional life table model. Chapter 3 also provided a description of the accuracy by which the independent sources of data were resolved into a cohesive group of cohort-specific estimates for the model using DisMod II. However, an additional triangulation of the model outputs against known prevalence in the English population is also informative.

A visual comparison of the estimates for myocardial infarction and for stroke are provided in Figure 4.3 and Figure 4.4 respectively. The comparison figures were drawn from estimates from the Office of National Statistics (ONS) and from the Health Survey for England (HSE), presented in a paper by Bhatnagar, Wickramasinghe, Wilkins, and Townsend (2016). The ONS data are for the United Kingdom, while the HSE data are specific to England. The data sets were drawn from 2011 as this was the last occasion prior to the focus year within the model (2013) at which both were collected. Both graphs indicate that while the population-level estimates are largely comparable, and the pattern of increasing prevalence with age is clearly visible. While there is a tendency within the model to over-

estimate the prevalence of both myocardial infarction and stroke in the older age-groups, this is likely due to a loss of fidelity within older age groups due to declining sample size.

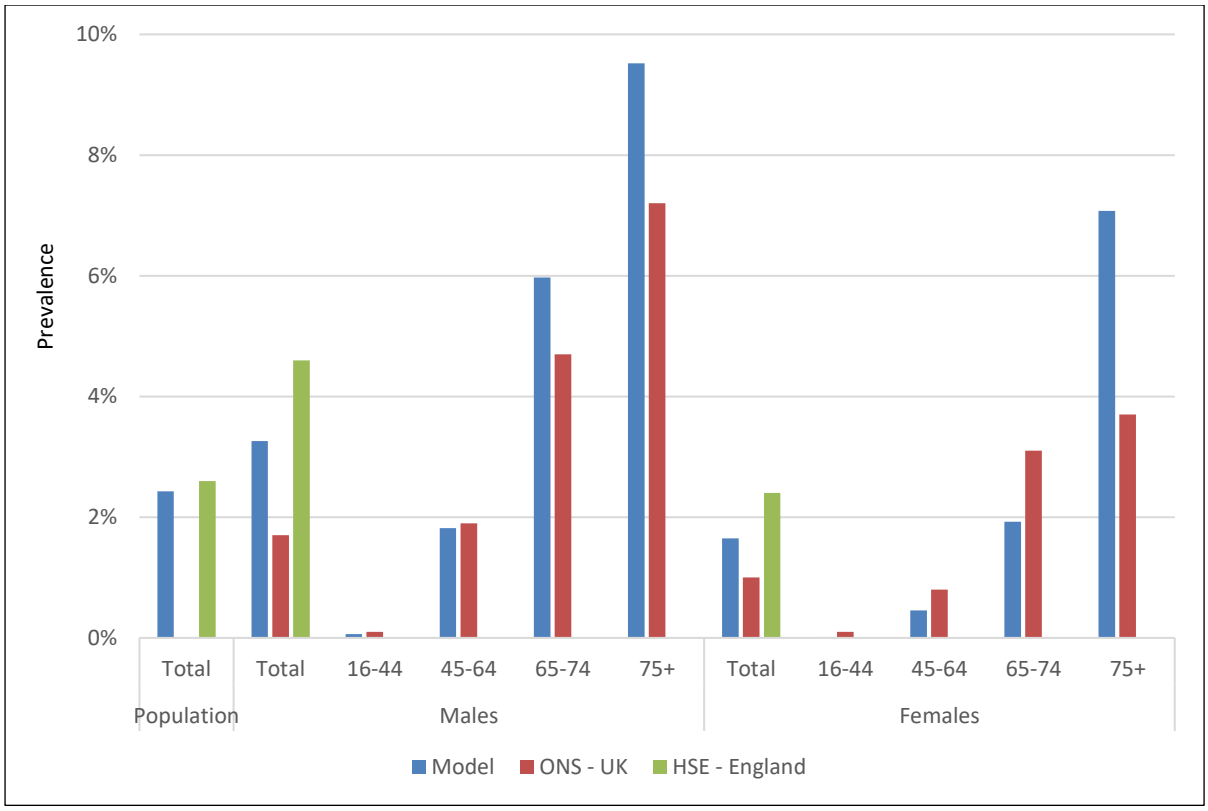


Figure 4.3 - Column graph showing the model outputs for prevalence of myocardial infarction against data from the Office for National Statistics (UK) and Health Survey for England (England) from 2011 provided in Bhatnagar et al. (2016).

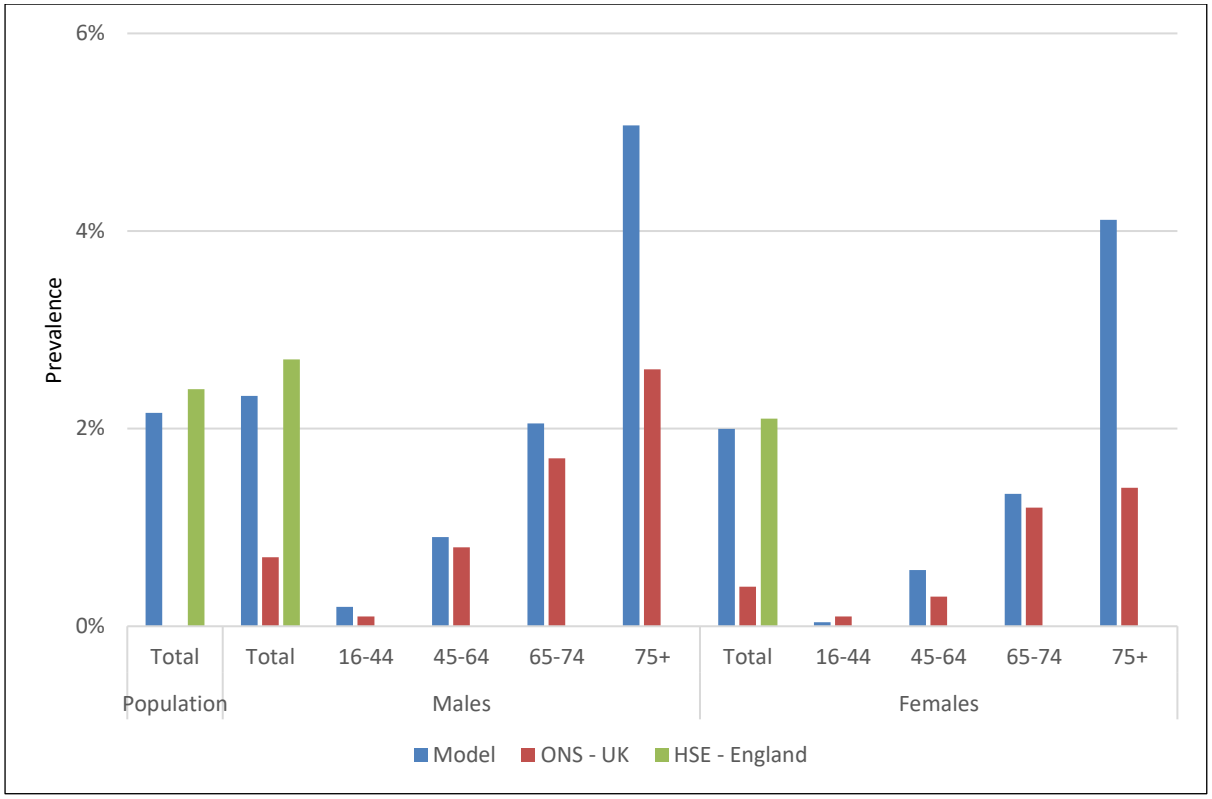


Figure 4.4 - Column graph showing the model outputs for prevalence of stroke against data from the Office for National Statistics (UK) and Health Survey for England (England) from 2011 provided in Bhatnagar et al. (2016)

A comparison between model outputs and reference data on the prevalence of type 2 diabetes is presented in Figure 4.5. The comparison data was produced by Public Health England (PHE) by modelling the trends in type 2 diabetes prevalence within the English population from previous HSE iterations and then projecting these trends forwards to provide a forecast. The PHE figures included all diabetes, and were adjusted to only represent type 2 diabetes by reducing them by 10% in accordance with the broad estimate of relative contribution to overall prevalence (González, Johansson, Wallander, & Rodríguez, 2009). Type 1 diabetes was removed as physical activity is not implicated in the development of this disease, in which the immune system mistakenly destroys insulin-producing cells in the pancreas (González et al., 2009). Overall, the prevalence estimates from the core model closely match those from the PHE projections in both pattern and value. The model appears to slightly underestimate the difference in relative prevalence between males and females, with this difference being more pronounced in the real population.

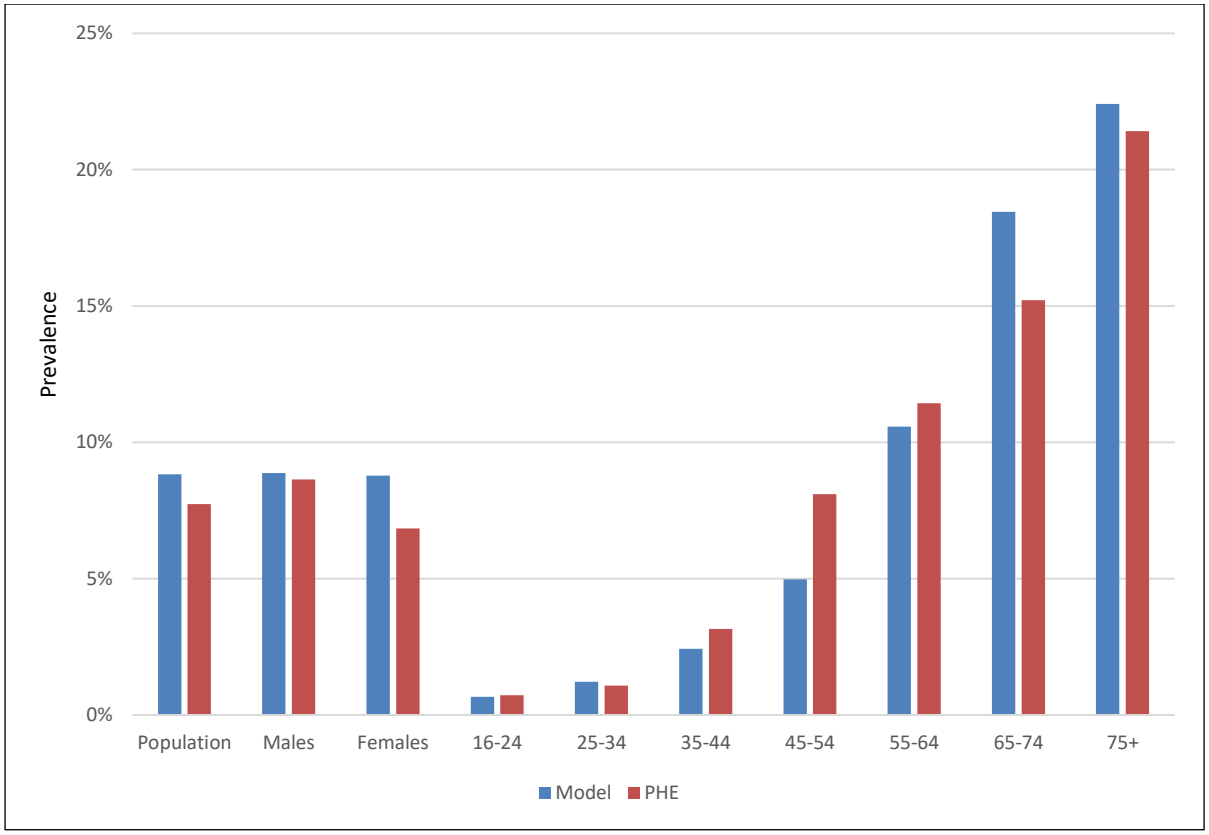


Figure 4.5 - Column graph showing the comparison between model outputs and adjusted diabetes prevalence estimates from the Public Health England Diabetes Prevalence Model.

Overall, in terms of both face validity and reference to available data on health outcomes, the model outputs appear to provide a credible baseline upon which to build the counter-factual scenarios. The physical activity estimates, derived from disaggregated point estimates taken from the HSE 2012 follow a logical pattern over the life-course and do not intersect. The totals estimated for each disease outcome also match up well, although care will need to be taken when comparing outcomes for specific age bands.

4.4. Baseline Profile of England

The baseline outputs from the core model specify the outcomes against which each subsequent scenario is compared. The primary outputs constituting the main outcomes of interest in these analyses are life expectancy, years of life in disability, and years of life lost (or gained). Life expectancy and years of life in disability estimates are presented in Table 6; years of life lost is a measure only

appropriate for direct comparisons. Note that total life expectancy, i.e. as if from birth, is approximately five years greater than that stated in the table.

Output	Estimate (years)	Lower uncertainty interval	Upper uncertainty interval
Life expectancy at five years old			
Cohort	77.37	77.35	77.40
Males	75.17	75.17	75.17
Females	79.69	79.69	79.69
Years of life in disability per 100,000 population			
Cohort	1009153.17	999140.64	1013930.64
Males	919546.10	906179.36	925822.14
Females	1098738.24	1092108.84	1102059.44

Table 6 - Primary outputs and uncertainty intervals (2.5th & 97.5th percentiles) from the application of the meta-analysis estimate for population interventions scenario, presenting changes in life expectancy at five years of age and years of life in disability per 100,000 population, using multivariate parameters.

The profile for life expectancy at five years of age is presented in Figure 4.6. The difference between males and females is clearly visible, as is the case for the English population. In addition, a life expectancy gradient, showing a positive association with physical activity level, is clearly observable in the graph. Overall, deterministic life expectancy estimates generated by the model are comparable to those from the ONS for males, with a model output of 80.33 compared to an ONS figure of 79.55, and females, with a model output of 84.57 compared to an ONS figure of 83.20 (Office for National Statistics, 2014). The slight differences in both estimates in favour of the figures derived from the model are expected given that the model presents period estimates, which constitutes a synthetic projected estimate from cross-sectional annual data from a single year (in this case 2013) and assumes all individuals are subject to these fixed rates throughout their lives (Goldstein & Wachter, 2006). In reality, however, people are subject to changing rates throughout their lifespan and therefore the ONS presents cohort estimates, which build life expectancies through a combination of layering

historical rates and projections about likely, typically positive, changes to future rates (Goldstein & Wachter, 2006).

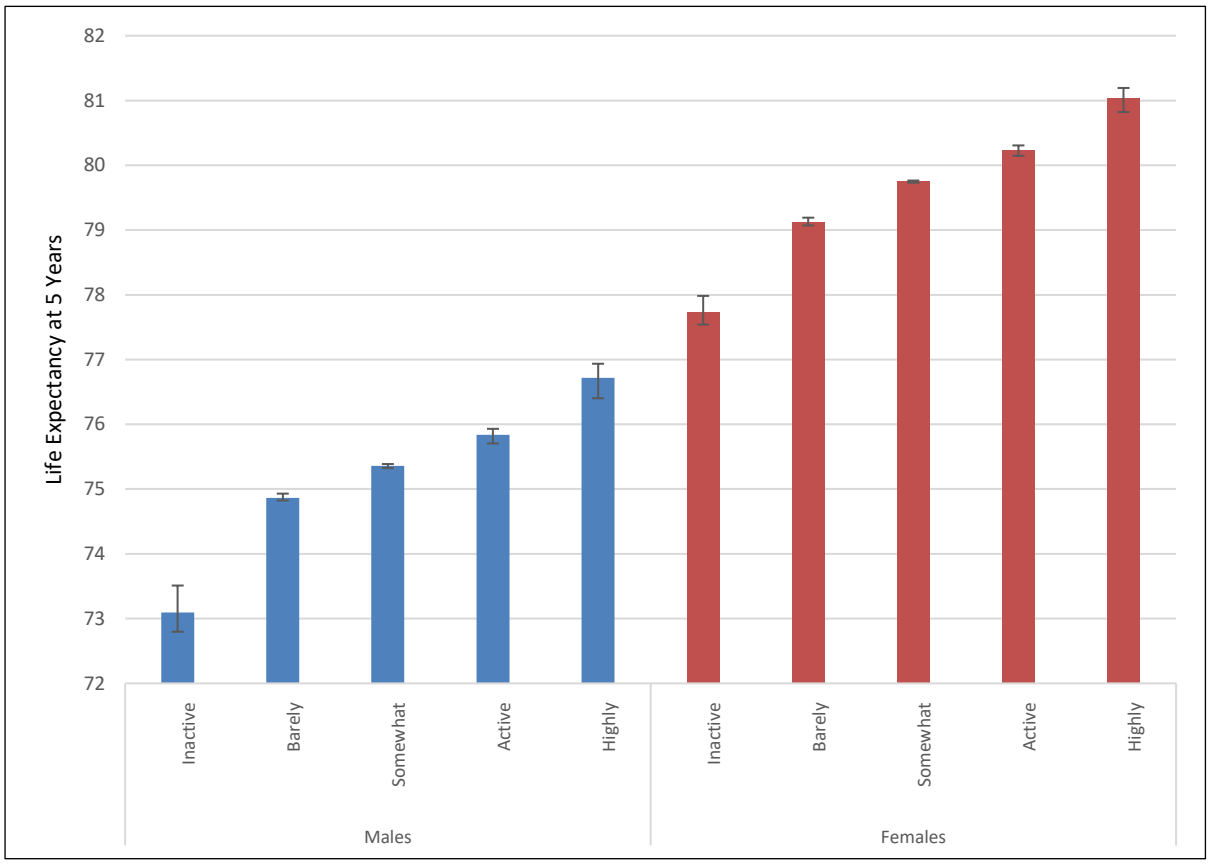


Figure 4.6 - Column graph showing the relative life expectancy estimates and uncertainty intervals (2.5th & 97.5th percentiles) for each physical activity strata within the model, at five years of age.

The cohort profile for years of life in disability, which is an estimate of the total number of years spent alive but ill with at least one of the diseases of interest, is presented in Figure 4.7. Once again, the profile follows an expected pattern of decline as physical activity levels increase, showing years of life in disability to be negatively associated with lifetime levels of physical activity. Females appear to experience slightly a higher number of years of life in disability, potentially due to additional diseases of interest, longer lifespan, lower average levels of physical activity, or a combination of all three factors.

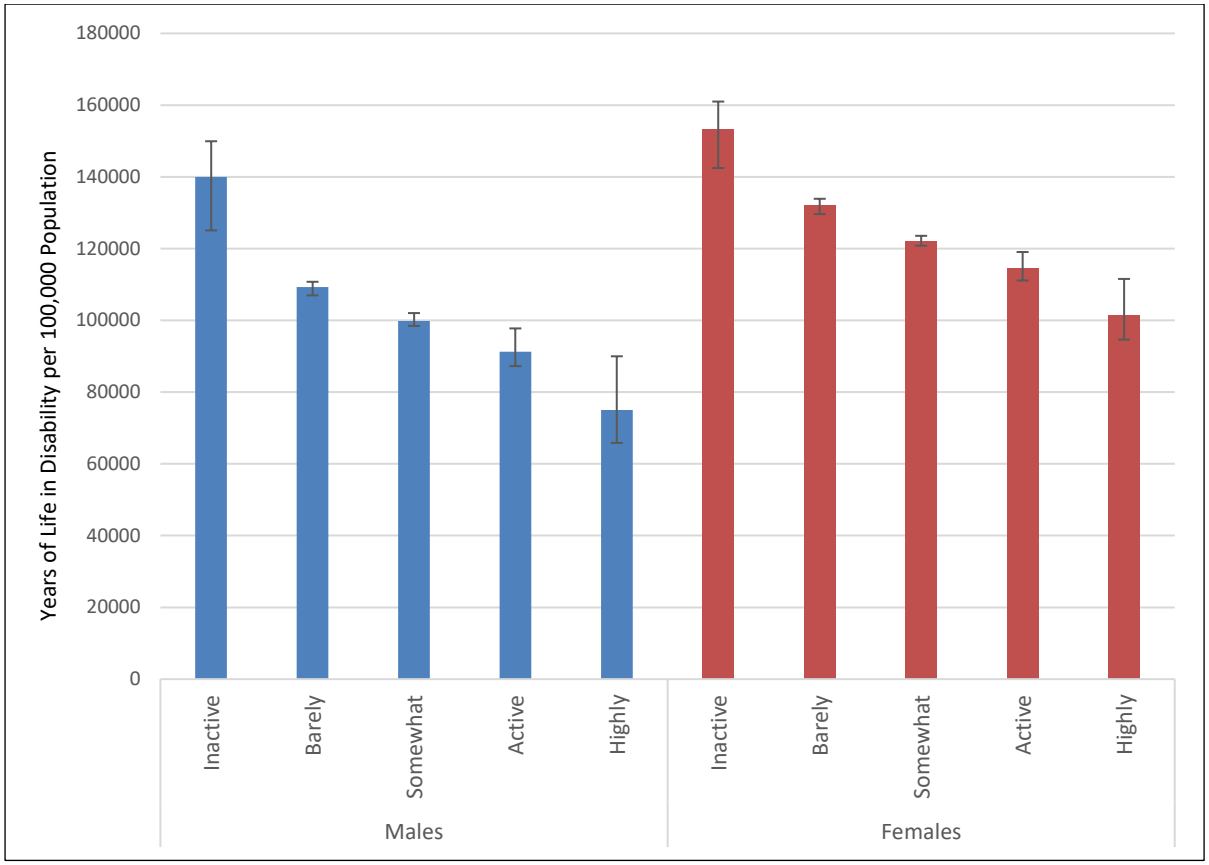


Figure 4.7 - Column graph showing respective years of life in disability per 100,000 population and uncertainty intervals (2.5th & 97.5th percentiles) for all physical activity strata within the model.

With the establishment of a credible baseline scenario, in which the physical activity estimates and disease specific parameters are appropriate, a brief analysis on these data becomes possible. Figure 4.8 presents the baseline survival curve within the simulated cohort along with the proportion of live cases who are either well or ill. The lower line represents incidence, with the upper line representing mortality. Overall, Figure 4.8 reinforces the interpretation from Figure 4.6 above, that the model follows a clearly appropriate pattern.

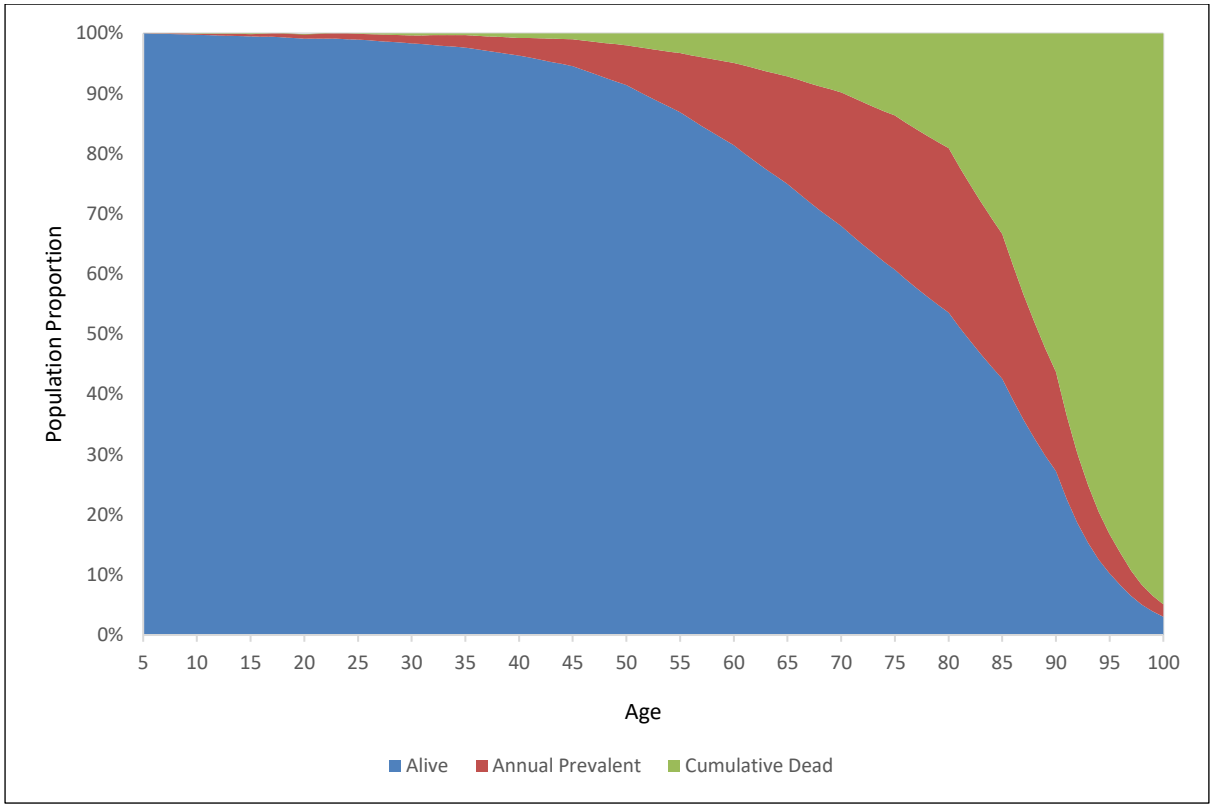


Figure 4.8 - Area graph showing the survival curve and relative wellness and illness within the baseline simulated cohort over the modelled life-span.

A more detailed presentation of the relative prevalence of the outcomes of interest within the live population is presented in Figure 4.9 and Figure 4.10 for males and females respectively. The area graphs demonstrate the progression of disease prevalence across the life-span, although care should be taken not to interpret these figures as absolute, as clearly the live population is reducing with each year.

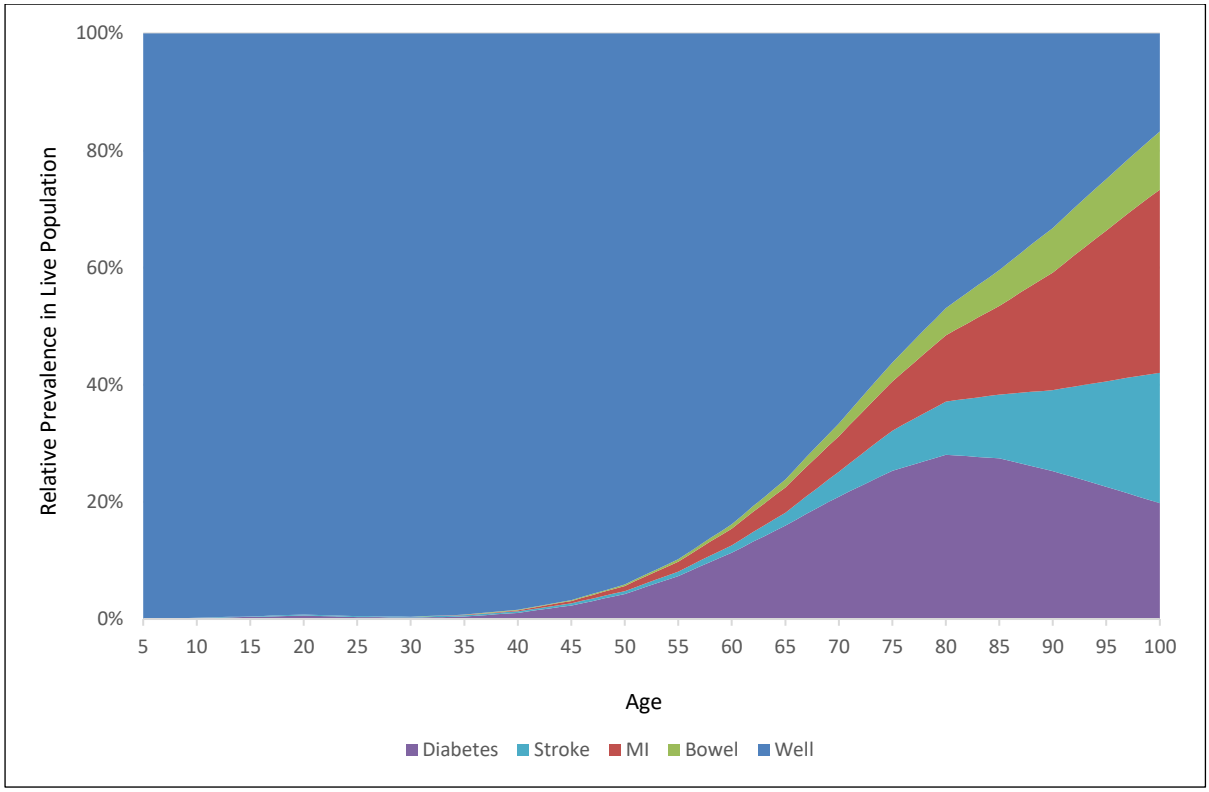


Figure 4.9 – 100% area graph showing the relative prevalence of specific disease outcomes over the life course within the live male cohort.

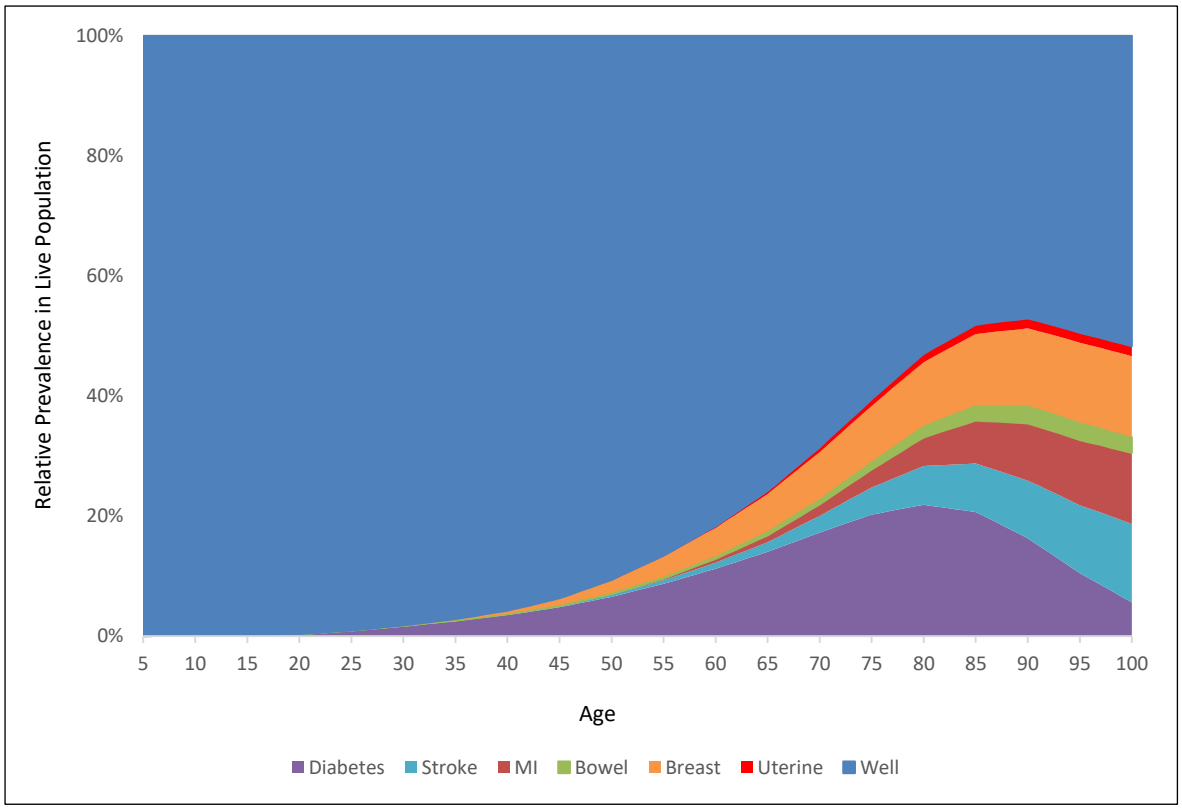


Figure 4.10 – 100% area graph showing the relative prevalence of specific disease outcomes over the life course within the live female cohort.

The figures and commentary above provide an overview and interim evaluation of the baseline outputs from the core model specified in Chapter 3. Overall, the model produces appropriate and intuitive outputs that correspond favourably to known data for the target population. The input parameters and model structure would therefore appear to be sufficiently valid to withstand the application of counter-factual scenarios and subsequently produce meaningful outputs.

4.5. Refinement of Uncertainty and Sensitivity Analysis Process

The method for analysis of uncertainty within the outputs is described and justified in Chapter 3. However, an initial observation of the raw results was needed in order to specify the number of iterations required for an appropriately powered Monte Carlo analysis. An initial stochastic run of the core model was therefore completed with 5000 iterations. Figure 4.11 shows the confidence interval stability for the estimate of change in life expectancy at five years of age by each counterfactual scenario, while Figure 4.12 shows the confidence interval stability for the estimate of change in years of life in disability by each counterfactual scenario. Graphs for additional outcomes, including disease specific estimates, are presented in Appendix 47 to Appendix 53. All graphs consistently demonstrate that confidence interval stability is achieved within 2500 iterations. Subsequent utilisation of a 2500 iteration Monte Carlo analysis is therefore used for sensitivity and uncertainty analysis throughout the thesis.

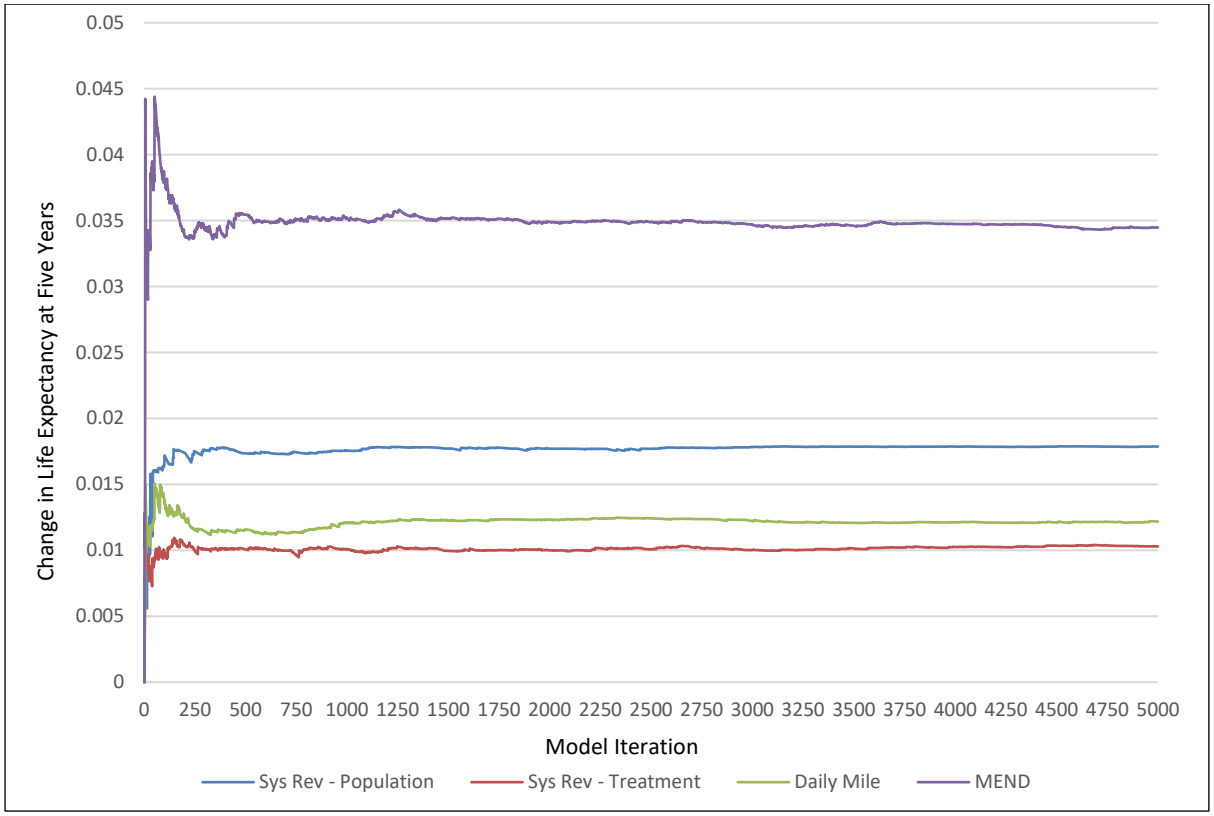


Figure 4.11 - Line graph showing stability of confidence interval for life expectancy at five years of age against number of iterations for each counterfactual scenario.

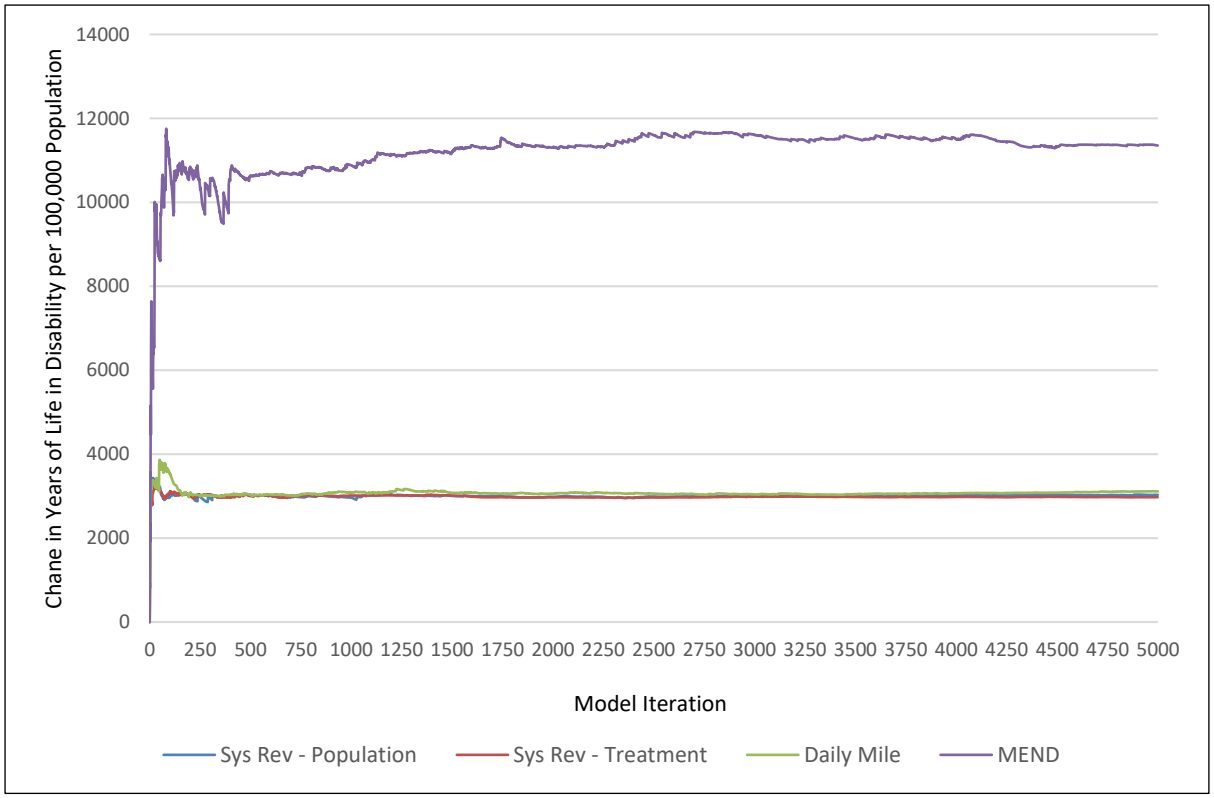


Figure 4.12 - Line graph showing stability of confidence interval for years of life in disability per 100,000 population against number of iterations for each counterfactual scenario.

4.6. Baseline Uncertainty and Sensitivity Analysis

In line with the process for sensitivity and uncertainty analysis specified in Chapter 3 and refined above, parametric uncertainty was assessed using 2500 iterations of a Monte Carlo analysis. The uncertainty bars in Figure 4.6 and Figure 4.7 are generated from this process, specifying the 2.5th and 97.5th percentile, while the point estimate itself is produced from a deterministic run of the model. Confidence intervals are also presented for estimates of life expectancy and years of life in disability in Table 6. The contribution of specific input parameters to this uncertainty are presented for life expectancy in Figure 4.13, illustrating little sensitivity to variation in any input parameter, and for years of life in disability in Figure 4.14, suggesting this outcome is most sensitive to variation in type 2 diabetes estimates. Tornado plots for the remainder of the outcomes are available in Appendix 54 to Appendix 59.

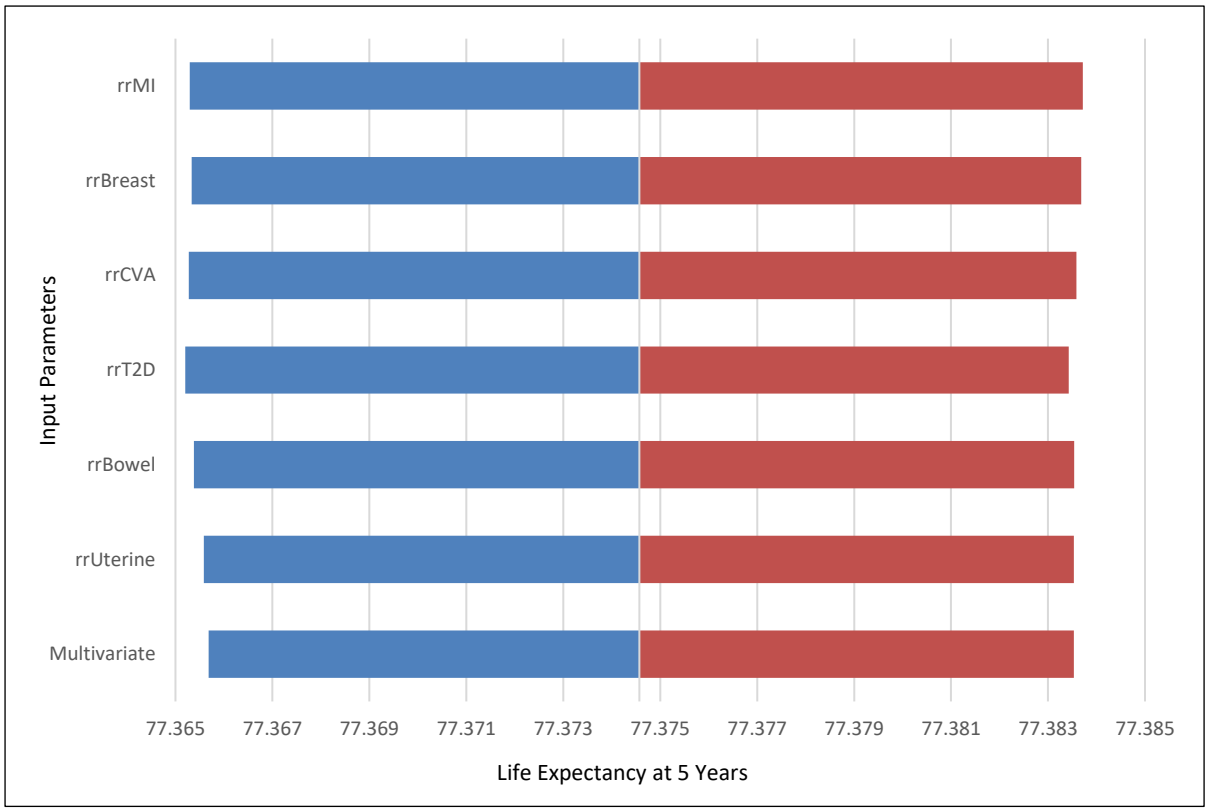


Figure 4.13 - Tornado plot showing the sensitivity of the estimate for life expectancy at 5 years (77.37) due to uncertainty within specific input parameters within the baseline model.

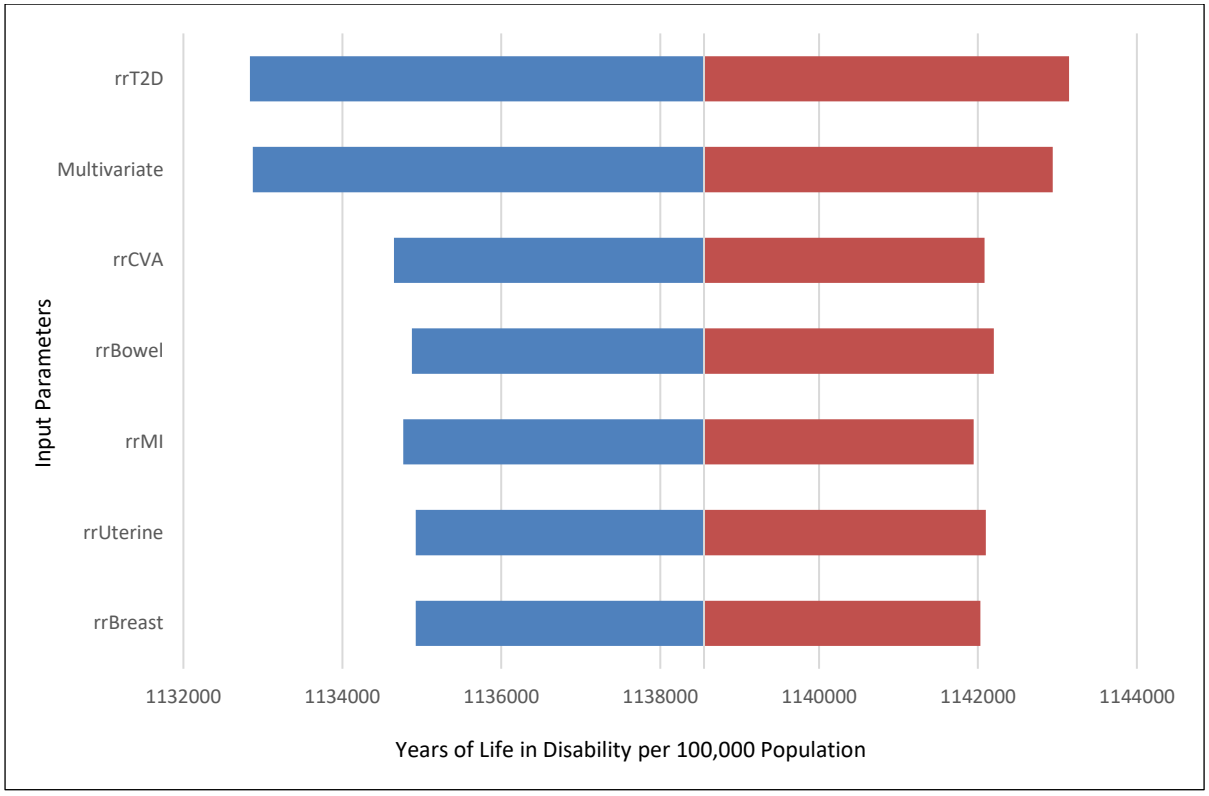


Figure 4.14 - Tornado plot showing the sensitivity of the estimate for years of life in disability (1138552) per 100,000 population due to uncertainty within specific input parameters within the baseline model.

4.7. Chapter Summary

The above chapter provides the first presentation of outputs from the completed model. While the focus of the thesis is primarily on the analysis of counter-factual scenarios, the establishment of a valid baseline is essential against which to evaluate any change. The chapter above therefore provides an important interim evaluation of the model outputs.

Chapter 5 - Systematic Review and Meta-Analysis

5.1. Chapter Overview

In order to proceed with modelling a series of relevant counterfactual scenarios it was necessary to conduct a more detailed review of the pertinent literature from which to specify the initial front ends to be applied within the baseline model. The present chapter provides the justification, methods, findings, and conclusions from a systematic review conducted as part of the overall scheme of work for this thesis. In particular, and with a clear focus on the requirements of modelling, the systematic review specifically concentrated on published results from studies that included sufficient methodological rigour from which to parameterise accurate and meaningful counterfactual scenarios.

The following chapter, therefore, provides both a systematic review of the most relevant studies as well as a meta-analysis of included studies that forms the basis for the formal derivation of the initial counterfactuals. The protocol for this systematic review and meta-analysis was registered on PROSPERO (CRD42014007545) in March 2014 and subsequently published in PLoS One in July 2015 under the title "The effectiveness of interventions on sustained childhood physical activity: A systematic review and meta-analysis of controlled studies" (see Sims et al., 2015).

5.2. Review of Previous Studies

While many previous reviews included criteria that an intervention must last a minimum requirement, and others included stratification by long- and short-term duration of intervention or between measurements, there were no reviews specifically reporting on the longer-term effects of interventions of childhood MVPA. Such a review was therefore warranted to address uncertainty regarding the stability of interventions over time and to compliment tracking studies (e.g. Hayes et al., 2019; Malina, 2001; Telama et al., 2013). The importance of conducting longer-term follow-up studies in childhood interventions has been demonstrated previously (Jones et al., 2011) and was partially addressed through an investigation of school-based intervention follow-up data (Lai et al., 2014). Previous reviews suggested that a minimum of a six-month follow-up period is required to advance

knowledge on the maintenance of behaviour change (Dobbins et al., 2013), which is broadly consistent with the timeframes indicated by Trans-Theoretical Model of Change (TTM) (Prochaska & DiClemente, 1982). However, while measurement of physical activity levels may be captured and may provide an assessment of immediate intervention uptake it supplies little indication of consequential behaviour change; in order to capture this, it is necessary to establish relative physical activity levels in the period once intervention phase has concluded.

The inception of many risk factors have been observed as commencing in childhood (Biddle, Gorely, & Stensel, 2004; Boreham & Riddoch, 2001), with a lack of physical activity leading to impaired childhood health outcomes, increased risk factors, and subsequent ill-health outcomes in adulthood (Ekelund et al., 2012), and a compromised attitude towards physical activity (Biddle et al., 2004; Sallis et al., 2000). As outlined in Chapter 1, physical activity behaviour tracks 'reasonably well' across time, although this relative stability reduces in adolescence and periods of transition (Hayes et al., 2019; Telama, 2009). In addition, evidence indicates that physical activity levels enter a broad decline in later childhood and adolescence (Dumith, Gigante, Domingues, & Kohl, 2011), resulting in insufficient levels of physical activity during the transition into adulthood (Corder et al., 2013; Gordon-Larsen, Nelson, & Popkin, 2004).

In an attempt to reverse the trend of declining physical activity, and consequential increase in disease outcomes and economic burden (Lee et al., 2012; Scarborough et al., 2011), the commissioning of childhood interventions appears to be a logical course of action to address development of formative risk factors and to promote healthy habits and attitudes towards physical activity (Blanchard, Shilton, & Bull, 2013; Dobbins et al., 2013). Interventions have taken either a population approach, with a focus on the reduction of the typical trend towards physical inactivity across a population, or a treatment approach, with a focus on increasing physical activity amongst individuals at an existing high risk, often obese and/or sedentary children.

The effectiveness of interventions to increase childhood physical activity has previously been systematically reviewed; specifically investigating preventative studies (Kamath et al., 2008a; Waters et al., 2011), treatment-based studies (Oude Luttikhuis et al., 2009), school-based studies (Dobbins et al., 2013; Lai et al., 2014), and community-based studies (van Sluijs et al., 2008), as well as comparative policy reviews (NICE, 2010). The magnitude of measured effects on levels of physical activity following intervention is typically small and, considering consistently high levels of heterogeneity, the risk of small sample bias, and an over-reliance on self-report measurement, caution is essential when interpreting positive findings. In addition, reviews have often included studies reporting measurement of physical activity or sedentary behaviour within limited times of day (e.g. school recess, travel time, or the immediate after-school period), thereby often failing to account for potential substitution (Ridgers, Timperio, Cerin, & Salmon, 2014).

These shortfalls were partially addressed in a systematic review by Metcalf et al. (2012) who investigated the effectiveness of interventions on levels of childhood physical activity across 30 controlled studies. Meta-analyses revealed only small-to-negligible effect on levels of Moderate to Vigorous Physical Activity (MVPA) and Total Physical Activity (TPA) immediately following intervention as measured by accelerometry, highlighting the potential for self-report bias in previous reviews and the importance of drawing data from studies specifically reporting whole-day physical activity (Metcalf et al., 2012). However, with the exception of Lai et al. (2014), which focused exclusively on school-based interventions, published reviews provide little detail regarding the maintenance of effects on whole-day physical activity in children and therefore do not account for the potential effects of habit formation (Lally, Van Jaarsveld, Potts, & Wardle, 2010) and stage of change (Marshall & Biddle, 2001).

5.3. Methods

5.3.1. Objectives

Given this specific shortfall in the literature, the primary objective was to conduct a systematic review to explore the effect of intervention on maintained whole-day childhood physical activity.

Furthermore, it was necessary to explore sustained effect sizes following a period of at least six months post-intervention (see Figure 5.1). Admissible interventions were delivered at any time and across any domain, and included both prevention and treatment strategies, but must have reported the effect on MVPA or TPA. In addition, measurement must have been conducted across the whole day, i.e. at least two domains of either leisure-time, domestic, transportation, or occupation/compulsory education behaviour. Where numbers permitted, stratification of MVPA and TPA was planned by age, gender, intervention type, intervention duration, measurement strategy, and treatment vs. prevention to provide a more detailed analysis of the findings.

These objectives were achieved by:

- Conducting a narrative systematic review of peer-reviewed studies meeting selection criteria below
- Conducting a meta-analysis for pooled effects of maintained change in post-intervention MVPA and/or TPA

The *a priori* methods for this review were detailed and registered with PROSPERO (CRD42014007545).

5.3.2. Inclusion Criteria

Peer-reviewed studies were included if they utilised a controlled trial design, irrespective of whether they used randomisation. No minimum or maximum duration of intervention was specified for inclusion, nor was any restriction placed on the personnel or settings involved with the intervention delivery.

The specific inclusion criteria were that each study:

Population

- Described an intervention(s) targeting children/adolescents aged between 5-18 years inclusive. Studies were included irrespective of the weight status of the participants but were excluded if they represented a specific clinical population.

Intervention

- Described an intervention(s) that intentionally increased physical activity levels of participants, either in isolation or as part of a multi-component programme. No restrictions were placed on the setting, delivery personnel, theoretical orientation, or duration of the intervention described.

Comparators

- Reported a control group that did not include any physical activity content beyond baseline provision.

Outcomes

- Utilised a global measure of MVPA or TPA spanning at least two domains. Outcome data must have been obtained either by an objective measure or by a validated self-report measure and additionally must have presented follow-up measurement data at least six months post-intervention (T_2) for the same participants measured at baseline (T_0) (see Figure 5.1). Where reported, Body Mass Index (BMI) was collected as a secondary outcome.

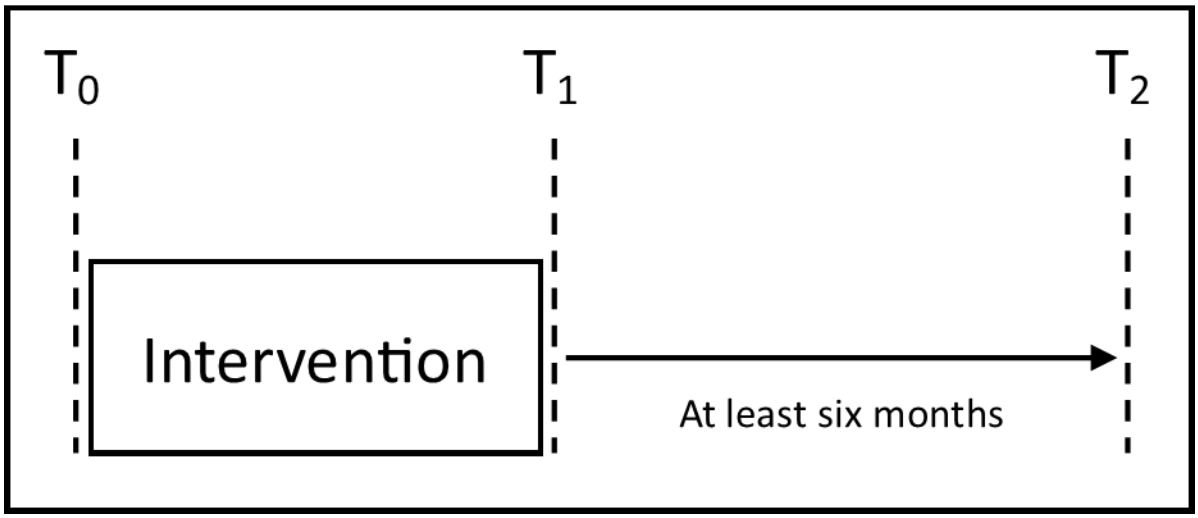


Figure 5.1 - Graphical representation of the study design required for inclusion.

5.3.3. Search Strategy

The search encompassed seven electronic databases (PubMed, MEDLINE, EMBASE, PsychINFO, ScienceDirect, SportDiscus and Google Scholar) for studies published between January 1991 and December 2013. Google Scholar was searched last with only the first 1,000 studies being considered due to the exhaustive nature of this search engine. Additionally, the reference lists of included studies and relevant published reviews were hand searched for additional studies. The search strategy was conducted using English search terms and included only English language studies due to the unavailability of appropriate translation services. A comprehensive table of the search terms entered by database is available in Appendix 60. Table 7 contains the base search terms for the initial screening of the databases specified above.

child OR adolescen* OR "young people"* *AND* *"physical activity" OR sport* OR cycl* OR walk* OR "physical education" OR "television view*" OR "tv view*" OR sedentary OR danc* OR "physical inactivity" OR "physical fitness" OR lifestyle OR exercise OR screen time OR "active travel*" OR commut** *AND* *clinical trial OR control* trial OR random* OR trial OR evaluation OR effect* OR random* sample OR control**

Table 7 - Base terms for database search.

5.3.4. Study Selection

The lead researcher (JS) examined the titles of all studies identified from the initial database results and excluded all publications that were unambiguously irrelevant and removed all duplications. Abstracts were then examined by the lead researcher (JS) and allocated to 'relevant,' 'irrelevant' and 'undecided' groups, with all undecided studies discussed and resolved with a second researcher (PS). Full text articles were then accessed and reviewed by the lead researcher (JS), with a second researcher (PS) cross-checking all included studies and a third researcher cross-checking a 10% sample of excluded studies (CF).

5.3.5. Data Extraction and Management

A data extraction form was utilised to extract primary and secondary data and assess quality of the study design and measurement protocol. The data extraction form was piloted against ten papers by the lead researcher (JS). The final data extraction form (see Appendix 61) was used by the lead researcher (JS) to extract information from all included studies. A second researcher cross-checked a random extraction sample of 10% of studies (PS). Disagreements were resolved in discussion with a third researcher (CF).

Study level characteristics extracted included: author(s), project title, nation, design, inclusion criteria, randomisation procedure where applicable, intervention and control descriptions, length of follow-

up, losses to follow-up and/or drop out, measurement strategy, secondary outcome measures, and results. The nature of outcome measurement was taken, along with the specific questionnaire or accelerometer and the length of the measurement period. Participant characteristics were extracted on relative gender percentages within the cohort, baseline age, baseline BMI or zBMI scores, as well as baseline global physical activity and MVPA levels.

Targets for sub-group analysis were specified *a priori* in order to reduce the likelihood of spurious findings (Higgins & Green, 2009). It was therefore planned to conduct subgroup analysis on: participant characteristics (gender, age, and cohort size); intervention characteristics (prevention vs. treatment, physical activity included vs. physical activity not included, intervention duration, and school vs. community setting), outcome characteristics (objective vs. subjective measurement and post-intervention follow-up delay); and, quality characteristics (high quality studies vs. lower quality studies). The number of participants providing valid data at the follow-up measurement point for each study was recorded. For the purposes of meta-analysis, the group means were extracted for the experimental and control groups at follow-up measurement, along with standard deviations, standard errors, or confidence intervals.

5.3.6. Standardisation of Data

All extracted data were entered into an Excel spreadsheet (Microsoft, 2013) for the purposes of recording and standardisation. Measurement strategy and measurement tool, along with target outcome and quality of reporting, varied considerably between papers necessitating a number of assumptions and transformations.

In order to utilise the mean difference within the meta-analysis and gain an intuitively meaningful estimate of effect it was necessary to transform data from some included studies into a common outcome metric, which permitted meta-analysis on the raw mean differences (Borenstein, Hedges, Higgins, & Rothstein, 2011). The majority of studies' reported outcomes were provided in mean minutes per day; therefore, this was selected as the common metric of MVPA. Where outcomes were

reported as minutes per week (Araujo-Soares, McIntyre, MacLennan, & Sniehotta, 2009) this total was divided by seven. Where MVPA was reported as number of sixty-minute blocks per week (Wright, Giger, Norris, & Suro, 2013) it was assumed that the full sixty-minute block was spent in MVPA and these were totalled and divided by seven to provide minutes per day. Where Moderate PA and Vigorous PA were presented separately (McManus et al., 2008) they were combined to produce a single MVPA outcome according to the procedure outlined in the Cochrane Manual (Higgins & Green, 2009). Where only Moderate or Vigorous Physical Activity was reported (Hovell et al., 2009) this was taken to be sufficiently conceptually similar to MVPA and entered into the meta-analysis as an equivalent main effect. Where MVPA was presented as a percentage of TPA (Dewar et al., 2013; Wake et al., 2009) the means and standard deviations were multiplied out to provide minutes per day. If results were given as amount of change (Wright et al., 2013), this change was added to baseline figures to arrive at a follow-up figure. In this case, the follow-up standard deviations were calculated by adjusting the baseline figures according to amount of change, under the assumption that the groups would retain an equivalent distribution to baseline figures. Where TPA was presented on a log scale (Black et al., 2010), means and standard deviations were transformed using standard processes (Higgins & Green, 2009). Where geometric means were reported (Hovell et al., 2009), it was assumed that these corresponded to the arithmetic means. Where intra-quartile range was reported as the indication of dispersion (Hovell et al., 2009), the quartile points were plotted on an assumed normal distribution and the corresponding standard deviations were entered into the analysis. Where data were presented for separate experimental groups, primarily by gender but also for staggered intervention cohorts, the numbers, means, and standard deviations were combined for entry into the primary meta-analysis (Higgins & Green, 2009), although the separate scores were reserved for secondary stratified analyses.

Where several different interventions were compared to control in each case only the primary intervention outcome data were entered into the meta-analysis. In the case of Chen, Weiss, Heyman, and Lustig (2010), the control group was assessed at immediate post-intervention, two months post-

intervention, and four months post-intervention but not six months post-intervention. However, the paper was retained in the meta-analysis given that the data points were consistent over time though the preceding measurements and therefore sufficiently justified an assumption that the control figures would not have significantly deviated after two further months. Where specific data was missing from a paper two attempts were made to contact the correspondence author by email.

5.3.7. Calculation of Effects

The group sizes, means and standard deviations were entered into RevMan 5.3 (The Cochrane Collaboration, 2012). MVPA, TPA, and BMI were entered as separate outcomes. The effect sizes of all outcome-relevant studies were combined to provide the overall effect for MVPA, TPA, and BMI. The planned outputs were overall effect estimates and 95% confidence intervals using random effects modelling with an inverse variance method. Random effects was chosen *a priori* as a moderate to high degree of heterogeneity was anticipated between studies (Higgins, Thompson, Deeks, & Altman, 2003). Initial analysis of the papers revealed TPA to have been measured and reported using varied strategies, therefore the effect measure for TPA was standardised mean difference, while mean difference was calculated for MVPA and BMI.

5.4. Results

5.4.8. Literature Search

The searches were conducted and completed in February 2014. The initial search of databases resulted in 15,696 identified studies, with a further thirteen potential studies identified from relevant systematic reviews, which was refined down to 15,412 studies following removal of duplicates. Analysis of titles then allowed unambiguously ineligible studies to be excluded, leaving a 1,493 sub-total. Scrutiny of abstracts of the remaining studies revealed 138 potentially relevant studies. Full text articles were then accessed and checked. No further relevant studies were identified from the reference lists of included studies, producing a total of eighteen preliminarily core studies. Four further studies were excluded at the data extraction stage, leaving fourteen studies for the final

systematic review. A PRISMA flow-chart (Moher, Liberati, Tetzlaff, & Altman, 2009) of the study selection process is presented in Figure 5.2.

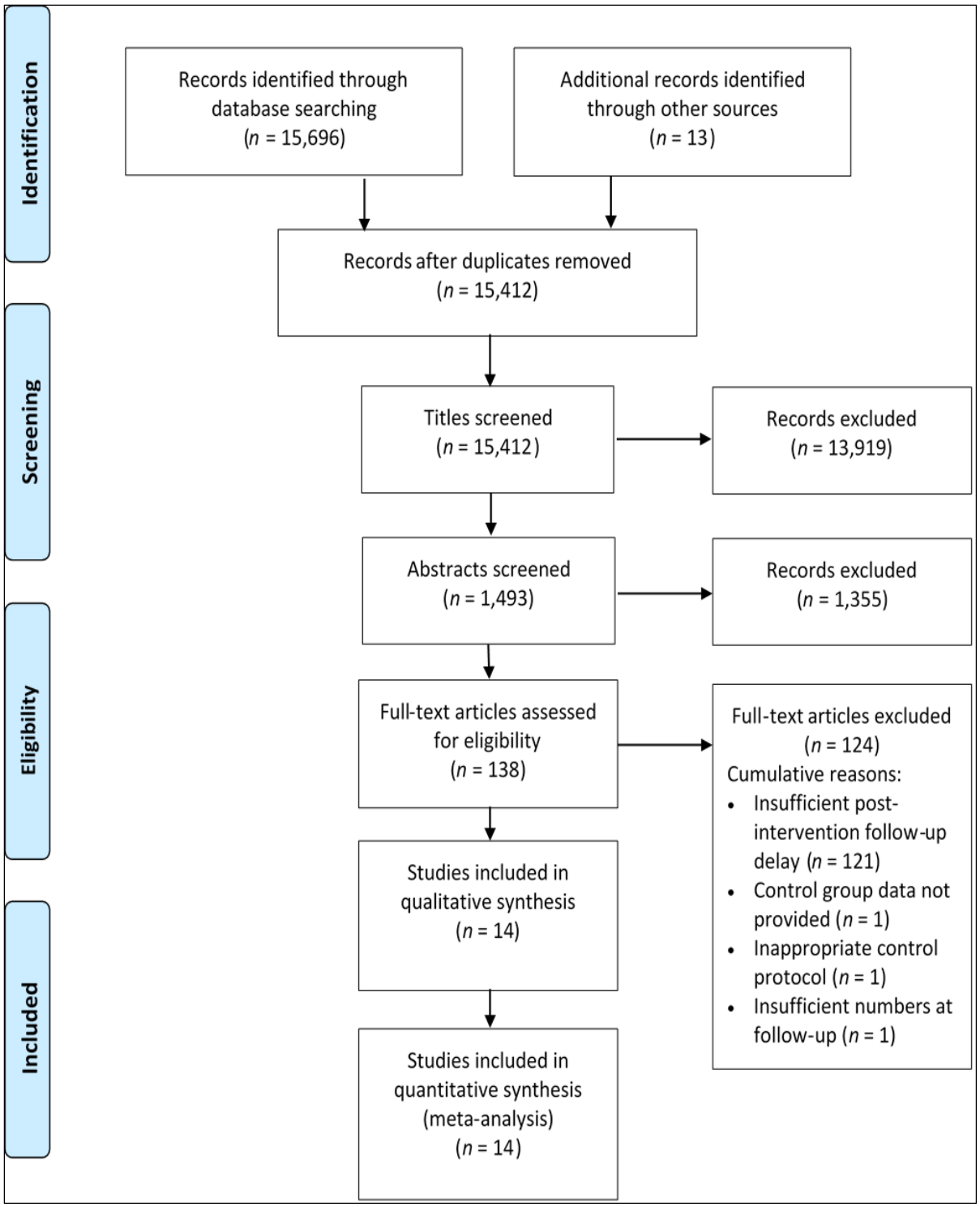


Figure 5.2 - PRISMA flow chart summarising the study selection process.

5.4.9. Summary of Characteristics of Excluded Studies

Exclusions at the initial stage were conducted following a screening of the study titles and were typically done on the basis of a clear lack of relevance. The exclusions at the second stage were made on the basis of the information in the abstracts. The most common reasons for exclusion at this stage were that the studies targeted either adult populations or did not stratify by age in sufficient detail to permit the adult and child data to be extracted separately. Further exclusions were made on the basis of experimental design, most particularly those studies utilising uncontrolled, observational or cross-sectional designs.

5.4.10. Assessment of Methodological Quality and Risk of Bias

The included studies were assessed for quality using the Methodology Checklist for Randomised Controlled Trials (NICE, 2012) (see Appendix 62). A summary graph indicating methodological quality across the included studies is given in Figure 5.3, with a study-by-study table provided in Appendix 63. Overall, there was a high number of 'uncertain' verdicts against the papers, potentially indicating the reporting of relevant information within the published articles was more pertinent that the actual methodological quality of the studies.

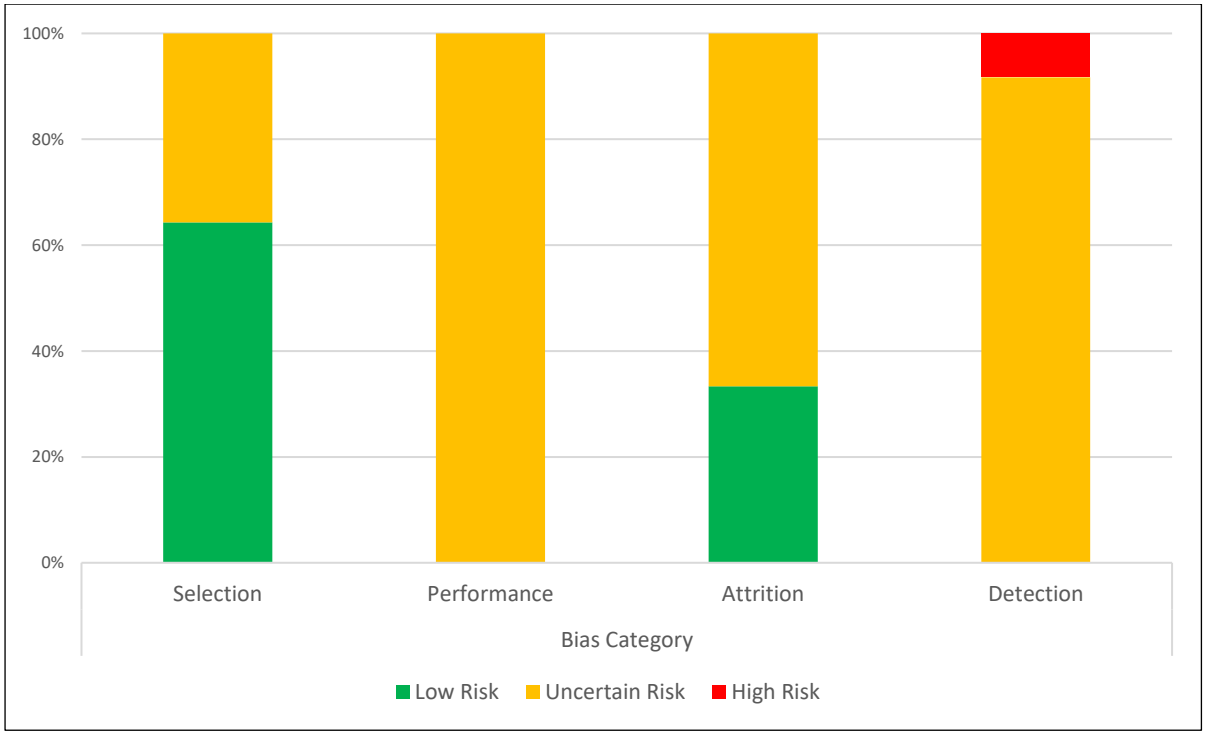


Figure 5.3 – Bar chart showing the overall assessed risk of bias within the 14 included studies.

Selection Bias

Studies typically reported a viable randomisation sequence generation procedure, either using a coin toss, a random number generator, or a lottery, although reporting of random sequence generation was sporadic. One study, Bugge et al. (2012), did not randomise classes as the intervention was implemented in a particular group of schools, with control schools identified by deliberate selection, with differences between groups reported on key variables. However, of more concern, many studies (see Appendix 63) did not report following a method by which the allocation was conducted by researchers blinded to number (Wood et al., 2008). All studies reported group comparisons for main effect at baseline and accounted for any differences in subsequent analysis. Baseline BMI was reported in all but Hovell et al. (2009). Overall, the risk of bias within this category was therefore low, although what risk that did exist was judged to be in the direction of the intervention group.

Performance Bias

All papers used a meaningful control protocol which differed from the intervention group only on intervention content, with controls either provided 'normal care' or allocated to a waiting list. Several

studies reported that intervention delivery followed a pre-designed manual in order to maintain intervention fidelity and to some extent reduce performance bias. Due to the nature of the delivery of physical activity programmes it was impossible to blind either participants or programme delivery staff to group allocation (Foster, Hillsdon, Thorogood, Kaur, & Wedatilake, 2005). It was therefore typical of the physical activity literature for performance bias to remain uncertain, with the direction of any bias likely to be in favour of the intervention.

Attrition Bias

With the exception of Chen et al. (2010) all studies followed intervention and control groups for the same time period. Chen et al. (2010) followed the intervention group for six months, but only followed the control group for four months, although this constituted six months post-*baseline*. With the exception of Nemet et al. (2005) all studies provided some level of statistical analysis on attrition to identify any systematic differences between those participants who completed the measurement series and those who did not (Wood, White, & Thompson, 2004). Despite low-level uncertainty within the study reporting it was judged that a high degree of risk of attrition bias was unlikely, and that any overall bias was not in a specific direction (Higgins & Green, 2009).

Detection Bias

The application of the inclusion criteria ensured that all studies followed the cohort for a suitable period of time, possessed a valid measurement protocol and defined either MVPA and/or TPA as an outcome. The reporting was less clear regarding the blinding of assessors to group allocation, resulting in a high risk of bias in several studies in the direction of the experimental group (Wood et al., 2008). With the exception of Nemet et al. (2005), which possessed a small sample (n = 41), all studies reported statistical methods by which to control for differences in baseline characteristics. This typically involved adjusting for variables identified as relevant within the analysis, including age, gender, social-economic status, BMI, energy intake, parental education, and parental marital status.

Publication Bias

The potential for the contribution of publication bias to the inconsistency between studies was assessed via a visual inspection of funnel plots for both outcomes (Figure 5.4). The plots are consistent with the potential for small-study bias but remain inconclusive due the low number of included studies.

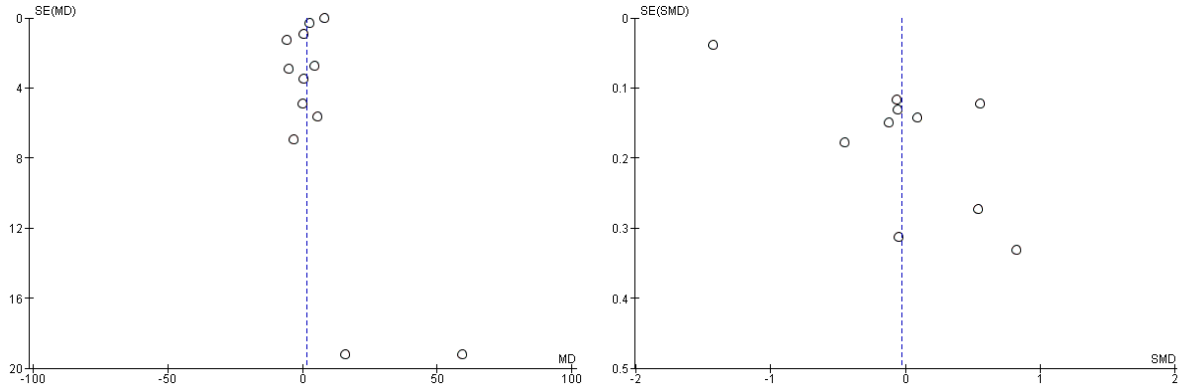


Figure 5.4 - Funnel plots showing the observed effects for the twelve studies reporting MVPA (left) and the ten studies reporting TPA (right).

Other Methodological Issues

Nine of the included studies utilised a cluster randomised control design (Araujo-Soares et al., 2009; Bugge et al., 2012; Cui et al., 2012; Dewar et al., 2013; Hovell et al., 2009; Jago et al., 2006; McManus et al., 2008; Nader et al., 1999; Wright et al., 2013). Uncorrected randomisation by cluster typically leads to an underestimation of standard error and therefore an increased relative weighting within a meta-analysis (Hahn, Puffer, Torgerson, & Watson, 2005). Jago et al. (2006) conducted analyses and presented findings on individual clusters, which were then combined for the purposes of analysis within the current review following recommended methods (Higgins & Green, 2009). Of the nine studies utilising clustered randomisation eight (Araujo-Soares et al., 2009; Bugge et al., 2012; Cui et al., 2012; Dewar et al., 2013; Hovell et al., 2009; Jago et al., 2006; Nader et al., 1999; Wright et al., 2013) provided a description of an appropriate statistical technique to account for clustering within the aggregated outcome.

The final stage of selection involved accessing full text articles. Exclusions at this stage were typically conducted on the basis of methodological concerns or the lack of provision of required information in the published paper. Additional exclusions were made at the point of data extraction at which point additional issues were identified that litigated against inclusion. Example exclusions included inadequate control group follow-up (Robertson, 2013), absence of published control group follow-up data (Salmon, Ball, Hume, Booth, & Crawford, 2008), and insufficient return on follow-up physical activity data (Hughes et al., 2008). Where there were notable absences of information the nominated authors were contacted on two occasions in an attempt to access missing data or seek clarification.

5.4.11. Overview of Characteristics of Included Studies

Appendix 64 provides a study-by-study description of the individual characteristics of included studies. Seven of the fourteen studies were conducted in the USA (Black et al., 2010; Cui et al., 2012; Hovell et al., 2009; Jago et al., 2006; Nader et al., 1999; Roemmich et al., 2012; Wright et al., 2013), two in Australia (Dewar et al., 2014; Wake et al., 2009), one in China (Chen et al., 2010) with one in Hong Kong (McManus et al., 2008), and one each in Denmark (Bugge et al., 2012), Israel (Nemet et al., 2005) and Portugal (Araujo-Soares et al., 2009). All but one of the studies, therefore, were conducted in high-income nations according to the World Bank economic classifications, with one being in the upper middle-income bracket (Chen et al., 2010).

Participant Characteristics

The number of participants ranged between the smallest study of just 41 participants (Nemet et al., 2005) and the largest of 3,714 participants (Nader et al., 1999). The median sample size was 255, with a total number of 7883 participants. Just over half the participants were female (52%) with one study recruiting only females (Dewar et al., 2013) and one using only males (Jago et al., 2006). Only two of the twelve studies including both genders reported gender-specific results (Bugge et al., 2012; Hovell et al., 2009). Mean baseline age was 10.67 (± 1.91) years, with eight studies targeting participants of primary education age (Bugge et al., 2012; Chen et al., 2010; McManus et al., 2008; Nader et al., 1999;

Nemet et al., 2005; Roemmich et al., 2012; Wake et al., 2009; Wright et al., 2013) and six studies targeting secondary education age participants (Araujo-Soares et al., 2009; Black et al., 2010; Cui et al., 2012; Dewar et al., 2013; Hovell et al., 2009; Jago et al., 2006). No included studies targeted tertiary education age participants. Three studies were treatment orientated (Nemet et al., 2005; Wake et al., 2009; Wright et al., 2013), recruiting specifically overweight or obese participants, with the remainder of studies being promotional or preventative, recruiting participants from across the distribution of weight.

Intervention Characteristics

There was a wide variety of intervention strategies across the included studies. Studies provided extra physical education classes in curriculum time (Araujo-Soares et al., 2009; Bugge et al., 2012; Dewar et al., 2013; McManus et al., 2008; Nader et al., 1999; Wright et al., 2013), physical activity delivery outside curriculum time (Chen et al., 2010; Jago et al., 2006; Nemet et al., 2005), counselling (Wake et al., 2009), goal-setting sessions (Araujo-Soares et al., 2009; Black et al., 2010; Wright et al., 2013), incentive-based intervention (Jago et al., 2006; Roemmich et al., 2012), and peer-modelling (Black et al., 2010; Cui et al., 2012) either singularly or in combination. Five studies (Araujo-Soares et al., 2009; Black et al., 2010; Chen et al., 2010; Cui et al., 2012; Dewar et al., 2013) reported explicitly grounding an intervention strategy in Social Cognitive Theory (Bandura, 2001). Seven studies (Araujo-Soares et al., 2009; Bugge et al., 2012; Cui et al., 2012; Dewar et al., 2013; McManus et al., 2008; Nader et al., 1999; Wright et al., 2013) involved a school setting within the intervention delivery, and seven in a community setting; four in a standard community approach (Black et al., 2010; Chen et al., 2010; Hovell et al., 2009; Roemmich et al., 2012), two in a primary care setting (Nemet et al., 2005; Wake et al., 2009), and one as part of a scout group (Jago et al., 2006). Intervention duration lasted between six weeks (McManus, Mandic, Carle, & Robert, 2012) and three years (Bugge et al., 2012; Nader et al., 1999).

Control Characteristics

None of the control groups included a physical activity component, excepting those comparisons which were made between additional physical activity and 'normal practice' in which case the participants completed standard physical education classes within curriculum time. Differences in characteristics between baseline and intervention groups were reported in all cases, with no comparisons deemed to be at high risk of bias. Control strategies included intention to treat or waiting lists, normal practice, and no-treatment comparisons.

Outcome Characteristics

Four studies reported only MVPA, two studies reported only TPA, and eight reported both MVPA and TPA. Overall, twelve studies reported MVPA and ten studies reported TPA. TPA was measured using either an accelerometer (Black et al., 2010; Bugge et al., 2012; Chen et al., 2010; Dewar et al., 2013; Jago et al., 2006; Roemmich et al., 2012; Wake et al., 2009) or questionnaire (McManus et al., 2008; Nader et al., 1999; Nemet et al., 2005). MVPA was also measured using accelerometer (Black et al., 2010; Bugge et al., 2012; Dewar et al., 2014; Jago et al., 2006; Roemmich et al., 2012; Wake et al., 2009) or questionnaire (Araujo-Soares et al., 2009; Cui et al., 2012; Hovell et al., 2009; McManus et al., 2008; Nader et al., 1999; Wright et al., 2013). The self-report measures included standardised questionnaires, 24-hour recall, and participation tick-sheets. Of the sixteen studies, four reported both TPA and MVPA, while nine studies reported BMI outcomes. Thirteen studies conducted outcome measurement immediately post-intervention; in two cases this was delayed by three months (Hovell et al., 2009; Wake et al., 2009) and in one case by two months (Cui et al., 2012). Follow-up measurement ranged from six months (Chen et al., 2010; Cui et al., 2012; Jago et al., 2006; McManus et al., 2008) to four years (Bugge et al., 2012), with a median delay of nine months post-intervention.

5.4.12. Overall Effect Sizes

The collated results from twelve included studies showed weak evidence for a small increase in MVPA in favour of the intervention group with a mean difference of 1.47 minutes per day (95% CIs: 1.88,

4.82; p = 0.39) (Figure 5.5). For the ten studies reporting TPA the analysis showed no difference between the pooled effects of the intervention and those for the control group, with a standardised mean difference of -0.13 (95% CI's: -0.74, 0.48; p = 0.67) (Figure 5.6). On the basis of this evidence it was concluded that interventions to increase physical activity in childhood had a slight effect on sustained MVPA and no effect on sustained TPA. I^2 values of 98% for both MVPA and TPA revealed a high level of statistical heterogeneity between studies in both outcomes. A further analysis exploring intervention effect on BMI is presented in Appendix 65, with a forest plot in Appendix 66.

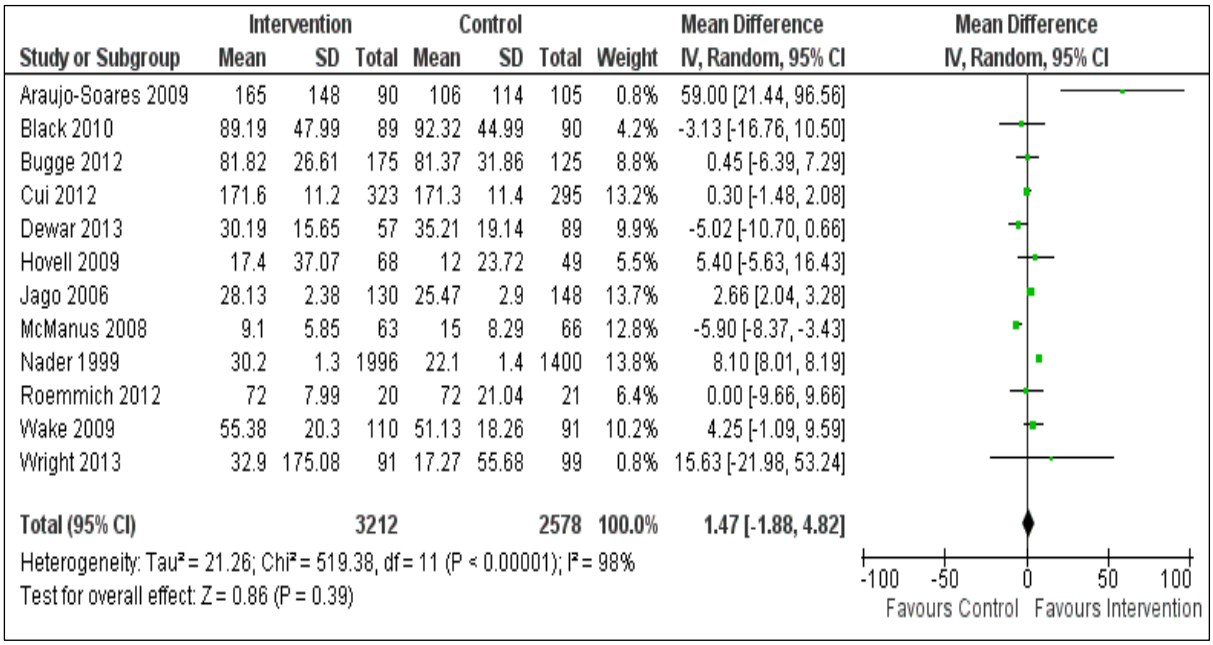


Figure 5.5 - Forest plot of mean difference in change in MVPA between intervention (n = 3212) and control (n = 2578) groups across the 12 included studies reporting MVPA data.

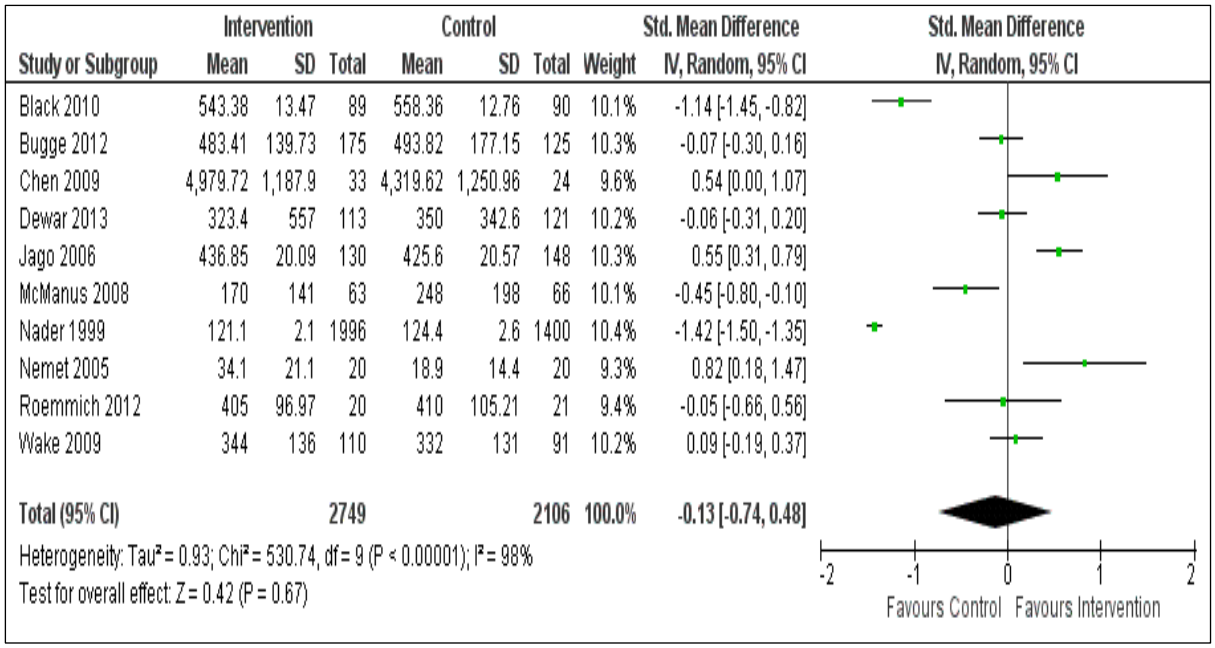


Figure 5.6 - Forest plot showing the standardised mean difference in change in TPA between intervention (n = 2749) and control (n = 2106) groups across the 10 included studies reporting TPA data.

5.4.13. Subgroup Analyses

In order to examine the data in more detail, as well as partially address the high statistical heterogeneity within the outcomes, a number of analyses were run on sub-groups of the data. Although the number of studies in the meta-analysis was low, meta-regressions were run on potential effect moderators as a means of further exploring the data.

Effects of Intervention by Gender

Two studies reported MVPA data stratified by gender (Bugge et al., 2012; Hovell et al., 2009) with one study recruiting only males (Jago et al., 2006) and a further study recruiting only females (Dewar et al., 2013). Outcomes for males showed a statistically significant effect in favour of intervention with a mean difference of 2.65 minutes per day of MVPA (95% CI's: 2.03, 3.27; $p < 0.001$) (Figure 5.7). Outcomes for females showed a non-significant mean difference of -0.42 (95% CI's: -7.77, 6.94; $p = 0.94$). The positive finding for males is largely accounted for by the Jago et al. (2006) study, which carried a large percentage of the weighting within the result. Removal of Jago et al. (2006) from the analysis reduced the result to a non-significant difference ($p = 0.90$). The difference between males and females was statistically non-significant ($\chi^2 = 0.66$, $p = 0.42$).

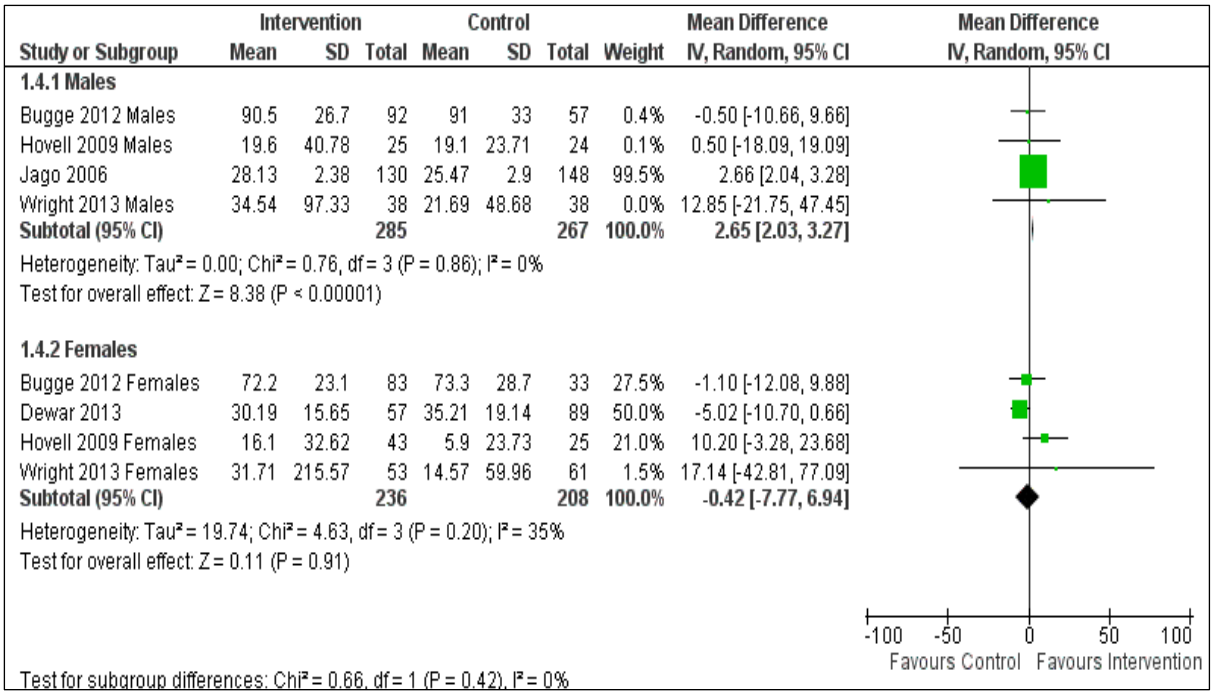


Figure 5.7 - Forest plot showing the mean difference in change in MVPA between intervention (n = 521) and control (n = 475) groups stratified by gender (males: intervention n = 295, control n = 267 across 4 studies; females: intervention n = 236, control n = 208 across 4 Studies).

Only Bugge et al. (2012) reported TPA data for both genders and was entered into the analysis along with the male only outcome data from Jago et al. (2006) and the female only data from Dewar et al. (2013). The standardised mean difference for males of 0.24 (95% CI's: -0.39, 0.87; p = 0.46) and for females of -0.08 (95% CI's: -0.28, 0.12; p = 0.44) revealed non-significant results (Figure 5.8). The difference between sub-groups was statistically non-significant (χ^2 = 0.89, p = 0.35).

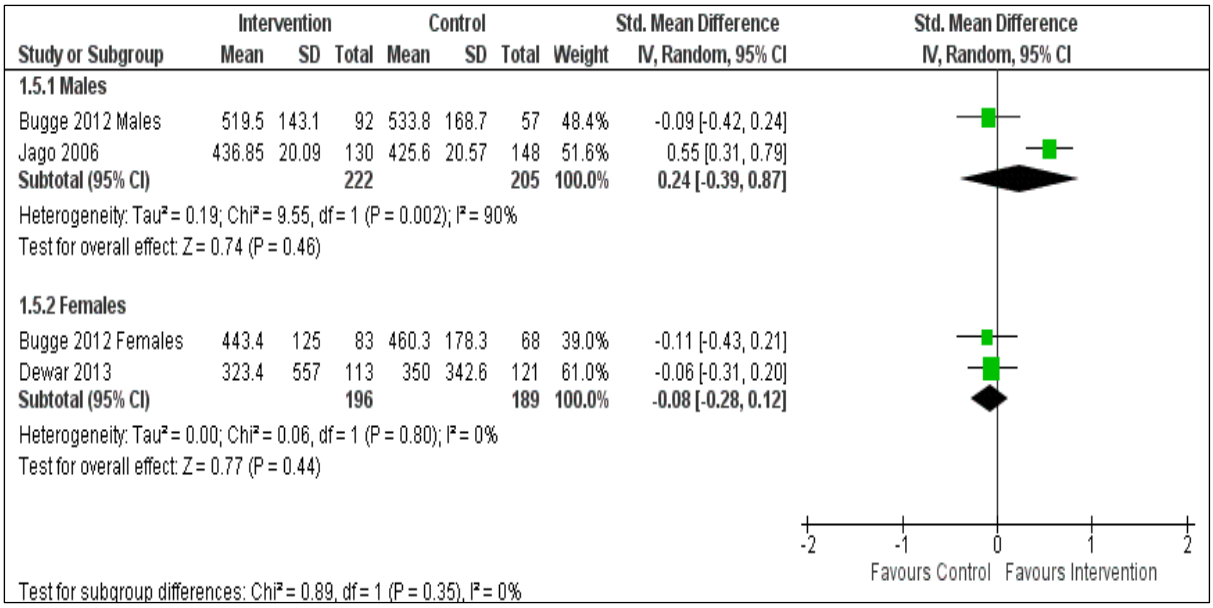


Figure 5.8 - Forest plot showing the standardised mean difference in change in TPA between intervention (n = 418) and control (n = 394) groups stratified by gender (males: intervention n = 222, control n = 205 across 2 studies; females: intervention n = 196, control n = 189 across 2 studies).

Effect of Intervention by Approach

Ten studies reported MVPA data for interventions that took a preventative approach (Araujo-Soares et al., 2009; Black et al., 2010; Bugge et al., 2012; Cui et al., 2012; Dewar et al., 2013; Hovell et al., 2009; Jago et al., 2006; McManus et al., 2008; Nader et al., 1999; Roemmich et al., 2012) while two studies reported data for treatment interventions (Wake et al., 2009; Wright et al., 2013). Studies were considered to be treatment-orientated if they specifically recruited participants with a pre-existing designation of overweight or obese at baseline. The ten studies taking a prevention approach returned a mean difference of 1.03 minutes per day of MVPA (95% CI's: -2.54, 4.60; $p = 0.57$) (Figure 5.9), while the studies taking a treatment approach returned a mean difference of 4.47 minutes per day (95% CI's: -0.81, 9.76; $p = 0.10$) which neared statistical significance, although was underpowered with only two studies in this sub-group. There was no significant difference between the sub-groups ($\chi^2 = 1.12$; $p = 0.29$).

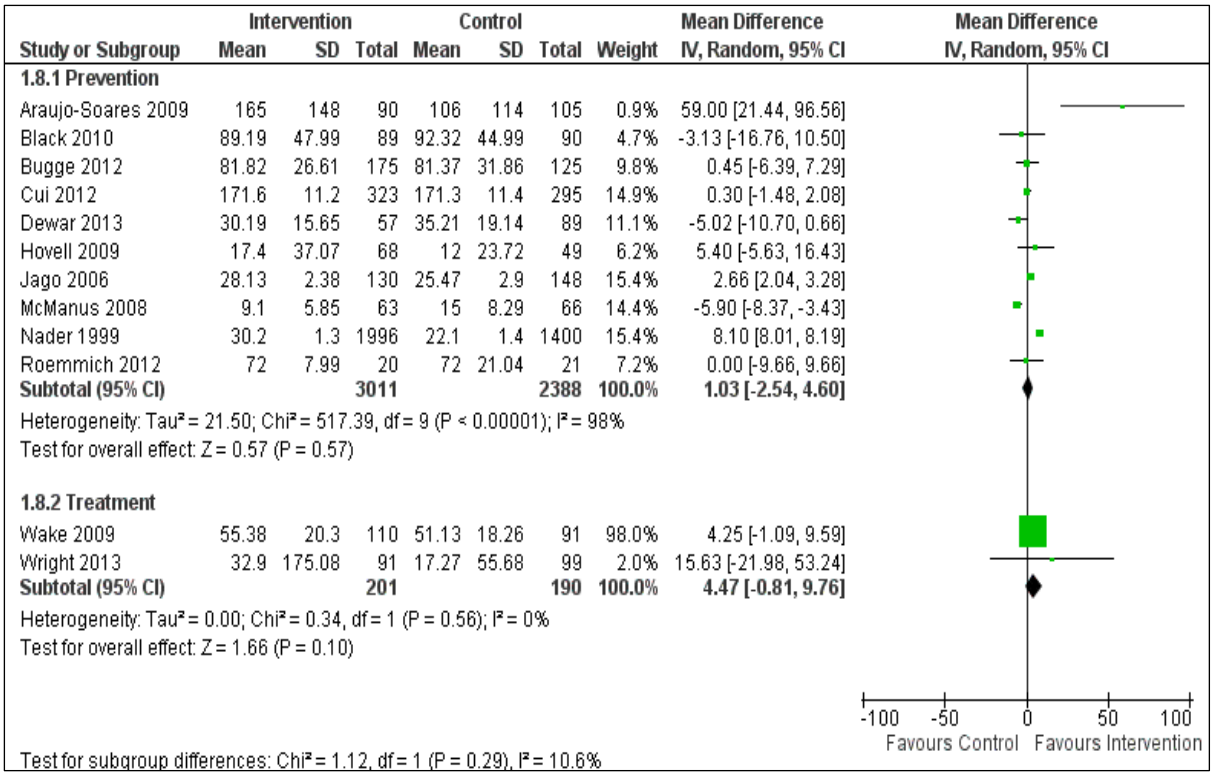


Figure 5.9 - Forest plot showing the mean difference in change in MVPA between intervention (n = 3212) and control (n = 2578) groups stratified by intervention approach (prevention: intervention n = 3011, control n = 2388 across 10 studies; treatment: intervention n = 201, control n = 190 across 2 studies).

Eight studies reported TPA data for interventions that utilised a preventative approach (Black et al., 2010; Bugge et al., 2012; Chen et al., 2010; Dewar et al., 2013; Jago et al., 2006; McManus et al., 2008; Nader et al., 1999; Roemmich et al., 2012) while two studies reported TPA for treatment-based interventions (Nemet et al., 2005; Wake et al., 2009). Analysis of the prevention-based studies revealed a standardised mean difference of -0.27 (95% CI's: -0.95, 0.71; $p = 0.43$), with the treatment-based approached providing a standardised mean difference of 0.40 (95% CI's: -0.31, 1.11; $p = 0.27$) (Figure 5.10). Neither analysis revealed statistically significant differences, nor was there a significant difference between the sub-groups ($\chi^2 = 1.78$; $p = 0.18$).

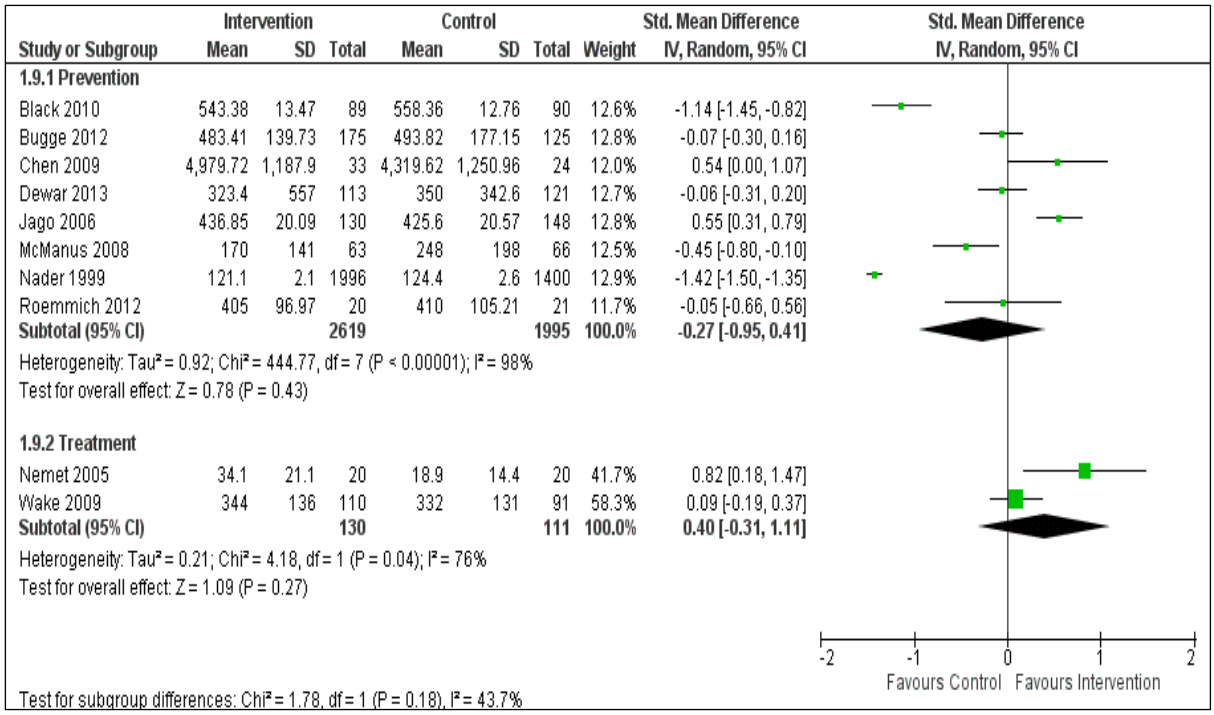


Figure 5.10 - Forest plot showing the standardised mean difference in change in TPA between intervention (n = 2749) and control (n = 2106) groups stratified by intervention approach (prevention: intervention n = 2619, control n = 1995 across 8 studies; treatment: intervention n = 130, control n = 111 across 2 studies).

Additional sub-group analysis were conducted for: baseline BMI on MVPA (Appendix 67) and TPA (Appendix 68); age of participants (Appendix 69) on effect for MVPA (Appendix 70), and TPA (Appendix 71) including meta-regressions for MVPA (Appendix 72) and TPA (Appendix 73); intervention duration (Appendix 74) on effect for MVPA (Appendix 75) and TPA (Appendix 76) including meta-regression for MVPA (Appendix 77) and TPA (Appendix 78); nature of intervention (Appendix 79) on effect for TPA (Appendix 80); intervention setting (Appendix 81) on effect for MVPA (Appendix 82) and TPA (Appendix 83); type of report measure (Appendix 84) on effect for MVPA (Appendix 85) and TPA (Appendix 86); post-intervention follow-up duration (Appendix 87) on effect for MVPA (Appendix 88) and TPA (Appendix 89) including meta-regression for MVPA (Appendix 90) and TPA (Appendix 91); meta-regression by baseline cohort size for MVPA (Appendix 92) and TPA (Appendix 93); and for study quality effect for MVPA (Appendix 94) and (Appendix 95).

5.4.14. Summary of Subgroup Effects

Subgroup	MVPA Effect Estimate (mean difference in mins/day)	95% Confidence Intervals	TPA Effect Estimate (standardised mean difference)	95% Confidence Intervals
Overall	1.47	-1.88, 4.82	-0.13	-0.74, 0.48
Participant Characteristics				
Gender				
Males	2.65**	2.03, 3.27	0.24	-0.39, 0.87
Females	-0.42	-7.77, 6.94	-0.08	-0.28, 0.12
Educational Age				
Primary	1.96	-5.75, 9.67	-0.10	-0.84, 0.64
Secondary	0.86	-2.31, 4.04	-0.21	-1.12, 0.71
Cohort Size				
<=Median Participants	0.10	-5.76, 5.96	-0.09	-0.79, 0.62
>Median Participants	2.49	-1.47, 6.44	-0.18	-1.11, 0.74
Intervention Characteristics				
Intervention Approach				
Prevention	1.03	-2.54, 4.60	-0.27	-0.95, 0.41
Treatment	4.47*	-0.81, 9.76	0.40	-0.31, 1.11
Intervention Strategy				
Physical Activity Included	1.57	-1.89, 5.04	-0.17	-0.86, 0.52
Physical Activity Not Included	0.00	-9.66, 9.66	0.07	-0.19, 0.32
Intervention Setting				
School	1.70	-4.84, 8.25	-0.50	-1.37, 0.36
Community	2.67**	2.05, 3.28	0.12	-0.49, 0.73
Outcome Characteristics				
Measurement Strategy				
Objective	1.03	-1.80, 3.85	-0.03	-0.44, 0.38
Self-Report	4.04	-3.26, 11.34	-0.39	-1.50, 0.71
Intervention Duration				
<4 Months	0.89	-2.80, 4.59	0.05	-0.54, 0.64

>=4 Months	1.75	-5.66, 9.16	-0.41	-1.34, 0.52
Follow-Up Duration				
<=9 Months	0.69	-3.10, 4.48	0.23†	-0.15, 0.60
>9 Months	1.99	-4.77, 8.75	-0.67†	-1.49, 0.15

** $p < 0.05$, * $p < 0.10$ for within group effect

† $p < 0.05$ for between group effect

Table 8 - Summary of effects and p values for MVPA and TPA outcomes by sub-group across 14 studies.

5.5. Discussion

5.5.15. Summary of Main Results

Twelve of the fourteen studies meeting the inclusion criteria reported MVPA data, while ten reported TPA data. For MVPA there was a statistically non-significant ($p = 0.39$) mean difference in favour of intervention, approximating to an average improvement of 1.47 minutes per day compared to controls, although this figure is well below the sensitivity of the utilised measurement tools. This result falls well short of the recommended levels of physical activity for children (World Health Organization, 2010) and is unlikely to be clinically significant even if maintained over time. For TPA there was no statistically significant ($p = 0.67$) difference in standardised mean difference in change between intervention and control groups at follow.

There were no statistically significant differences in outcomes across the majority of study level characteristics, summarised in Table 8. An exception to this trend was that male participants showed a statistically significant ($p < 0.001$) mean difference in MVPA between intervention and control groups at post-intervention follow-up measurement, approximately equivalent to 2.65 minutes of extra MVPA per day compared to controls. However, this weighted average difference was generated from a sub-group of only four studies, with the male-only Jago et al. (2006) figure carrying the vast majority of the weighting due to the relatively tight standard deviations provided by this study. The standardised mean difference from the same study did not produce a statistically significant result, indicating that firm conclusions from these findings are not appropriate (Higgins & Green, 2009). The

only other statistically significant (p = 0.05) difference was observed between short and long follow-up duration sub-groups, with longer follow-up delay showing a decrement in TPA relative to controls.

5.5.16. Potential Explanations

Sub-Group Analyses

The sub-group of interventions that took place outside a school environment, including leisure centres and primary care settings, showed a statistically significant (p < 0.05) mean difference in MVPA between intervention and control groups. Initial inspection revealed the Jago et al. (2006) paper to have taken the majority of the weighting; removal of this paper from the sub-group analysis produced a non-significant result. In addition, the standardised mean difference of this sub-group was not significant. However, the sub-group of studies that provided TPA data also showed an approaching statistically significant (p < 0.10) difference between intervention and control groups for community-based interventions. The relative success of community-based interventions may be due in part to small study effect, as four of the studies in this subgroup possessed comparatively small cohort sizes. In addition, the treatment-based sub-group (Wake et al., 2009; Wright et al., 2013) approached significance (p < 0.10) for MVPA and the Nemet et al. (2005) study, which evidenced a positive effect on TPA at follow-up, were all conducted in community settings, potentially indicating factors that may cluster to promote effectiveness in increasing physical activity.

Potential Bias

In physical activity studies it is typically not possible to blind the participants or instructors to allocation, opening a potential source of bias into the delivery (Foster et al., 2005). In addition, the measurement was often conducted by researchers not blinded to allocation. This has been shown to be a practice associated with high risk of bias when using self-report measurement, but not objective measurement (Wood et al., 2008). However, sub-group analysis (Appendix 84) showed that self-report measurement did not show a significant difference when compared to objective measures for MVPA (Appendix 85) or TPA (Appendix 86). Although the risk of bias was uncertain across a number of

studies, the direction of risk was consistently in favour of the intervention group. Given this direction, the potential for a Type II error was reduced which, against the already negligible findings in the overall meta-analysis, lends further support for the null hypothesis.

Methodological Issues

It is possible that some inconsistency between studies contributing to the high I^2 statistics was due to a difference in thresholds set for MVPA. Certainly Hovell et al. (2009) only included vigorous physical activity, and other studies may have used differing interpretations of minutes per day of MVPA. In addition, the levels of heterogeneity apparent between studies that used self-report was consistently high across both outcomes (MVPA I^2 = 98%; TPA I^2 = 97%), potentially compromising the sensitivity of this measurement strategy to reliably demarcate significant from non-significant results in small studies. The effect of this potential lack of specificity would have been to increase the likelihood of a Type II error as the confidence intervals would have broadened, with a consequential reduction of weighting within the meta-analysis.

Study Quality

It is important to note that the included studies were not selected on the basis of strong methodological rigour or freedom from risk of bias; the primary inclusion criterion specified that studies include at least a six-month post-intervention follow-up. There exists the possibility that alternative intervention studies, those of a higher methodological quality, would have shown a positive effect had they been measured at follow-up. However, the results of recent reviews that have included larger numbers of studies (Metcalf et al., 2012; van Sluijs et al., 2008) do provide evidence that this is not the case. In addition, bubble plots of included studies did not reveal a pattern indicating an association between sample size and effect size for either MVPA (Appendix 92) or TPA (Appendix 93), nor was a relationship indicated between effect sizes and study quality (see Appendix 94 & Appendix 95).

Comparison with Other Reviews

The main outcome that interventions do not lead to meaningful increases in physical activity in children relative to controls at six months follow-up is consistent with a recent review by Metcalf et al. (2012), who conducted a meta-analysis on 30 studies measured by accelerometer immediately post-intervention, with Dobbins et al. (2013), who reviewed 44 studies specifically regarding school-based interventions, and with Kamath et al. (2008a), who reviewed 18 studies on levels following physical activity interventions within a wider review into prevention of childhood obesity. There was only a small amount of overlap between these reviews, with only a maximum of three studies common to other reviews and the present study, indicating that the minimal return following intervention is common across a larger number of studies. Increasing the length of intervention did not produce a corresponding increase in physical activity levels at follow-up (see Appendix 74 to Appendix 78). This was consistent with an observation by Metcalf et al. (2012) that interventions demonstrated greatest impact in the first three months, followed by a typical levelling out in effect.

There appeared to exist a trend towards statistical significance across studies that were implemented in a community setting. The studies in the community delivery sub-group also featured in the small cohort sub-group and the treatment approach subgroup. This is consistent with Metcalf et al. (2012) who found a statistically significant effect in both MVPA and TPA for studies recruiting exclusively overweight and/or obese participants but noted that it was impossible to distinguish whether this effect was due to a treatment approach or an effect of small studies, as the majority of treatment studies recruited relatively small cohorts. This may indicate a single factor which is consistent with successful intervention or it may indicate that a community setting, small cohort, and a treatment approach jointly contribute towards success, but due to underpowered analyses it is not possible to establish with any certainty. A more recent systematic review found no evidence of effect for physical activity or adiposity of intervention in individuals with pre-existing obesity or overweight, either at post-intervention or follow-up (Nooijen, Galanti, Engström, Möller, & Forsell, 2017b) and no pattern was evident on forest plots of effects by adiposity (see Appendix 67 & Appendix 68).

5.5.17. Strengths and Limitations

The comparatively few studies that were included in this systematic review and meta-analysis left the meta-analysis somewhat underpowered, particularly with regard to sub-group analyses and meta-regressions. As such it was only possible to infer patterns from the analyses rather than report statistically and clinically significant findings. In addition, the overall quality of the reporting of the studies contained a high degree of uncertainty regarding risk of bias. The high levels of heterogeneity between the studies in the main findings potentially undermined the assumption that studies were reporting on an equivalent outcome, although MVPA meta-analyses run using standardised mean difference do not differ in their broad patterns from those presented above.

This limitation, however, also represented the strength of the current review as the specificity of the inclusion criteria permitted a more focussed consideration of the relevant studies. In addition to the requirement for at least six-month post-intervention follow-up data, a key inclusion criterion for this review was the requirement for studies to report physical activity across the entire day, rather than accepting data from studies focussing solely on physical activity within recess, school travel, or after-school periods. Previous reviews without this criterion have not been able to exclude the possibility of substitution, nor have they been able to generalise findings to whole-day behaviour of children.

5.5.18. Adjunct Update to Intervention Studies

While modelling over previous chapters, and most particularly the systematic review and meta-analysis competed in Chapter 5 and modelled in Chapter 6, constitutes a period-specific analysis focused on 2013 data, there exists the possibility that more recent interventions and subsequent publications have demonstrated greater effectiveness in the effort to sustain increased physical activity levels in children. Below is a brief review of publications since 2013, followed by a brief synopsis of publications that broadly meet the inclusion criteria of the Sims et al. (2015) systematic review. The section concludes with a discussion of the likely impact of any changes to the modelled outcomes.

An increasing number of systematic reviews and meta-analyses have been published in recent years, and while the intervention studies included in the analysis in Sims et al. (2015) also appear in more contemporary reviews, additional studies have been added to the evidence base. In general, the field has seen an increased number of systematic reviews with no corresponding increase in intervention studies. As a result, the focus of these reviews and consequent inclusion criteria have become rather more specific. However, this has largely seen a falling number of included studies in each meta-analysis, with a consequential reduction in power and generalisability. One example of this specificity includes a focus on physical activity within specific population sub-groups, such as people with sleep disorder (e.g. Mendelson et al., 2018), wheelchair users (e.g. O'Brien et al., 2016), cerebral palsy (e.g. Reedman, Boyd, & Sakzewski, 2017), or learning disabilities (e.g. Willems et al., 2018). additionally, physical activity behaviours have been addressed within specific contexts, such as school classrooms (e.g. Watson, Timperio, Brown, Best, & Hesketh, 2017), after-school clubs (e.g. Mears & Jago, 2016), active travel (e.g. Pang, Kubacki, & Rundle-Thiele, 2017), or community sports clubs (e.g. Lee, Pope, & Gao, 2018).

Mannocci et al. (2020) conducted an umbrella review of systematic reviews and meta-analyses on the effectiveness of interventions to increase physical activity in children and young people published since 2010. They included 30 reviews, including fifteen meta-analyses, finding that the majority focused on school-based interventions, while others included community and family settings. Eight of the meta-analyses evidenced a small effect of intervention, but none reported large differences between pooled effects of intervention and control groups. A broader meta-synthesis was not possible due to the low quality of several reviews, as well as the low quality of some contributing studies even to the higher quality reviews. Mannocci et al. (2020) concluded that long-term multi-component interventions based in schools showed the greatest relative effectiveness, although effect size remained modest at best.

Russ, Webster, Beets, and Phillips (2015) conducted a systematic review of 'whole school' approaches to increasing daily physical activity, with interventions including family engagement projects, enhancements to physical education classes, after-school clubs, and lunchtime activities. Of the fourteen included studies they found a standardised mean difference of 0.11 (95% CI's: 0.03, 0.14), representing a statistically significant but pragmatically small effect, although changes were based on measurement immediately post-intervention and as such effects are likely to be higher than at follow-up. Owen, Curry, Kerner, Newson, and Fairclough (2017) focused on the effects of school-based interventions specifically on adolescent girls, identifying twenty studies of which seventeen were included in a meta-analysis. The three studies not included within the meta-analysis showed positive effects, but either did not report variance, did not report group sizes, or did not recruit a control group. Meta-analysis revealed a small but statistically significant standardised mean difference of 0.07 (95% CI's: -0.00, 0.14), with the authors again suggesting that while multi-component interventions underpinned by theory represent a potential avenue of promise, meaningful improvement in adolescent girl's physical activity remains challenging within the school setting.

Mears and Jago (2016) focused on the efficacy of after-school clubs to increase whole day MVPA in children. Of the fifteen eligible studies, six were included in the meta-analysis, finding a non-significant effect of 4.84 (95% C's: -0.94, 10.61) additional minutes of MVPA per day in favour of intervention at post-intervention measurement. The two studies including an extended follow-up period (Dzewaltowski et al., 2010; Madsen, Thompson, Adkins, & Crawford, 2013) both reported non-significant effects. Mears and Jago (2016) suggest that interventions specifically targeting obese or overweight children show higher rates of success.

Further studies have investigated the domain of active travel, including Larouche, Mammen, Rowe, and Faulkner (2018) who included 27 papers in a systematic review. Interventions included publication of safe routes to school, 'Bikeability' training, walking buses, distal drop-off locations, and specific education content. However, while thirteen studies reported statistically significant effects, the

heterogeneity of measurement, in several cases using direct observation or head-counts, resulted in the authors declining to proceed with meta-analysis. While Jones et al. (2019) published an updated meta-analysis focused on the active travel domain, again this was underpowered due to measurement inconsistency and heterogeneity.

Outside school-based interventions, Brown et al. (2016) reviewed 47 publications detailing family-based approaches to increasing physical activity, including goal-setting, community education programmes, positive behaviour reinforcement, and role-modelling. Due to data reporting constraints, only nineteen studies were included in a meta-analysis, which produced a statistically significant standardised mean difference of 0.41 (95% CI's: 0.15, 0.67) in favour of intervention groups. The authors suggest that explicit goal-setting and positive reinforcement constitute the most effective combination in increasing child physical activity.

Corepal, Tully, Kee, Miller, and Hunter (2018) focused on the effectiveness of behavioural interventions, rather than on intervention delivery within a specific domain of physical activity, including publications focused on material incentive and rewards (e.g. Roemmich et al., 2012; Suchert, Isensee, Sargent, Weisser, & Hanewinkel, 2015), social support mechanisms (Goldfield et al., 2006), or goal setting (e.g. Hardman, Horne, & Fergus Lowe, 2011; Horne, Hardman, Lowe, & Rowlands, 2009). Reviewing 22 studies, with nineteen in their meta-analysis, the authors found minimal support for efficacy in increasing physical activity in children, with a standardised mean difference of 0.31 (95% CI's: -0.27, 0.88). Although the authors conclude there is some support for the use of behavioural interventions for increasing physical activity in childhood, their meta-analysis was completed only on comparisons immediately post-intervention, rather than including any follow-up data.

Focusing specifically on high risk children, Nooijen, Galanti, Engström, Möller, and Forsell (2017a) conducted a systematic review on the effectiveness of physical activity intervention with obese or overweight children. Interventions included direct physical fitness programmes, environmental management, and behavioural incentives. Meta-analysis found no group effect for intervention, with

a standardised mean difference of -0.02 (95%CI's: -0.15, 0.11) in daily physical activity. The authors conclude that there was no evidence that interventions were able to increase physical activity levels in overweight or obese children.

In summary, a scan of the available systematic reviews of contemporary interventions to increase physical activity in children shows that effects are inconsistent and, where present, remain modest. A number of potentially positive results from individual studies were rejected from inclusion in both the systematic reviews and their subsequent meta-analyses due to non-availability of appropriate data or poor quality of design. Importantly, there have been no formal updates to large-scale systematic reviews, most particularly Cochrane reviews (e.g. Dobbins et al., 2013; Oude Luttikhuis et al., 2009). As such, it would be reasonable to conclude that there has been no substantial increase in consolidated intervention effectiveness in the years since the meta-analysis in Chapter Five was completed.

In addition to a broader summary of the developments in physical activity, it is important to consider publications which are likely to have been included in an updated systematic review in order to evaluate the potential change in pooled effects and conclusions contained in the original systematic review and consequentially on the modelling. The papers outlined below, while not systematically reviewed nor entered into a meta-analysis, all broadly meet the criteria for the original review, i.e. that they must focus on interventions in children, with a control group, and that physical activity levels are recorded at least six weeks post-intervention.

Verbestel et al. (2015) completed a multi-national cluster-controlled trial of a community-based obesity prevention programme, including food and hydration targets, reducing screen time, improving sleep quality, increasing family time, and increasing levels of physical activity. A random subsample (n = 9,184) wore accelerometers at baseline, of which 3,010 children provided follow-up data. At follow-up measurement, there was no group difference between intervention and control group in time

spent in MVPA, although there was an increase in sedentary time and a corresponding reduction in time spent in light physical activity across both groups.

Corder et al. (2020) conducted a UK school-based cluster-randomised controlled trial, in which 2,862 participants at 16 schools were allocated to either control or intervention arms. Intervention was a theoretically driven mentor- and peer-leader school-based programme encouraging children to engage with new activities. At ten-month follow up, both control and intervention arms had reduced MVPA compared to baseline, with an intervention effect of -1.91 (95% CI's: -5.53, 1.70) minutes of MVPA per day difference. The authors concluded that, despite meticulous planning, the intervention was neither efficacious beyond typical school provision nor cost effective, suggesting that stake-holders and policy-makers must be realistic about the extent of improvements that can be made in school physical activity.

Additional intervention studies have shown minimal or no change in physical activity levels at follow-up measurement. These include an after-school dance project aimed specifically at girls (Jago et al., 2015) which found a non-significant -1.52 (95% CI's: -4.76, 1.73) minutes of daily MVPA six months post-intervention. Nyberg, Sundblom, Norman, and Elinder (2011) found a non-significant difference of -3.6 (95% CI's: -8.9, 1.8) minutes of MVPA per week at five months follow-up subsequent to a multi-component intervention to increase health behaviours in overweight primary school children. Lubans et al. (2016) found a mere 0.1% (95% CI's: -0.8, 1.0) difference in percentage of total physical activity spent in MVPA ten months post-intervention following an intervention targeted at obesity prevention in disadvantaged school-aged boys. Taken together, the evidence from studies including follow-up measurement appear to indicate that the modest effects revealed by meta-analyses based solely on measurements taken immediately post-intervention are not maintained.

However, other intervention studies have found differences that persist at post-intervention follow-up. For example, following a peer training intervention with girls, Sebire et al. (2018) found a significant effect of 6.09 minutes (95% CI's: 1.43, 10.76) of MVPA per weekday compared to controls

six months post-intervention, despite a non-significant effect immediately post-intervention, potentially indicating increasing efficacy post intervention period. A multi-component intervention by Toftager et al. (2014) found minor changes in school and recess time, but not total daily, MVPA at two year follow-up, concluding that mandatory and environmental interventions are potentially more effective. Another multi-component school-based intervention, conducted by Sutherland et al. (2016), resulted in an additional seven minutes (95% CI's: 2.7, 11.4) of daily MVPA compared to controls at two year follow-up.

Without further systematic review and an additional meta-analysis, definitive claims cannot be made regarding the direction nor extent of change in the findings of the Sims et al. (2015) and the subsequently derived estimates for modelling in the thesis. However, even where an effect is recorded, the changes in physical activity observed are modest at best and rarely persist at follow-up. As such, it can be conservatively inferred that meaningful change in the effectiveness of physical activity interventions is not evident from a broad review of systematic reviews and meta-analyses that have occurred since the publication of Sims et al. (2015), nor from a sample of intervention studies aligned to the inclusion criteria from that review. A small number of studies have demonstrated efficacy and offer tentative evidence that theoretically informed, multi-component interventions that include changes to the social and physical environment to increase physical activity and health behaviours appears to provide the most promising avenue of research for effective intervention to increase childhood physical activity levels.

5.6. Conclusions and Directions

This review reinforced previous evidence that physical activity interventions have, on average, little effect on measured TPA or MVPA levels in children, either immediately post-intervention or at six-month post-intervention. The possibility remains that the included studies, plus physical activity interventions in general, are ineffective due to insufficient intensity, duration, delivery quality, theoretical grounding, and implementation or measurement sensitivity. However, changes in physical

activity behaviour have been insufficient for clinical effect in this review and others before, both at post-intervention and follow-up. Although the benefits of physical activity in childhood are intuitive, the evidence has yet to demonstrate that interventions can be relied upon to produce sustained increases in physical activity and resources may be better invested in alternative approaches to achieve positive effects, a finding which remains true following a review of more recent publications. The findings do demonstrate, however, that interventions do not reduce levels of physical activity.

At the time of writing no publication had specifically investigated the maintenance of physical activity levels at follow-up post-intervention; this represented an important gap in knowledge addressed by the current review. Sub-group analysis revealed a potential area of promise with the utilisation of physical activity intervention to treat high-risk children and warrants further investigation. The challenge remains to ensure that high methodological quality, particularly regarding measurement tools, is adhered to in future studies to build a meaningful evidence base.

5.7. Chapter Summary

The systematic review and meta-analysis reported in the present chapter forms an underpinning for the subsequent chapter in which the outputs from the meta-analysis are contrasted with the baseline output from the model. Following a summary of more recent publications, no substantive difference in parameters was required. While the number of studies meeting the inclusion criteria for the above meta-analysis are comparatively few, these studies represent the best available evidence by which to parameterise the first examples of front-end scenarios. The figures presented in Table 8, specifies the estimates for effectiveness for the population and the treatment approaches, are therefore applied in the following chapter.

Chapter 6 - Application of Counterfactuals from Systematic Review

6.1. Overview of Chapters Six, Seven, and Eight

In order to conduct the analysis of childhood physical activity interventions against a baseline simulated cohort, the following three chapters specify and then conduct a systematic analysis on two distinct counterfactual scenarios. For Chapters 6 and 7, two counterfactuals comprise one 'population' approach in which an intervention is applied to the entire cohort, and one 'treatment' approach, in which an intervention is applied only to the least active strata of the cohort. Within both chapters, findings from the application of each counterfactual approach is first analysed individually and then contrasted. Chapter 8 then explores the necessary physical activity increases required to meet two desirable health outcomes.

In order to provide the basis for comparison, Chapter 6 presents an evaluation of the impact of an application of the estimates drawn from the meta-analysis presented in Chapter 5. Chapter 7 presents two further specific counterfactual scenarios derived from contemporary interventions implemented within the English population, in this case the Daily Mile and the MEND interventions. Chapter 8 then uses the model to examine the extent to which physical activity can contribute to contemporary health goals.

Each chapter presents a rationale for selection and a specification for how scenarios were parameterised and applied to the baseline model. Deterministic results are presented to illustrate the consequences of applying these front-ends to the model. Uncertainty analyses are then completed in order to demonstrate the stochastic uncertainty around the input parameters within the model. Lastly, a comparison of population versus treatment approaches is presented.

6.2. Section Introduction

The following analysis presents the outputs from the application of the estimates derived from the systematic review and meta-analysis conducted on randomised controlled studies investigating

interventions to increase levels of physical activity, described in detail in Chapter 5. The section below applies an abstracted population and treatment scenario to the baseline scenario presented above.

6.3. Population Intervention Context

The meta-analysis presented in Chapter 5 drew output data from fourteen studies, specified via a systematic review of the literature, of which eleven studies described a population approach to increasing physical activity levels. There was a wide variety of intervention strategies across the included studies. As specified in Chapter 5, the studies adopting a population approach included interventions such as providing extra physical education classes in curriculum time (Araujo-Soares et al., 2009; Bugge et al., 2012; Dewar et al., 2013; McManus et al., 2008), PA delivery outside curriculum time (Chen et al., 2010; Jago et al., 2006), goal-setting sessions (Araujo-Soares et al., 2009; Black et al., 2010), incentive-based intervention (Jago et al., 2006; Roemmich et al., 2012), and peer-modelling (Black et al., 2010; Cui et al., 2012), either singularly or in combination. Intervention duration lasted between six weeks (McManus et al., 2012) and three years (Bugge et al., 2012; Nader et al., 1999). The systematic review and subsequent meta-analysis specifically excluded any studies which did not provide follow-up data for at least six months post-intervention.

6.3.1. Scenario Parameterisation and Formal Scenario

Meta-analysis of the eleven studies indicated above produced an estimate of 1.03 (95% CI's: -2.54, 4.60) minutes per week of additional physical activity resulting from a population approach to intervention. Given the heterogeneous nature of the interventions and measurement practices, and in the absence of data that permitted differentiation of effectiveness by pre-existing levels of physical activity, no distinction or graded application across the physical activity strata was applied. This derived estimate presented in Table 9 is directly applied to all children, regardless of gender, within the simulated cohort in each year of childhood, from five to fifteen years of age, constituting a physical activity increase for eleven consecutive years.

Minutes of additional MVPA per week	95% CI's	MET equivalent	Point estimate MET minutes per week	CI's MET minutes per week
1.03	-2.54, 4.60	5.11	5.26	-12.97, 23.49

Table 9 - Showing calculations of input parameters for the Population scenario drawn from Sims et al. (2015) meta-analysis of eleven physical activity intervention papers reporting follow-up data.

The MET equivalent conversion figure of 5.11 in Table 9 is unique to this project. Ainsworth et al. (2011) suggest a figure of 4.5 MET minutes for moderate physical activity and 6.5 for vigorous physical activity. Previous studies, for example Wahid et al. (2016), have taken the average of 5.5 as reflecting MVP. However, in an examination of school recess time behaviour, Ridgers, Stratton, and Fairclough (2005) showed that only 16% of moderate-to-vigorous physical activity consists of vigorous physical activity, resulting in the potential for overestimate (i.e. 16% of vigorous physical activity and 84% moderate physical activity). In addition, Hamer and Stamatakis (2018) analysed accelerometry data from 4770 children from the Millennium Cohort Study, principally to assess the association between relative intensities of physical activity and risk of obesity in later childhood. Vigorous physical activity was found to comprise 30.4% of recorded MVPA which, when used to weight the relative contribution, produces the MET equivalent value used above. Given the availability of an objectively measured, whole-day estimate of the relative proportion of vigorous to moderate physical activity, the figure from Hamer and Stamatakis (2018) was therefore used to parameterise physical activity levels in the thesis.

6.3.2. Effect of Intervention

Application of the scenario parameters derived from the Sims et al. (2015) meta-analysis within the simulated cohort resulted in an absolute gain of 5.26 MET minutes per week for both males and females, comprising a mere 0.21 and 0.30 percent increase for males and females respectively, compared to the baseline scenario across the school-aged population (i.e. five to fifteen years old inclusive). Under the benchmark physical activity legacy scenario as specified in Chapter 3, the intervention led to an average cohort lifetime increase of 1.65 MET minutes per week. Figure 6.1

presents the baseline and counterfactual scenario physical activity trajectories for individuals under 40 years of age revealing the stratum-specific benefits. The benefits are modelled to follow an exponential decay pattern towards baseline levels. The benefits of the meta-analysis estimate intervention for school-aged children are presented in Figure 6.2, which illustrates the relative benefit experienced by strata of physical activity and sex. Both figures display the fractional effects afforded by the intervention estimate across the simulated population.

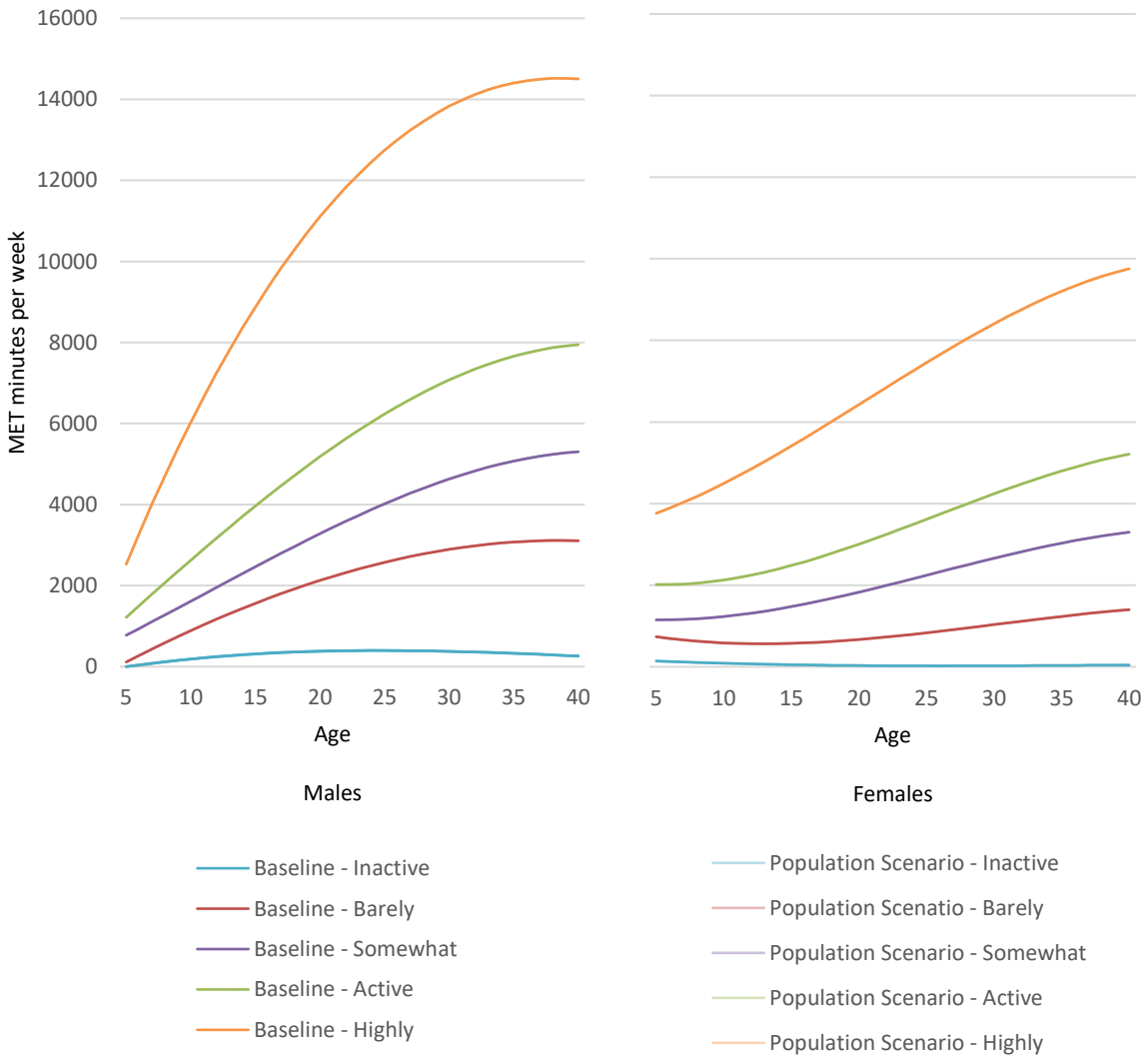


Figure 6.1 - Line graphs showing impact on MET minutes per week trajectories following population intervention estimate scenario, by physical activity strata and sex.

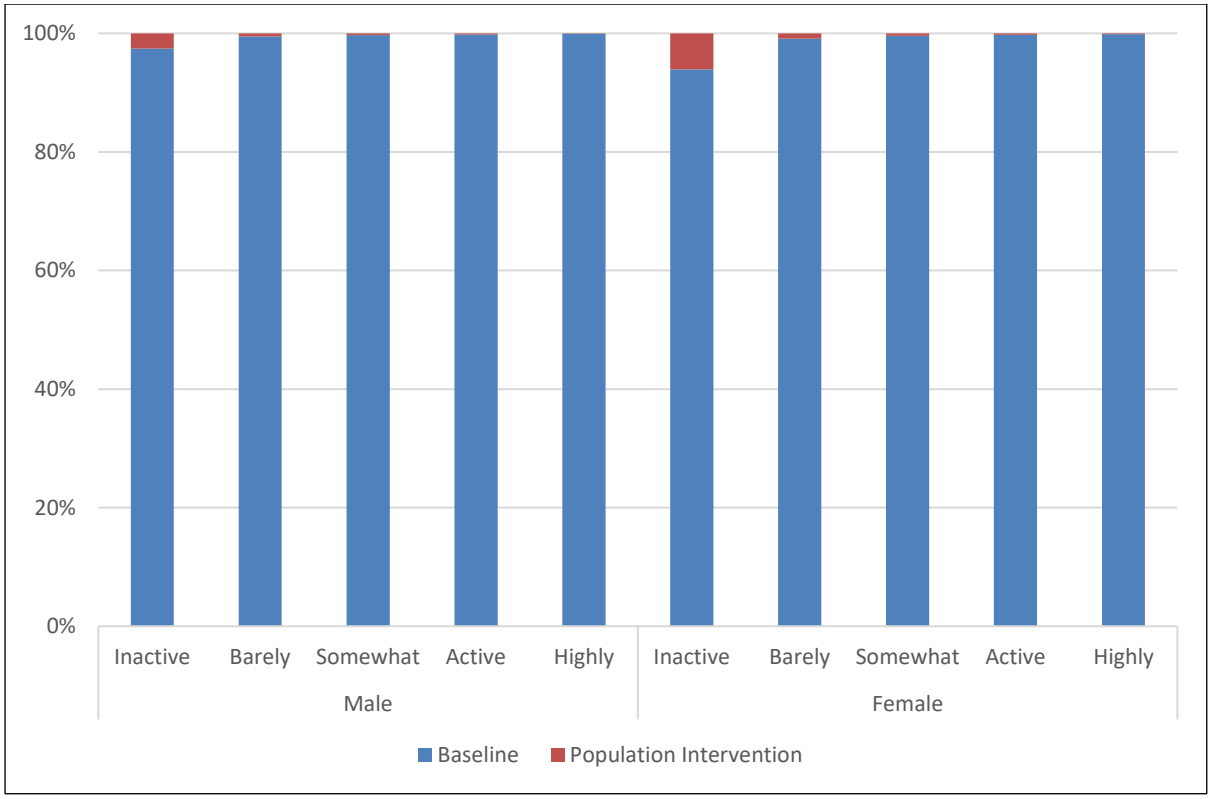


Figure 6.2 - 100% Stacked column graph showing the benefit of application of the meta-analysis estimate for population interventions in total MET minutes per week, by sex and physical activity strata.

6.3.3. Primary Outputs

The modelled implementation of the population scenario resulted in an estimated 0.01 years of life gained, which approximates to 4.50 days of additional life per person across the simulated population of 100,000. The primary findings are presented in Table 10; the point estimates are produced from a deterministic run of the core model, with the confidence interval produced by taking the 2.5th and 97.5th percentiles from 2500 iterations of a Monte Carlo analysis. The intervention had a negligible effect on life expectancy but showed a small reduction in years of life lost and years of life in disability.

Output	Estimate (years)	Lower uncertainty interval	Upper uncertainty interval	Estimate in days
Change in life expectancy at five years old				
Cohort	0.01	0.00	0.02	4.50
Males	0.02	0.00	0.04	8.61
Females	0.00	0.00	0.01	0.47
Cohort change in years of life lost per 100,000				
Cohort	-2.15	-3.63	0.28	-767.85
Males	-4.10	-6.38	0.06	-1462.98
Females	-0.20	-0.92	0.50	-68.50
Years of life in disability per 100,000				
Cohort	-1855.98	-3666.49	923.34	-668942.43
Males	-3204.82	-5403.44	747.46	-1150537.94
Females	-507.16	-2034.68	1091.86	-183991.32

Table 10 - Primary outputs and uncertainty intervals (2.5th & 97.5th percentiles) from the application of the meta-analysis estimate for population interventions scenario, presenting changes in life expectancy at five years of age, years of life lost, and years of life in disability.

The changes following application of the meta-analysis estimate for population specific interventions on prevalence of specific health outcomes are presented in Table 11. The greatest benefit is observed for type 2 diabetes, with a lesser effect for myocardial infarction. There is a small preventative effect on all health outcomes, but the intervention has only a small effect on stroke and the three forms of cancer.

Change in number of prevalent cases per 100,000	Estimate	Lower uncertainty interval	Upper uncertainty interval
MI			
Cohort	-5.84	-14.37	2.27
Males	-11.52	-27.68	3.62
Females	-0.16	-0.92	0.46
Stroke			
Cohort	-3.94	-8.41	1.46
Males	-7.66	-15.78	2.32
Females	-0.22	-1.06	0.60
Type 2 Diabetes			
Cohort	-33.33	-69.57	20.28
Males	-59.62	-109.36	22.20
Females	-7.06	-31.44	18.30
Bowel Cancer			
Cohort	-1.03	-2.34	0.33
Males	-2.00	-4.38	0.52
Females	-0.06	-0.34	0.16
Breast Cancer			
Females	-0.12	-0.64	0.32
Uterine Cancer			
Females	-0.08	-0.48	0.24

Table 11 - Changes in prevalent cases per 100,000 for specific disease outcomes following modelling application of the meta-analysis estimate for population interventions scenario, including uncertainty intervals (2.5th & 97.5th percentiles).

Comparisons between baseline and the population intervention estimate derived from meta-analysis for life expectancy are presented in Figure 6.3, broken down by physical activity strata and sex, with a corresponding presentation for years of life in disability in Figure 6.4. Figure 6.5 presents the comparison between baseline and population intervention estimate scenarios, showing no discernible reductions in any health outcome for both males and females.

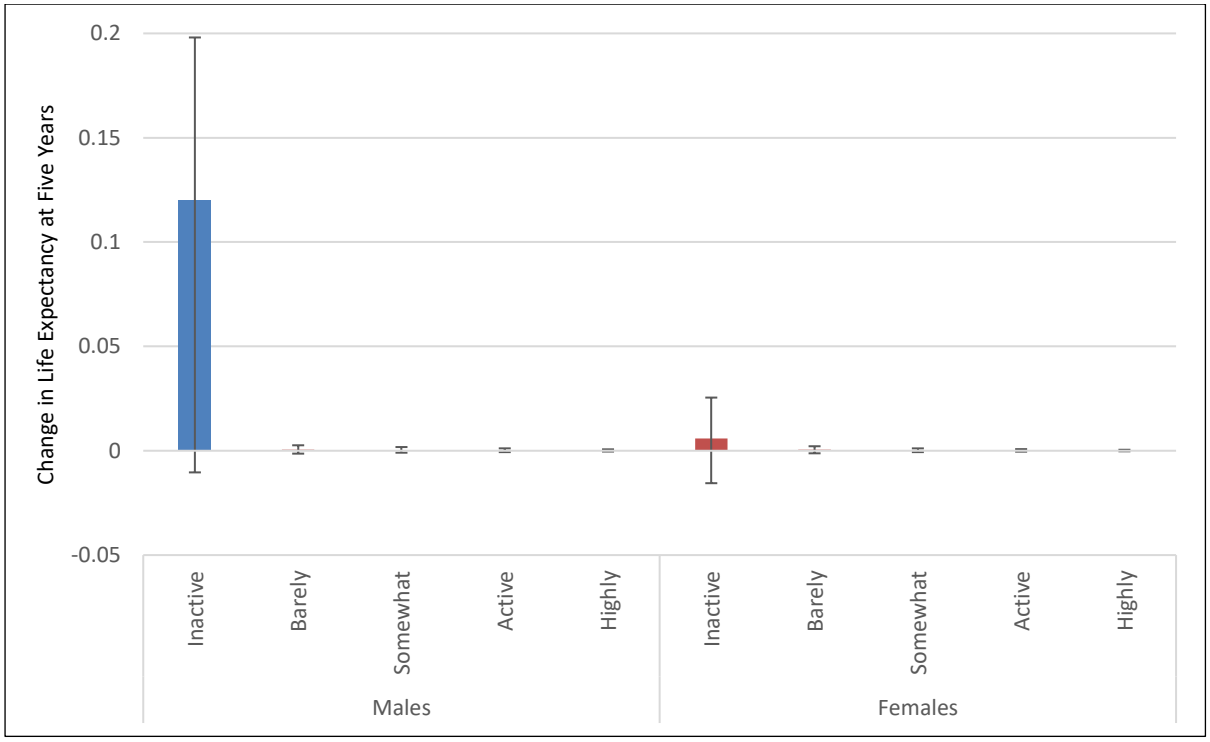


Figure 6.3 - Column graph showing the estimate for change in life expectancy at five years of age following application of the meta-analysis estimate for population interventions relative to baseline, by physical activity strata and sex, with uncertainty intervals (2.5th & 95th percentiles).

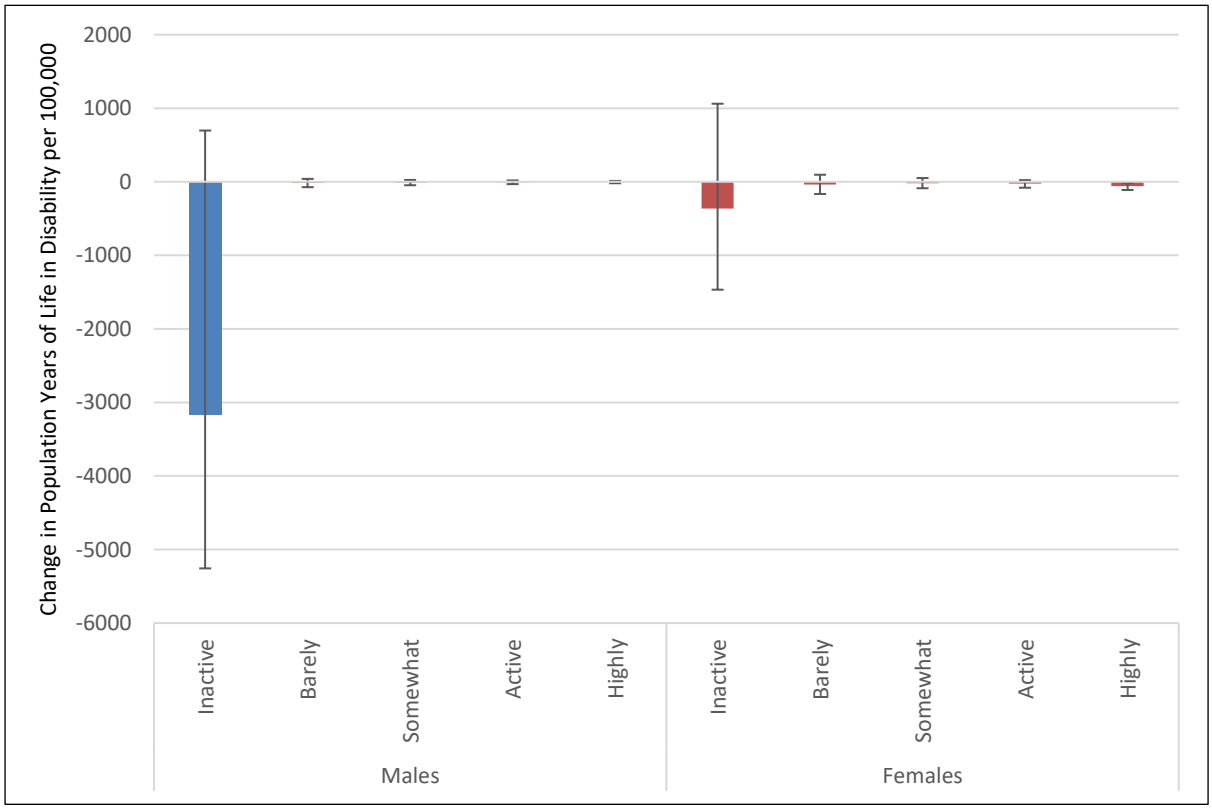


Figure 6.4 - Column graph showing the benefit of application of the meta-analysis estimate for population interventions relative to baseline on years of life in disability, physical activity strata and sex, with uncertainty intervals (2.5th & 95th percentiles).

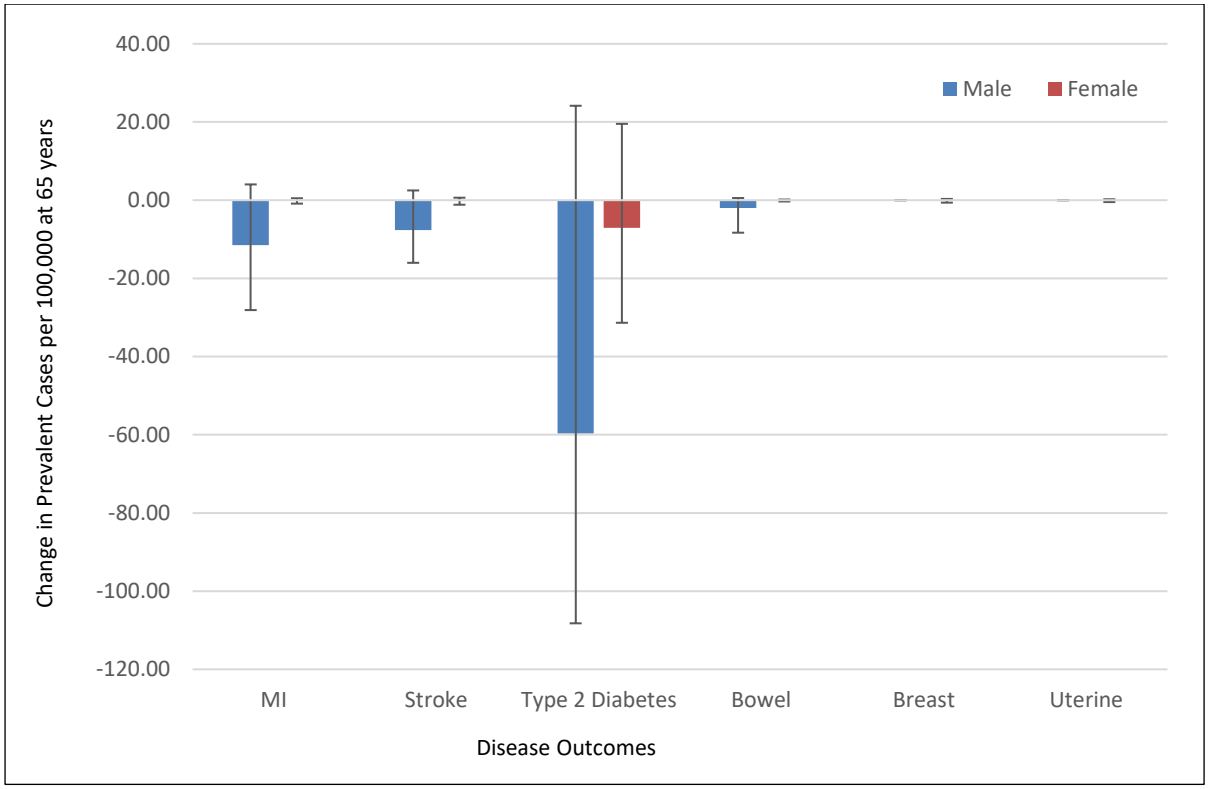


Figure 6.5 - Column graph showing comparison of baseline and application of the meta-analysis estimate for population interventions on prevalent cases per 100,000 of specific health outcomes at 65 years of age, by sex, with uncertainty intervals (2.5th & 95th percentiles).

6.3.4. Uncertainty and Sensitivity Analysis

In line with the process for sensitivity and uncertainty analysis specified in Chapter 3, parametric uncertainty was assessed using 2500 iterations of a Monte Carlo analysis. The uncertainty bars in Figure 6.3, Figure 6.4, and Figure 6.5 are generated from this process, specifying the 2.5th and 97.5th percentile, while the point estimate itself is produced by a deterministic run of the model. The contribution of specific input parameters to this uncertainty are presented for life expectancy in Figure 6.6 and years of life in disability in Figure 6.7.

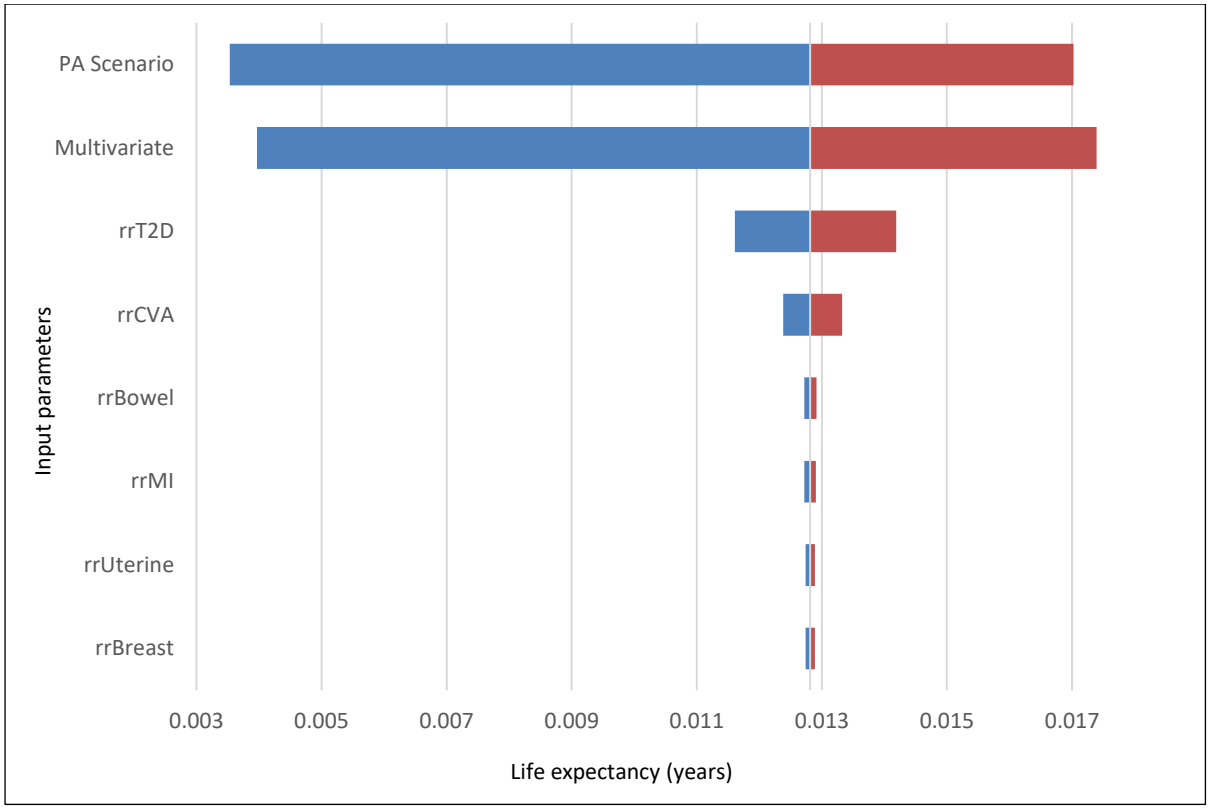


Figure 6.6 - Tornado plot showing the sensitivity of the estimate for change in life expectancy (0.01) due to uncertainty within specific input parameters following modelling of the population intervention estimate scenario.

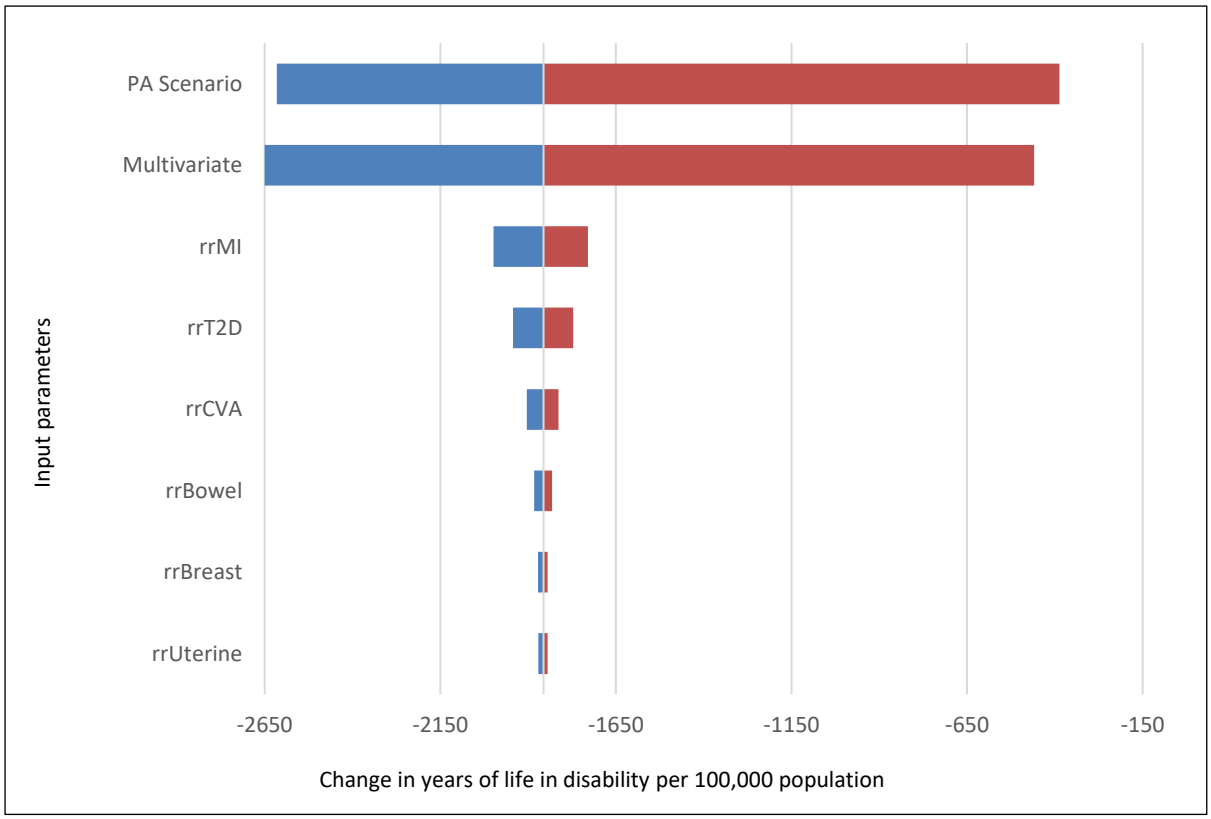


Figure 6.7 - Tornado plot showing the sensitivity of the estimate for change in years of life in disability (1855.98) due to uncertainty within specific input parameters following modelling of the population intervention estimate scenario.

6.3.5. Interim Discussion of the Meta-Analysis-Derived Population Estimate

With the input estimate for improvements in physical activity being so small it is of little surprise to observe that there were no discernible benefits following scenario modelling. The impact of the estimate on levels of physical activity was minimal even for the Inactive strata (see Figure 6.2) and as a consequence made negligible impact on the health outcomes of interest.

6.3.6. Strengths and Limitations

While the estimate applied to the baseline scenario was very small, modelling of such a benefit is not without precedent (e.g. Barrett et al., 2015), and represented an important use of the model. The input physical activity increase parameter was systematically derived to represent the best available estimate of the sustained effect of population-based interventions designed to increase levels of physical activity in children.

The input parameter generated from the meta-analysis was inevitably a summary of the data from papers that described heterogeneous approaches to the increase of physical activity in children. As such the estimates and outcomes presented above do not directly represent a real-world intervention. In addition, the blanket application of the physical activity benefit across the cohort and throughout childhood was not representative of the interventions in the contributing papers. However, the specific parameterisation of an evidenced-based estimate and application to a simulated cohort is representative of the modelling approach.

6.4. Treatment Intervention Context

The meta-analysis presented in Chapter 5 drew output data from fourteen studies, specified via a systematic review of the literature, of which three studies described a treatment approach to increasing physical activity levels, i.e. an approach specifically targeting a high-risk section of the population. There was a variety of intervention strategies across the included studies. As specified in Chapter 5, the studies adopting a treatment approach included interventions such as providing extra physical education classes (Wright et al., 2013), primary-care family counselling sessions (Wake et al.,

2009), and a community-based combined diet and activity programme (Nemet et al., 2005). Intervention duration lasted either three (Nemet et al., 2005; Wake et al., 2009) or four (Wright et al., 2013) months. The systematic review and subsequent meta-analysis specifically excluded any studies which did not provide follow-up data for at least six months post-intervention.

6.4.7. Scenario Parameterisation and Formal Scenario

Meta-analysis of the three studies indicated above produced an estimate of 4.47 (95% CI's: -0.81, 9.76) minutes per week of additional physical activity resulting from a treatment approach to intervention. Unlike the population approach specified above, the estimate summarising treatment approaches is applied only to the Inactive strata within the simulated cohort, but again using the MET minutes conversion figure of 5.11. This derived estimate presented in Table 12 is directly applied only to children in the Inactive strata, regardless of gender, within the simulated cohort in each year of childhood, from five to fifteen years of age, constituting a physical activity increase for eleven consecutive years.

Minutes of additional MVPA per week	95% CI	MET equivalent	Point estimate MET minutes per week	CI's MET minutes per week
4.47	-0.81, 9.76	5.11	22.83	-4.14, 49.84

Table 12 - Showing calculations of input parameters for the Treatment scenario drawn from Sims, Scarborough, and Foster (2015) meta-analysis of eleven physical activity intervention papers reporting follow-up data.

6.4.8. Effect of Intervention

Application of the scenario parameters derived from the Sims et al. (2015) meta-analysis within the simulated cohort resulted in an absolute gain of 22.83 MET minutes for each individual, comprising a 0.18 and 0.26 percent increase for males and females respectively, compared to the baseline scenario across the school-aged population (i.e. five to fifteen years old inclusive). Under the benchmark physical activity legacy scenario as specified above, the intervention led to an average cohort lifetime increase of 0.04 percent. Figure 6.8 presents the baseline and counterfactual scenario physical activity trajectories for individuals under 40 years of age revealing the stratum-specific benefits. The benefits

are modelled to follow an exponential decay pattern towards baseline levels. The benefits of the meta-analysis estimate intervention for school-aged children are presented in Figure 6.9, which illustrates the relative benefit experienced by strata of physical activity and sex. Once again, the figures both reveal a small benefit in outcome.

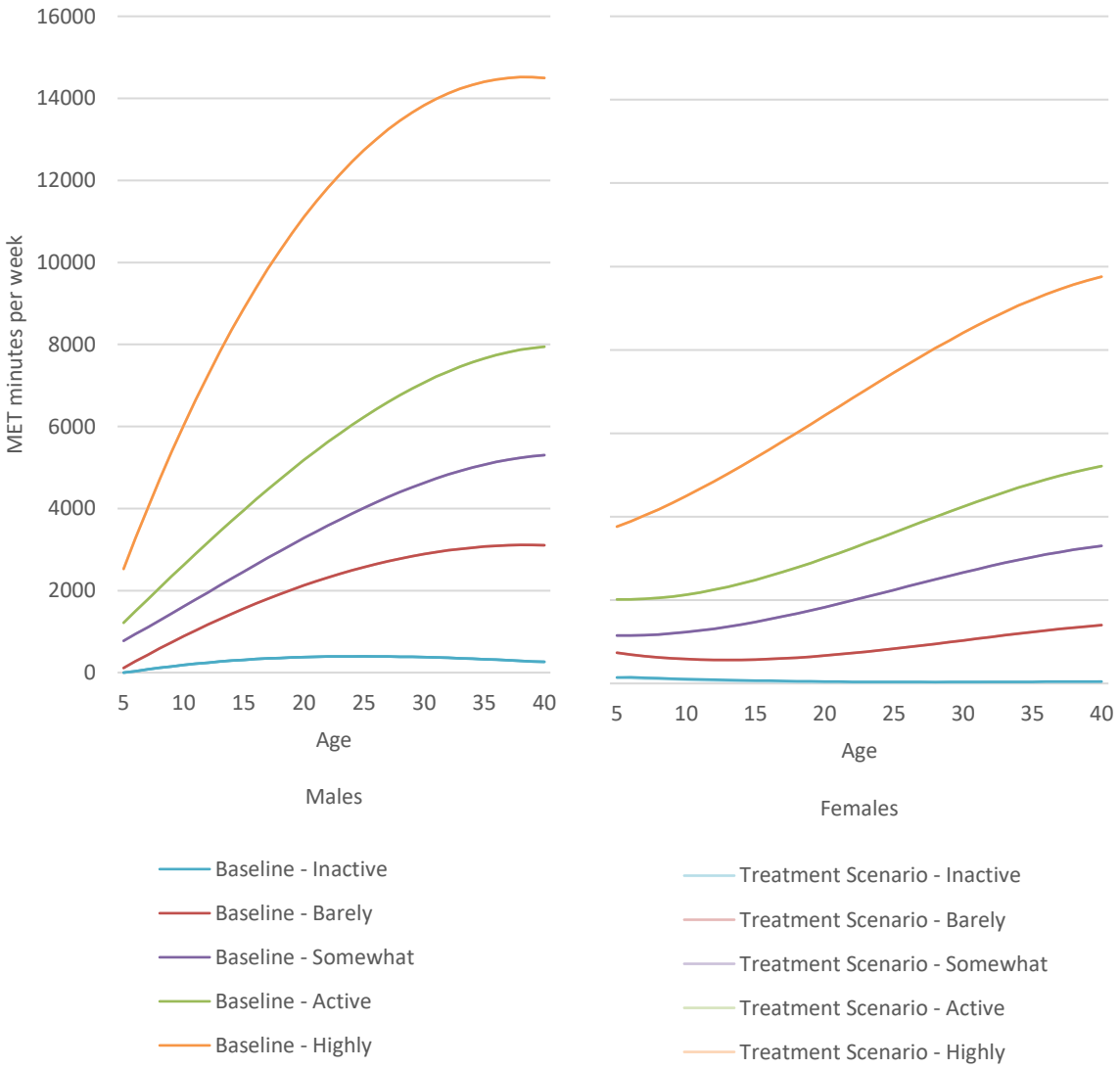


Figure 6.8 - Line graphs showing impact on MET minutes per week trajectories following treatment estimate scenario, by physical activity strata and sex.

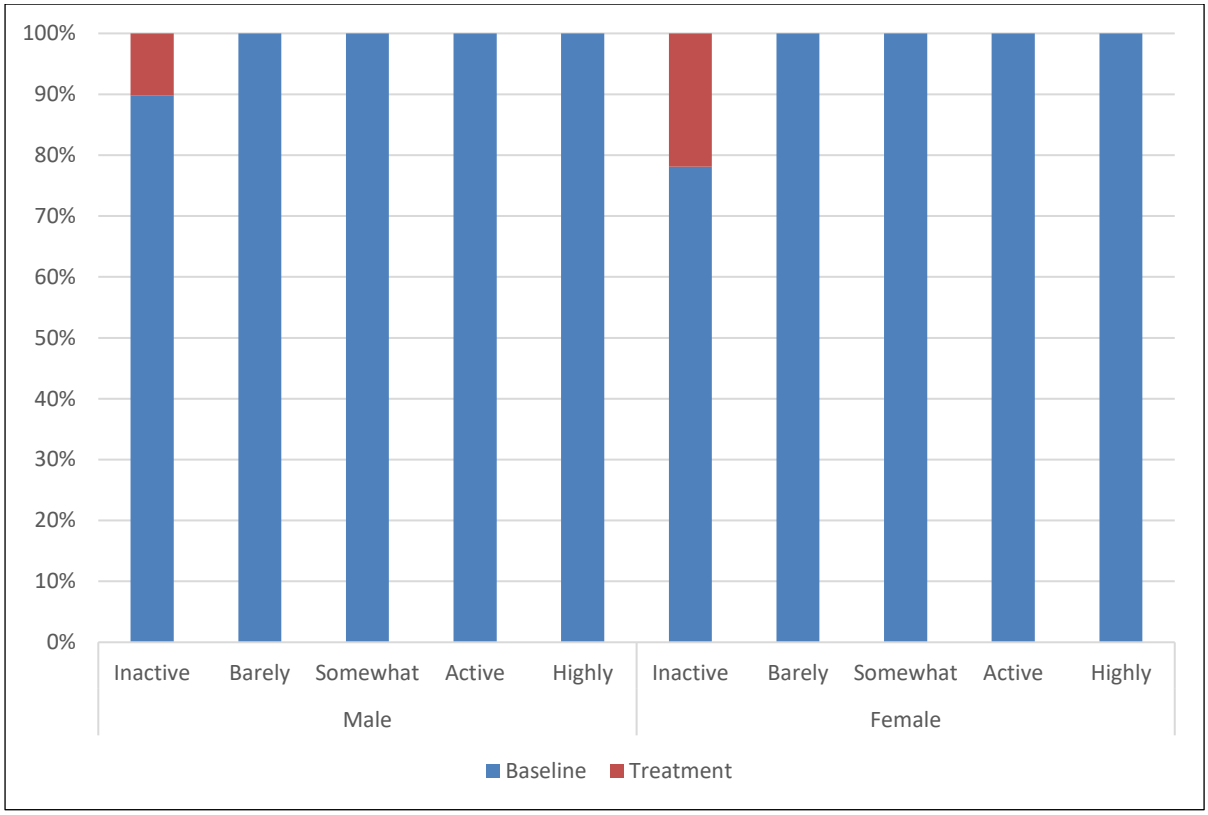


Figure 6.9 - 100% Stacked column graph showing the benefit of application of the meta-analysis estimate for treatment interventions in total MET minutes per week, by sex and physical activity strata.

6.4.9. Primary Outputs

The modelled implementation of the treatment scenario resulted in an estimated 0.02 years of life gained, which approximates to 7.46 days of additional life per person across the simulated population. The primary findings are presented in Table 13, the point estimates are produced from a deterministic run of the core model, with the confidence interval produced by taking the 2.5th and 97.5th percentiles from 2500 iterations of a Monte Carlo analysis. The intervention had a negligible effect on life expectancy but showed a small reduction in years of life lost and years of life in disability.

Output	Estimate (years)	Lower uncertainty interval	Upper uncertainty interval	Estimate in days
Change in individual life expectancy at 5 years old				
Cohort	0.02	0.00	0.03	7.46
Males	0.04	0.00	0.04	13.10
Females	0.00	0.00	0.01	1.85
Cohort change in years of life lost per 100,000				
Cohort	-3.35	-4.68	0.10	-1215.52
Males	-5.98	-7.86	0.02	-2163.72
Females	-0.72	-1.56	0.18	-264.12
Years of life in disability per 100,000				
Cohort	-1890.70	-3552.94	1050.69	-701076.58
Males	-2281.04	-6298.86	4120.08	-816062.60
Females	-1500.36	-3208.76	332.80	-554810.66

Table 13 - Primary outputs and confidence intervals following the application of the meta-analysis estimate for treatment interventions scenario, presenting changes in life expectancy at five years of age, years of life lost, and years of life in disability.

The changes following application of the meta-analysis estimate for treatment specific interventions on prevalence specific health outcomes are presented in Table 14. The greatest benefit is observed for type 2 diabetes, with a lesser effect for myocardial infarction. There is a small preventative effect on all health outcomes, but the intervention has only a marginal effect on stroke and the three forms of cancer.

Change in number of prevalent cases per 100,000	Estimate	Lower uncertainty interval	Upper uncertainty interval
MI			
Cohort	-5.74	-14.13	2.27
Males	-10.88	-27.68	3.62
Females	-0.60	-1.82	0.14
Stroke			
Cohort	-4.05	-8.36	1.46
Males	-7.30	-15.44	3.16
Females	-0.80	-2.14	0.22
Type 2 Diabetes			
Cohort	-39.82	-68.87	4.90
Males	-56.46	-106.74	28.52
Females	-23.18	-50.4	6.68
Bowel Cancer			
Cohort	-1.03	-2.34	0.37
Males	-1.84	-4.40	0.98
Females	-0.22	-0.62	0.04
Breast Cancer			
Females	-0.42	-1.10	0.10
Uterine Cancer			
Females	-0.28	-0.96	0.08

Table 14 - Changes in prevalence for specific disease outcomes following the application of the meta-analysis estimate for treatment interventions scenario, including 95% uncertainty intervals.

Comparisons between baseline and the treatment intervention estimate derived from meta-analysis for life expectancy are presented in Figure 6.10, broken down by physical activity strata and sex, with a corresponding presentation for years of life in disability in Figure 6.11. Figure 6.12 presents the comparison between baseline and treatment intervention estimate scenarios, showing no discernible reductions in any health outcome for both males and females.

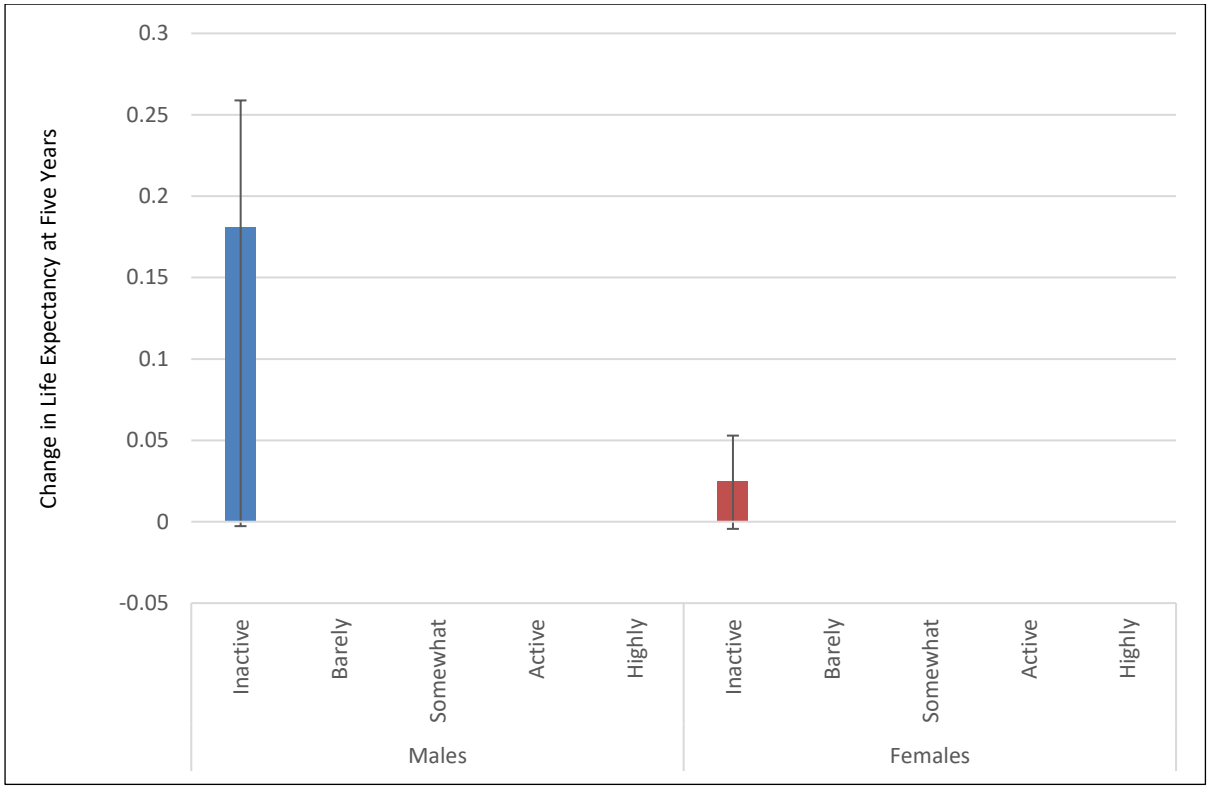


Figure 6.10 - Column graph showing the benefit of application of the meta-analysis estimate for treatment interventions relative to baseline on life expectancy at five years of age, by physical activity strata and sex, with uncertainty intervals (2.5th & 95th percentiles).

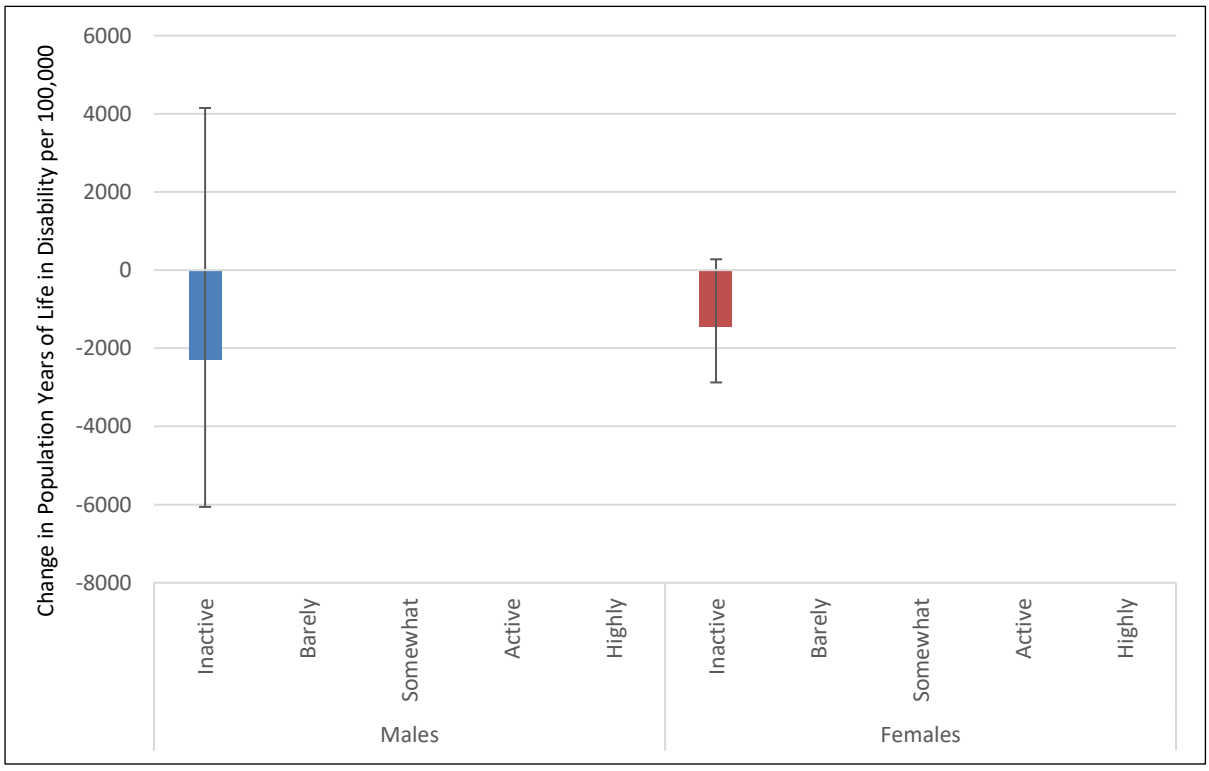


Figure 6.11 - Column graph showing the benefit of application of the meta-analysis estimate for treatment interventions relative to baseline on years of life in disability, physical activity strata and sex, with uncertainty intervals (2.5th & 95th percentiles).

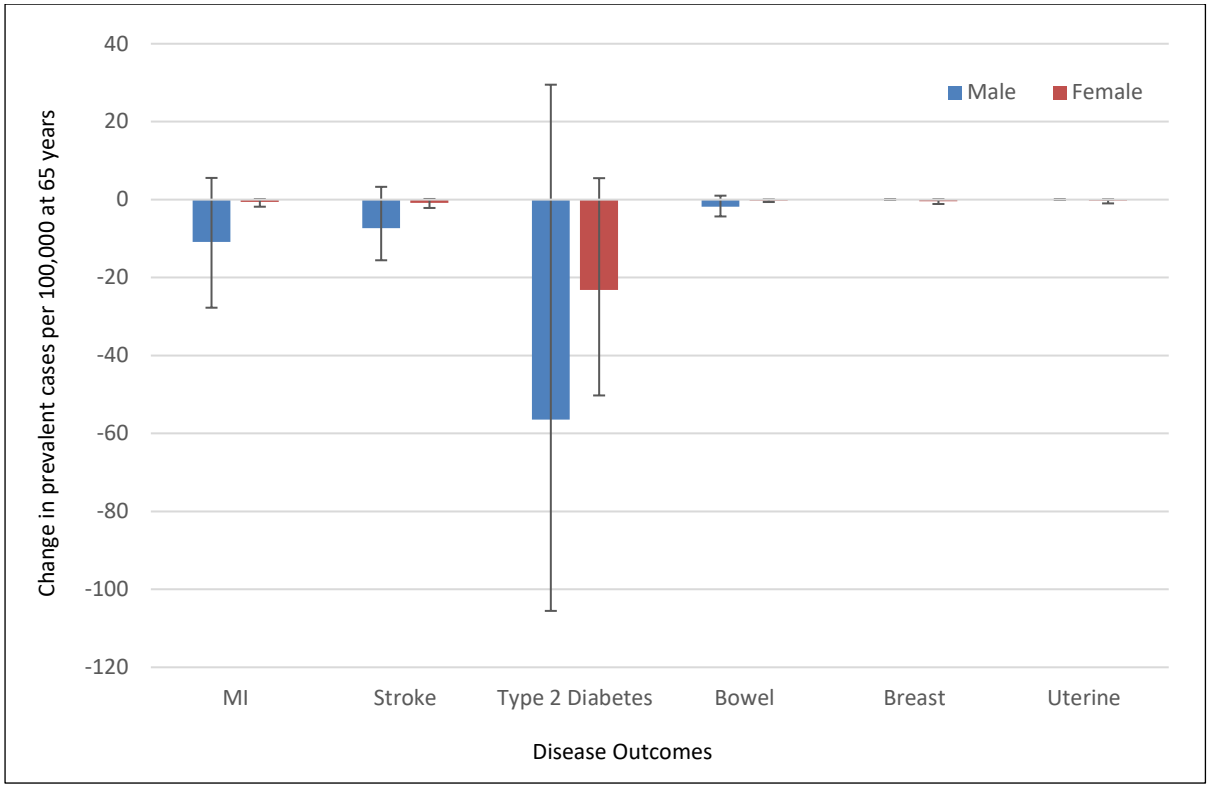


Figure 6.12 - Column graph showing comparison of baseline and application of the meta-analysis estimate for treatment interventions on prevalent cases of specific health outcomes at 65 years of age, by sex, with uncertainty intervals (2.5th & 95th percentiles).

6.4.10. Uncertainty and Sensitivity Analysis

In line with the process for sensitivity and uncertainty analysis specified in Chapter 3, parametric uncertainty was assessed using 2500 iterations of a Monte Carlo analysis. The uncertainty bars in Figure 6.10, Figure 6.11, and Figure 6.12 are generated from this process, specifying the 2.5th and 97.5th percentile, while the point estimate itself is produced by a deterministic run of the model. The contribution of specific input parameters to this uncertainty are presented for life expectancy in Figure 6.13 and years of life in disability in Figure 6.14.

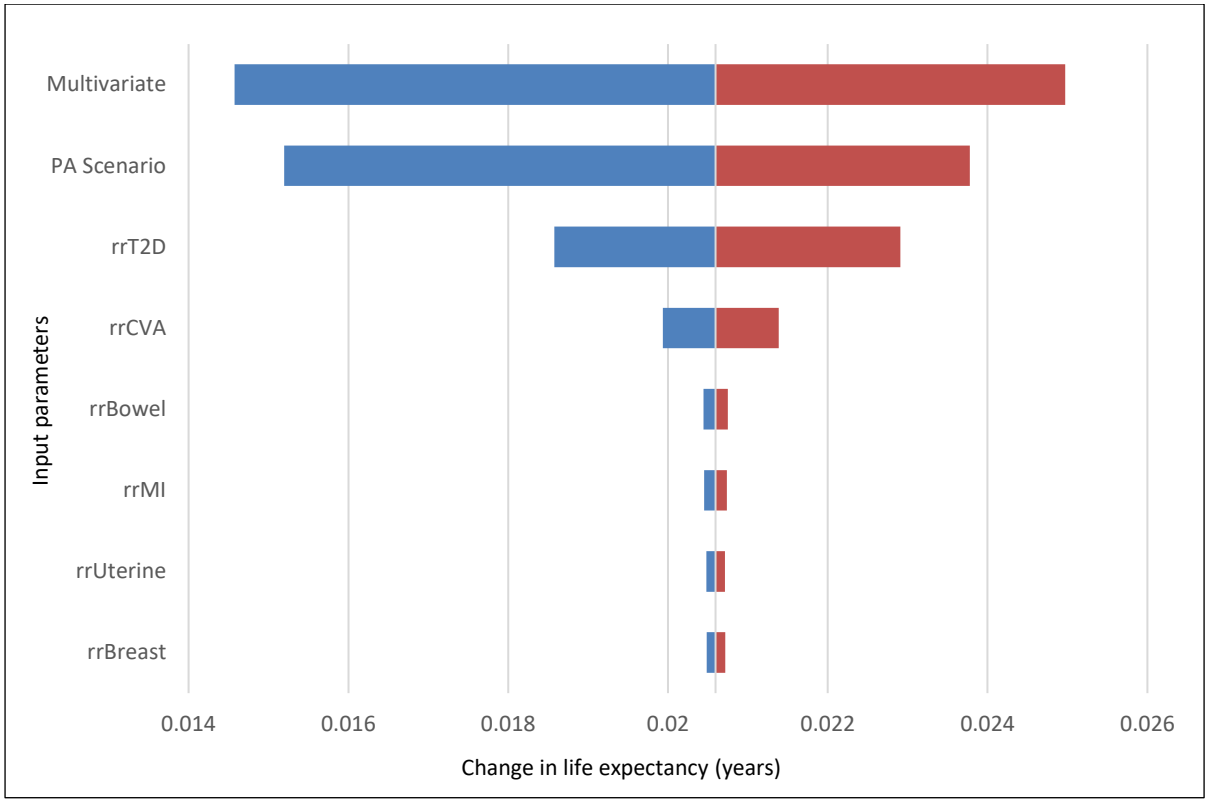


Figure 6.13 - Tornado plot showing uncertainty of input parameters for Life Expectancy estimate (0.02) following modelling of the application of the meta-analysis estimate for treatment interventions.

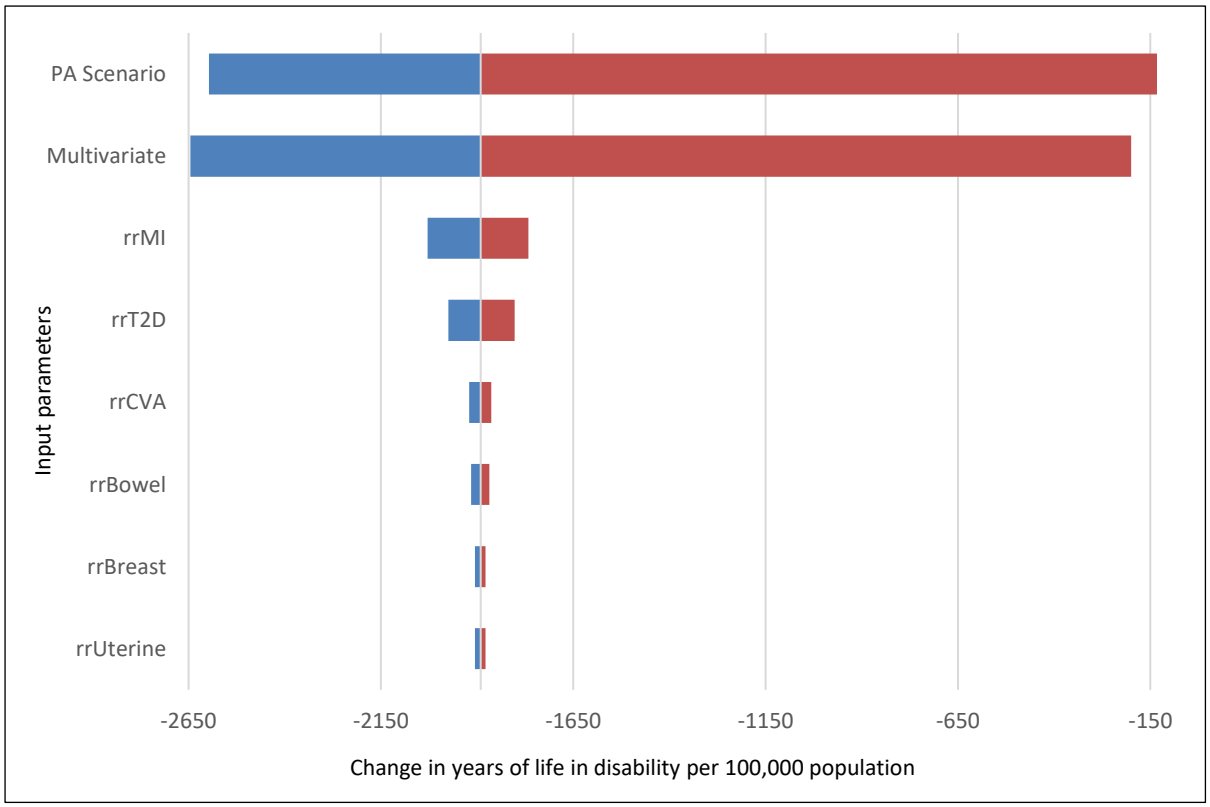


Figure 6.14 - Tornado plot showing uncertainty of input parameters for Years of Life in Disability estimate (1890.70) following modelling of the application of the meta-analysis estimate for treatment interventions.

6.4.11. Interim Discussion of the Meta-Analysis Treatment Estimate

Although the estimate for improvements in physical activity due to treatment approaches was larger than that for population approaches it was only applied to the Inactive strata and as such any effect is diluted across the remainder of the cohort. Once again, the minimal benefit to physical activity levels due to intervention meant there was little observable improvement in outputs. The impact of the estimate on levels of physical activity was minimal even for the targeted Inactive strata (see Figure 6.9) and as a consequence made negligible impact on the health outcomes of interest. This absence of discernible effect is subsequent to a modelling scenario in which the benefit was applied for all years of childhood, boosting the physical activity by the specified amount in each year.

6.4.12. Strengths and Limitations

While the estimate applied to the baseline scenario was minimal, once again the input represented the best available evidence for the sustained effects of treatment-oriented intervention. With many studies reporting post-intervention gains in physical activity, the comparative rarity of a systematically and rigorously measured and controlled trial incorporating meaningful follow-up data does not yet allow such claims to be substantiated.

The input parameter generated from the meta-analysis was inevitably a summary of the data from papers that described heterogeneous approaches to the increase of physical activity in children. As such the estimates and outcomes presented above do not directly represent an actual intervention. In addition, the application of the input parameter to only the Inactive strata does not map precisely from the target client groups described within the intervention studies, as some selected children due to obesity or additional criteria. However, the specific parameterisation of an evidenced-based estimate and application to a simulated cohort is representative of the modelling approach.

6.5. Comparison of the Population and Treatment scenarios

The respective estimates for the population and the treatment approach to physical activity intervention were derived from meta-analysis and therefore represent abstractions from multiple

sources. As a consequence, the brief comparison below is not intended to provide a direct comparison of the two approaches, as this comparison would require a health economic analysis in order to provide a true comparator.

Table 15 presents direct comparisons of the primary outputs from both scenarios, broken down by physical activity strata and sex. The figures under the two scenarios match predicted patterns. Under the population scenario, the relative benefit of intervention on the three primary outputs follows a pattern of sharply diminishing return for strata of increasing physical activity. However, while the treatment scenario clearly benefits only the Inactive strata, it shows a slightly superior cohort-level benefit on all three primary outputs, potentially indicating that a focus on maximal increases in the physical activity levels of the inactive proportion of the population is more effective than a population approach that necessarily dilutes impact across the whole cohort. A large proportion of the benefits accrued by implementation of the population scenario are observed within the Inactive strata, but when compared to an intervention that specifically targets these strata is unable to match this effectiveness. The lack of impact on disease specific outcomes is further reinforced by the data presented in Figure 6.15, which clearly show that any observed impact is minimal at best.

	Population		Treatment	
	Males	**Females**	**Males**	**Females**
Life Expectancy at 5 years				
Inactive	73.21	77.73	73.27	77.75
Barely	74.87	79.12	74.87	79.12
Somewhat	75.36	79.75	75.36	79.75
Active	75.84	80.24	75.84	80.24
Highly	76.72	81.04	76.72	81.04
Totals	75.20	79.58	75.21	79.58
Cohort Total	-	77.39	-	77.40
Change in Years of Life Lost per 100,000				
Inactive	-4.10	-0.16	-5.98	-0.72
Barely	<-0.00	-0.01	0	0
Somewhat	<-0.00	<-0.00	0	0
Active	<-0.00	<-0.00	0	0
Highly	<-0.00	<-0.00	0	0
Totals	-4.10	-0.20	-5.98	-0.72
Cohort Total	-	-2.15	-	-3.34
Change in Years of Life in Disability per 100,000				
Inactive	-12158.80	-1518.39	-8709.74	-6086.60
Barely	-72.56	-137.54	0	0
Somewhat	-47.79	-71.82	0	0
Active	-34.84	-50.80	0	0
Highly	-21.61	-31.19	0	0
Totals	-3204.81	-507.15	-2281.04	-1500.36
Cohort Total	-	-1855.98	-	-1890.70

Table 15 - Comparison between primary outputs from the population and treatment estimates from the Sims et al. (2015) systematic review and meta-analysis, by physical activity strata and sex.

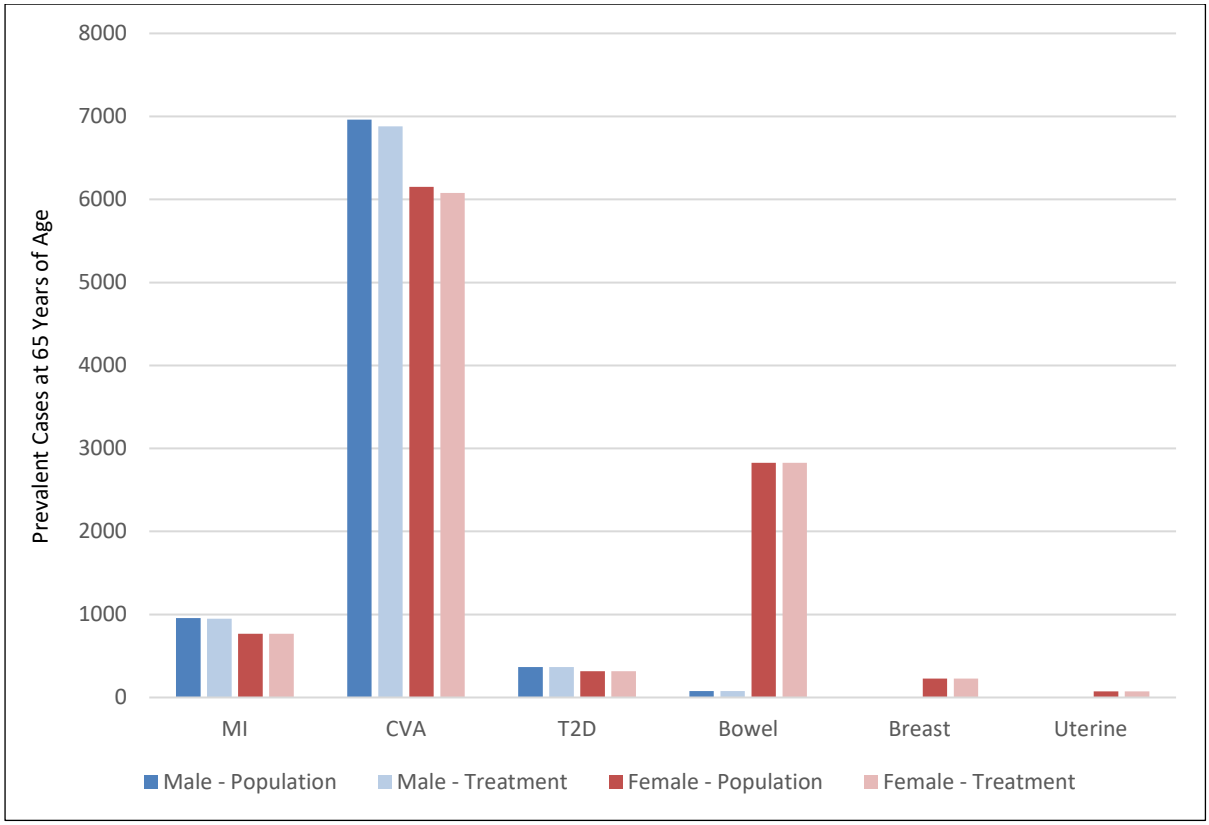


Figure 6.15 - Column graph showing comparison of Population and Treatment scenarios on prevalent cases of specific health outcomes at 65 years of age, by sex, per 100,000 population.

6.6. Chapter Summary

The present chapter formally applied the results from the systematic review and meta-analysis presented in Chapter 5 to the baseline model described in Chapter 4. While both population and treatment estimates for the increases in physical activity achieved through respective approaches to intervention are abstract figures derived from meta-analysis, they are drawn from systematically derived publications that satisfy conditions indicating that the effects on physical activity levels are plausible. Both estimates can be considered to be rather low in the face of additional publications that claim much higher levels success. However, until such publications evidence that effects persist when a study incorporates both a viable control group and meaningful post-intervention follow-up measurement, the estimates used in this chapter represent the best available evidence on the sustained effects of intervention.

Chapter 7 - Application of Counterfactuals from Specific Intervention Scenarios

7.1. Chapter Overview

In contrast to the previous chapter, in which the focus was on the application of physical activity change estimates derived from a systematic aggregation of controlled studies including follow-up measurement, the present chapter profiles and analyses the impact of two specific contemporary interventions on the simulated cohort within the model. Faithful to the core theme of the thesis, this chapter explores the impact of a population strategy, one in which all participants are eligible regardless of their existing level of physical activity, and a treatment strategy, one in which participants were specifically selected based on existing criteria. Both these interventions have been directly applied within an English context and therefore allow a more specific modelling application.

7.2. Population Intervention Context

The Daily Mile (Daily Mile Foundation, 2016) was selected for modelling due to the intervention clearly representing a preventative programme approach and one that is potentially scalable to a population level. This intervention is also relevant for policy, particularly the possibility of implementation across the UK and beyond, and has penetrated the national press (e.g. Phillips & Moses, 2016), has been the subject of contemporary parliamentary debate (*HC Deb*, 2017), and indeed was specifically mentioned in the recent government Childhood Obesity Plan (Department of Health and Social Care, 2018a). The premise is simple; school children of primary age are required to complete fifteen minutes of 'running', aiming to complete a mile in this time, on each school day. The Daily Mile must be implemented in classroom time, replacing neither break/recess time, standard physical education allocation, nor before and after-school time. Children can run at any speed, or walk, but travel must be done by foot, i.e. no scooters or bicycles are permitted.

In a preliminary evaluation at the founding school, it was estimated that of the children aged 4-7 years, 50% ran approximately one mile, while 25% ran over, and the remaining 25% ran under one mile. Of

those children aged 8-11 years, 50% ran one mile, 40% ran over, and 10% ran less than one mile (Daily Mile Foundation, 2016). The report mentions that children with special educational needs or mobility issues were supported to participate, but not whether any such children were included in the figures within this initial assessment.

A further case-study was conducted at a London primary school (LPFF, 2017) in which children completed the fifteen minutes of running, but only three times per week. Fitness was measured using a modified Cooper Run, a norm-referenced measure of cardio-respiratory fitness requiring a participant to walk/run as far as possible in six minutes (Cooper, 1968; Van Mechelen, Hlobil, & Kemper, 1986). Children's self-esteem, physical self-efficacy, and well-being were measured by self-report, and children's classroom behaviour was assessed by staff. A sample of 76 pupils (42 boys & 34 girls) showed a 19% improvement in aerobic fitness over a four-month period, with broad improvements in reported classroom performance and self-report measures (LPFF, 2017). However, it must be highlighted that the above case-studies do not represent high-quality data, comprising little more than observational studies. Furthermore, there has been some variation in the implementation of the programme leading to different levels of success; an analysis of implementation was conducted by Ryde et al. (2018), who suggested that while flexibility for schools to adapt the programme to suit the time and space parameters for their individual context is important, a delivery that remains faithful to the simple core principles of duration, activity type, and frequency is key to successful implementation.

A pilot study was conducted at two primary schools (Chesham et al., 2018) intending to implement The Daily Mile; the intervention was conducted in one school with the other providing a delayed control in which a normal curriculum was continued. The intervention group contained 247 of the 355 eligible children and the control group contained 124 of 169 eligible children, the remaining 30% did not participate due to lack of consent. Group changes in moderate-to-vigorous physical activity (MVPA) were measured using waist-mounted accelerometry worn for eight days, fitness using an age

and gender corrected shuttle run test, and adiposity using a skinfold test and Body Mass Index (BMI) z-score. Group differences in pre- to post-intervention showed 9.1 minutes per day improvement relative to control, although it was not detailed whether this mean change included weekends. Relative increases in MVPA predicted reductions in sedentary time, indicating that substitution was not occurring, but did not predict changes in fitness or adiposity. Chesham et al. (2018) conclude that modest differences were found for each outcome measure and that these are potentially relevant for health outcomes if maintained.

More recently, Morris et al. (2019) conducted a randomised controlled trial to assess the amount of MVPA associated with participation in The Daily Mile, as well as any subsequent effects on executive function and academic performance. 303 children (aged $\bar{x}$ = 8.99 ± 0.5) across eleven primary schools were individually randomised to either intervention or control conditions. Participants in the intervention group completed The Daily Mile within curriculum time, while those in the control group completed normal classroom activity. Physical activity was measured using accelerometry within a testing period on day seven of the intervention, during which participants completed the executive function and academic performance tests, and either the intervention or control condition. Morris et al. (2019) report a significant difference in physical between groups, with the intervention group completing a mean additional 10.23 (± 2.90) minutes of MVPA compared to control, as well as reductions in sedentary time, but no significant impact on executive function or academic performance tests. Although Morris et al. (2019) conducted a rigorous investigation, incorporating objective assessment of physical activity levels in a large sample of children, they caution against over-interpretation of their physical activity data, stating that this provides a snapshot only rather than indication of change subsequent to intervention, and as such it is not appropriate to use the findings from this study as the basis to parameterise subsequent modelling.

7.2.1. Scenario Parameterisation

The Daily Mile intervention specifies 15 minutes of 'running' within curriculum time in each school day, for the duration of the school year, throughout primary school education. The programme indicates that this activity should be completed irrespective of the weather, facilitated by the identification of a clear and pragmatic route, or circuit, that permits such continuity (Daily Mile Foundation, 2016). Table 16 displays the sources and data informing the input estimates by which the Daily Mile intervention was modelled. The age-specific MET values for children aged five to seven years, and eight to eleven years, were taken from Butte et al. (2018) for running at four miles per hour on the assumption that the cohort completed a mile within the allocated fifteen-minute timeframe.

Age Group	Source study	Mean (95% CI's) change in minutes of MVPA/day	Assigned MET equivalent value	Weekly Benefit in MET mins/week (95% CI's)
5-7 years	Chesham et al. (2018)	9.1 (5.1 – 13.2)	6.5	295.8 (165.8 – 429.0)
8-11 Years	Chesham et al. (2018)	9.1 (5.1 – 13.2)	7.2	327.6 (183.6 – 475.2)

Table 16 - Sources, point estimates and 95% CI's (adjusted for age and sex), and MET minutes per week estimates for two age groups following implementation of the Daily Mile intervention.

7.2.2. Formal Scenario

The scenario applies the Daily Mile intervention to the simulated population of the core model for each year of primary school attendance, without exception for age and sex. No provision is made for school refusal, ambulatory disability, sickness days, nor any lack of compliance. It is assumed that children perform the Daily Mile for the full intervention period of fifteen minutes, five days a week and for 37 weeks per year, representing the typical full academic term of attendance. The intervention occurs within curriculum time, and not within any break/recess nor before or after school. No Daily Mile benefit was applied once children reached secondary school age (twelve years). In line with the model specifications, a legacy of increased physical activity is assumed to persist post-intervention, following an exponential decay to baseline levels over subsequent years of life. For the purposes of

sensitivity analysis two further legacy patterns are applied, one with no legacy of improved post-intervention physical activity and one in which physical activity increases persist throughout lifetime.

7.2.3. Effect of Intervention

Application of the Daily Mile scenario within the simulated cohort resulted in an absolute gain of 1156.9 and 1309.7 MET minutes for male and female individuals respectively over the course of the intervention, comprising an average nine percent increase, compared to the baseline scenario within the primary school-aged population (i.e. five to eleven years old). Under the benchmark physical activity legacy scenario as specified above, the intervention led to an average lifetime increase of 54.2 and 60.8 MET minutes per week for males and females respectively, comprising an average of two percent per individual. Figure 7.1 presents the baseline and counterfactual scenario physical activity trajectories for individuals under 40 years of age revealing the stratum-specific benefits. The benefits are modelled to follow an exponential decay pattern towards baseline levels; benefits are largely negligible after 40 years of age. The benefits of the Daily Mile intervention for primary school-aged children are more explicitly presented in Figure 7.2, which illustrates the relative benefit experienced by strata of physical activity and sex.

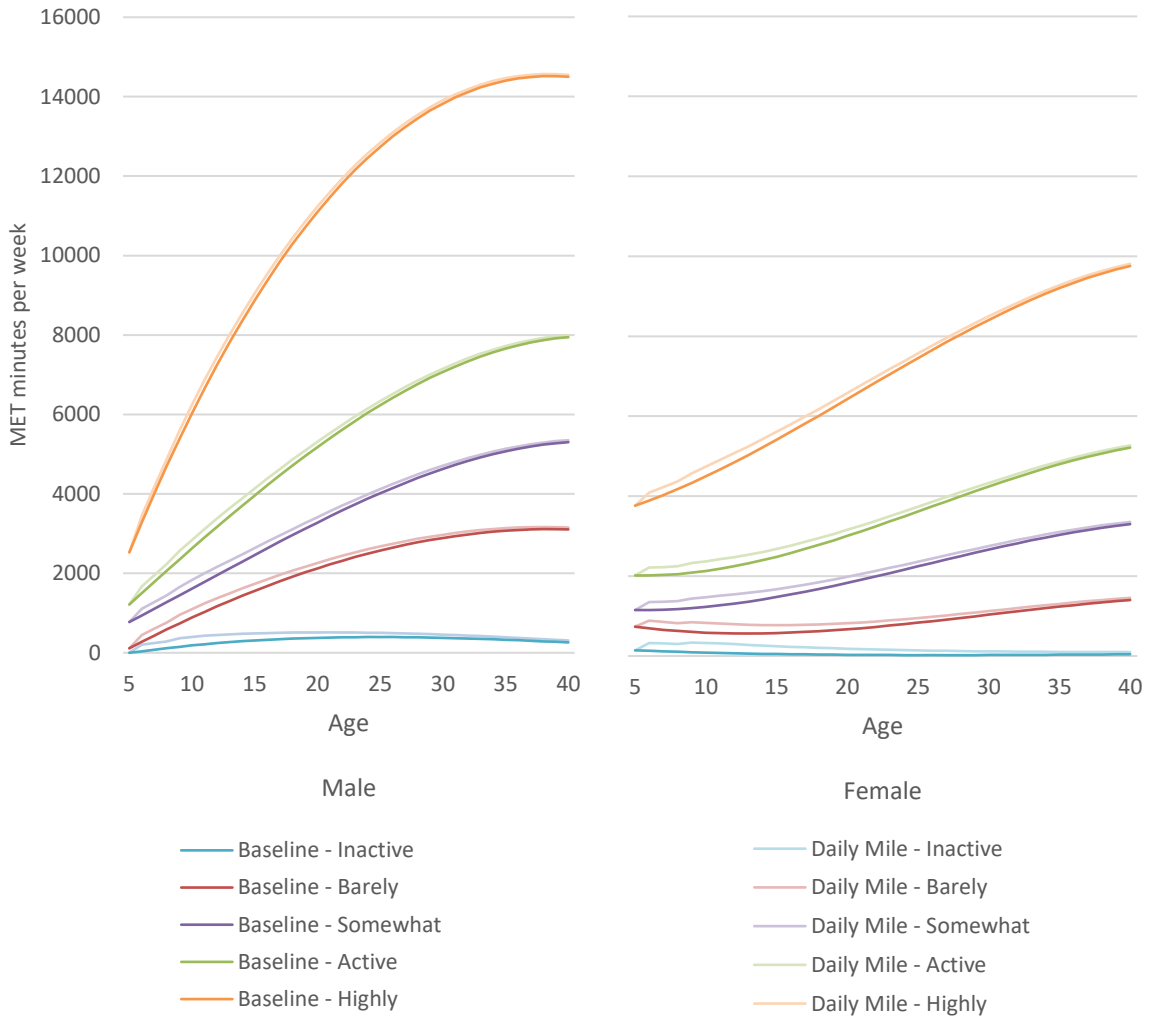


Figure 7.1 - Line graphs showing impact on MET minutes per week trajectories following Daily Mile scenario, by physical activity strata and sex.

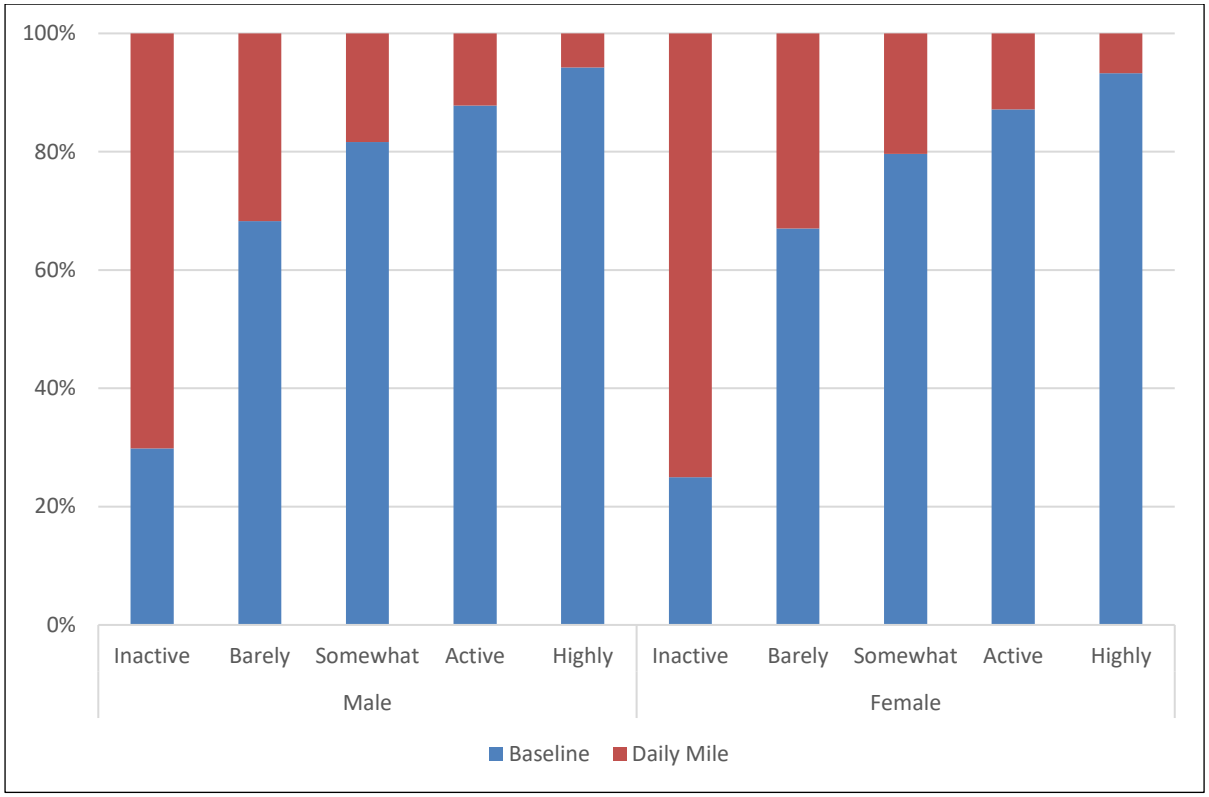


Figure 7.2 - 100% Stacked column graph showing the additional minutes due to implementation of the Daily Mile intervention on total MET minutes per week, by sex and physical activity strata.

7.2.4. Primary Outputs

The modelled implementation of the Daily Mile scenario resulted in an estimated 0.07 years of life gained, which approximates to 26.72 days of additional life per person across the simulated population. The primary findings are presented in Table 17, the point estimates are produced from a deterministic run of the core model, with the confidence interval produced by taking the 2.5th and 97.5th percentiles from 2500 iterations of a Monte Carlo analysis. The intervention had a limited effect on life expectancy but showed a notable reduction in years of life lost and years of life in disability.

Output	Estimate (years)	Lower uncertainty interval	Upper uncertainty interval	Estimate (days)
Change in individual life expectancy at 5 years old				
Cohort	0.07	0.04	0.11	26.72
Males	0.10	0.06	0.14	34.64
Females	0.05	0.02	0.08	18.80
Cohort change in years of life lost per 100,000				
Cohort	-9.88	-13.60	-5.89	-3631.80
Males	-12.00	-15.28	-4.38	-4370.52
Females	-7.60	-12.08	-3.22	-2837.74
Reduction in years of life in disability per 100,000				
Cohort	-13748.20	-20188.33	-7601.12	-5070799.44
Males	-14055.64	-19316.76	-8843.00	-5153190.00
Females	-13440.72	-21319.48	-6243.16	-4950879.92

Table 17 - Primary outputs and confidence intervals from the application of the Daily Mile scenario, presenting changes in life expectancy at five years of age, years of life lost, and years of life in disability.

The changes following implementation of the Daily Mile intervention on prevalence of specific health outcomes are presented in Table 18. In line with findings from the previous chapter the greatest benefit is observed for diabetes, with a lesser effect for myocardial infarction and stroke. There is a small preventative effect on all health outcomes, but the intervention has only a small effect on the three forms of cancer.

Change in number of prevalent cases at 65 years in the live population, per 100,000	Estimate	Lower uncertainty interval	Upper uncertainty interval
Myocardial Infarction			
Cohort	-27.30	-59.26	-7.23
Males	-47.90	-103.14	-13.08
Females	-6.72	-10.04	-2.94
Stroke			
Cohort	-19.66	-34.95	-7.99
Males	-30.72	-53.54	-12.90
Females	-8.60	-16.90	-2.70
Type 2 Diabetes			
Cohort	-251.52	-390.93	-127.44
Males	-281.44	-420.74	-159.18
Females	-221.60	-362.70	-96.04
Bowel Cancer			
Cohort	-4.65	-9.25	-0.94
Males	-7.04	-13.40	-1.60
Females	-2.26	-5.00	-0.28
Breast Cancer			
Females	-4.40	-8.90	-0.48
Uterine Cancer			
Females	-3.18	-8.84	-0.38

Table 18 - Changes in prevalence for specific disease outcomes following modelling application of the Daily Mile intervention, including 95% uncertainty intervals.

Comparisons between baseline and the Daily Mile for life expectancy are presented in Figure 7.3, broken down by physical activity strata and sex, with a corresponding presentation for years of life in disability in Figure 7.4. Both Figure 7.3 and Figure 7.4 clearly show that, consistent with the relative gains in physical activity displayed in Figure 7.2, the greatest benefits on health outcomes from the implementation of the Daily Mile is seen within the Inactive stratum. Figure 7.5 presents the

comparison between baseline and Daily Mile scenarios on the specific health outcomes, with type 2 diabetes showing the greatest benefit from the application of this intervention.

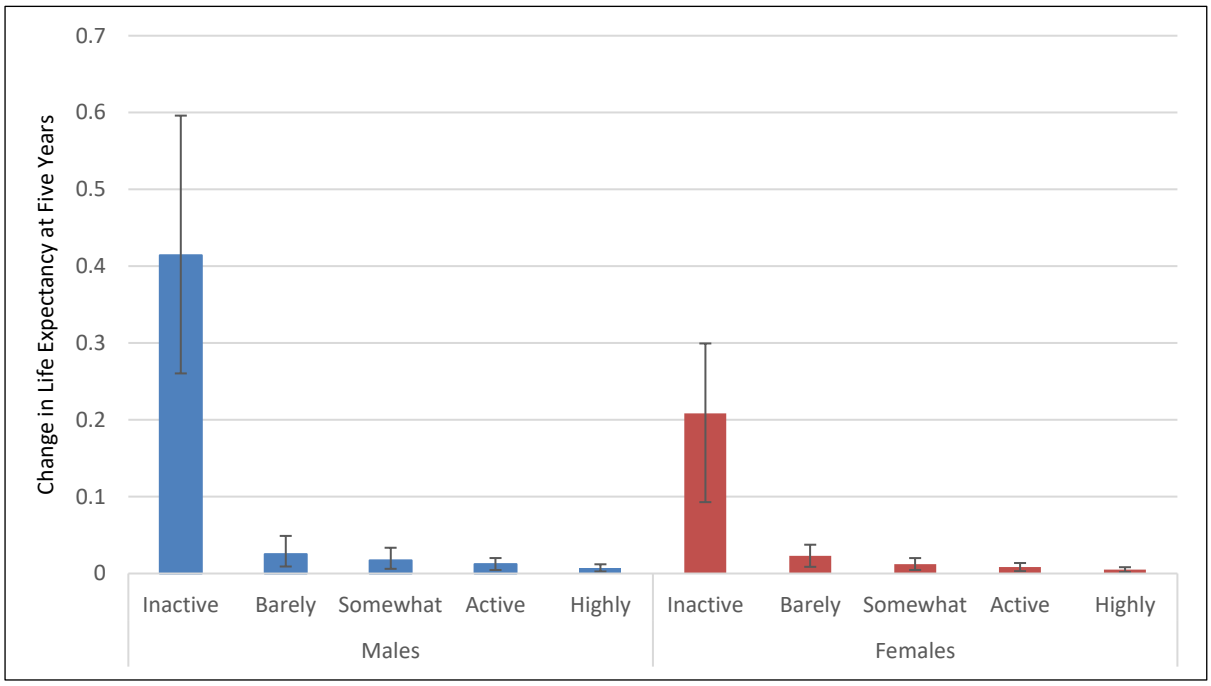


Figure 7.3 - Column graph showing the impact of participation in the Daily Mile relative to baseline on life expectancy at five years of age, by physical activity strata and sex, with uncertainty intervals (2.5th & 97.5th percentiles).

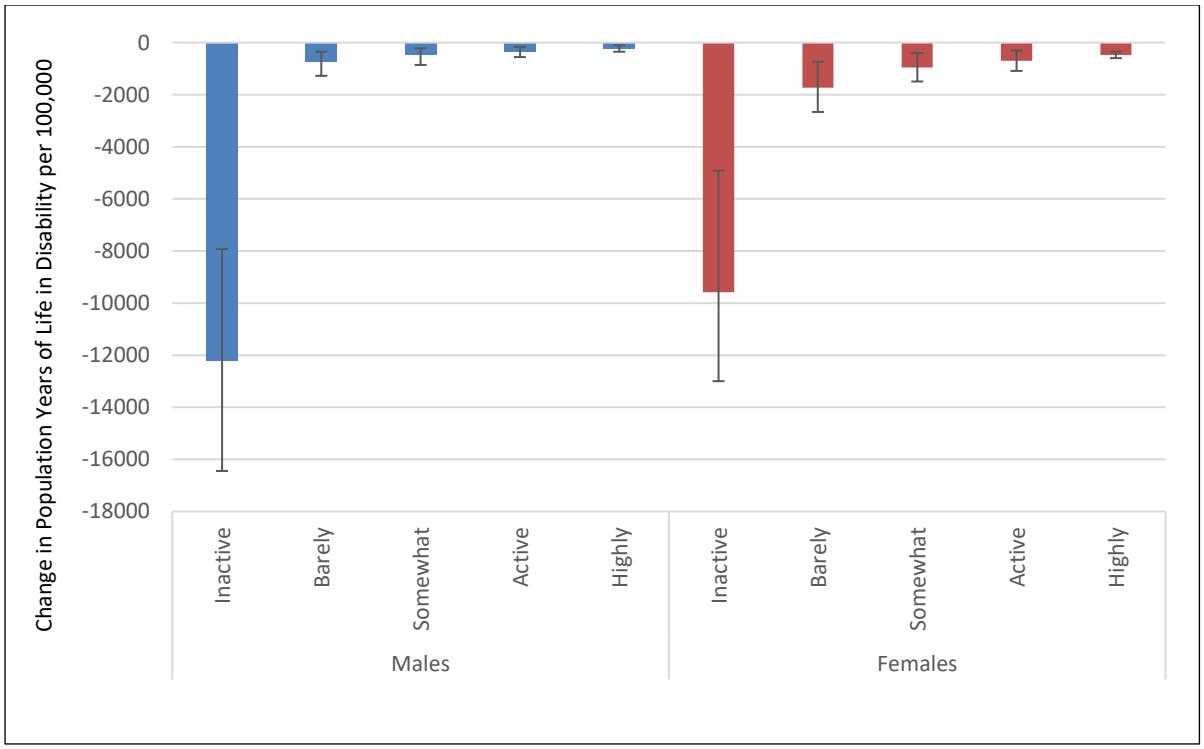


Figure 7.4 - Column graph showing the impact of participation in the Daily Mile relative to baseline on years of life in disability, physical activity strata and sex, with uncertainty intervals (2.5th & 97.5th percentiles).

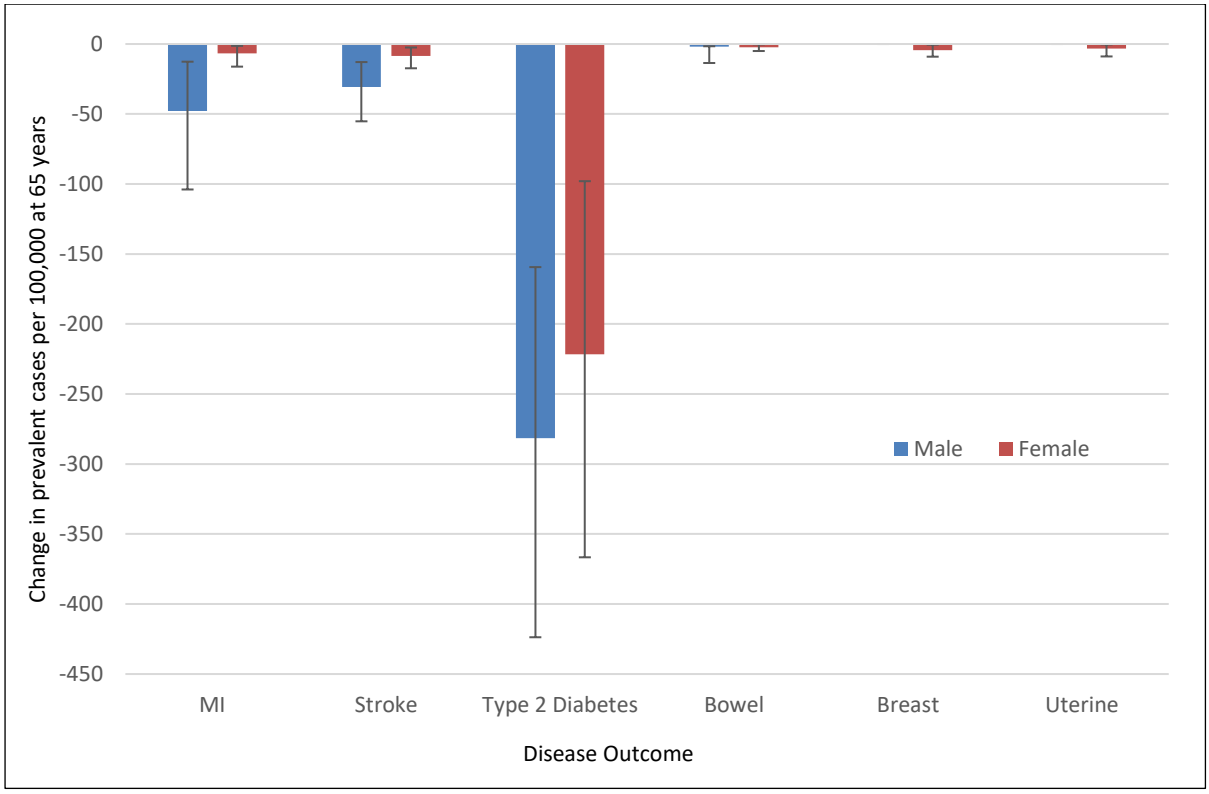


Figure 7.5 - Column graph showing comparison of baseline and Daily Mile scenarios on prevalence cases of specific health outcomes at 65 years of age, by sex, with uncertainty intervals (2.5th & 97.5th percentiles).

7.2.5. Uncertainty and Sensitivity Analysis

In line with the process for sensitivity and uncertainty analysis specified in Chapter Three, parametric uncertainty was assessed using 2500 iterations of a Monte Carlo analysis. The uncertainty bars in Figure 7.3, Figure 7.4, and Figure 7.5 are generated from this process, specifying the 2.5th and 97.5th percentile, while the point estimate itself is produced by a deterministic run of the model. The contribution of specific input parameters to this uncertainty are presented for life expectancy in Figure 7.6 and years of life in disability in Figure 7.7.

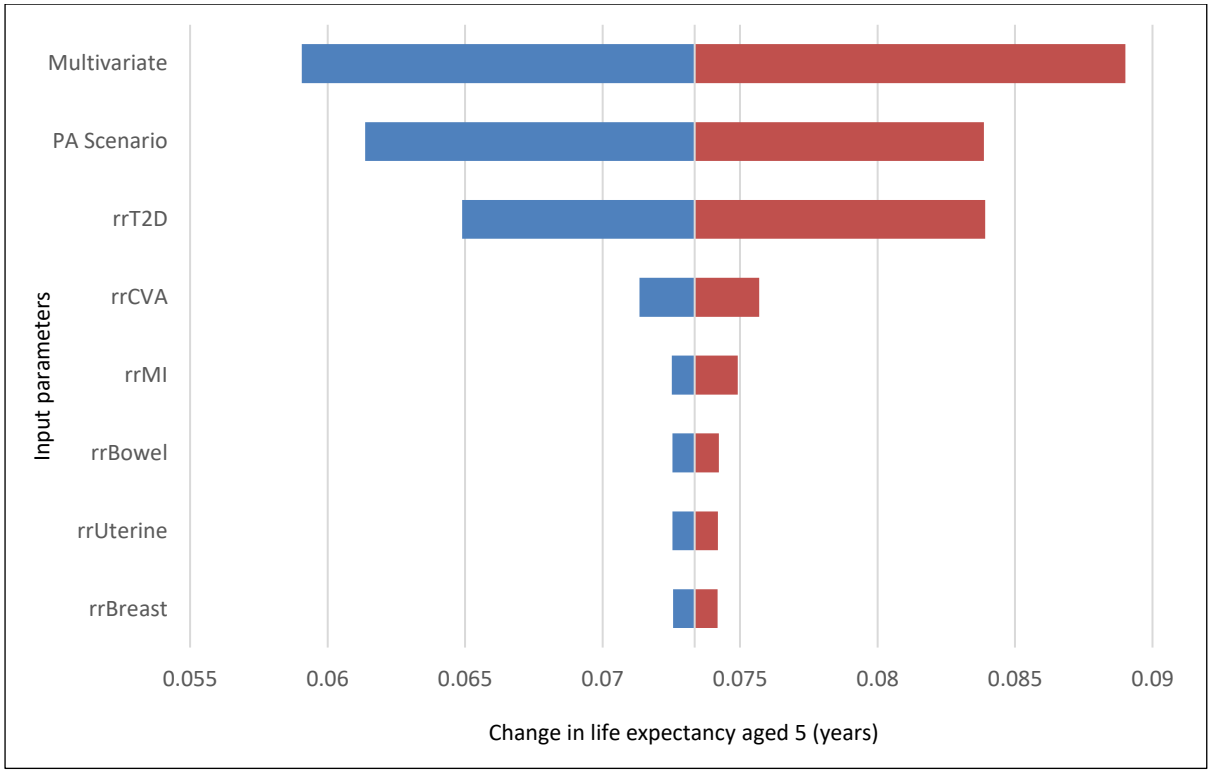


Figure 7.6 - Tornado plot showing the sensitivity of the estimate for change in life expectancy at five years old (0.07) due to uncertainty within specific input parameters following modelling of the Daily Mile scenario.

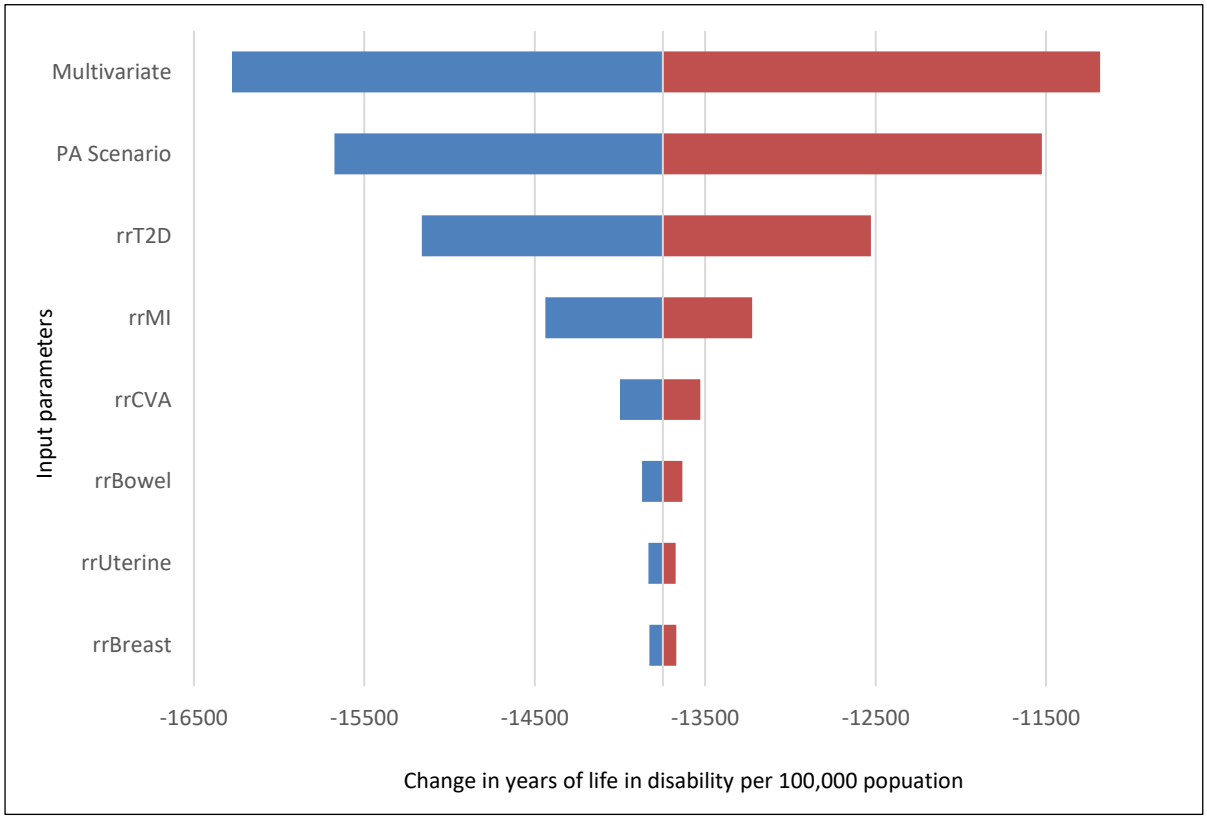


Figure 7.7 - Tornado plot showing the sensitivity of the estimate for change in years of life in disability (-13748.20) due to uncertainty within specific input parameters following modelling of the Daily Mile scenario.

While not included within the multivariate sensitivity analysis, the physical activity legacy following the implementation of the Daily Mile is also pertinent to an exploration of uncertainty within the model outputs. In Chapter 4 there were follow up data available which permitted a broad specification of a reduction in effect post-intervention, this parameter was included in the multivariate sensitivity analysis. There are no such data available for the Daily Mile and therefore the post-intervention rate of decay in benefit from Chapter 4 was also applied in this case. However, there remains the possibility that all children return immediately to baseline levels of physical activity once the Daily Mile intervention ceases (i.e. conceptually this would correspond with progression from primary to secondary school age).

The hypothesised trajectories in average MET minutes per week are presented in Figure 7.8, providing a visual representation of impact of this element of the modelling process. It is clear that if the gains in physical activity can be retained by individuals there will be a benefit that far exceeds that which may be attained within the period of the intervention itself, approximating an extra 1473 and 959 MET minutes per week for males and females respectively, in comparison to the modelled legacy scenario. However, as indicated within the systematic review presented in Chapter 4 (and see Sims et al., 2015) there is little evidence that this is the case with physical activity interventions. By contrast, modelling a legacy scenario in which no sustained benefit was observed within the simulated cohort, revealed an approximate average reduction of 211 and 236 MET minutes per week for males and females respectively across the lifespan.

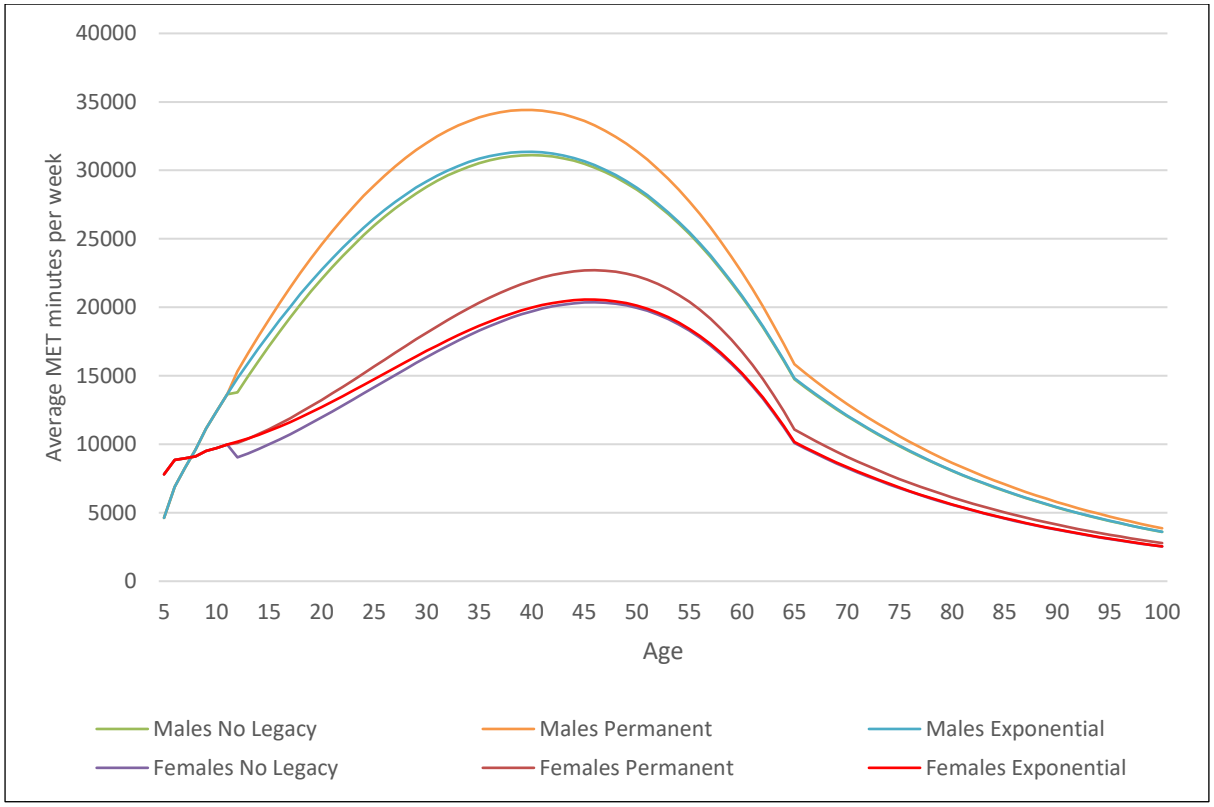


Figure 7.8 - Line graph showing the hypothesised trajectories in average MET minutes per week following different intervention legacy scenarios following the Daily Mile intervention.

7.2.6. Interim Discussion of Daily Mile Intervention

In contrast to the results in Chapter 6, the implementation of the Daily Mile showed a benefit subsequent to application throughout primary school. The greatest benefit was observed in the Inactive strata. Indeed, and by way of example, approximately 88% and 77% of the entire reduction of years of life in disability, for males and females respectively, within the simulated cohort is seen in the Inactive strata, clearly evidencing that a non-volitional physical activity intervention can be targeted at population level, but the benefits are observed at the high-risk end of the distribution. Following the application of the Daily Mile within the simulated cohort there was a small increase in life expectancy, a reduction in years of life lost, and a reduction in years of life in disability. Of the disease specific health outcomes, the reduction in diabetes prevalence was the most notable, with reductions in prevalence of myocardial infarction also evident.

7.2.7. Strengths and Limitations

The parameterisation of the Daily Mile intervention within the analysis above to some extent addresses the potential for substitution. While non-experimental reviews may report only the absolute benefit in physical activity due to an intervention, the figures above analyse the relative benefit of implementing the Daily Mile in a typical primary school lunch time, with a broad estimate of an eleven percent increase in physical activity across the age-relevant simulated population. This may, to a certain extent, account for why the Inactive can be expected to receive the greater benefit of this compulsory physical activity intervention, as they can be expected to have been largely sedentary in their lunch hour when compared to the more active children. The scenario takes no further account of substitution, for example whether the children perform less physical activity in their other break times, or after school.

While the scenario was parameterised on the available data there was comparatively little methodologically rigorous physical activity results regarding the effectiveness of the Daily Mile. The failure of Chesham et al. (2018) to report absolute pre-post data following an assessment of this intervention is unfortunate and forced the parameterisation to include a greater level of assumption. In addition, while the scenario allowed for different levels of attainment within the fifteen minutes of 'running', there was no differentiation between physical activity strata when applying these levels. As such the large benefit within the Inactive and Barely Active strata may represent an overestimate, with a corresponding underestimate of benefit for the Active and Highly Active, as it could be expected that a comparatively larger proportion of Inactive children will fail to achieve the optimum distance within the specified time.

7.3. Treatment Intervention Context

The Mind, Exercise, Nutrition, Do It! (MEND) project was an intervention specifically targeting overweight and obese children (Sacher et al., 2005), initially those aged from eight to thirteen. MEND followed a twice-weekly programme delivered at sports centres over a period of three months. The

primary aim was a reduction in waist circumference, with BMI, self-esteem, body composition, blood pressure, recovery heart rate, sedentary behaviour, and physical activity also measured. Physical activity was measured using a child and parental self-report questionnaire developed by Slemenda, Miller, Hui, Reister, and Johnston (1991), which gathered time spent in specific activities and provided a total estimate of hours per week of physical activity.

Sacher et al. (2010) conducted a small-scale randomised controlled trial of the MEND programme with a sample of 116 obese (BMI≥98th percentile) children referred by a school, health professional, or by parental request. Separate programmes were run at five community leisure centres using different delivery teams, with random allocation to intervention or waiting-list control group occurring after baseline assessment. Further measurements were taken at six and at twelve months post-intervention, although the control group commenced the intervention at six months and therefore prevented twelve-month post-intervention comparisons between groups. The MEND programme offered twice weekly sessions with the child and at least one parent, involving classroom activities on diet or healthy living, followed by activities for the children and further discussions with the parents. Within subject changes indicated significant twelve-month improvements in all measures except Body Mass Index (BMI) (both child and maternal), sedentary time, and diastolic blood pressure (Sacher et al., 2010).

Following the initial roll-out of the MEND intervention, additional programmes were added for specific age groups, including a MEND 5-7 adapted for younger children (Smith et al., 2013) and a Mini-MEND that targeted pre-school children (Sacher et al., 2008). Smith et al. (2013) conducted an uncontrolled repeated measures evaluation of the MEND 5-7 programme with 440 overweight or obese children across 37 venues. Significant positive changes were observed for BMI, waist circumference, child psychological symptoms, parenting self-efficacy, physical activity, sedentary behaviour, and fruit and vegetable consumption, with a 70% retention rate over the twelve weeks of the programme. The

authors concluded that MEND 5-7 appeared effective but noted a requirement for subsequent controlled trials (Smith et al., 2013).

Although not specifically an intervention for low physical activity levels, there is sufficient evidence to justify the use of MEND in this study. Firstly, the intervention was implemented within an English setting. Secondly, there are evaluation data available. Thirdly, baseline assessment indicated that self-reported physical activity levels were low (Sacher et al., 2010) compared to age-group profiles (e.g. Colley et al., 2011; Nader et al., 2008) and as such MEND can be considered a physical activity intervention for the high-risk group.

7.3.8. Scenario Parameterisation

The MEND intervention ran for twelve weeks and delivered a specific physical activity programme on a twice-weekly basis, typically one episode of 'wet' activity and one of 'dry' activity. The participants were originally recruited if they were above the 96th percentile on BMI measurement. However, MEND subsequently recruited any child to their programmes who possessed a BMI of over 25, which therefore classified them as 'overweight'. The source studies do not differentiate by sex therefore the changes were applied equally to both sexes within the core model.

Age Group	Source study	Mean (CI) change in hours of physical activity/week	Assigned MET minute value for MEND intervention gain	'MEND-like' Weekly Benefit (MET mins/week)
5-7 years	Smith et al. (2013)	2.90 (1.20 - 4-70)	5.11	888.61 (367.70 – 1440.19)
8-13 Years	Sacher et al. (2010)	4.00 (1.90 - 6.00)	5.11	1225.67 (582.19 – 1838.50)
14-16 Years	Sacher et al. (2010)*	4.00 (1.90 - 6.00)	5.11	1225.67 (582.19 – 1838.50)

Table 19 - Sources, changes in time spent in physical activity, and MET minutes per week estimates for three age groups following implementation of the MEND programme.

**No specific data for this age group, data taken from Sacher et al. (2010) from the 8-13 years age group.*

Table 19 presents the findings from evaluations conducted on the MEND programmes. Twelve-month changes in physical activity hours per week were reported for the 8-13 programme (Sacher et al., 2010), while for the 5-7 programme the reported data were a pre-post difference over the duration of the intervention (Smith et al., 2013). The gains were reported as additional hours of physical activity per week following the programme. These figures were then multiplied by 60 to provide a figure for minutes and then by a figure of 5.11, representing a balanced MET equivalence estimate of moderate and vigorous physical activity (Hamer & Stamatakis, 2018). The product of this provides the overall weekly benefit of participation in the MEND programme. Although MEND was a term-time intervention, no reduction in effect was applied as the input data were drawn from follow-up measurement and therefore represented a lifestyle improvement rather than merely attendance at the MEND exercise classes.

The initial intention was to model the MEND programme estimates to all people within the simulated cohort who possessed a BMI of 25 or above within the relevant age groups. However, an analysis of the HSE 2012 data revealed that, irrespective of age, the proportion of people reporting a BMI of 25 or over was almost uniform across the physical activity quintiles. Instead, therefore, a 'MEND-like' application of the intervention programme within the simulated cohort was applied based on physical inactivity rather than adiposity status. This adaptation remains faithful to the treatment philosophy of

intervention while proving applicable within the structure of the core model; the estimates from Table 19 were therefore applied only to the Inactive strata within the core model.

7.3.9. Formal Scenario

The scenario applies the MEND intervention to the Inactive strata only within simulated population of the core model for each year of school attendance, without exception for age and sex. No provision is made for lack of attendance or adherence. The intervention occurs outside curriculum time and within a community setting. In keeping with the MEND delivery system and available age-specific interventions, the modelled benefit was applied throughout childhood. A legacy of increased physical activity was assumed to persist post-intervention, following an exponential decay to baseline levels over subsequent years of life. For the purposes of sensitivity analysis two further legacy patterns are applied, one with no legacy of improved post-intervention physical activity and one in which physical activity increases persist throughout lifetime.

7.3.10. Effect of Intervention

Application of the MEND scenario within the whole simulated cohort resulted in an absolute gain of 19747.56 MET minutes across the cohort, comprising an average 10.9% increase within the ten-year period of the intervention compared to the baseline scenario, and a 2.4% increase across the lifespan. Looking specifically within the Inactive strata, the MEND scenario resulted in an average gain of 83.2% in MET minutes per week over the period of the intervention, with a 72.6% average lifetime increase. Figure 7.9 presents the baseline and counterfactual scenario physical activity trajectories for individuals under 40 years of age within the Inactive stratum. The benefits are modelled to follow an exponential decay pattern towards baseline levels; benefits are largely negligible after 40 years of age. The benefits of the MEND intervention for inactive children are more explicitly presented in Figure 7.10, which illustrates the relative benefit by age-group and sex.

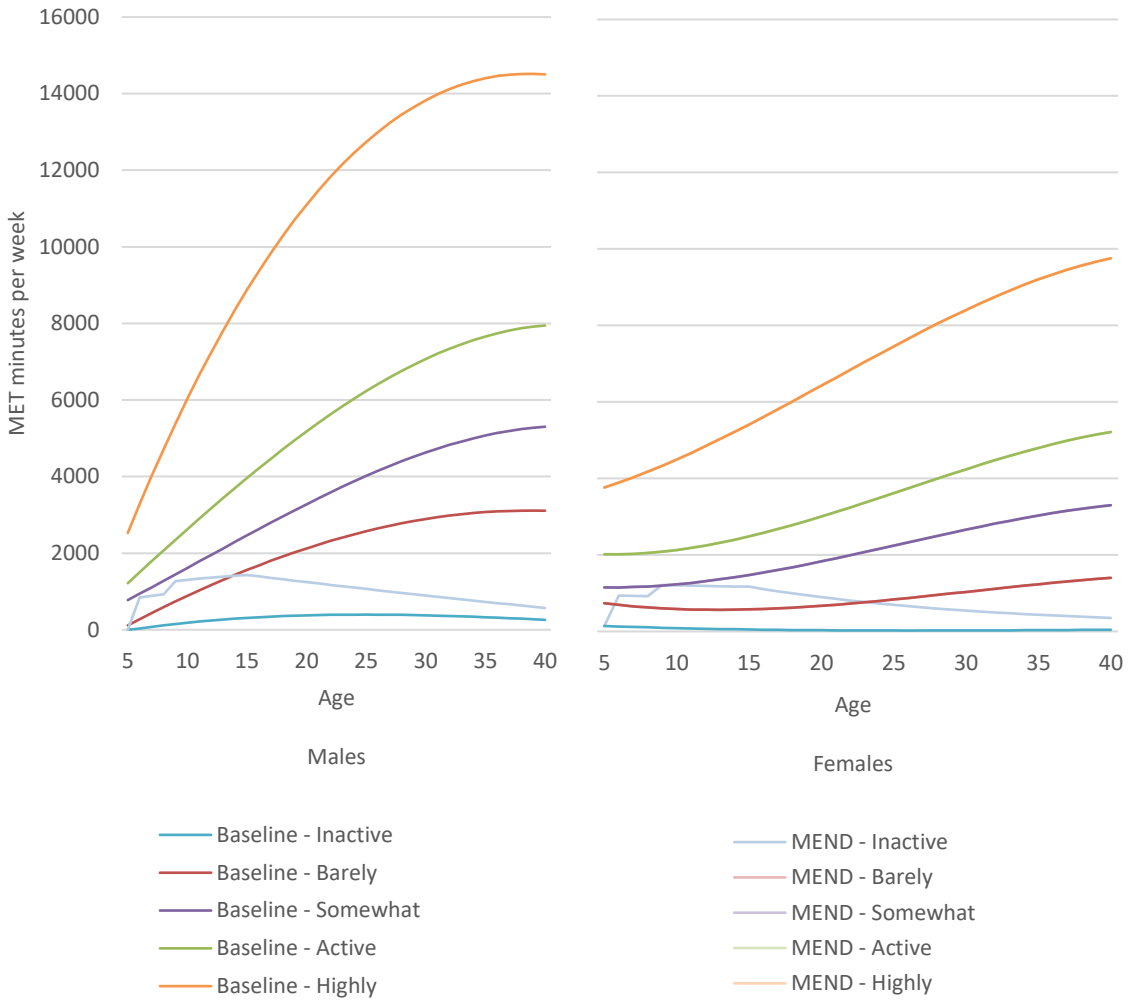


Figure 7.9 - Line graphs showing impact on MET minutes per week trajectories following MEND scenario, by physical activity strata and sex.

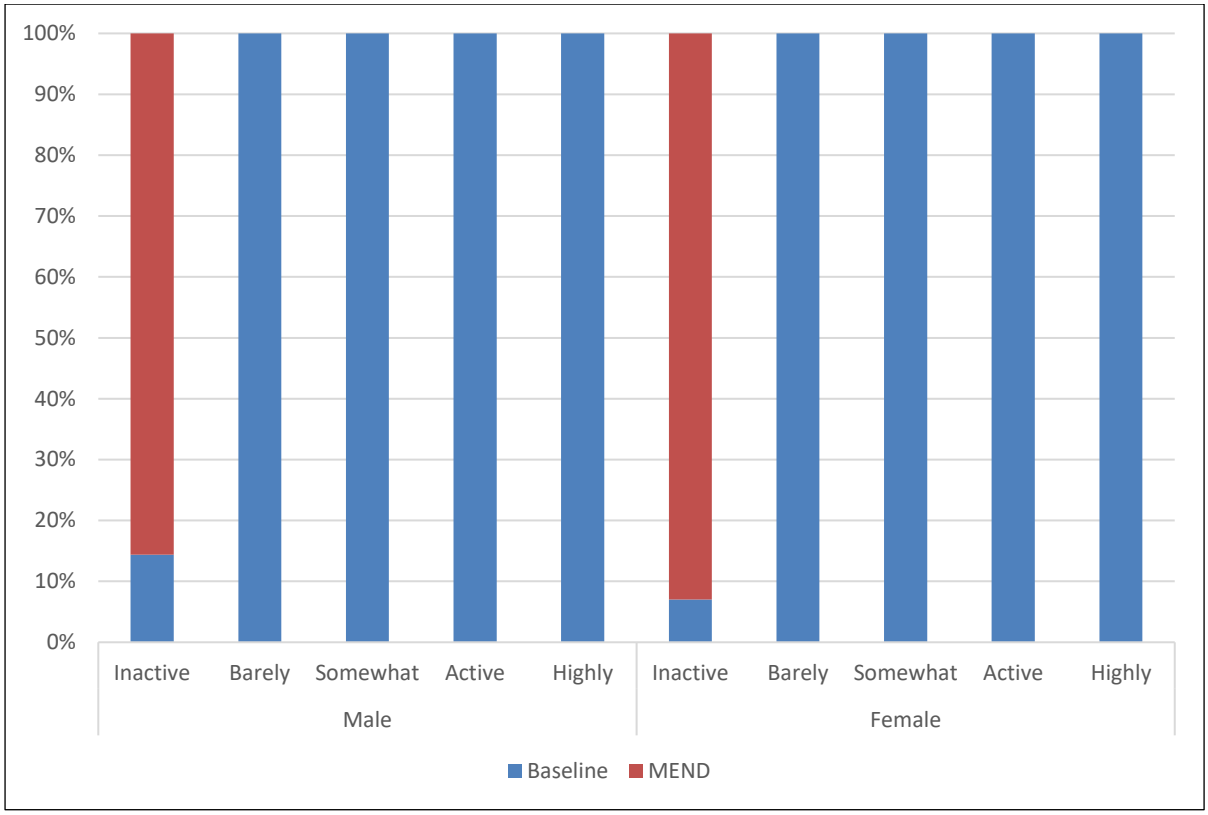


Figure 7.10 - 100% Stacked column graph showing the benefit on implementation of the MEND intervention on total MET minutes per week, by sex and physical activity strata.

7.3.11. Primary Outputs

The modelled implementation of the MEND scenario resulted in an estimated 0.14 years of life gained, which approximates to 50.21 days of additional life per person among the Inactive strata. The primary findings are presented in Table 20, the point estimates are produced from a deterministic run of the core model, with the confidence interval produced by taking the 2.5th and 97.5th percentiles from 2500 iterations of a Monte Carlo analysis. The intervention had a limited effect on overall cohort life expectancy but showed a notable reduction in years of life lost and years of life in disability.

Output	**Estimate** (years)	**Lower uncertainty interval**	**Upper uncertainty interval**	**Estimate** (days)
Change in life expectancy at 5 years old				
Cohort	0.14	0.08	0.20	50.21
Males	0.16	0.10	0.24	57.95
Females	0.12	0.07	0.17	42.23

Cohort change in years of life lost per 100,000				
Cohort	-16.80	-22.44	-10.95	-6116.91
Males	-15.68	-20.20	-11.10	-5707.36
Females	-17.92	-25.00	-10.60	-6526.50
Change in years of life in disability per 100,000				
Cohort	-23494.90	-32234.38	-15405.69	-8565615.16
Males	-23655.93	-31645.98	-16102.28	-8580023.10
Females	-23477.90	-33666.48	-14451.84	-8576590.66

Table 20 - Primary outputs and confidence intervals from the application of the MEND scenario within the Inactive strata only, presenting changes in life expectancy at five years of age, years of life lost, and years of life in disability.

The changes following implementation of the MEND intervention on the prevalence of specific health outcomes are presented in Table 21. In line with findings from the previous chapter the greatest benefit is observed for type 2 diabetes, with a lesser effect for myocardial infarction and stroke. There is a small preventative effect on all health outcomes, but the intervention has only a small effect on the three forms of cancer.

Change in number of prevalent cases at 65 years in the live population, per 100,000	**Estimate**	**Lower uncertainty interval**	**Upper uncertainty interval**
Myocardial Infarction			
Inactive Cohort	-50.42	-109.75	-13.74
Inactive Males	-84.76	-183.70	-23.58
Inactive Females	-16.08	-36.12	-3.82
Stroke			
Inactive Cohort	-34.78	-62.00	-14.53
Inactive Males	-47.46	-86.94	-21.50
Inactive Females	-20.10	-37.04	-7.62
Type 2 Diabetes			
Inactive Cohort	-458.76	-685.60	-271.34
Inactive Males	-501.82	-742.76	-304.06

Inactive Females	-415.70	-627.76	234.66
Bowel Cancer			
Inactive Cohort	-8.32	-16.62	-1.62
Inactive Males	-11.50	-22.50	-2.42
Inactive Females	-5.14	-10.76	-0.72
Breast Cancer			
Inactive Females	-10.12	-19.02	-1.44
Uterine Cancer			
Inactive Females	-7.66	-19.88	-0.94

Table 21 - Changes in prevalence for specific disease outcomes following modelling application of the MEND intervention within the Inactive strata only, including 95% uncertainty intervals.

Comparisons between baseline and the MEND intervention for life expectancy are presented in Figure 7.11, broken down by physical activity strata and sex, with a corresponding presentation for years of life in disability in Figure 7.12. Figure 7.13 presents the comparison between baseline and MEND scenarios, showing reductions in type 2 diabetes for both males and females as well as a reduction in myocardial infarction prevalence in males. Clearly, no benefits are observed on any outcome outside the Inactive strata.

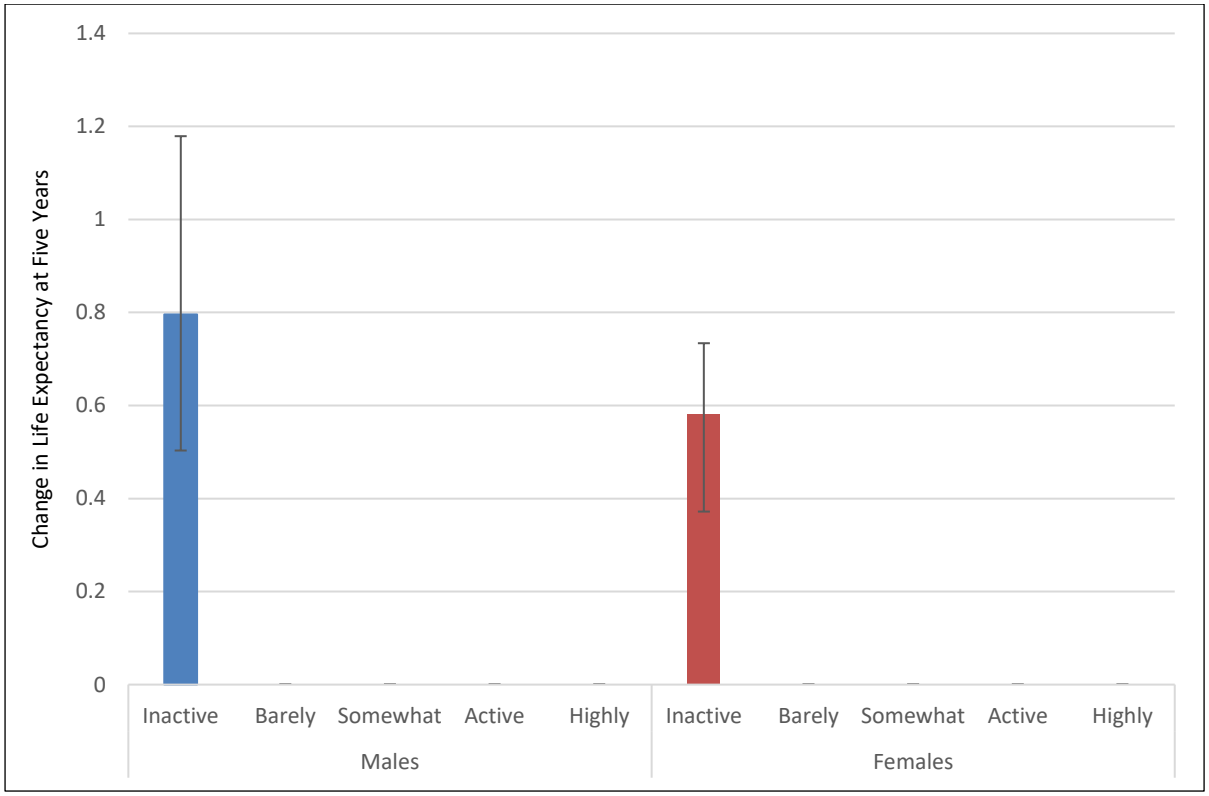


Figure 7.11 - Column graph showing the benefit of participation in the MEND relative to baseline on years of life in disability, physical activity strata and sex, with uncertainty intervals (2.5th & 97.5th percentiles).

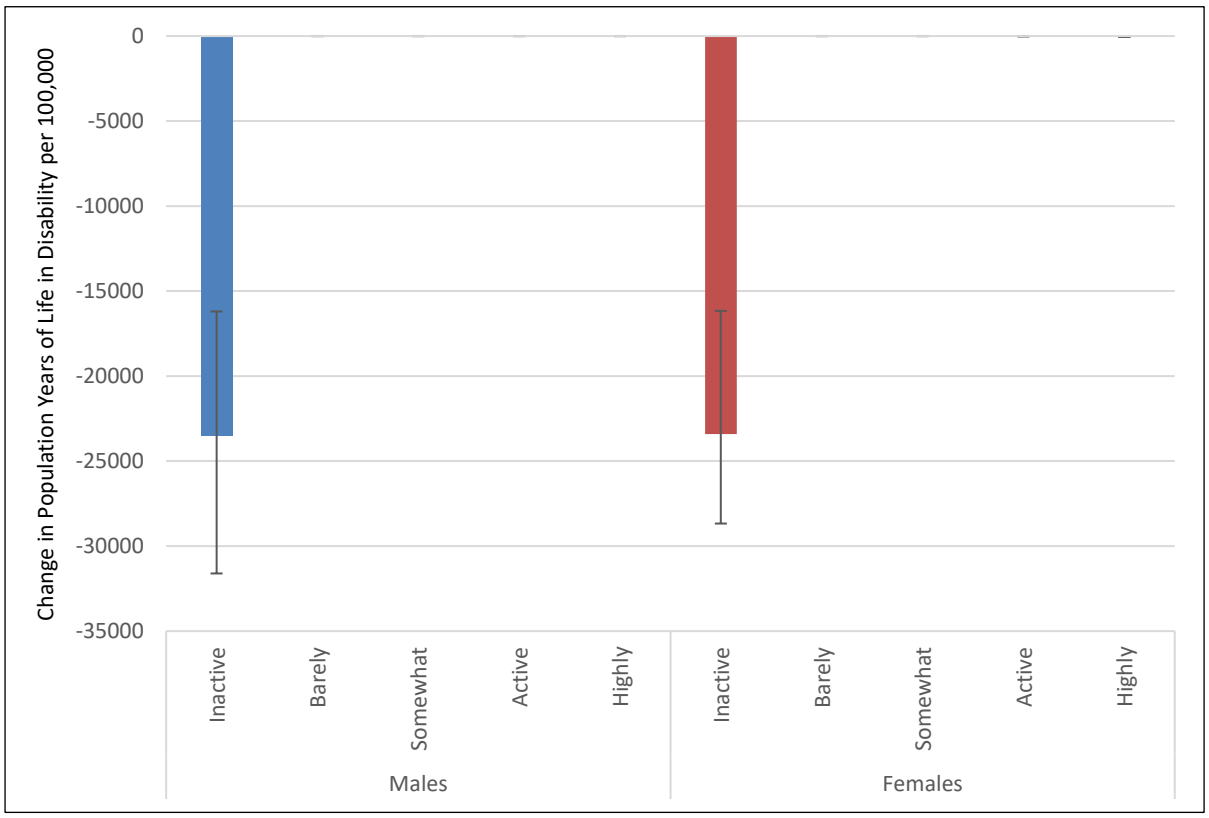


Figure 7.12 - Column graph showing the benefit of participation in the MEND relative to baseline on years of life in disability, by physical activity strata and sex, with uncertainty intervals (2.5th & 97.5th percentiles).

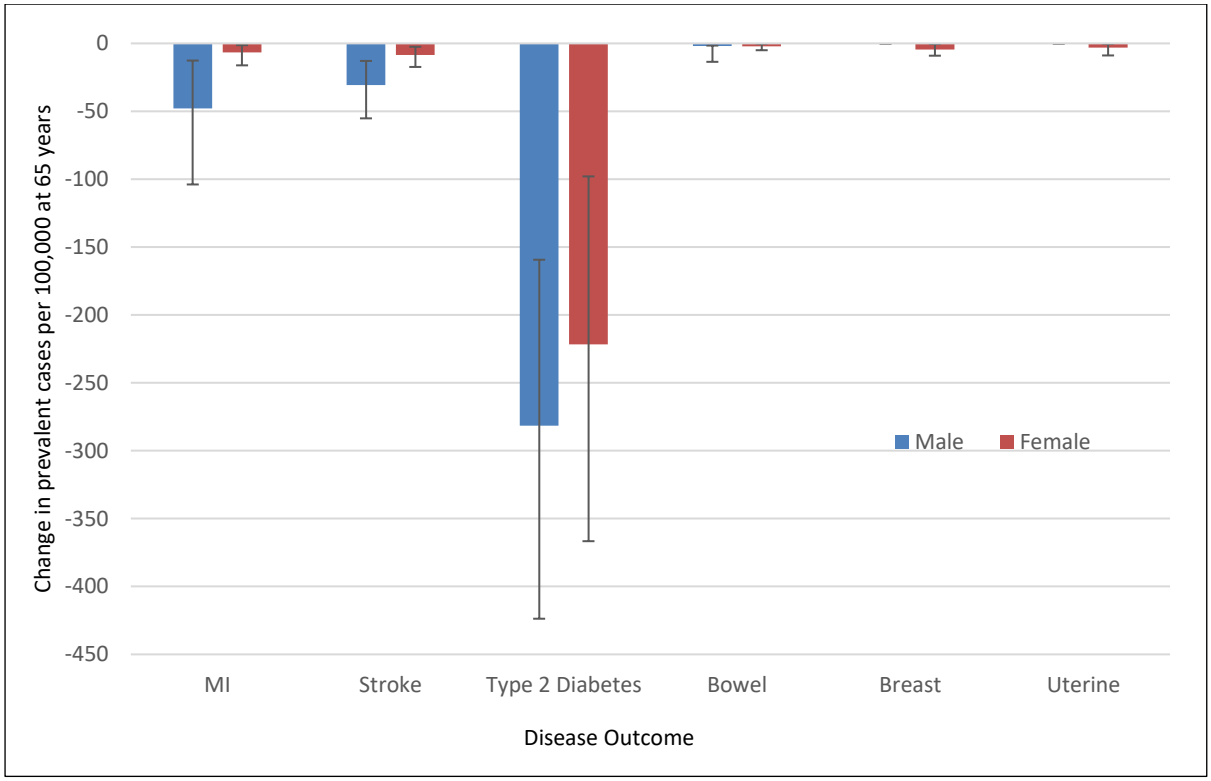


Figure 7.13 - Column graph showing comparison of baseline and MEND scenarios on prevalence cases of specific health outcomes at 65 years of age, by sex, with uncertainty intervals (2.5th & 97.5th percentiles).

7.3.12. Uncertainty and Sensitivity Analysis

In line with the process for sensitivity and uncertainty analysis specified above, parametric uncertainty was assessed using 2500 iterations of a Monte Carlo analysis. The uncertainty bars in Figure 7.11, Figure 7.12, and Figure 7.13 are generated from this process, specifying the 2.5th and 97.5th percentile, while the point estimate itself is produced by a deterministic run of the model. The contribution of specific input parameters to this uncertainty are presented for life expectancy in Figure 7.14 and years of life in disability in Figure 7.15.

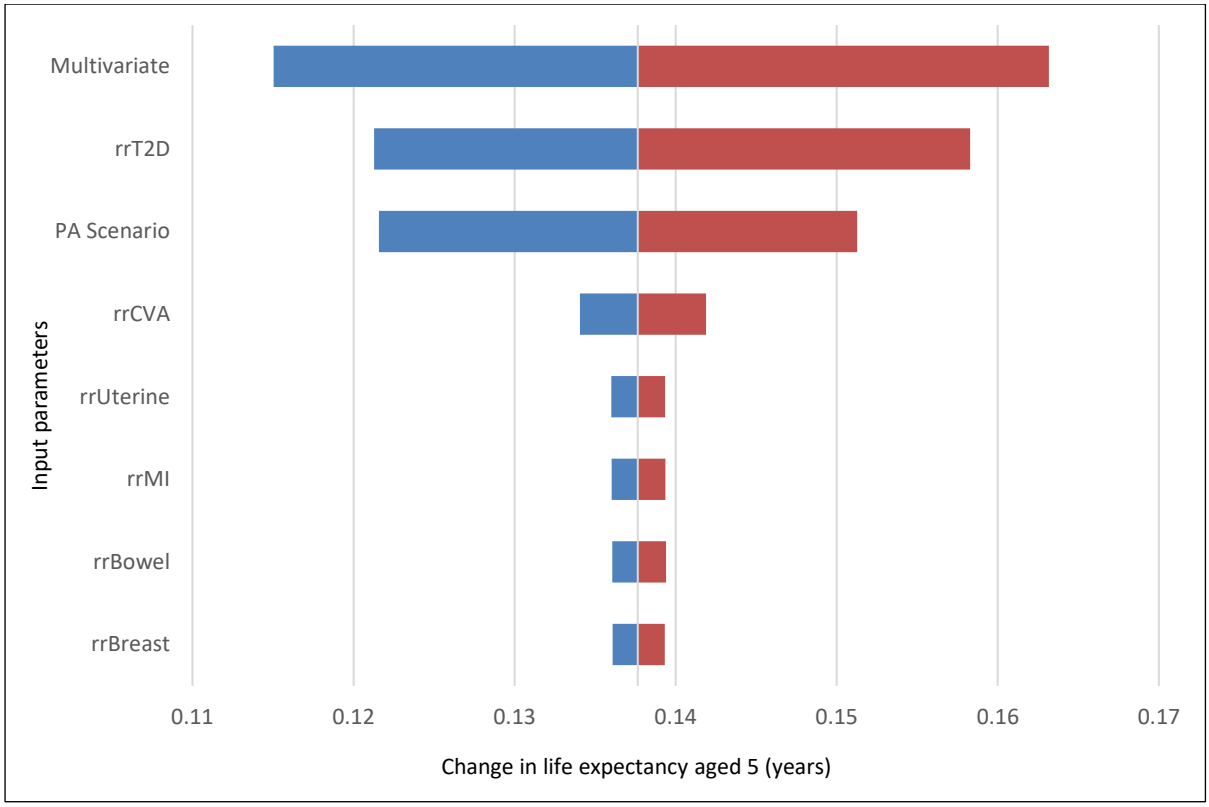


Figure 7.14 - Tornado plot showing the sensitivity of the estimate for change in life expectancy (0.14) due to uncertainty within specific input parameters following modelling of the MEND scenario.

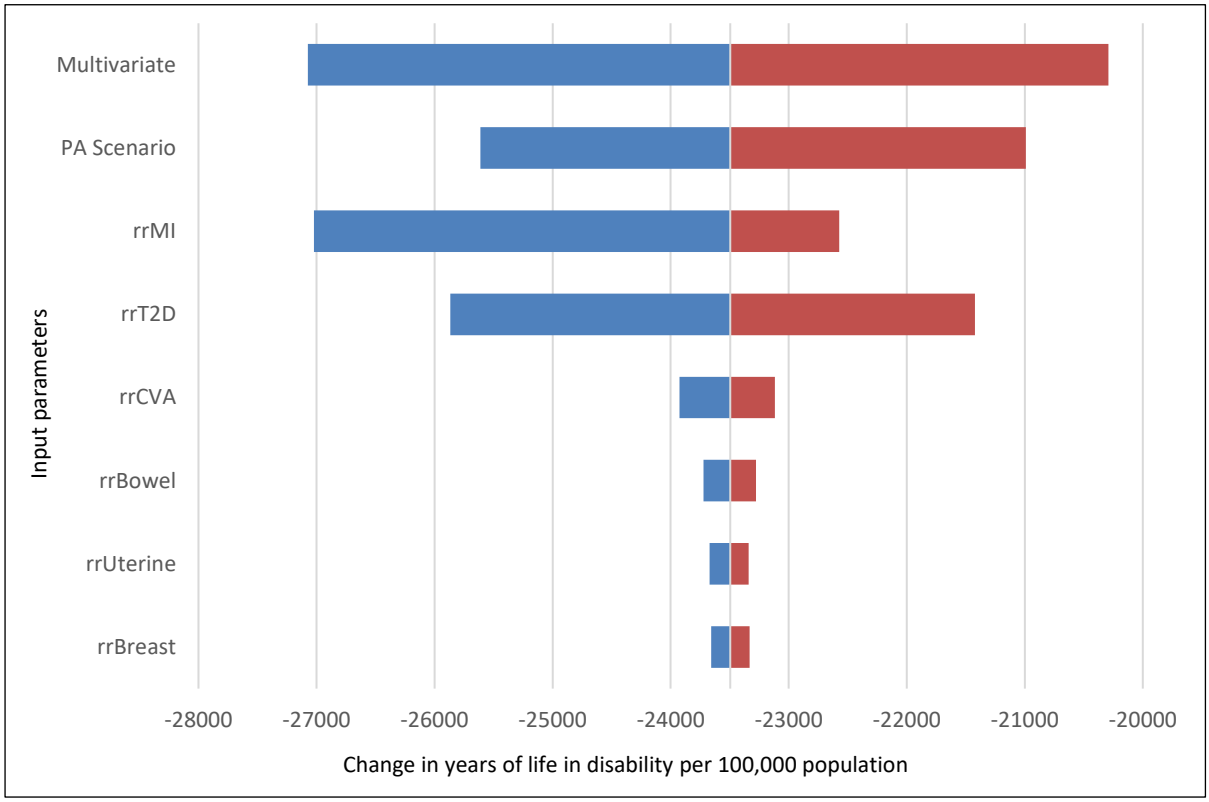


Figure 7.15 - Tornado plot showing the sensitivity of the estimate for change in years of life in disability (-23494.90) per 100,000 population due to uncertainty within specific input parameters following modelling of the MEND scenario.

The physical activity legacy following the implementation of the MEND scenario was also explored following the process outlined above. While some follow-up data were presented for the MEND intervention, control group data were not collected, and therefore were not used to parameterise the model inputs or physical activity legacy effects. The three legacy scenarios outlined within the Daily Mile scenario were also applied for the MEND scenario, i.e. degrading legacy, permanent legacy, and no legacy. The hypothesised trajectories in average MET minutes per week are presented in Figure 7.16, providing a visual representation of impact of this element of the modelling process.

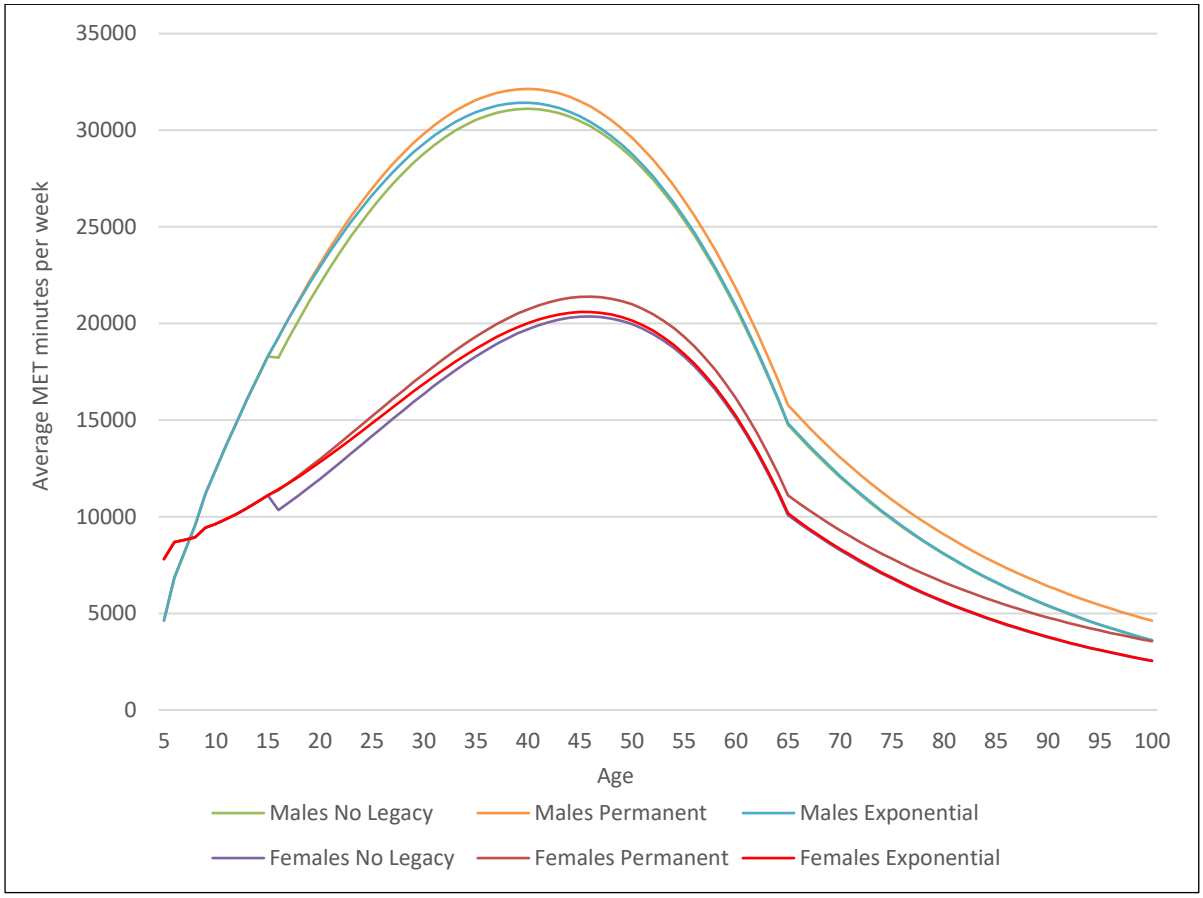


Figure 7.16 - Line graph showing the hypothesised trajectories in average MET minutes per week following different intervention legacy scenarios following the MEND intervention.

Once again, the maintenance of post-intervention physical activity gains brings a benefit that clearly exceed that gained by alternative maintenance trajectories, approximating an extra 690 MET minutes per week for inactive males and females, in comparison to the modelled legacy scenario. By contrast, modelling a legacy scenario in which no sustained benefit was observed within the simulated cohort,

revealed an approximate average reduction of 219 MET minutes per week for inactive males and females respectively across the lifespan.

7.3.13. Interim Discussion of MEND Intervention

Implementation of the MEND-like scenario showed a benefit subsequent to application throughout primary and secondary school age. The intervention only targeted the Inactive strata for males and females and therefore 100% of the benefit was observed here. Following the application of the MEND within the simulated cohort there was a small increase in life expectancy, a reduction in years of life lost, and a reduction in years of life in disability. In line with previous scenario outputs, the reduction in diabetes prevalence was the most notable, with reductions in prevalence of breast cancer, myocardial infarction, and stroke also evident.

7.3.14. Strengths and Limitations

The parameterisation of the MEND intervention within the analysis did not formally address the potential for substitution. However, given the input parameters were drawn from follow up data, albeit without a control group comparison, and were drawn from whole day activity this allows substitution to be taken into account. The formal scenario only applies the intervention to the Inactive strata, and as such raises the levels of physical activity in those strata to above those in the Barely strata (see Figure 7.9). The structural constraints of the model prevent a more nuanced application of the scenario, involving additional strata.

As with the Daily Mile intervention detailed above, there were comparatively little rigorous empirical data available. The three papers specifically investigating MEND programmes provided some insight into the effectiveness of the intervention. In particular, the randomised controlled trial conducted by Sacher et al. (2010) recruited a large sample size and conducted follow-up measurement. The MEND intervention itself, however, was designed and targeted at obese children, rather than physically inactive children, and therefore the formal scenario was necessarily an extrapolation rather than a

direct application. Given the subsidiary nature of physical activity within the MEND studies, the measurement tool lacked some specificity and therefore introduces further parametric uncertainty.

7.4. Comparison of the Daily Mile and MEND scenarios

While specific interventions have been selected as exemplars of both the population and the treatment approach, the analyses made below are not intended to represent a direct comparison between the Daily Mile and MEND programmes. Instead, these analyses are intended to investigate the relative utility of a population and a treatment approach to intervention in children with low levels of physical activity and the consequential benefit of these approaches over the life-course. In contrast to the previous chapter, which explored the application of a largely abstract number which signified the likely benefit of any intervention, the scenarios in this chapter are presented both in order to demonstrate the utility of the model and to evidence a more grounded approach to intervention effectiveness assessment.

Table 22 presents direct comparisons of the primary outputs from both scenarios, broken down by physical activity strata and sex. The figures under the two scenarios match predicted patterns. Under the Daily Mile scenario, the relative benefit of intervention on the three primary outputs follows a pattern of sharply diminishing return for strata of increasing physical activity. However, while the MEND scenario clearly benefits only the Inactive strata, it shows superior cohort-level benefits on all three primary outputs, potentially indicating that a focus on maximal increases in the physical activity levels of the inactive proportion of the population is more effective than a population approach that necessarily dilutes impact across the whole cohort. A large proportion of the benefits accrued by implementation of the Daily Mile scenario are observed within the Inactive strata, but when compared to an intervention that specifically targets these strata is unable to match the effectiveness, although as indicated in Chapter Six a true comparison is only appropriate when intervention costs are taken into consideration. In the absence of controlled follow-up data from either intervention it is not possible to reliably assert that the maintenance trajectories following these interventions (see Figure

7.8 & Figure 7.16) would not differ dramatically, and potentially balance such benefits, but within the modelled scenarios the treatment-orientated approach is favoured.

	Daily Mile		MEND	
	Males	**Females**	**Males**	**Females**
Life Expectancy at Five Years of Age				
Inactive	73.51	77.94	73.89	78.31
Barely	74.89	79.14	74.87	79.12
Somewhat	75.38	79.76	75.36	79.75
Active	75.85	80.25	75.84	80.24
Highly	76.73	81.04	76.72	81.04
Totals	75.27	79.63	75.33	79.69
Cohort Total	-	77.45	-	77.51
Change in Years of Life Lost per 100,000				
Inactive	-11.42	-6.20	-17.68	-17.92
Barely	-0.26	-0.72	0	0
Somewhat	-0.16	-0.40	0	0
Active	-0.10	-0.26	0	0
Highly	-0.06	-0.16	0	0
Totals	-12.00	-7.76	-15.68	-17.92
Cohort Total	-	-9.88	-	-16.80
Change in Years of Life in Disability per 100,000				
Inactive	-44224.10	-36275.05	-107656.00	-106407.73
Barely	-2523.19	-5167.39	0	0
Somewhat	-1681.93	-2769.19	0	0
Active	-1230.48	-1971.39	0	0
Highly	-764.28	-1216.69	0	0
Totals	-14055.60	-13440.70	-23511.97	-23477.90
Cohort Total	-	-13748.20	-	-23494.93

Table 22 - Comparison between primary outputs from Daily Mile and MEND scenarios, by physical activity strata and sex.

This implication is further supported by the disease specific outcomes presented in Figure 7.17. The data clearly show that the MEND scenario leads to a greater reduction in type 2 diabetes for both sexes, as well as a greater reduction in myocardial infarction in males.

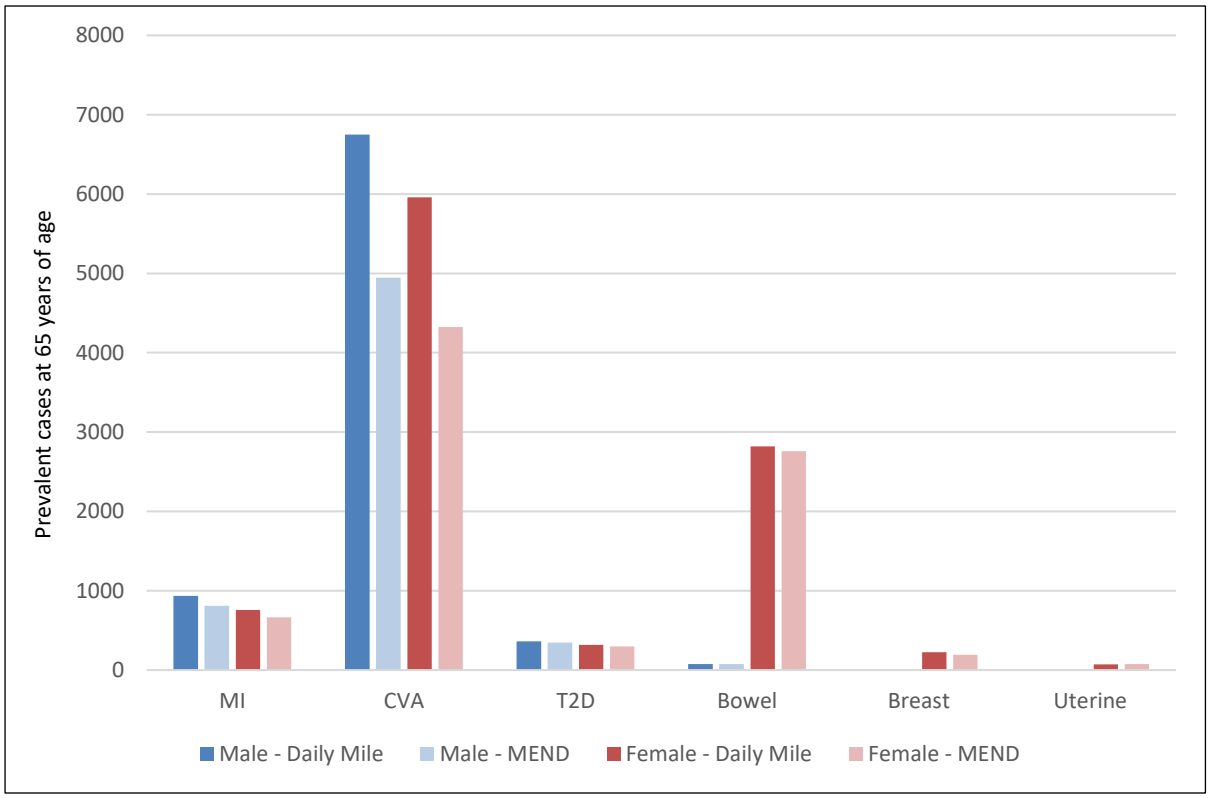


Figure 7.17 - Column graph showing comparison of Daily Mile and MEND scenarios on prevalence cases of specific health outcomes at 65 years of age, by sex.

7.5. Chapter Summary

The present chapter compliments and extends the results presented in Chapter 6 by formally parameterising two scenarios from existing and relevant interventions. The Daily Mile is an increasingly familiar initiative focussing on British primary school children's physical activity, while MEND programmes remain prevalent across community settings throughout England. While Chapter 6 presented the results from an application of well-evidenced but ultimately abstract scenarios, the present chapter drew data from real-world interventions.

The primary outputs suggested that implementation of both scenarios results in modest benefits for life expectancy, years of life lost, and years of life in disability. Specifically, within the Daily Mile

scenario, these benefits were largely observed within the inactive proportion of the population, with diminishing benefits as extant levels of physical activity rose. While the MEND scenario only targeted the inactive proportion, the clearly superior gains in physical activity levels led to a greater benefit on all primary outputs. These findings are concordant with the those presented in Chapter 6 and suggest that a focus on increasing physical activity levels of the least active results both in greater levels of physical activity and in greater benefits from intervention.

Chapter 8 - Application of Hypothetical Outcome Counterfactuals

8.1. Chapter Overview

Chapters 6 and 7 respectively explored the effects and consequences of implementation of systematically derived intervention data and specific contemporary interventions within the simulated cohort. The approach taken within the previous two chapters involved specifying input parameters derived from known intervention effects and exploring the health benefits within the population. However, while the chapters provide an analysis of what specific physical activity interventions can offer, there is no information on the potential contribution that increases in physical activity could produce at higher levels. In particular, the health benefit for the simulated cohort on years of life in disability, or type 2 diabetes prevalence, is not yet quantified. Given the deterministic structure of the core model, it is also possible to specify a desired outcome and then explore hypothetical inputs required to achieve this outcome, or 'reverse-engineering' the core model. Examples of desired changes in outputs might be a one-year increase in population life expectancy, a 10% reduction in lifetime prevalence of type 2 diabetes, or a 5% reduction in years of life in disability within females.

This chapter therefore presents two outcome-based scenarios drawn from contemporary narratives in the mainstream press. The first explores the recent initiative by the UK government indicating a desire to increase healthy life expectancy through a focus on preventative measures, specifically targeting five additional years of healthy living. The second explores a specific health outcome, type 2 diabetes, following reports that incidence of this disease has doubled over the previous two decades, and explores the extent to which increases in childhood physical activity may assist with the reduction of this trend.

8.2. Output Context - "Five extra years of healthy, independent life"

In a recent policy document, "Prevention is better than cure: Our vision to help you live well for longer", the Department of Health and Social Care (2018b) presented a goal of increasing healthy

living by an average of five years by 2035. The document outlines the necessity to reduce risk factors in an effort to increase independence, reduce the economic burden of ill-health, and reduce the pressure on the NHS and social public services. While there has been a notable increase in life expectancy over the last decades due to improvements in medical care, an average of 18 years per individual remain spent in ill-health. The document recognises that given the changing landscape of disease epidemiology, gains in life expectancy are less likely to occur, but propose that reductions in years of ill-health are achievable through a greater focus on prevention (Department of Health and Social Care, 2018b).

The document identifies broader socio-economic issues, including residential neighbourhood, air quality, social grouping, and work environments, in recognition that prevention of ill-health is a nuanced issue, as well as recognising that socio-economic inequalities represent a significant problem. However, the focus is weighted towards individual behaviour and personal responsibility, citing smoking, alcohol consumption, high levels of obesity, excessive screen-time, and insufficient sleep, as the primary drivers of ill-health (Department of Health and Social Care, 2018b). The document suggests individuals should avoid smoking, reduce intake of sugar and salt, consume five portions of fruit and vegetables per day, eat more high-fibre foods, take regular exercise, and limit alcohol intake in an effort to address "rising levels of obesity, mental illness, age-related conditions like dementia, and a growing, ageing and diversifying population, often living with multiple, long-term conditions such as diabetes, asthma and arthritis" (Department of Health and Social Care, 2018b).

8.2.1. Scenario Parameterisation

Using the core model in reverse requires only small changes to the modelling approach. While there is no requirement for a 'real world' front-end scenario, the method of increasing physical activity levels must possess ecological validity, i.e. a plausible method attainable by intervention. This was completed using an 'enforced benchmark' method. Firstly, a physical activity 'floor' was imposed on the population, such that a minimum amount of MET minutes per week was specified and enforced

throughout childhood. Secondly, constraints were imposed such that no quintile could be overtaken by the quintile below; for example, at the point at which the Inactive quintile increases to equal the Barely Active quintile then both these quintiles would increase by the same amount (see Figure 8.1).

In consideration of the findings from Chapters 6 and 7, this approach was taken as it was expected to deliver the most efficient gains, i.e. prioritising the section of the population at highest risk, in comparison to population approaches which potentially dilute the effect of increased childhood physical activity due to diminishing health returns at higher levels of physical activity. This approach also broadly replicates the principle of national physical activity guidelines, in that a minimum figure is specified above which a health gain is expected. In keeping with the benchmark-based approach to increases in physical activity, the analyses are conducted under the assumption that the benefits are experienced throughout the lifespan, rather than just in childhood. While, this represents a slight deviation from the central thrust of the thesis it does so in order to provide a more appropriate answer to the outcome-focused questions.

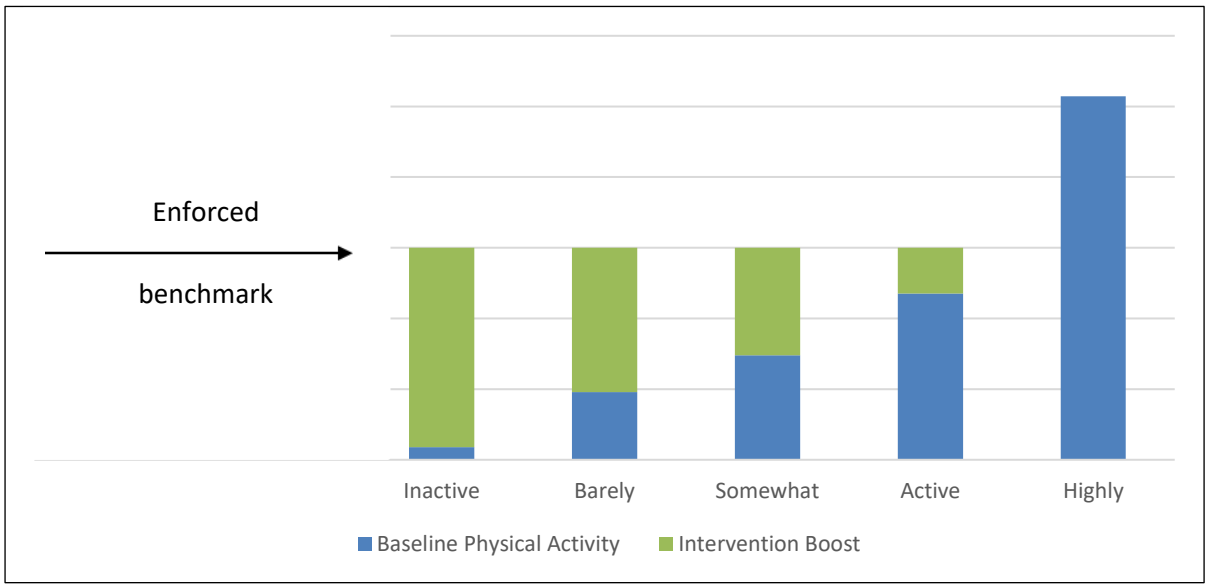


Figure 8.1 - Illustration of 'enforced benchmark' scenario in which all strata are increased to meet a specified population criterion.

8.2.2. Primary Outputs

In order to achieve an increase of one full year in life expectancy as an average across the simulated cohort, it was necessary to raise the minimum level of physical activity to 86658.84 MET minutes per week. This clearly nonsensical requirement can be stated as needing to run at nine miles per hour, for sixteen hours every day throughout childhood, without major reductions in energy outputs in adult life. This finding reinforces previous suggestions that it is very difficult to further increase life expectancy among the English population, and that life expectancy is not particularly sensitive to increases in physical activity within realistic boundaries. The physical activity requirements for a small range of life expectancy changes is presented in Figure 8.2. In each case there is a greater increase required in physical activity for females than males to receive the same benefit in life expectancy.

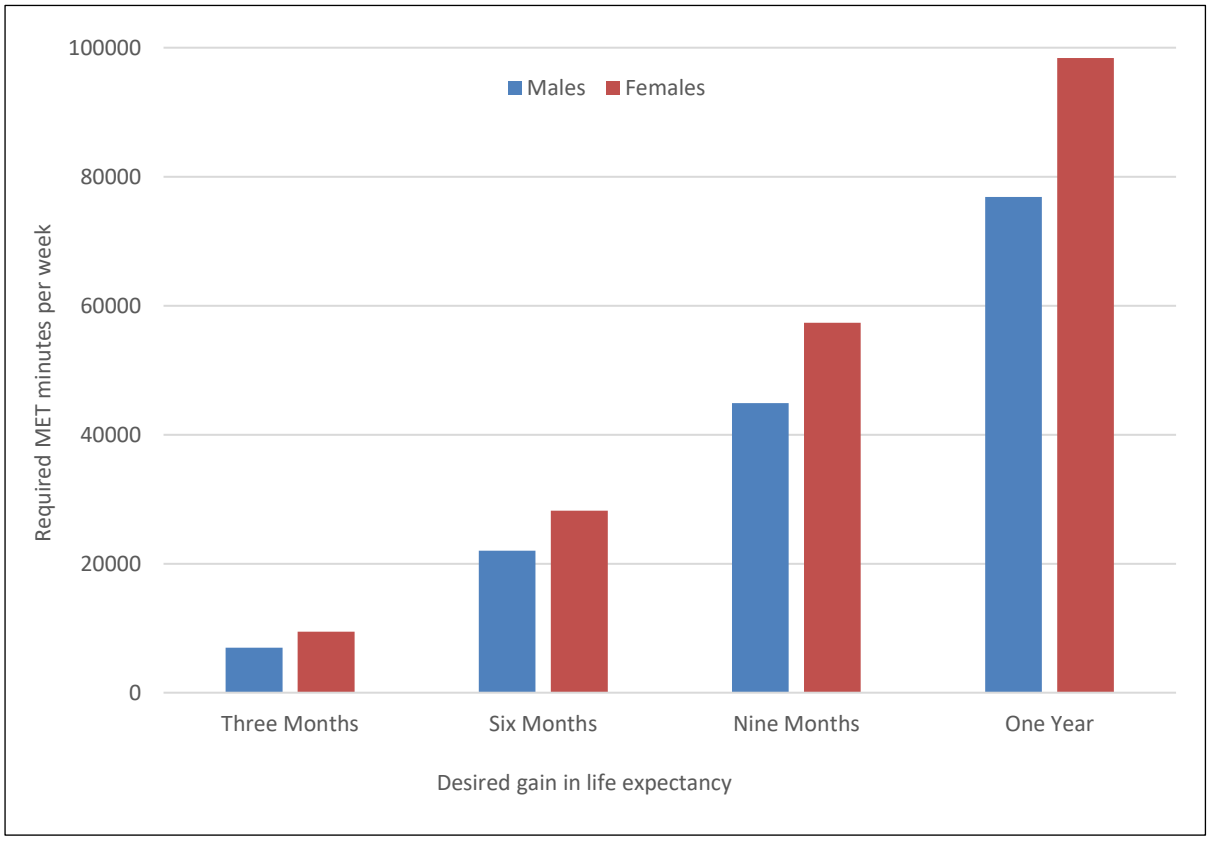


Figure 8.2 - Column graph showing the minimum levels of cohort physical activity require to increase life expectancy, by sex.

Focusing on the increase of healthy living years, or a reduction in years spent in disability, it is necessary to raise the minimum level of physical activity to 8010.95 MET minutes per week in order to produce an average benefit of one years of additional healthy liver per individual. This could be

expressed as four hours per day of walking at a brisk pace (moderate physical activity), or as two hours per day of basketball practice (vigorous physical activity). The required increases in minimum levels of physical activity required to produce a range of increases in years of healthy living are presented in Figure 8.3.

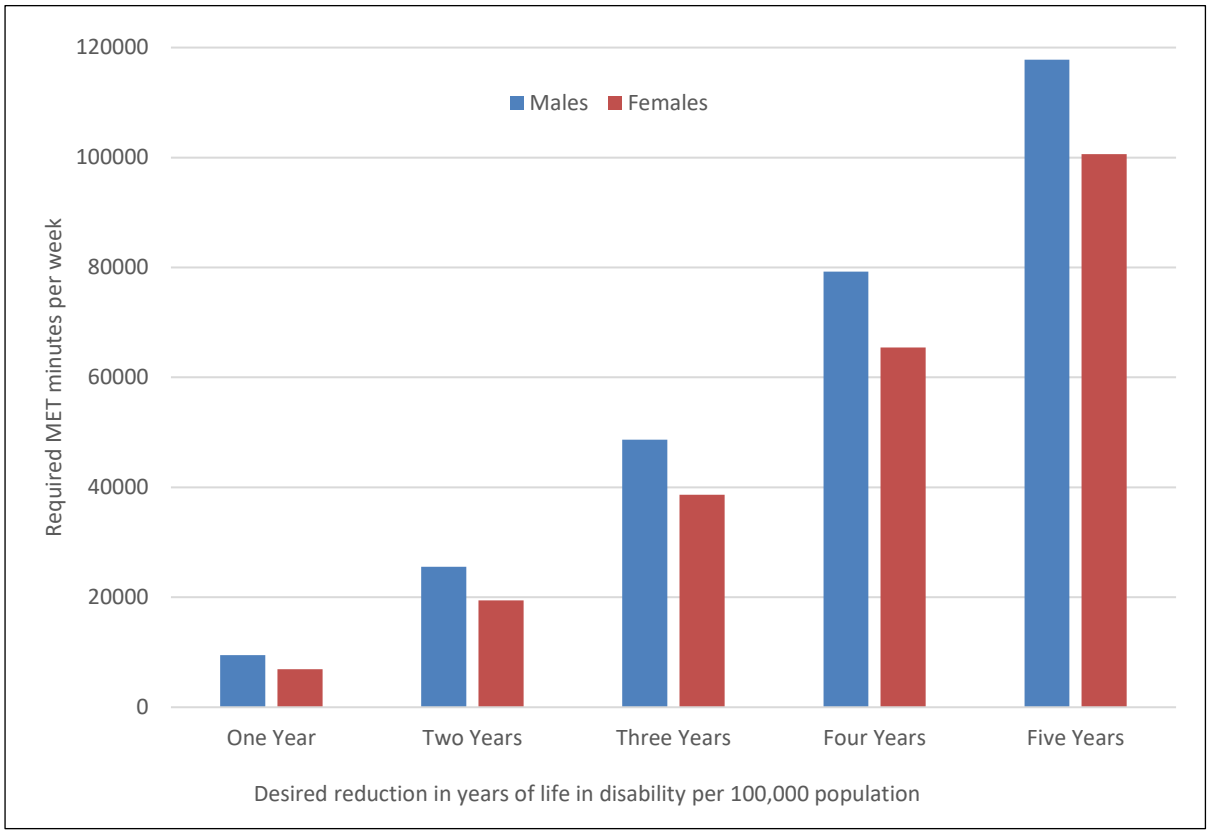


Figure 8.3 - Column graph showing the increase in physical activity required to produce reductions in years of life in disability per 100,000 population, by sex.

While the required increase in physical activity in order to achieve an average on one extra healthy year is highly ambitious, it is not impossible. The benchmark requirement is presented along with the actual data for each physical activity strata in Figure 8.4 and Figure 8.5 for males and females respectively from 2012 HSE data. Figure 8.4 shows an overlap between the benchmark requirement and the amount of physical activity currently achieved by Highly Active male children, although Figure 8.5 shows that female children fall short of this benchmark throughout childhood.

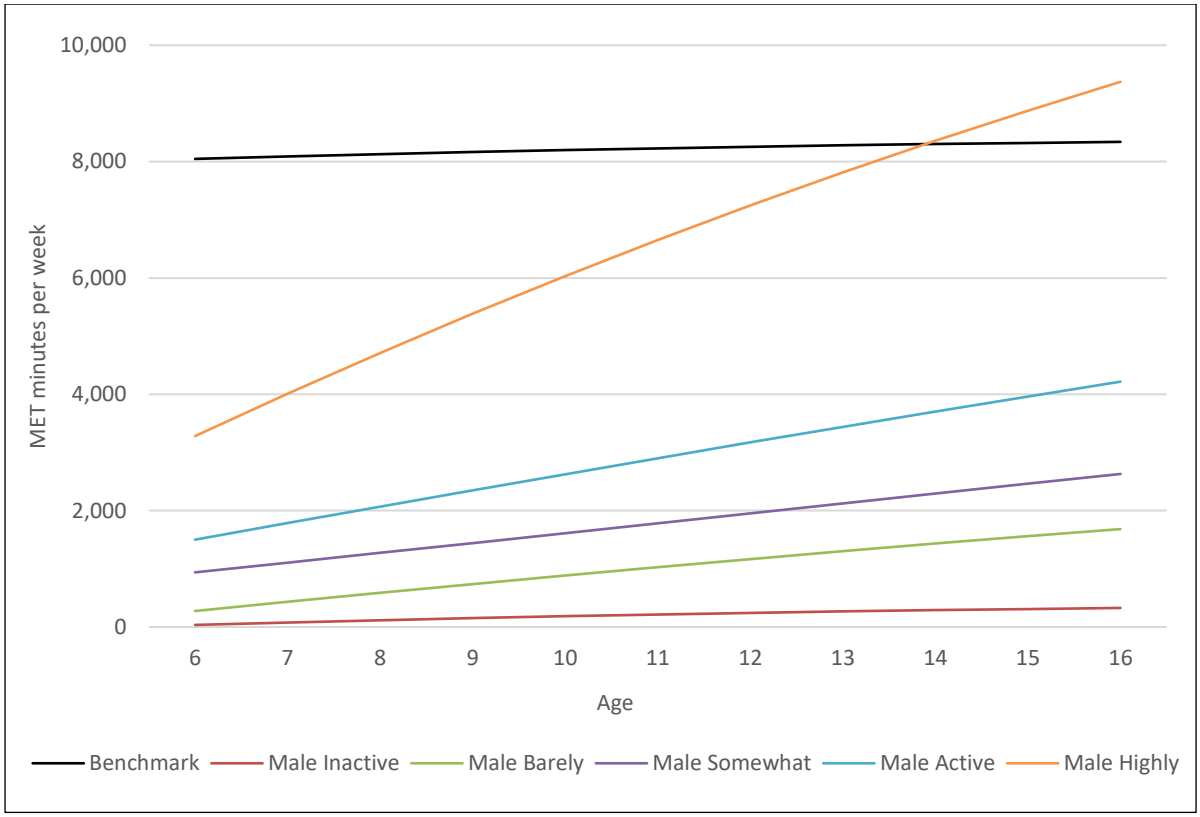


Figure 8.4 - Line graph showing the benchmark level of physical activity required to achieve one additional year of healthy life in comparison to five strata of physical activity reported in the Health Survey for England 2012 for males.

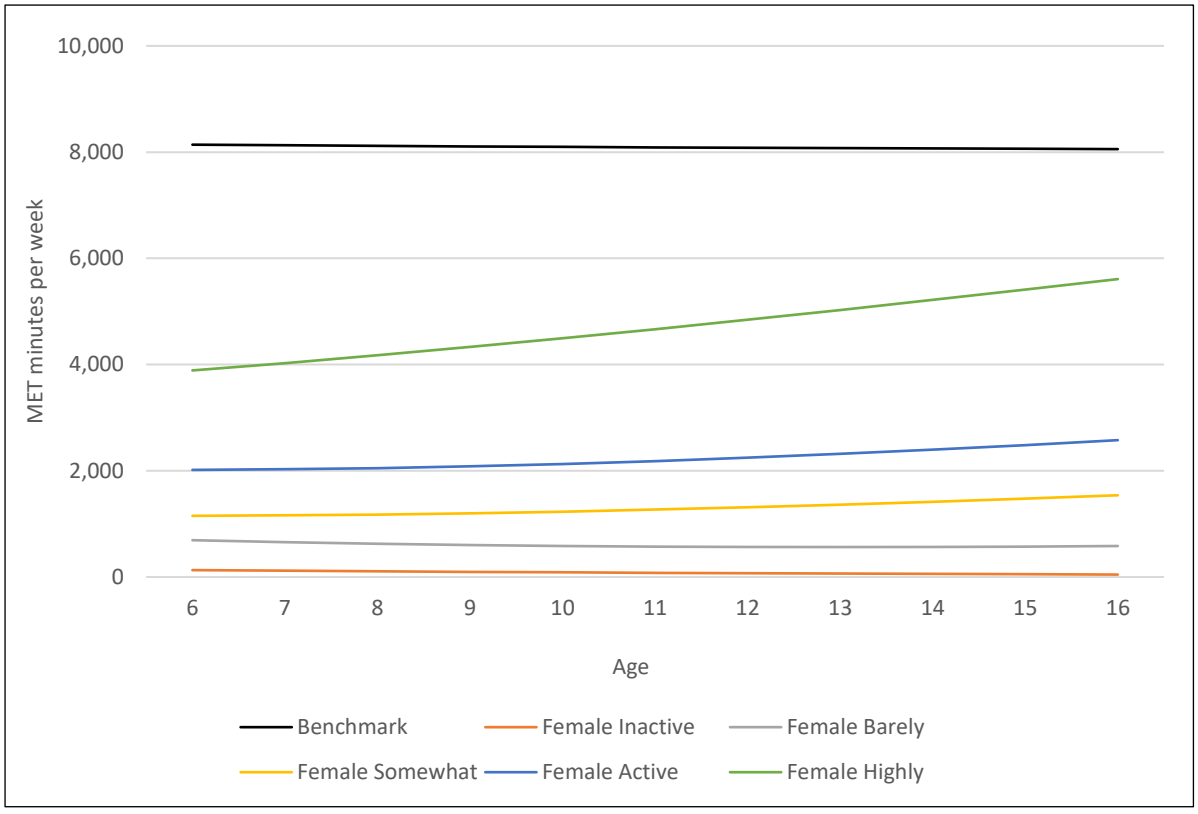


Figure 8.5 - Line graph showing the benchmark level of physical activity required to achieve one additional year of healthy life in comparison to five strata of physical activity reported in the Health Survey for England 2012 for females.

8.3. Additional Analyses

While large increases in life expectancy are not realistic, an increase in physical activity could contribute to a modest reduction in years of life in disability. Taking the example of a sufficient increase in physical activity to reduce years of life in disability by one year, or a year of extra healthy living, it is possible to ascertain the relative contribution to this year from the specific diseases within the model. The contributions are presented in Figure 8.6 and Figure 8.7 for males and females respectively. A sharp reduction between Inactive and Barely Active males is clearly visible, less so in females. The reduction in change between the physical activity strata mirrors the reduction in relative risk of incidence. Across both males and females, and across the physical activity strata, the vast majority of the reduction in years of life in disability is accrued from a reduction in the prevalence of type 2 diabetes. In addition, the contribution of type 2 diabetes relative to the other diseases appears to increase as physical activity strata increases.

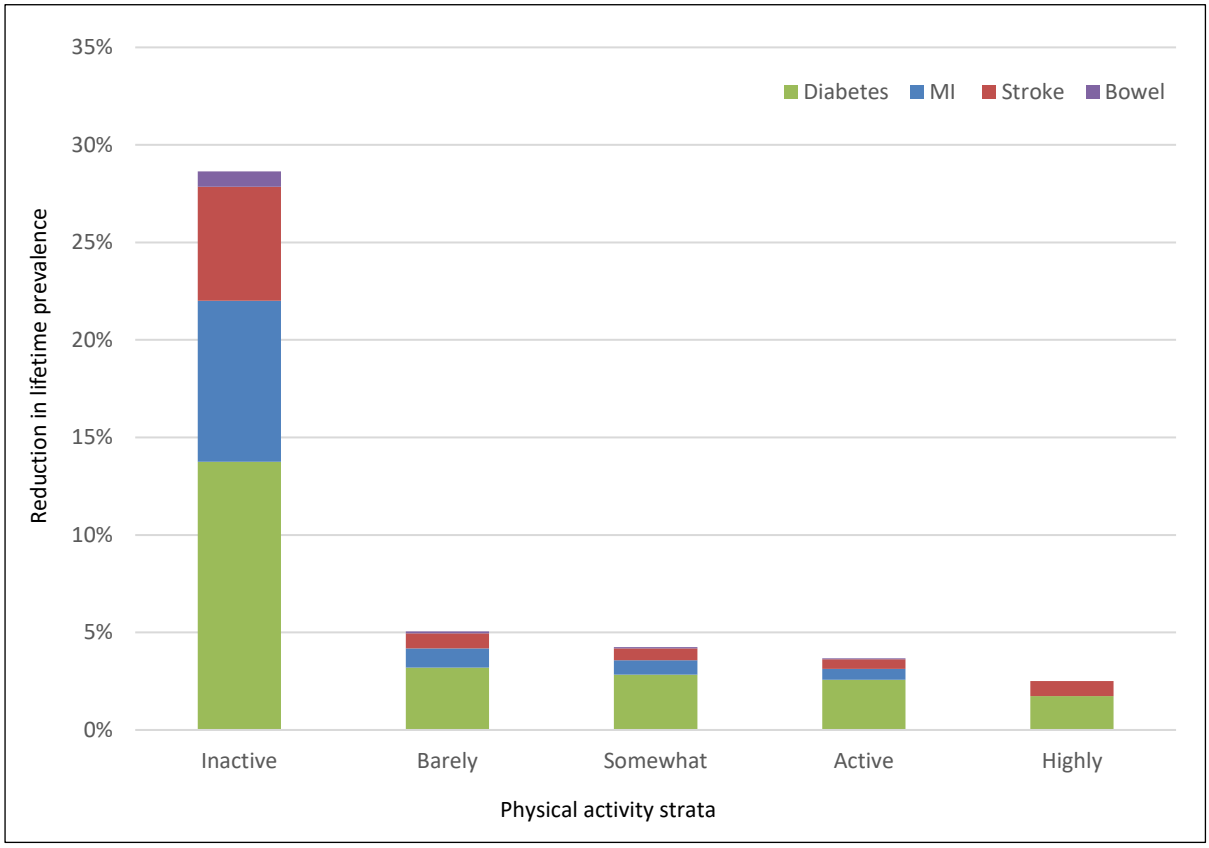


Figure 8.6 - Stacked column graph showing the relative contributions from each disease outcome to achieve a one-year reduction in years of life in disability per 100,000 population in males, by physical activity strata.

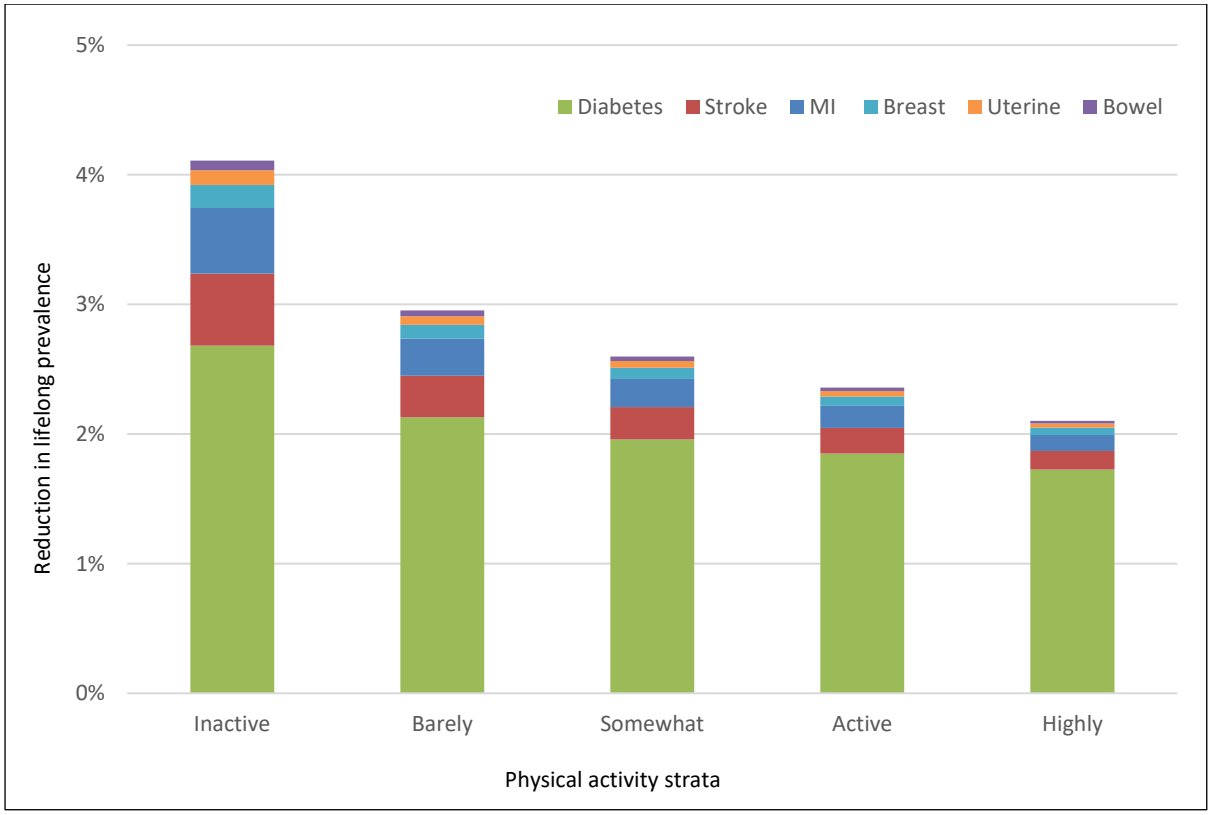


Figure 8.7 - Stacked column graph showing the relative contributions from each disease outcome to achieve a one-year reduction in years of life in disability per 100,000 population in females, by physical activity strata.

While not directly stated in the policy document it is implicit that the least healthy will contribute more years towards this desired outcome than the healthiest, as there is good evidence that the least active strata of the population gain the most from any increase in physical activity due to the dose-response relationship between physical activity and the health outcomes of interest. The relative contribution of each strata, by disease outcome, is presented in Figure 8.8 and Figure 8.9 for males and females respectively. In each disease outcome, and across both males and females, there is a clear reduction in benefit from increased physical activity as according to an individual's pre-existing levels, with the Inactive strata experiencing the greatest reduction in years of life in disability and the Highly Active receiving the least benefit. Of interest is that type 2 diabetes shows a less obvious delineation by existing physical activity level, with the benefit of additional physical activity much more evenly spread across the physical activity strata.

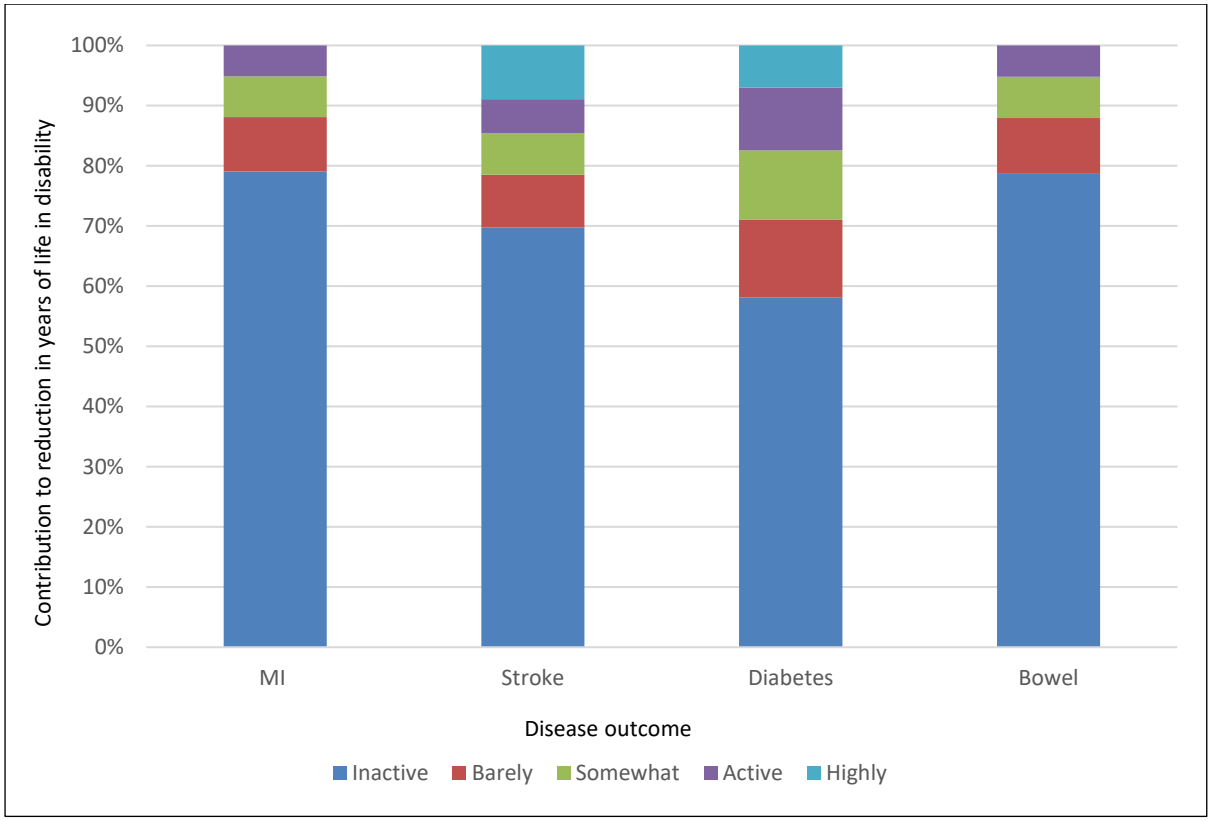


Figure 8.8 - 100% stacked column graph showing the relative contribution towards reduction in years of life in disability by one year per person from the five physical activity strata in males.

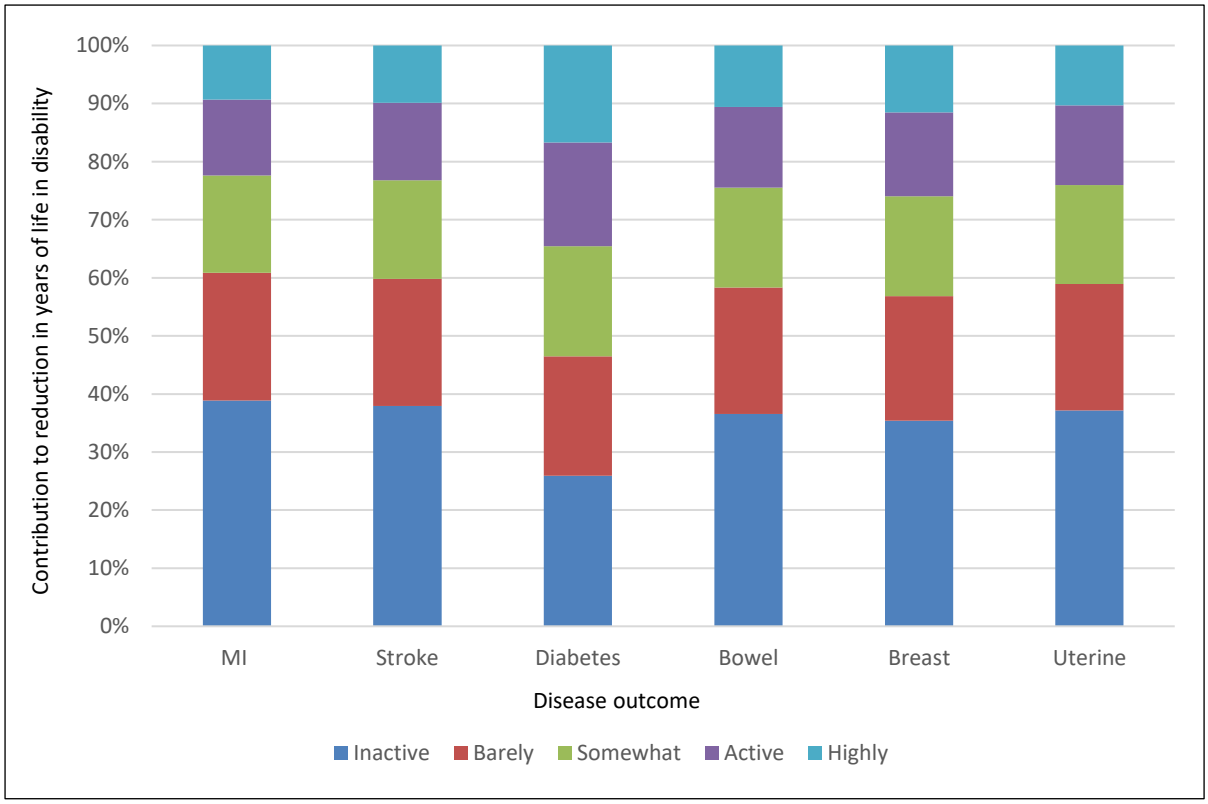


Figure 8.9 - 100% stacked column graph showing the relative contribution towards reduction in years of life in disability by one year per person from the five physical activity strata in females.

8.4. Interim Discussion

The above scenario explores the potential role for increased physical activity in addressing the desired outcome of five extra years of healthy living. "Prevention is better than cure: Our vision to help you live well for longer" clearly acknowledges that increases in physical activity levels would need to form just part of a holistic approach to reducing unhealthy behaviour (Department of Health and Social Care, 2018b). Life expectancy appears largely impervious to realistic, and even unrealistic, increases in childhood physical activity levels. However, the document specifically suggests that a reduction in the years of life spent in ill-health is the primary goal, rather than an increase in years lived. To this end, the government strategy of providing "five extra years of healthy, independent life" appears to be a reasonable goal in which to invest.

The results above suggest that increasing childhood physical activity has the potential to modestly but meaningfully contribute to a holistic package, although alternative modelling of the extent to which levels of physical activity persist throughout the life course would change the figures. More work needs to be integrated into the narrative regarding the potential for the other strands of this package to be quantified, such as diet, as well as the potential for synergistic effects to further increase any benefit. Lastly, the additional analysis suggests that within any reduction in years of life in disability due to increases in childhood physical activity, it is type 2 diabetes that contributes the majority of this benefit. Furthermore, and in contrast to the other diseases of interest, all strata of physical activity appear to benefit from increased physical activity levels with regard to reductions in type 2 diabetes. Given this disease appears most sensitive to changes in physical activity, further analysis of the potential population benefits is warranted.

8.5. Output Context - "The number of people diagnosed with diabetes has doubled in the last 20 years"

Data from NHS England suggest that the prevalence of diabetes has doubled in the last two decades, leading to an estimated annual direct cost to the NHS of approximately £10 billion (Hex et al., 2012). The story was covered by the BBC following the report on both the mainstream news and on the BBC

Health website (Ives, 2018). This rising trend is projected to continue, with prevalence expected to increase to nearly five million, approximating nearly 10% of the adult population (Wild, Roglic, Green, Sicree, & King, 2004), broadly matching age-standardised trends in type 2 diabetes globally (NCD Risk Factor Collaboration, 2016).

8.5.3. Scenario Parameterisation

The following analysis assesses the extent to which increases in childhood physical activity levels can reduce the prevalence of type 2 diabetes in the English population. It is not possible to estimate the impact intervention might have on the increasing trend due the way the model is structured, i.e. a time-limited closed cohort simulation. The target for intervention would be to reduce the prevalence of diabetes by fifty percent, and reverse the trends over the last two decades. The inputs and analysis process follow the methods presented in Scenario One above, involving the specification of a 'floor' level of childhood physical activity, and the subsequent incremental increase of this floor to meet specific outcomes.

8.5.4. Primary Outputs

In keeping with the findings from Scenario One above, the more demanding requirements rapidly become nonsensical, as presented in Figure 8.10. However, the lowest benchmark outcome, that of reducing the prevalence of diabetes by 10% appears within the bounds of possibility. A figure of 4,745 MET minutes per week of physical activity throughout childhood approximately doubles that of the current UK guidelines, but would not be impossible to achieve. For example, this could take the form of running at 8.5 mph for one hour per day of childhood, or two hours of horse-riding or badminton per day, or four hours of slow walking per day. Given the lower level of physical activity typically achieved by females in England, the benefits of increased physical activity more rapidly accrue when increasing female physical activity.

A comparison of a benchmark guideline of 4,745 MET minutes per week of physical activity to the stratified estimates reported within the HSE 2012 shows that Highly Active boys are already meeting

and exceeding this benchmark for the majority of their childhood, and that by the time they are sixteen the Active boys are also approaching this benchmark Figure 8.11. Figure 8.12 shows that Highly Active girls are also meeting or exceeding this benchmark figure by the time they are twelve years old.

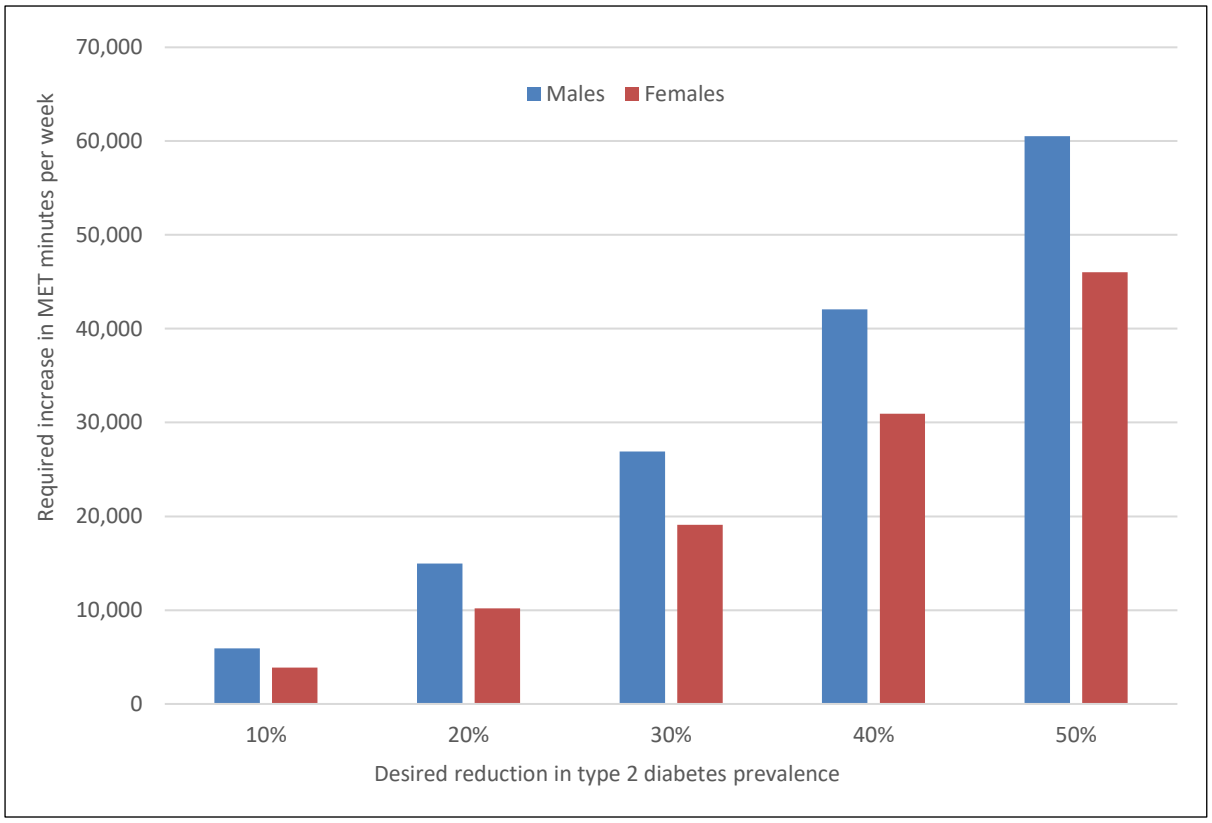


Figure 8.10 - Column graph showing the required increase in MET minutes per week to produce a desired reduction in type 2 diabetes within the modelled population, by sex.

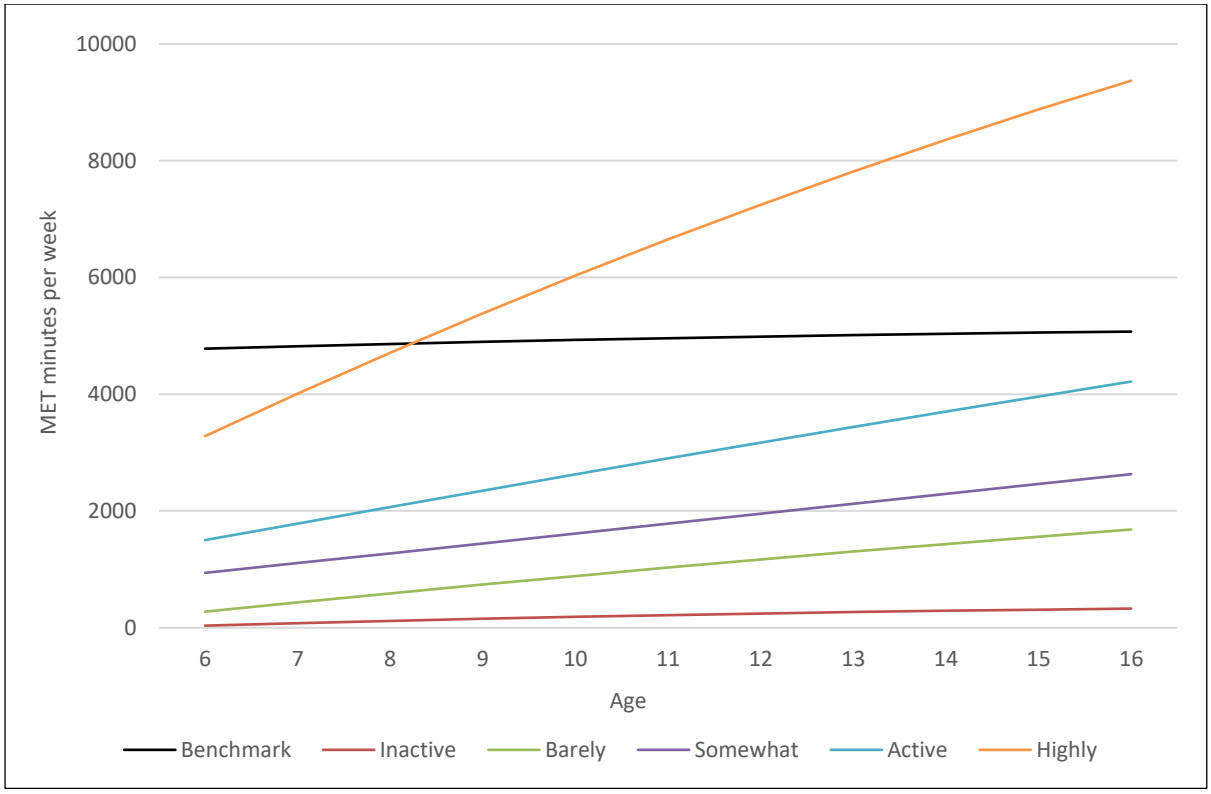


Figure 8.11 - Line graph showing the benchmark level of physical activity required to achieve a 10% reduction in lifetime prevalence of type 2 diabetes in comparison to five strata of physical activity reported in the Health Survey for England 2012 for males.

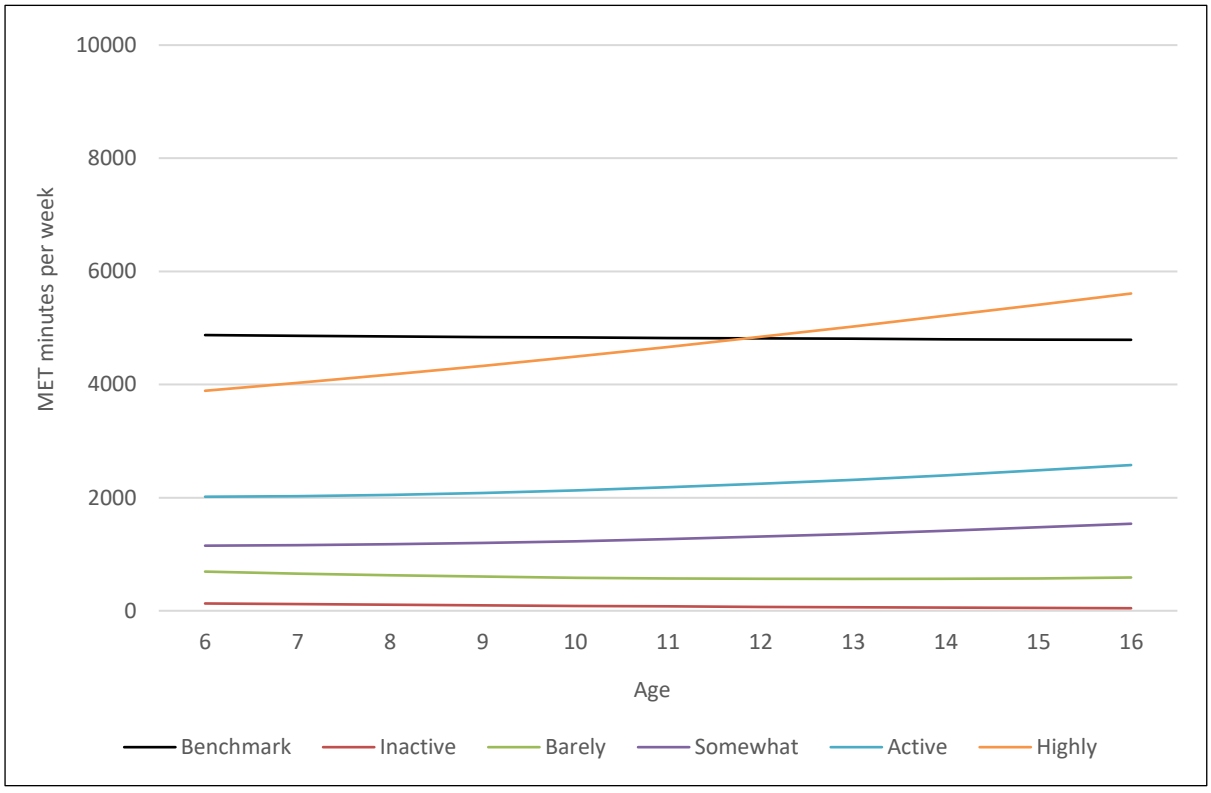


Figure 8.12 - Line graph showing the benchmark level of physical activity required to achieve a 10% reduction in lifetime prevalence of type 2 diabetes in comparison to five strata of physical activity reported in the Health Survey for England 2012 for females.

While the more ambitious targets are not achievable, a 10% reduction in type 2 diabetes would carry a multitude of health and economic benefits. Exploring this target in more detail, the typically modest benefits for life expectancy are presented in Figure 8.13. The familiar pattern of the greatest benefit occurring within the Inactive strata emerges again, across both males and females. A similar and more robust pattern of benefit is observed when exploring effects on reduction in years of life in disability, presented in Figure 8.14.

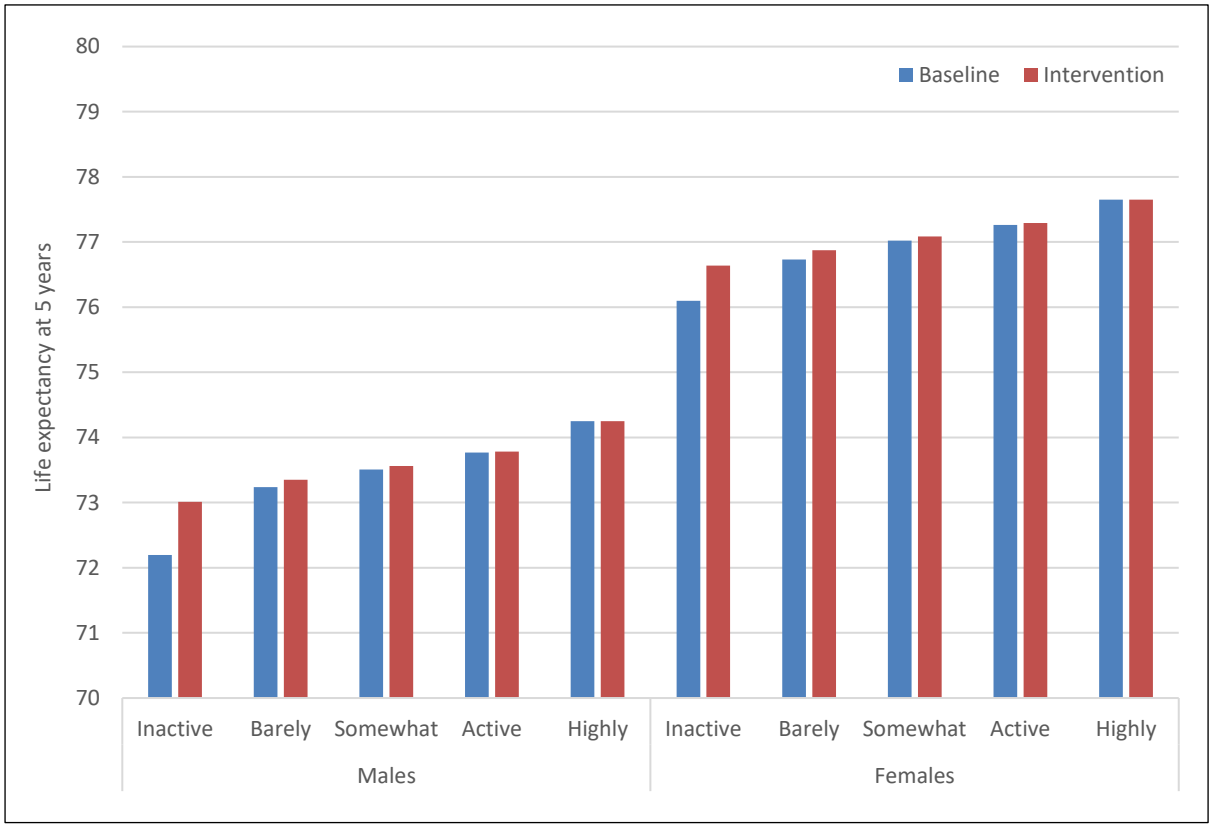


Figure 8.13 - Column graph showing the effect of a childhood physical activity intervention sufficient to reduce type 2 diabetes prevalence by 10% on life expectancy at five years, by physical activity strata and sex.

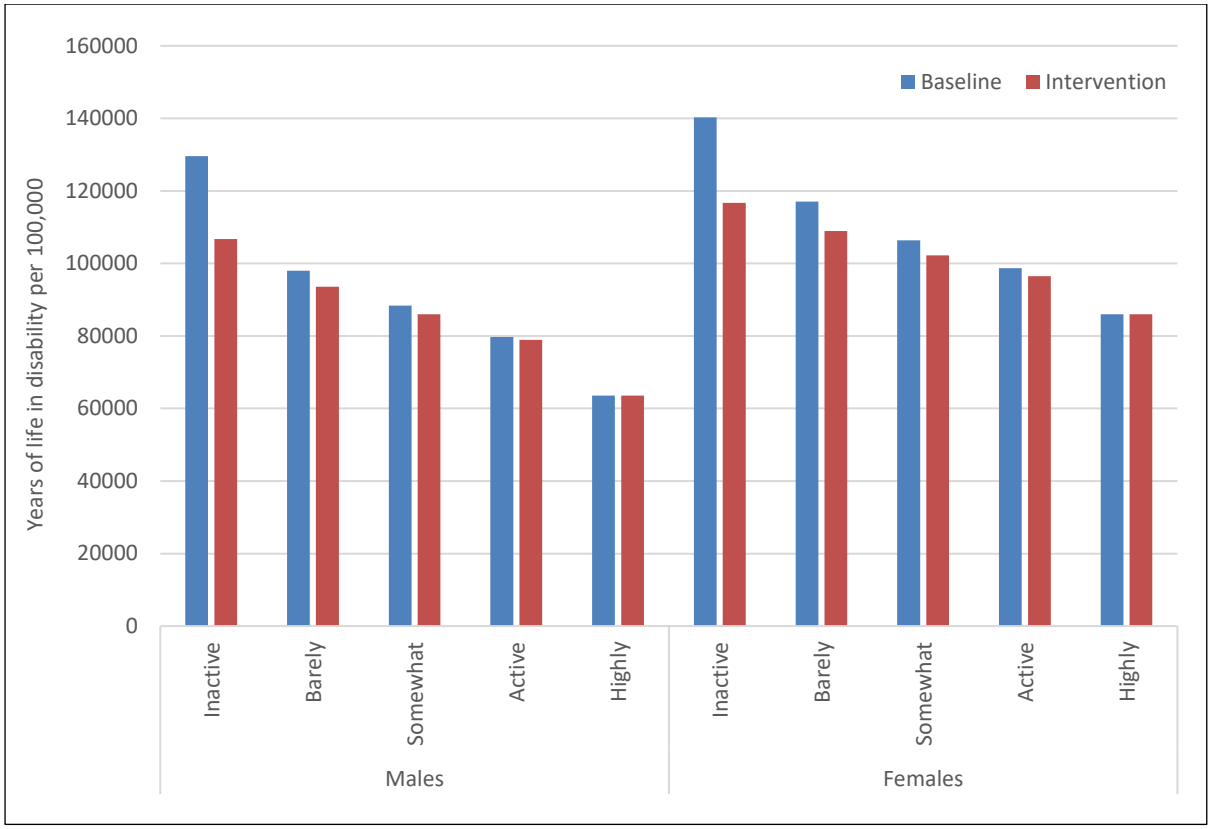


Figure 8.14 - Column graph showing the effect of a childhood physical activity intervention sufficient to reduce type 2 diabetes prevalence by 10% on years of life in disability, by physical activity strata and sex

8.6. Discussion

Analysis in previous chapters indicate that of all the outcomes of interest, a reduction in type 2 diabetes prevalence appears to be particularly sensitive to increases in childhood physical activity levels. However, it was not previously known the extent to which childhood physical activity levels, and subsequent increases in life-time physical activity, might scale to population-level reductions. The above scenario presents an exploration of the extent to which increases in childhood physical activity levels can mitigate the increase in prevalence of type 2 diabetes. Concordant with analyses of increased physical activity levels from previous chapters, the pattern of maximum benefit experienced in the Inactive strata of the population emerges, with diminishing returns observed for incrementally more physically active strata. Again, life expectancy shows only minimal gains, but there is a modest reduction in years of life in disability. However, while increases in physical activity levels in childhood may contribute towards a reduction in prevalence, even modest reduction requires a drastic increase in physical activity for the entirety of childhood and favourable a favourable legacy over the life course.

8.7. Chapter Summary

The above chapter presents the analyses of two brief hypothetical scenarios drawn from contemporary narratives regarding physical activity or related health outcomes. When reading these outputs, it must be borne in mind that they are generated through an application of one type of hypothetical intervention, although the evidence of previous chapters suggest that this approach is the optimal solution to increasing childhood physical activity levels. In addition, while the trend data are observed at all levels of 'benchmark', absolute outputs depend on the placement of the benchmark. Lastly, the exponential decay in physical activity increases post childhood is the only legacy scenario modelled in these analyses, and naturally any change in this scenario will alter the outputs.

Chapter 9 - Discussion and Conclusion

9.1. Chapter Overview

The primary aim of this thesis was to explore the effects that physical activity interventions implemented in childhood have on non-communicable disease outcomes across the lifespan of a simulated cohort. The preceding chapters outlined the context and issues surrounding childhood physical activity levels and interventions, and reviewed the available evidence on childhood physical activity levels in England, defined a method of modelling by which the thesis aims could be satisfactorily addressed, provided a systematic review a meta-analysis of the sustained effects of physical activity interventions, and presented the findings from estimates based on both pooled and 'real world' interventions. The present chapter provides an overall summary and discussion of the main findings within the thesis, a comparison with other relevant research, a brief review of the contributions and limitations of the method and findings, and concludes with suggestions for additional research within this area.

9.2. Summary of Principle Findings

The principle findings of this investigation are the extent to which actual and hypothetical interventions affect the levels of physical activity in childhood and the consequential effect this increase holds for lifelong non-communicable disease incidence, prevalence, and mortality. The thesis is structured to first explore the current context and sources of data, to present a viable method by which the central research question could be answered, to explore preliminary outputs from the core model, to ascertain the extent to which current interventions increase child physical activity levels and the effect these hold for lifetime health outcomes, and finally to explore the potential effects that known or hypothetical childhood interventions could possess for health outcomes across the lifespan. The main findings for each of these sections are summarised below.

9.2.1. Child Physical Activity in England

The exploration of the Health Survey for England (HSE) responses from the 2012 and 2015 iterations revealed a number of interesting patterns, as well as confirming some stereotypes, regarding children's physical activity levels. Boys total more activity than girls throughout childhood, both in terms of minutes spent being active and in MET minutes per week. This pattern holds across all domains of physical activity except active transport. An interesting pattern showed that as boys get older, formal sport replaces informal activity to broadly maintain physical activity levels throughout childhood; in girls, however, informal activity levels also decline with age but are not then replaced with formal sport participation, leading to a sharp decline in girls physical activity levels in the teenage years.

There was very little variation in levels of childhood physical activity across geographical region within England. While an overall negative correlation emerged between quintile of index of multiple deprivation (QIMD) this was weaker than might be predicted from the literature (e.g. De Vet, De Ridder, & De Wit, 2011; Fairclough, Ridgers, & Welk, 2012), particularly for leisure time physical activity (Gidlow, Johnston, Crone, Ellis, & James, 2006). A similar pattern was evident for physical activity levels and weight status, with only a weak negative correlation. There were, however, some clearer variations apparent across ethnic groups, specifically indicating that children identifying as white report higher average levels of physical activity than other broad ethnic groups.

In a comparison between data across the 2012 and 2015 iterations of the HSE, there were no systematic differences in either total physical activity levels, domains of physical activity, or within levels when stratified geographical region, QIMD, or ethnicity. This suggests that the patterns identified within the 2012 iteration, used as the physical activity level inputs within the core model, were robust over time. The HSE 2015 included a measure of school-time physical activity for the first time within the survey. While the amount of school-time physical activity was low relative to other

domains it, along with active travel, appeared largely impervious to change across age, sex, or other variables, indicating a small but resilient contribution to childhood physical activity levels.

9.2.2. Systematic Review of Intervention Effectiveness

A review of the available literature revealed both a lack of consensus on the effectiveness of intervention in childhood and a lack of quality information on the sustained effectiveness of such interventions. In addition, a systematic review by Metcalf et al. (2012) questioned whether any effect was observable following intervention at all when study quality was high and measurement was objective. A systematic review was therefore conducted to assess whether interventions were effective at a follow-up of at least six months.

At the time of review and subsequent publication, only fourteen studies provided controlled follow-up data at least six months post-intervention. Meta-analysis revealed negligible gains in measured childhood moderate-to-vigorous physical activity following intervention, with a mean difference of only 1.47 (95% CI's: -1.88, 4.82) additional minutes per week when compared to controls. Sub-group analyses revealed few statistically significant differences, but did suggest that males receive a greater benefit following interventions than females, community-based interventions appear to be more effective than those implemented within a school setting, and that 'treatment' style interventions specifically targeting those with low levels of baseline physical activity appear more effective than 'population' style interventions that recruit no specifically targeted participants.

When those low incremental levels of physical activity, identified by meta-analysis, were entered into the core model there was a predictably small benefit observed in health outcomes. When applied, the pooled estimate for population approach interventions resulted in a mere 0.01 (95% CI's: 0.01, 0.02) years increase in life expectancy at five years of age, or a -2.15 (95% CI's: -3.63, 0.28) change in years of life lost within the total simulated population of 100,000. Of the specific disease outcomes, the highest benefit was observed for type 2 diabetes with a change of -33.33 (95% CI's: -69.57, 20.28) change in prevalent cases per 100,000 within the simulated cohort at 65 years of age. The pooled

estimate for treatment interventions produced marginally more success, with a 0.02 year (95% CI's: 0.00, 0.03) increase in life expectancy at five years and a change of -3.35 (95% CI's: -4.68, 0.10) years of life lost for the simulated cohort of 100,000. Again, type 2 diabetes showed the most benefit with a change of -39.82 (95% CI's: -68.87, 4.90) prevalent cases per 100,000 at 65 years.

9.2.3. Modelling of Specific Interventions

To supplement the estimates of effects drawn from systematic review and meta-analysis, two 'real world' childhood physical activity interventions were simulated and applied within the core model. This was completed for two primary reasons, firstly because the pooled estimates produced by meta-analysis contained significant heterogeneity and as such did not precisely represent an identifiable intervention, and secondly because there is no evidence of the effects of scaling up known interventions to a population level. Therefore, in keeping with the exploration of both population and treatment effects when applying the estimates from the systematic review, this analysis selected one population intervention, The Daily Mile, which makes no discrimination with regard to participation, and one treatment intervention, Mind Exercise Nutrition Do it! (MEND), which was targeted specifically at the high-risk sub-section of the child population.

Modelling of the Daily Mile scenario (Daily Mile Foundation, 2016) suggested that modest benefits are achievable from a continual application of a physical activity intervention. Changes in life expectancy were negligible, but there was a reduction of over 10,000 years of life in disability within the simulated cohort of 100,000 following application of the Daily Mile throughout primary school years and under specific legacy conditions. Type 2 diabetes saw the greatest reduction in prevalence subsequent to intervention, with nearly 200 fewer cases occurring within the same simulated cohort. Of particular note was the extent to which the population benefit was accrued within the least active quintile of the population, with over 80% of the total health benefit observed within the Inactive strata, even though the Daily Mile intervention was implemented across the whole child population.

Modelling the MEND intervention (Sacher et al., 2010), targeted exclusively at the Inactive strata of the simulated population, also revealed health benefits subsequent to intervention. While changes in life expectancy remained very small, there was a reduction of over 20,000 years of life in disability across the simulated cohort of 100,000. This gain was produced despite the intervention only targeting 20% of the population. Again, type 2 diabetes was the health outcome in which the greatest reduction in prevalence was observed.

9.2.4. Modelling for Hypothetical Outcomes

Following the results generated by modelling specific interventions, summarised above, it was evident that some health benefit was achievable through application of child physical activity interventions within the simulated cohort. It was not known, however, the extent to which childhood physical activity interventions could address or contribute to addressing the desired population health increases to which they may be logically applied. Therefore, two contemporary outcomes were selected in order to further explore this issue. Firstly, the UK Government's publicised goal to increase the health of the population to provide five additional healthy years, was explored. Secondly, the potential contribution that physical activity interventions may play in partially reversing the trend of rising prevalence of type 2 diabetes was investigated.

Both scenarios involved 'reverse engineering' the core model; rather than parameterising a specific input and allowing the figures to work through the deterministic model, a desired outcome was pre-determined and the level of childhood physical activity was incrementally increased until the outcome was achieved. In both scenarios, the amount of additional physical activity required to meet the original outputs was pragmatically unachievable. However, were the child population moved to benchmark levels of physical activity, meaningful reductions in health outcomes were observed. In particular, were all children to increase physical activity levels to achieve a minimum of 8,000 MET minutes per week, equivalent to a Highly Active male in their mid-teenage years, the simulated population experienced an average of one additional year of healthy life per person.

9.3. Methodological Critique

While the above summary of results summarises the results from interventions applied within the simulated cohort, there are a number of issues that must be borne in mind when evaluating the findings. Many of the limitations within the method and analyses are consequential to the modelling approach, a justification for which is made in Chapter 3. Here, an argument is made both to justify the approach and to clarify the limitations such that an informed evaluation of the findings is possible. Further uncertainties arise from the availability and quality of the sources of data, and the structural uncertainty within the model itself. The main limitations to the findings within this thesis are discussed briefly below.

Overall, the indications from published studies of physical activity levels and health outcomes are echoed in the present study, concordant in the finding that increased amounts of routine physical activity are independently associated with lowered risk of health outcomes, and most particularly chronic disease incidence and morbidity. Those individuals meeting physical activity guidelines are therefore consequentially less likely to experience non-communicable disease morbidity than those who do not. These specific health benefits follow a dose response relationship, with comparatively high reductions in disease morbidity following improvement from low levels of physical activity, following a subsequent pattern of diminishing returns for each unit of increase in physical activity. In studies investigating physical activity as a continuous, or at least ordinal, exposure (e.g. Kyu et al., 2016; Sattelmair et al., 2011; Wahid et al., 2016) and this pattern is indicated as a relationship that can be parameterised as a 0.25 power transformation for the included health outcomes.

9.3.5. Inclusion and Exclusion of Model Parameters

An *a priori* discussion of the limitations of modelling, the specific constraints and consequences regarding the choice of modelling strategy, and the inherent uncertainty for the current project, is provided in Chapter 3. However, given the summary of the findings immediately above, a revision of the limitations of the selected modelling approach is appropriate. As with all models, the core model

used within this thesis represents a simplification of the real world in order to explore a specific issue. The core model specifically explores the relationship between physical activity levels and selected non-communicable disease outcomes within a simulated population, and therefore removes a large number of potentially relevant variables from analysis that are present in the real-world context.

Specifically, in the case of the core model no encoding or analysis was conducted for: environmental factors such as relative urban/rural dwelling, region of residence in England, or environmental deprivation; social factors such as income, social networks and cohesion, or cultural background; nor individual factors such as level and quality of education, beliefs regarding food intake and exercise, or existing skill or experience with particular physical activities. Furthermore, no medical or physiological variables were included within the model, including levels of adiposity, cardio-respiratory fitness, illness or disability, or genetic predisposition. Finally, no concept of causal chain nor concurrent risk factors were encoded within the model, such as hypertension, obesity, unhealthy dietary intake, alcohol intake, or psychological factors such as depression or anxiety.

The above delimitations are not presented as weaknesses of the model, but rather in order to provide a transparent explanation of the model structure from which the findings may be correctly evaluated. The reasons for many of these modelling decisions are briefly addressed below. Firstly, the analyses conducted within Chapter 2 explored a number of the omitted variables mentioned above. Within the data from the HSE, no systematic variation was discovered for geographical region, level of obesity, or QIMD. Variation in physical activity levels was shown to be related to age and sex, and therefore those variables were included within the model. While ethnicity did show some effect for physical activity, no data are available by which to parameterise this within the model and therefore this was not included. Secondly, the absence of data on either the specific effects, or the effects in interaction, for the additional variables means that assumptions would be required to encode them within the model. For each assumption made, even if the assumption is that no interaction is to be modelled, the model becomes further abstracted from reality. Thirdly, while the additional outputs generated from

the inclusion of intermediate variables between physical activity level and health outcomes would welcome and, further, that intermediate variables would potentially add greater integrity to the data (i.e. increased use of physiological measures rather than survey and self-report), there is a clear argument for a more a more direct approach. In the case for salt intake, for instance, in which there exists more robust evidence for effect which includes the intermediate variable of hypertension, a viable mechanism, and meta-analysis of intervention studies (Aminde, Cobiac, & Veerman, 2019; He, Li, & MacGregor, 2013), there is a clear rationale for modelling these transition steps without the disadvantage of excluding potential additional influences on the health outcome. However, in the case of physical activity and health outcomes, the most convincing intermediate step would be adiposity (BMI), but the HSE data revealed no relationship between childhood physical activity and weight status, nor have meta-analyses revealed a consistent relationship between physical activity and childhood weight status (e.g. Poitras et al., 2016; Rauner, Mess, & Woll, 2013); furthermore, the meta-analysis by Wahid et al. (2016) found that adjustment for weight status only marginally attenuated relative risk estimates, suggesting the health benefits from increased physical activity are largely accumulated through alternative mechanisms.

The core model therefore explores the direct association between physical activity levels in MET minutes per week and the incidence and mortality rates of the included disease outcomes as it is these relationships for which there exists the best available evidence. Furthermore, the model does not explicitly model the effects of physical activity level on attenuating the effects of morbidity, for instance the use of physical activity in rehabilitation and 'prehabilitation' of people with cancer (Hunter, Gibson, Arbesman, & D'Amico, 2017) or heart disease (Dibben et al., 2018). In addition to positive effects for health outcomes included in the model, increased physical activity levels has been shown to hold a protective and rehabilitative effect in people with a diagnosis of chronic disease, for example those with type 1 diabetes (Tully, Aronow, Mackey, & Streisand, 2016) or cystic fibrosis (Cox & Holland, 2019).

In addition to the modelled benefits to incidence and mortality a number of wider benefits can be accrued from increases in physical activity both across the lifetime and within youth. While the analyses in the previous chapters are appropriate examples of health outcomes that are associated with physical activity levels, additional outcomes are indicated in the literature. These include: further negative associations with disease outcomes such as osteoporosis (Bland, Heatherington-Rauth, Howe, Going, & Bea, 2020), additional cancers (Moore et al., 2016), and dementia (Xu et al., 2017); positive associations with mental health and wellbeing in both youth (Bell, Audrey, Gunnell, Cooper, & Campbell, 2019) and adults (Bernard et al., 2018); and positive associations with child academic performance (McPherson, Mackay, Kunkel, & Duncan, 2018) and adult workplace productivity (López, Casajús, & Garatachea, 2018). However, in many of the above outcomes the contributing studies are lack rigor and there is typically insufficient evidence to parameterise a continuous dose response relationship.

The effects of levels of physical activity, and inclusion of specific opportunities to participate in episodes of physical activity, within the school day has received increasing attention in the literature, including increasing the intensity or duration of formal physical education (Bugge et al., 2012; Lonsdale et al., 2013), additional physical activity opportunities within the day (Daily Mile Foundation, 2016), active classrooms (Norris et al., 2020), and encouraging more active break and lunch periods (Parrish, Okely, Stanley, & Ridgers, 2013). The potential link between physical activity and academic performance, classroom concentration, and executive function has been explored in detail, although largely inconclusively (de Greeff, Bosker, Oosterlaan, Visscher, & Hartman, 2018; Morris et al., 2019; Watson et al., 2017). As such, interpretation of the results presented in the previous chapters should be limited only to those outcomes explicitly modelled, and not generalised to additional potential clinical and non-clinical benefits.

Beyond academic performance, the utility of physical activity in childhood, both in and out of school, has been shown to contribute to the development of mental and physical correlates that are

suggested to be indicative of higher levels of future physical activity. In particular, child participation in has been shown to increase physical activity self-efficacy (e.g. Pakarinen, Parisod, Smed, & Salanterae, 2017), motivation (e.g. Vasconcellos et al., 2019), and future intentions (e.g. Franco & Coterón, 2017), all of which are indicative of future physical activity. Furthermore, increasing the quantity and quality of participation has been shown to increase fundamental movement skills in children (Johnstone, Hughes, Janssen, & Reilly, 2017; Johnstone, Hughes, Martin, & Reilly, 2018), thereby encouraging future involvement in physical activity (Barnett et al., 2016; Lubans, Morgan, Cliff, Barnett, & Okely, 2010).

Lastly, the relevance of physical activity within health inequalities constitutes an important consideration (Arrigon, 2019). It is increasingly clear that the quantity and type of physical activity participation is linked to a social-economic gradient (Althoff, Hicks, King, Delp, & Leskovec, 2017; Chzhen, Moor, Pickett, Toczydlowska, & Stevens, 2018; O'Donoghue et al., 2018). Indeed, a recent review and modelling study suggested that even were 25% of the UK child population to achieve national physical activity guidelines with a consequential 5% reduction in childhood obesity, inequalities would persist due largely to the negative socio-economic gradient with physical activity levels (Pearce et al., 2019). Inequalities in overall physical activity levels are due to gender (Chaput et al., 2018) and ethnicity (Love et al., 2019), as replicated within the results presented in Chapter Two. Weight status has also been suggested to be associated with physical activity inequality (Public Health England, 2017), although the analysis from Chapter Two did not support this in childhood, a position concordant with other investigations on obesity and inequalities (e.g. Noonan & Fairclough, 2018).

9.3.6. Structural Modelling Limitations

A justification of the choice of model structure, in comparison with alternative structures, and for specific adaptations to the core model is provided in Chapter 3. However, a brief reiteration of the structural implications of the selected modelling strategy provides additional context for evaluation and is therefore summarised below. The proportional multi-state life table is an adaptation and

extension of the multi-state life table approach, allowing multiple health outcomes to be explored within the simulated cohort without the requirement for exponentially more complicated modelling.

The model remains 'memory-less', in that it does not differentiate between individuals who have become incident with disease either in the last year or twenty years previously, and each cycle sees the age, sex, and physical activity level adjusted transition probabilities applied afresh to the population at risk. The concepts of case-fatality, usually defined as death within 30 days of incidence, survival periods, and disease remission are not explicitly encoded within the model. Each disease state remains independent within the model, meaning that an individual with incident myocardial infarction possesses no additional risk of, for example, stroke than a 'healthy' individual, whether due to an increase risk consequential to the index disease or due to any risk factor common to both diseases. Furthermore, while there exists an implied time component there are no trend data encoded within the model; the physical activity estimates for age, sex, and physical activity level, entered into the model were all taken from the HSE 2012 as a cross-sectional dataset, and are not linked in any longitudinal manner.

9.3.7. Consequences for Interpreting Outputs

When interpreting the findings from this thesis the following cautionary notes need to be taken into account. The model directly links physical activity levels with health outcomes without accounting for mediating or moderating variables beyond age and sex, thereby essentially operating on an 'all other things being equal' basis. The model was designed to conduct analyses of hypothetical scenarios on a specific dataset and it is therefore not appropriate to forecast trends in the English population into the future due to the cross-sectional nature of the parameters. Firm conclusions regarding individuals or even small sub-groups are not appropriate given the extrapolation and stratification that has taken place within the data processing, instead the model was designed and employed to provide population-level outputs.

While every effort was made to source the most relevant data, some relative risks were taken from wider geographical areas and therefore may not precisely represent the English population as simulated within the model, although there is no evidence that the distribution within the English population differ in any systematic manner from the Western world in terms of physical activity levels, patterns, or subsequent risk of disease. Each parameter is taken from either a specific study which in turn represents average point estimates from a sample of the population, or at best from a meta-analysis of several studies, although these are typically high in heterogeneity; the parameters are then extrapolated over age and across physical activity strata and therefore the outputs are a combination of several levels of abstraction and summarisation. In particular, the relative risk estimate for uterine cancer was specified using assumptions, rather than by evidence-based parameterisation, and results should consequentially be viewed with appropriate caution.

9.4. Comparison with Published Research

Of the modelling studies discussed in Chapter 3, the majority were completed in order to produce cost-effectiveness estimates. For example, the appraisal of six physical activity interventions completed by Cobiac et al. (2009) as part of the ACE Obesity project estimated increases ranging between 57 MET minutes per week for an active travel intervention to 574 MET minutes per week for a pedometer campaign. The study by Roux et al. (2008) estimated increases between 32 MET minutes per week for a city-wide health promotion campaign to 1151 MET minutes per week for enhanced access to active environments. These estimates are higher than those included in the meta-analysis estimates, 5 and 21 MET minutes per week for population and treatment respectively, but broadly equivalent for the estimates used for the Daily Mile scenario which ranged between 165 and 475 MET minutes per week. Two further studies within the ACE Obesity project provided estimates of 212 MET minutes a week for a Smart Travel Plan (Moodie et al., 2011) and 580 MET minutes per week for an active after-school programme (Moodie, Carter, Swinburn, & Haby, 2010), again comparable with previous estimates. The estimate used within the analysis for the MEND scenario of additional values of between 367 and 1838 MET minutes per week is comparatively high, although this was only applied

to the Inactive strata of the simulated population. This figure represents the equivalent of just over four additional hours of brisk walking per week, so while it is high in comparison with other modelled effects it remains plausible.

Common among physical activity modelling studies is an acceptance of the lack of good data on the long-term sustainability of physical activity effects following interventions, both in terms of generic effect sustainability and individual types of intervention effect, and the clear recognition that the quicker any intervention effect is assumed to decline the greater the reduction in any health benefits (Cobiac et al., 2009). Cobiac et al. (2009) assumed that all intervention effects were sustained for one year, and subsequently decayed by 50%, leading to little discernible benefit five years post-intervention. Roux et al. (2008) and NICE (2006), used more generous legacy scenarios, although further differences in modelling approach, such as intervention period and scope, prevent a direct comparison of the effects of legacy assumptions. The two studies specifically modelling childhood interventions, Moodie et al. (2011) and Moodie et al. (2010), assumed a permanent benefit from interventions and still found interventions not to be cost-effective. Children arguably represent a more volatile group given observed changes in physical activity behaviour through adolescence (Dumith, Gigante, Domingues, & Kohl III, 2011) and key transition periods (Allender, Hutchinson, & Foster, 2008) with regard to intervention legacy scenario which, when combined with longer time horizons, represents a key potential weakness in all physical activity modelling studies. This potential lack of ecological validity, combined with the lack of intervention effects presented in recent meta-analyses (see Metcalf et al., 2012; Sims et al., 2015) may implicate a systemic over-estimate of the effect of physical activity interventions in the literature and therefore an explicit presentation of the legacy scenarios is essential in any modelling studies.

9.5. Improvements and Extensions to the Model

The core model is constrained due to the resources available for this thesis and the limitations to the availability of data. Inevitably, therefore, further improvements can be made to the model through

updated availability and improved quality of information regarding the population of interest. Principally, however, the model represented the time-frame for which it was designed, that being in or as close to 2012 as possible. Updates to any model parameter should therefore be accompanied by updates to all parameters and physical activity data in order to more accurately model the 'current state' within the population of interest.

The core model presents cross-sectional physical activity data and extrapolates this over time, using the implicit assumption that physical activity levels and relative risks exist in a steady state. However, it is hypothesised that this is not the case, as claims are common that population physical activity levels have undergone a reduction over the last few decades, although remain largely constant at present. If change has occurred over the last lifetime, then there is a lack of correspondence between the young and old within the model. In addressing this issue, it would also add trend data (i.e. 'time' as opposed to 'age') and allow cautious forecasting to occur.

There is more than one way to accomplish this. Initially, total physical activity levels could most easily be recruited from all iterations of the HSE that included sufficient data, currently including 1991, 1992, 1993, 1994, 1997, 1998, 1999, 2002, 2003, 2004, 2006, 2007, 2008, 2012, and 2015. Continuity on survey items is not precise, as the survey has been revised over the years, meaning that interpretation and assumptions would need to occur, but overall trend data by age-group and sex could be ascertained and then applied within the simulated cohort. This would at least control for population level changes within England and increase the specificity of the model. In addition, a further extension to the model would permit continuous modelling of time within the simulated population, with a new year group being 'born' with each cycle and maintaining the population within the model over time, thereby allowing projection into the future to occur. An alternative method by which to accomplish this would be to source physical activity data direct from a large cohort study such as ALSPAC or Biobank, data from which could then be directly modelled or extrapolated to provide a simulated population.

A further benefit for improved physical activity data from both longitudinal studies, and most particularly from intervention studies with lengthy follow up periods, would be an improved representation of the legacy effects post-intervention. While sensitivity analyses were completed in Chapters 5 and 6 regarding the effects of different legacy scenarios (i.e. exponential decay, zero legacy, and permanent legacy) this was necessarily assumption-based as there are no data on the pattern of benefit post-intervention. Tracking studies completed by Malina (2001) and Telama et al. (2013) provide an indication of stability of the relative rank of individuals physical activity level within the population over time, they provide little insight into change in absolute physical activity levels and no information on effects of interventions. That said, the findings of Metcalf et al. (2012) and Sims et al. (2015) indicate little sustained success is currently observed with childhood interventions at all.

While the diseases within the model were carefully selected to represent relevant and viable health outcomes, further research will continue to identify additional outcomes that are sensitive to physical activity levels. For example, additional cancer types have been shown to be more prevalent in those with lower levels of physical activity, including gastric, lung, pancreatic, prostate, and renal cancers (Leitzmann et al., 2015), as well as potentially bladder, gall-bladder, kidney, liver, and oesophageal cancer, and lymphoma and leukaemia (Moore et al., 2016). Increased levels of lifetime physical activity are also negatively associated with osteoporosis and consequences in later life, such as falls and fractures (Gregg et al., 2000). Lastly, increases in physical activity are also associated with favourable mental health outcomes, such as reduced lifetime prevalence of anxiety, depression and stress, reduced risk of dementia, and improved cognitive function and sleep (Bauman, Merom, Bull, Buchner, & Fiatarone Singh, 2016). Where a specific research question is posed, and a dose-response estimates are available for each of these outcomes, by age-group and sex, these may be relatively simply included in the model.

The final suggestion for extensions to the current model, and the most logical body of subsequent work, is the development of a health economic component to the project. The beneficial effect of

increasing physical activity levels on health has long been known, and the aim of the thesis was to quantify the extent to which increases in childhood physical activity levels following interventions led to meaningful reductions both in overall years of life in disability and in prevalence of specific non-communicable diseases, the analysis for which is presented over the preceding chapters. However, the inclusion of disease utility measures and associated costs would extend these findings to inform policy makers of the required investment against specific returns. Most importantly, this extension would provide a unit of comparison by which physical activity intervention approaches, either population or treatment, could be assessed directly against one another as well as alternative health interventions such as diet, transport, or smoking cessation.

9.6. Priorities for Future Research

In terms of areas of priority for future research implicated from the presentation and discussion of the results from this thesis, there is a clear requirement to extend the model further to include health utilities and incremental cost effectiveness estimates. This addition would facilitate a more detailed investigation of each physical activity scenario, but perhaps more importantly would permit a direct comparison of several intervention effects through a common metric. In particular, this would allow a comparative estimate to be made on whether a more expensive treatment-focused intervention on high-risk children would be more effective at alleviating population disease burden than a prevention-focused intervention that aimed to help the whole population. The combination of the relative effectiveness of treatment versus population approaches and the dose response curve, in which the least active benefit substantially more than the remainder of the population, makes this question of comparative urgency.

In order to compliment this extension, a corresponding expansion of the model to include further direct, and potentially indirect, health outcomes remain a clear avenue for development. Additional direct health outcomes would permit a broader analysis of both the relative effectiveness of interventions, but also a more comprehensive picture of the health economic benefits. Given the

increasing availability of data on their association with physical activity levels, appropriate additions include bone health and osteoporosis (Castrogiovanni et al., 2016), additional indicated types of cancer (World Cancer Research Fund/American Institute for Cancer Research, 2018), mental health in children (Biddle, Ciaccioni, Thomas, & Vergeer, 2019) and adults (Schuch et al., 2018), and cognitive decline (Xu et al., 2017). Indirect outcomes are considerably more difficult to parameterise, and typically involve a greater level of assumption; but could, for example, include workplace absenteeism due to back pain (e.g. Gordon & Bloxham, 2016), wellbeing (Kim, Kim, & Thapa, 2020), and rehabilitation and recovery from illness such as stroke (Kramer, Hung, & Brodtmann, 2019) or cancer (Onerup et al., 2017). Lastly, and with domain-specific systematic reviews and meta-analyses more prevalent in the literature (e.g. Bahls et al., 2018; Mahmood, MacInnis, English, Karahalios, & Lynch, 2017; White et al., 2017), a more nuanced analysis of physical activity is increasingly viable in which the relationship between domain-specific contributions to total physical activity and relevant health outcomes may be independently parameterised, allowing identification of areas of opportunity and facilitating implementation of more targeted intervention and policy.

The continued development of methods of population surveillance is therefore a clear requirement for a more informed approach to increasing levels of physical activity, especially with regard to targeting areas of need and maximising potential opportunities. The use of self-report methods is likely to continue in larger-scale surveys for the foreseeable future, and as such there is a evident interest in increasing the precision of these measures. The development and incorporation of calibration methods within larger scale surveys such as the HSE is particularly justified. Although limited to an adult sample, an accelerometry component was included within the wider capture of physical activity data on previous HSE iterations as an assessment of criterion validity (see Scholes et al., 2014b). As such, there exists scope to potentially increase the utility of this component to provide a representative calibration reference for self-report questionnaires. The difficulty for this implementation includes the potential to require a substantial revision of the current physical activity module within the HSE, while the benefits include a more accurate representation of national physical

activity levels, and therefore a more nuanced interrogation of the ensuing data for more precise policy decisions.

More accurate survey data, especially within children and youth, would permit further investigation into the role of light physical activity (LPA), particularly relevant as limited evidence suggests an association with childhood obesity (Kwon, Janz, Burns, & Levy, 2011). While the greater proportion of the literature, and national guidelines, focuses on MVPA as a primary target, there is evidence that increasing the volume of LPA independently confers benefits. Although not specific to children, these benefits include cardiometabolic health (Chastin et al., 2019), mental health (Ku, Steptoe, Liao, Sun, & Chen, 2018), cognitive reserve (Johnson et al., 2016), and the management of type 2 diabetes (Dempsey et al., 2016). Although LPA does not match the benefits of an equal volume of MVPA (Saint-Maurice, Troiano, Berrigan, Kraus, & Matthews, 2018), the protective effect of higher levels of LPA appear to manifest in older age and therefore potentially play an important role in the mitigation of symptoms in that age-group (Fuezeki, Engeroff, & Banzer, 2017). LPA remains comparatively difficult to capture through self-report measures, typically involving a significant component of incidental movement, potentially explaining the lack of focus on this stratum of physical activity, but represents an important part of the overall picture of health gain.

While individually-targeted or treatment-focused interventions may be more effective than population approaches, even when health outcomes are aggregated to a population level, there are additional areas of promise within the literature with regard to the implementation of physical activity interventions in children and youth. Multi-component interventions are consistently recommended as being comparatively effective (e.g. Kriemler et al., 2011; Messing et al., 2019; van Sluijs et al., 2008), although intervention effects remain small (Russ et al., 2015). In particular, those interventions which incorporate parental involvement, staff training, and changes to schools environments appear to show relative promise (Bellow, Cavill, Allender, Copeland, & Shearn, 2020; Messing et al., 2019), and have been incorporated into large-scale contemporary interventions (e.g. Sutherland et al., 2020; Telford

et al., 2020) which show at least modest gains in youth physical activity levels. In all future intervention studies, however, it remains important to implement a comprehensive measurement protocol that not only meets the specific context of the intervention (see Kelly et al., 2016) but also provides an indication of the longevity of intervention effects.

9.7. Conclusion

The primary aim of the thesis was to explore and quantify the extent to which childhood physical activity interventions are effective in reducing lifetime non-communicable disease outcomes across the English population. Through the construction of a proportional multi-state life table and the identification of relevant sources of data, a method for addressing this aim was developed. Using this method, a series of physical activity intervention scenarios were modelled, including estimates derived from systematic review, specific contemporary interventions, and hypothetical scenarios required to provide specific outcomes. In summary, while published intervention studies providing controlled follow-up data showed little sustained benefit following intervention, and the modelled health gains were therefore small, scenarios based on real-world interventions showed there was potential for modest increases in beneficial physical activity. However, further analysis suggested that consistently high levels of physical activity were needed throughout childhood in order to provide meaningful population benefits in isolation to complimentary interventions.

The secondary aim was to explore the effectiveness of both prevention and treatment approaches to physical activity interventions. While a direct comparison between approaches was not possible, the exploration across the scenarios reveals an interesting pattern. Firstly, systematic review of the literature, and considering those studies included and excluded from the meta-analysis, suggested that interventions which target less-active children produced a higher physical activity boost both immediately and at six months post-intervention. Secondly, prevention-focused interventions produced a pattern of diminishing health returns as baseline physical activity levels increase. In particular, the vast majority of the increase in physical activity levels and subsequent health benefit is

expressed in the Inactive strata of the population despite interventions targeting the entire population. Thirdly, treatment-focused interventions, both those derived from meta-analysis and from real-world scenarios, produced greater physical activity gain and therefore greater population health benefits than population-focused interventions. However, a systematic consideration of cost-effectiveness would need to be completed prior to a direct comparison.

1. An analysis of childhood physical activity data from the Health Survey for England 2012 and 2015.
• Across both data sets there was a consistent pattern regarding the contribution of informal physical activity to total physical activity across the childhood years. For boys, informal physical activity (e.g. walking, cycling and play) declines over the childhood years but is largely replaced by formal activity (e.g. sport). For girls, the same pattern of decline in informal physical activity is observed, but this is not compensated by increases by formal activity. Active travel and curriculum time activity contribute a comparatively small amount to total physical activity levels, but these levels are consistent across age and sex throughout childhood and represent an important contributor to total physical activity for the least active children.
• In terms of policy, the importance of physical activity accrued both within school curriculum time and through active travel to and from school appear impervious to age, sex, geographical region, ethnicity, and economic status. As a consequence, the contribution from these domains is most important for the least active children and should therefore be facilitated and protected as a means of providing a minimum level of physical activity throughout childhood. The decline in total physical levels for older girls represents a clear target for intervention, potentially through the provision of opportunities to participate in formal sport, or by alternative informal activities.
2. The success of interventions on increasing levels of physical activity is limited.
• Building on work completed by Metcalf et al. (2012), systematic review and meta-analysis of studies including follow-up measurement at least six months post-intervention revealed negligible effect of intervention on childhood physical activity levels. Although still minimal,

the most notable effects were observed in studies reporting impact of treatment-based, rather than population-based, interventions. Certainly, future studies claiming the potential benefit of particular interventions should evidence their sustained effect over time.
• While the results from the meta-analysis may appear somewhat pessimistic, the implications provide several potential implications for policy. Firstly, the limited but comparative success of treatment-based interventions suggest that a focus on the at-risk proportion of the population, i.e. the least active, and encouraging modest increases may prove more beneficial than population-wide initiatives. Secondly, given the apparent legacy of interventions is limited, but the potential impact of increased interventions remains clear, opportunities for non-volitional physical activity may be explored, potentially including curriculum-time interventions.
3. Treatment-type interventions which specifically target inactive children may be more beneficial than non-specific population-type approaches, even at population levels.
• Throughout the analyses in this thesis, a focus on meaningfully increasing physical activity levels in the least active portion of the population has produced a greater benefit than a population-level approach. While any increase in physical activity is advantageous, the health benefits display a diminishing return pattern that levels out comparatively quickly and to the extent that dedicated intervention within inactive children could produce a more meaningful improvement in population health than a population-wide effort.
• While additional research is required, the implications throughout the thesis largely supports the advantage of focused interventions targeted at the least active children. Under conditions of limited funding on physical activity interventions, there potentially

exists a greater return on investment through reducing entrenched inactivity when compared to non-specific population intervention.
4. The contribution of physical activity towards government targets for improvements in population health is limited.
• Very few modelling studies provide the exploration of potential gain that is provided in Chapter 8 of this thesis, focusing instead on comparative cost-effectiveness. The model outputs suggest that physical activity increases, even under arguably generous legacy conditions, are unlikely to significantly contribute towards government-level targets for either population health (e.g. five extra years of healthy life) or reductions in non-communicable disease burden. In particular, while increases in population physical activity levels provides a negligible increase in life expectancy, modest reductions in years of life in disability are viable, largely due to reduced prevalence of type 2 diabetes.
• While increases in physical activity levels in childhood are unlikely to address government targets for population health alone, the contribution is sufficient to be included within a comprehensive health package along with other health behaviours (e.g. reductions in smoking, improvement in diet). Prevalence of type 2 diabetes is the health outcome most sensitive to changes in physical activity levels and represents a viable opportunity for both increases in population health and reductions in disease burden.

Table 23 - Key contributions to the literature and to policy arising from this thesis.

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Category	*n*	Total Mean (SD)	Active Transport Mean (SD)	%	Non-Specific Mean (SD)	%	Formal Mean (SD)	%	Informal Mean (SD)	%
QIMD										
1 – Least Deprived	371	3409.0 (3006.1)	192.7 (277.3)	5.7	113.0 (487.1)	3.3	598.6 (882.4)	17.6	2504.7 (2812.4)	73.5
2	326	3423.8 (2878.3)	165.8 (252.3)	4.8	157.8 (659.4)	4.6	512.2 (923.6)	15.0	2588.0 (2617.2)	75.6
3	307	3315.2 (3145.5)	170.7 (286.3)	5.1	148.5 (620.0)	4.5	523.5 (1186.7)	15.8	2472.5 (2738.2)	75.6
4	360	3446.8 (3197.5)	200.9 (290.2)	5.8	124.4 (527.8)	3.6	438.6 (934.8)	12.7	2682.9 (3053.5)	77.8
5 – Most Deprived	368	3048.0 (3033.0)	182.3 (268.8)	6.0	30.0 (152.3)	1.0	290.8 (705.5)	9.5	2545.0 (2933.3)	83.5
Effect of QIMD		*B* = -84.36	*B* = 3.03		*B* = -15.26		*B* = -59.84 **		*B* = -12.57	
Ethnicity										
White	1380	3391.5 (3020.7)	190.6 (286.9)	5.6	128.9 (539.7)	3.8	494.8 (932.9)	14.6	2577.2 (2827.7)	76.0
Black	86	2514.4 (2611.7)	161.1 (239.4)	6.4	53.4 (287.4)	2.1	440.7 (778.1)	17.5	1859.2 (2352.9)	73.9
Asian	167	2739.1 (2732.1)	171.0 (196.6)	6.2	33.4 (156.4)	1.2	215.0 (584.0)	7.8	2320.0 (2693.6)	84.7
Mixed	77	4221.9 (4174.4)	110.8 (207.5)	2.6	83.4 (326.1)	2.0	675.8 (1567.7)	16.0	3352.0 (3451.6)	79.4
Other	15	4263.6 (3899.9)	183.4 (421.6)	4.3	24.0 (93.0)	0.6	154.6 (271.1)	3.6	3901.6 (3927.7)	91.5
Effect of Ethnicity		*F* = 6.02**	*F* = 1.26		*F* = 1.86		*F* = 5.83**		*F* = 4.54**	
Region										
North East	108	3399.7 (2901.4)	200.6 (249.3)	5.9	36.7 (190.2)	1.1	536.2 (855.5)	15.8	2626.1 (2679.2)	77.2
North West	232	3447.9 (3245.6)	171.9 (273.3)	5.3	113.0 (511.5)	3.3	517.7 (982.2)	15.0	2645.4 (3089.9)	76.7
Yorkshire	160	3351.1 (3059.9)	183.3 (314.3)	5.5	97.9 (553.2)	2.9	371.2 (759.6)	11.1	2698.8 (2891.3)	80.5

East Midlands	151	3310.4 (3042.2)	210.4 (283.1)	6.4	181.2 (589.7)	5.5	369.0 (677.5)	11.1	2549.7 (2809.3)	77.0
West Midlands	210	2812.2 (2668.2)	152.9 (274.9)	5.4	113.0 (584.1)	4.0	405.0 (952.0)	14.4	2141.3 (2356.3)	76.1
East	202	3181.6 (2756.0)	191.5 (276.3)	6.0	110.6 (374.7)	3.5	399.1 (732.4)	12.5	2480.3 (2602.0)	78.0
London	249	3551.2 (3414.4)	184.2 (233.8)	5.2	97.8 (425.3)	2.8	525.4 (1090.6)	14.8	2743.7 (3112.3)	77.3
South East	278	3462.9 (3116.1)	187.1 (266.4)	5.4	129.5 (548.7)	3.7	492.0 (961.0)	14.2	2654.3 (2949.7)	76.6
South West	142	3365.7 (2990.5)	183.3 (325.2)	5.4	106.7 (450.2)	3.2	621.6 (1168.4)	18.5	2454.1 (2774.6)	72.9
Effect of Region		*F* = 1.07	*F* = 0.74		*F* = 0.82		*F* = 1.96**		*F* = 0.95	

*Appendix 1 – Table presenting supplementary data to Table 2, effects of QIMD, ethnicity, and geographical region for the Health Survey for England 2012 data, by domain (QIMD: Quintile Index of Multiple Deprivation) ** p<0.05*

Category	n	Total Mean (SD)	Active Transport Mean (SD)	%	Non-Specific Mean (SD)	%	Formal Mean (SD)	%	Informal Mean (SD)	%	School Mean (SD)	%
1 – Least Deprived	990	3347.2 (3093.4)	182.6 (302.9)	5.5	97.4 (466.6)	2.9	744.7 (1684.6)	22.2	2322.5 (2404.2)	69.4	174.5 (316.5)	5.2
2	993	3592.5 (3566.5)	156.9 (271.7)	4.4	97.8† (358.9)	2.7	607.6 (1099.6)	16.9	2729.2 (3240.6)	76.0	188.8 (360.8)	5.3
3	999	3700.5 (3305.9)	145.0 (232.2)	3.9	80.6† (376.7)	2.2	534.7 (1119.2)	14.4	2940.2 (3206.3)	79.5	164.8 (267.0)	4.5
4	1036	3636.1 (3538.4)	139.5† (226.6)	3.8	71.5† (303.2)	2.0	513.6 (1261.5)	14.1	2911.4 (3206.3)	80.1	162.4 (281.0)	4.5
5 – Most Deprived	1418	3555.2† (3504.0)	159.7 (263.5)	4.5	43.4 (208.5)	1.2	354.9 (879.3)	10.0	2986.0† (3328.0)	84.0	167.2 (311.2)	4.7
Effect of QIMD		B = 19.10	B = -1.45		B =-12.62 **		B = -89.54 **		B =130.28 **		B = -7.58 **	
Ethnicity												
White	4102	3805.7† (3489.4)	164.6† (275.6)	4.3	87.2† (375.3)	2.3	584.5† (1296.0)	16.1	2969.6† (3135.5)	71.4	170.6 (317.5)	6.0
Black	259	2633.3 (3238.8)	158.2 (230.2)	5.8	28.0 (157.1)	0.9	338.4 (795.8)	12.3	2108.6 (3217.4)	72.9	175.1 (277.5)	8.1
Asian	643	2678.9 (2766.6)	134.7† (204.8)	4.9	42.2 (256.9)	1.4	305.2 (712.0)	11.9	2196.8 (2650.9)	74.1	162.0 (272.7)	7.7
Mixed	316	3257.7† (3255.4)	158.4 (232.4)	4.5	48.6 (206.2)	1.6	568.3 (1025.2)	17.1	2582.4† (3093.6)	69.3	203.1 (303.7)	7.6
Other	100	2525.4 (3112.0)	141.9 (263.2)	3.7	21.6 (100.0)	0.6	462.0 (1817.7)	15.5	1889.9† (2390.9)	75.1	156.0 (260.0)	5.0
Effect of Ethnicity		F = 28.97 **	F = 3.20 **		F = 6.39 **		F = 13.73 **		F = 16.79 **		F = 2.56 **	
Region												
North East	417	4024.1 (3991.3)	138.5† (234.3)	3.4	85.0 (286.5)	2.1	549.4 (1493.9)	13.7	3251.3 (3597.0)	80.8	141.7 (232.3)	3.5
North West	747	4051.7† (3445.5)	136.0 (228.7)	3.4	58.9† (249.9)	1.5	457.4 (865.9)	11.3	3399.4† (3258.6)	83.9	143.7 (279.3)	3.5
Yorkshire	514	3691.4 (3312.7)	157.7 (267.0)	4.3	62.9 (309.3)	1.7	445.3 (880.0)	12.1	3025.5 (3109.7)	82.0	158.9 (349.7)	4.3
East Midlands	536	3861.4 (4326.4)	170.5† (257.1)	4.4	86.4 (574.5)	2.2	487.8 (1341.5)	12.6	3116.6 (3899.8)	80.7	186.6 (276.2)	4.8
West Midlands	533	3181.4 (3237.2)	167.2 (279.9)	5.3	43.5† (224.3)	1.4	452.4 (945.3)	14.2	2508.4 (2975.1)	78.8	182.6 (355.6)	5.7
East	556	3554.9 (3163.9)	161.8	4.6	63.8 (293.9)	1.8	639.2† (1331.3)	18.0	2690.0 (2894.7)	75.7	189.4 (328.3)	5.3

			(280.7)									
London	841	3169.9 (3083.7)	177.5 (236.6)	5.6	82.8 (334.4)	2.6	571.3 (1206.9)	18.0	2338.4 (2730.6)	73.8	195.9 (311.6)	6.2
South East	879	3248.2 (2987.0)	170.1 (311.4)	5.2	85.4 (325.0)	2.6	548.7 (1297.3)	16.9	2444.1 (2549.4)	75.2	173.9 (318.9)	5.4
South West	413	3682.9 (3382.8)	142.2 (246.3)	3.9	106.1 (426.4)	2.9	701.7 (1493.9)	19.1	2733.0 (2960.3)	74.2	149.2 (281.3)	4.1
Effect of Region		F = 5.88 **	F = 1.56		F = 1.94 **		F = 4.66 **		F = 8.67 **		F = 3.23 **	

Appendix 2 - Table presenting supplementary data to Table 2, effects of QIMD, ethnicity, and geographical region for the Health Survey for England 2015 data, by domain (QIMD: Quintile Index of Multiple Deprivation)

*** p < 0.05* *† Significant difference (p < 0.05) between 2012 and 2015 data*

Gender

No differences were found in mean total MET minutes per week, which for this dataset excluded school physical activity, between survey years for either boys (t_{3558} = -1.471, p = 0.141) or girls (t_{3606} = -1.705, p = 0.088). A comparison of domain-specific physical activity, by sex, between survey years suggests boys reported lower levels of active travel (t_{3558} = 3.231, p = 0.001) and non-specific activity (t_{3558} = -2.117, p = 0.034) in 2015, while girls completed higher amounts of non-specific activity (t_{3606} = 2.777, p = 0.006).

Age

While weighted estimates and extent of statistical significance showed variation on total and domain-specific MET minutes per week between 2012 and 2015 surveys, there were few notable differences in total and domain-specific estimates between the survey years. Statistically significant reductions in active transport were observed for the 5-7 (t = 3.215, p = 0.001) and 8-10 (t = 3.692, p < 0.001) year-old age categories, while a reduction in non-specific exercise was noted in the 11-12-year-old category (t = 2.69, p = 0.007).

Deprivation

As detailed in Table 2, the totals and effects differ between HSE 2012 and 2015 survey responses. There are some specific instances of statistical significance within the permutations but there was no overall pattern within these examples.

Ethnicity

Investigating the differences between survey years with regard to ethnicity, those identifying as being from a white ethnic background reported higher levels of mean total MET minutes per week in 2015 than in 2012 for both boys (t_{2721} = -2.34, p = 0.026) and girls (t_{2757} = -2.88, p = 0.004). There were no statistically significant differences between the survey years for respondents from other identified ethnic backgrounds regarding total activity. Boys identifying as white (t_{2721} = 3.21, p = 0.001) and girls identifying as Asian (t_{393} = 2.712, p = 0.007) both reported less active travel in 2015

when compared to 2012. Boys identifying as white reported higher levels of formal (t_{2721} = -2.196, p = 0.028) and informal (t_{2721} = -2.22, p = 0.026) activity, while girls identifying as white reported higher levels of informal activity (t_{2757} = -2.98, p = 0.003) in 2015 when compared to 2012, with no further significant differences noted on formal or informal activity domains when stratified by ethnicity and sex. Comparison within the Mixed ethnicity category was not reliable due to low power, neither was it reliably possible to compare between survey years on the non-specific activity domain.

Region

There are isolated instances of significant differences across the domain-specific totals but no overall pattern of change within the data.

Informal

In terms of specific differences, there was little between-survey change in cycling (t_{7166} = 0.62, p = 0.537), hopscotch (t_{7166} = 0.93, p = 0.350), trampolining (t_{7166} = -1.19, p = 0.236), or dancing (t_{7166} = 1.06, p = 0.291); HSE 2015 saw increases in reported walking (t_{7166} = -5.43, p < 0.001), housework (t_{7166} = -2.46, p = 0.014), and playing (t_{7166} = -2.00, p = 0.003), while recording reductions in skating (t_{7166} = 3.86, p < 0.001) and skipping (t_{7166} = 2.55, p = 0.011). Analysis indicates that while total MET minutes per week of informal physical activity remains largely stable, there are variations between years on the constituent activities of this domain.

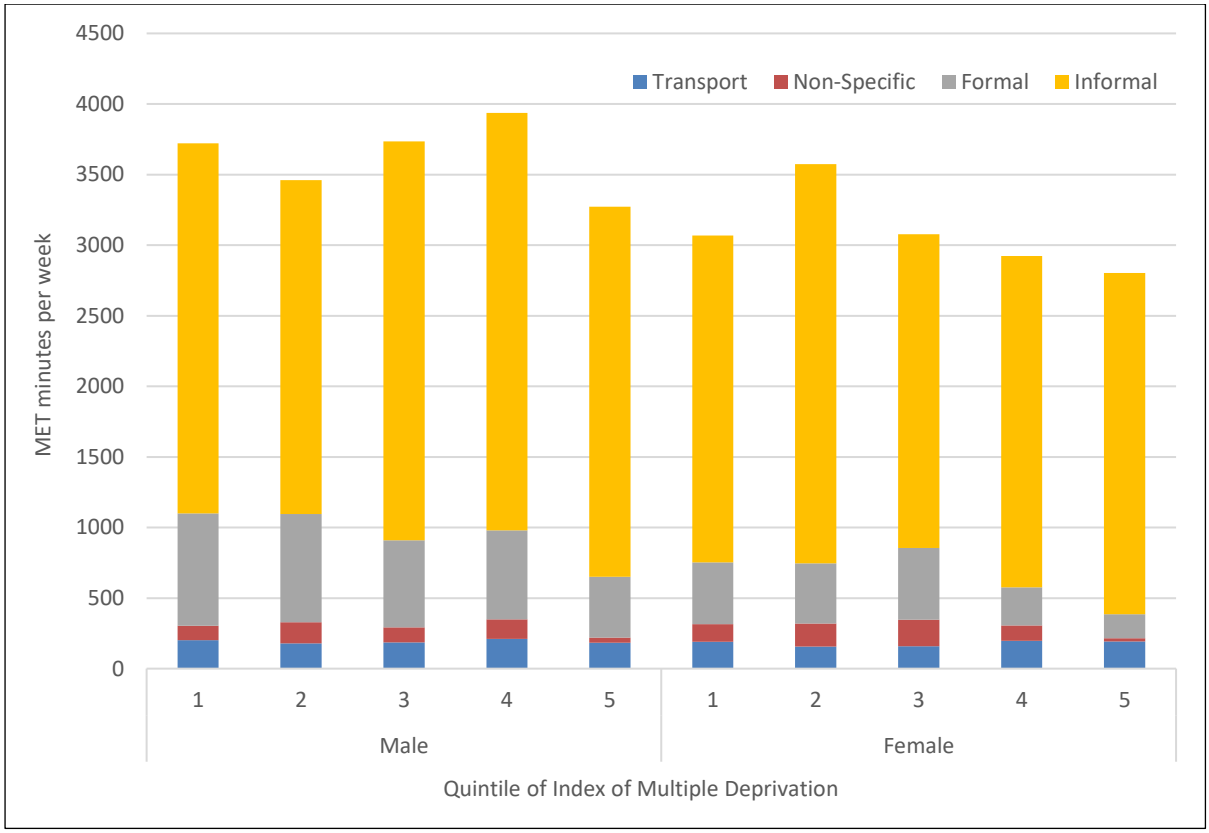
Appendix 3 - Summary of differences in childhood physical patters between 2012 and 2015 iterations of the Health Survey for England

	B	SE B	β	t	p	95% CI-	95% CI+
By Age							
Total	-119.39	50.99	-0.05	-2.34	0.019	-219.33	-19.31
Active Travel	45.11	4.62	0.23	9.76	<0.001	36.04	54.18
Non-Specific	45.44	8.47	0.13	5.36	<0.001	28.82	62.06
Formal	115.45	15.96	0.17	7.23	<0.001	84.15	146.75
Informal	-325.31	46.43	-0.17	-7.01	<0.001	-416.38	-234.25
By QIMD							
Total	-84.36	50.83	-0.04	-1.66	0.097	-184.06	-15.34
Active Travel	3.30	4.61	-0.02	0.72	0.474	-5.74	12.35
Non-Specific	-15.26	8.45	-0.04	-1.81	0.071	-31.82	1.31
Formal	-58.84	15.86	-0.09	-3.77	<0.001	-90.94	-28.74
Informal	-12.57	46.32	-0.01	-0.27	0.786	-103.42	78.28
By Weight							
Total	122.26	117.04	0.03	1.04	0.296	-107.34	351.86
Active Travel	-3.89	10.92	-0.01	-0.36	0.721	-25.32	17.53
Non-Specific	-29.77	20.94	-0.04	-1.42	0.155	-70.85	11.32
Formal	18.68	39.60	0.01	0.47	0.637	-59.01	96.36
Informal	137.25	104.95	0.04	1.31	0.191	-68.65	343.14

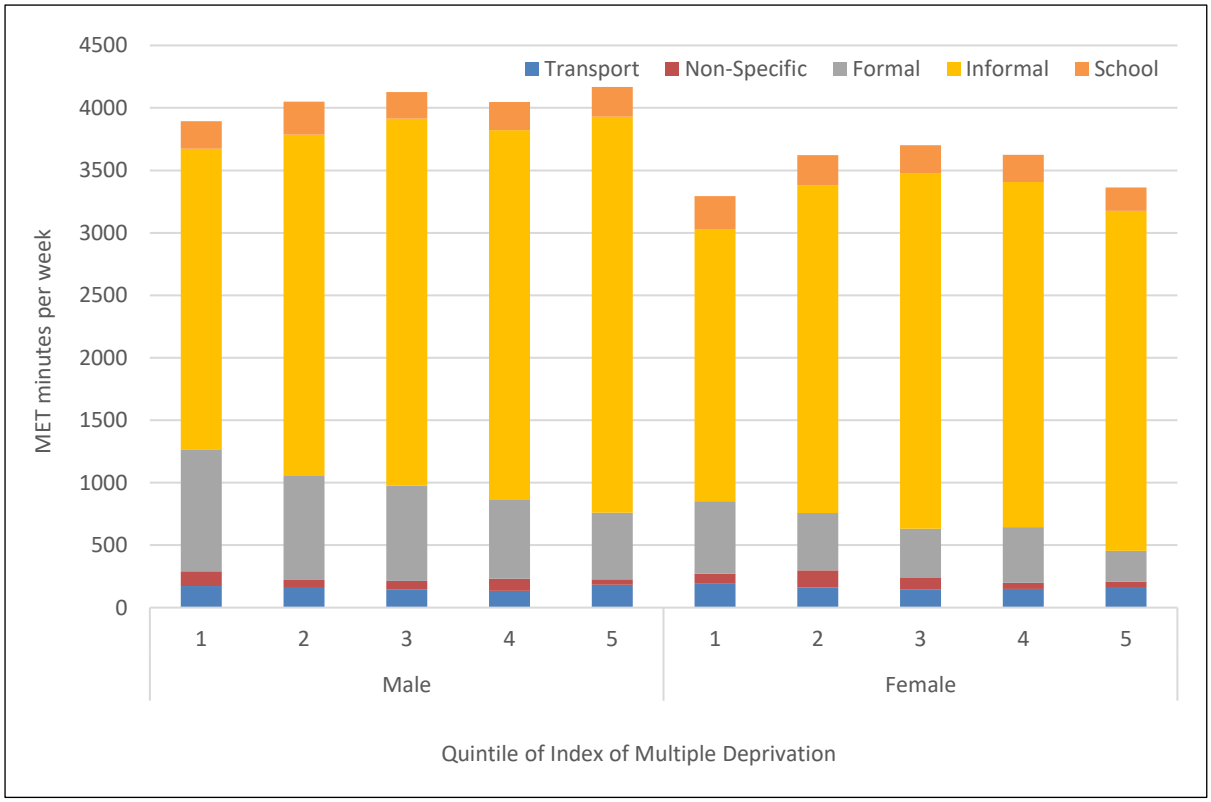
Appendix 4 – Table showing age-predicted outcomes on total MET minutes per week and all domain specific physical activity, for the HSE 2012 on linear regressions controlling for age and sex

	B	SE B	B	t	p	95% CI-	95% CI+
By Age							
Total	-183.00	33.05	-0.08	-6.72	<0.001	-248.79	-119.21
Total School	-102.08	33.18	-0.04	-3.08	0.002	-167.13	-37.04
Active Travel	47.18	2.58	0.25	18.28	<0.001	42.12	52.24
Non-Specific	23.73	3.53	0.09	6.73	<0.001	16.82	30.64
Formal	147.06	11.76	0.17	12.50	<0.001	123.99	170.12
Informal	-401.97	29.30	-0.19	-13.72	<0.001	-459.40	-344.53
School	81.91	3.22	0.34	25.46	<0.001	75.61	88.22
By QIMD							
Total	26.67	32.14	0.01	0.83	0.407	-36.34	89.68
Total School	19.10	32.27	0.01	0.39	0.554	-44.17	82.36
Active Travel	-1.45	2.51	-0.01	-0.58	0.564	-6.37	3.47
Non-Specific	-12.62	3.42	-0.05	-3.68	<0.001	-19.33	-5.90
Formal	-89.54	11.37	-0.11	-7.87	<0.001	-111.83	-67.25
Informal	130.28	28.44	0.06	4.58	<0.001	74.53	186.02
School	-7.58	3.13	-0.03	-2.42	0.015	-13.71	-1.45
By Weight							
Total	-222.60	70.73	-0.05	-3.15	0.002	-361.26	-83.93
Total School	-222.65	70.89	-0.05	-3.14	0.002	-361.63	-83.67
Active Travel	4.09	5.60	0.01	0.73	0.465	-6.88	15.07
Non-Specific	-0.80	8.14	-0.00	-0.10	0.922	-16.75	15.16
Formal	-50.94	26.33	-0.03	-1.94	0.054	-102.56	-0.67
Informal	-174.95	62.21	-0.04	-2.81	0.005	-296.92	-52.98
School	-0.05	7.13	-0.00	-0.01	0.994	-14.03	13.93

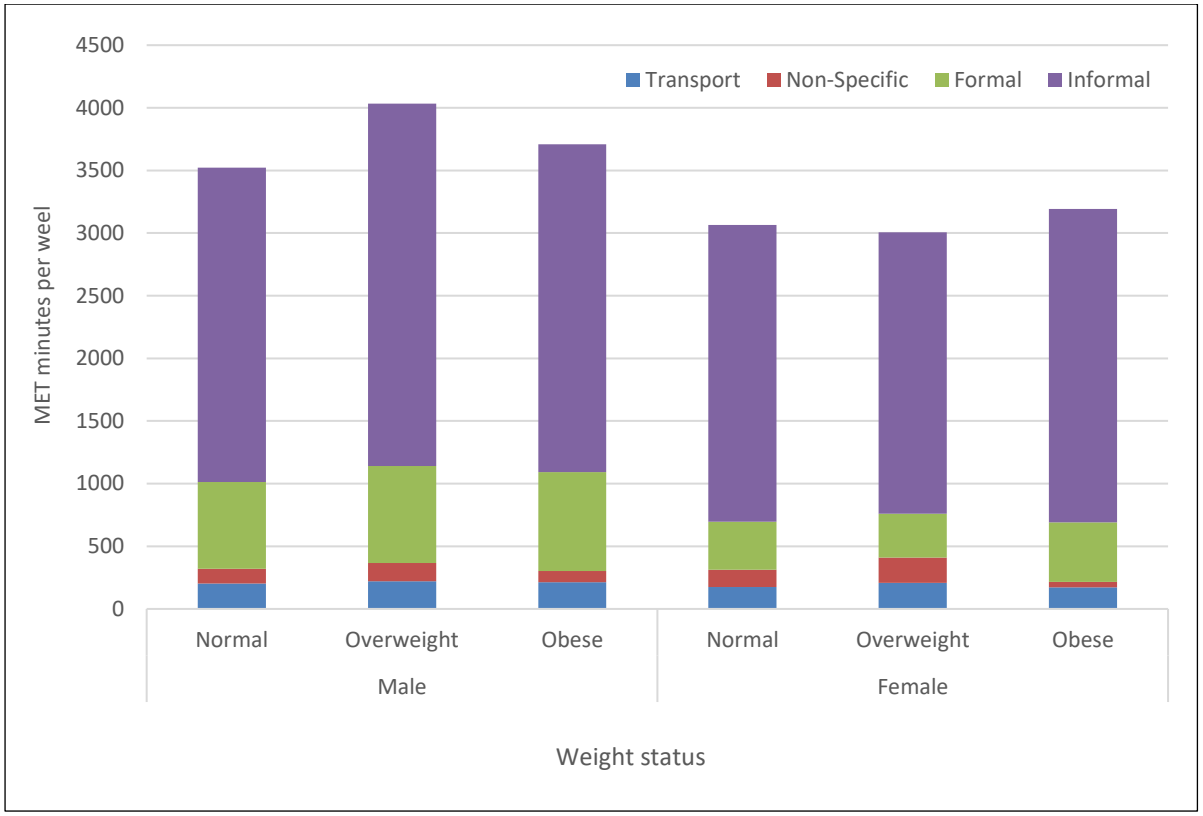
Appendix 5 - Table showing age-predicted outcomes on total MET minutes per week and all domain specific physical activity, both including and excluding school physical activity data, for the HSE 2015 on linear regressions controlling for age and sex



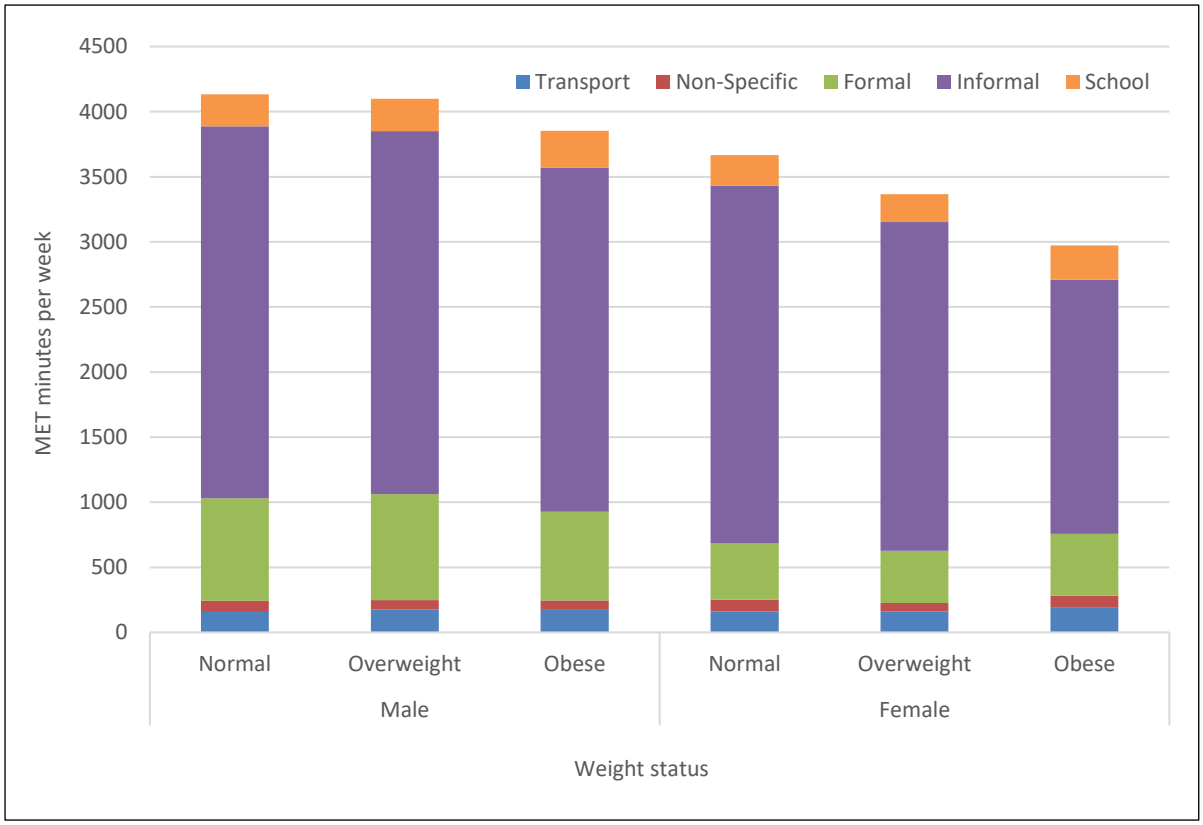
Appendix 6 - Stacked column graph showing the domain contribution to mean MET minutes per week for HSE 2012, by QIMD and sex



Appendix 7 - Stacked column graph showing the domain contribution to mean MET minutes per week for HSE 2015, by QIMD and sex



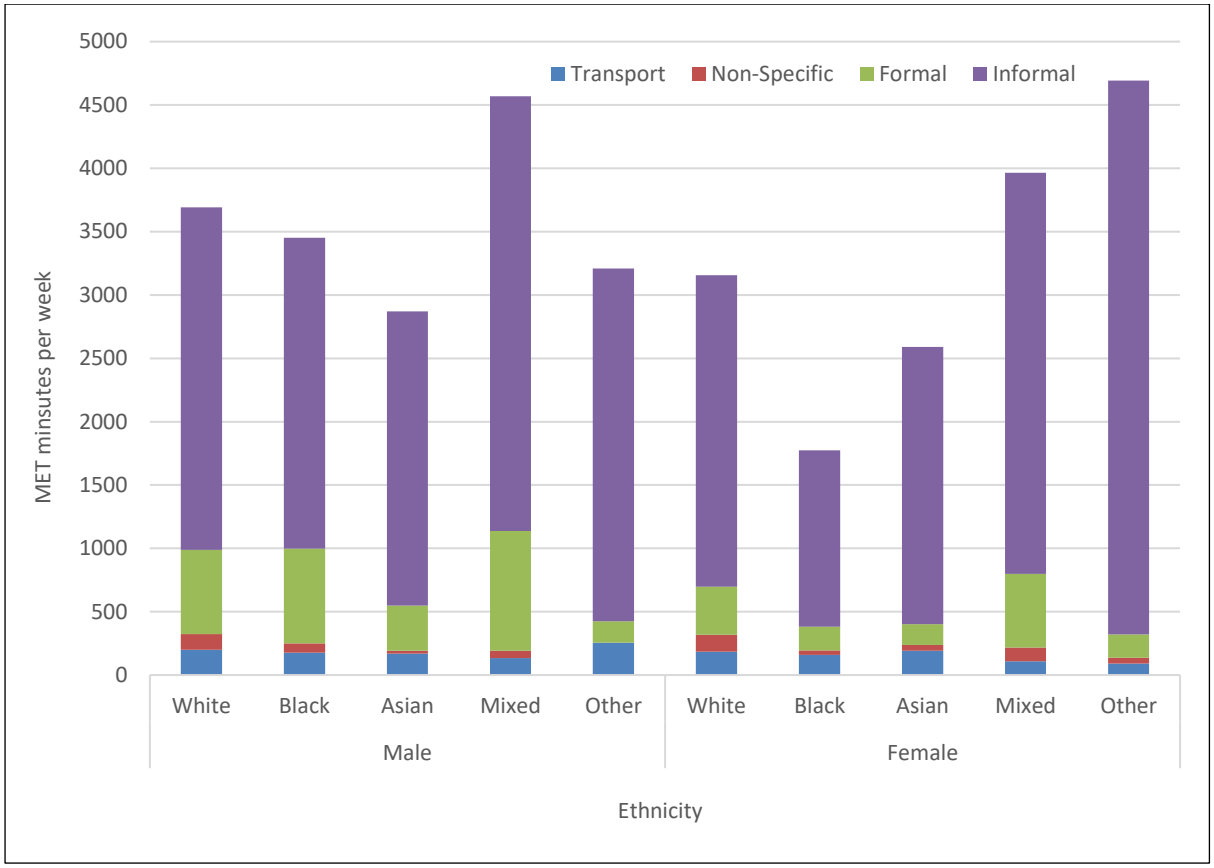
Appendix 8 - Stacked column graph showing the domain contribution to mean MET minutes per week for HSE 2012, by weight status and sex



Appendix 9 - Stacked column graph showing the domain contribution to mean MET minutes per week for HSE 2015, by weight status and sex

	Df	SS	MS	F	p
By Ethnicity					
Total	4	220100000	55017371	6.02	<0.001
Active Travel	4	379917	94979	1.26	0.285
Non-Specific	4	1907900	476975	1.86	0.115
Formal	4	20785447	5196362	5.83	<0.001
Informal	4	138200000	34556309	4.54	0.001
By Region					
Total	8	78994966	9874371	1.07	0.380
Active Travel	8	449943	56243	0.74	0.623
Non-Specific	8	1681041.5	210130.18	0.82	0.580
Formal	8	13995303	17494123	1.96	0.049
Informal	8	58104269	7263034	0.95	0.474

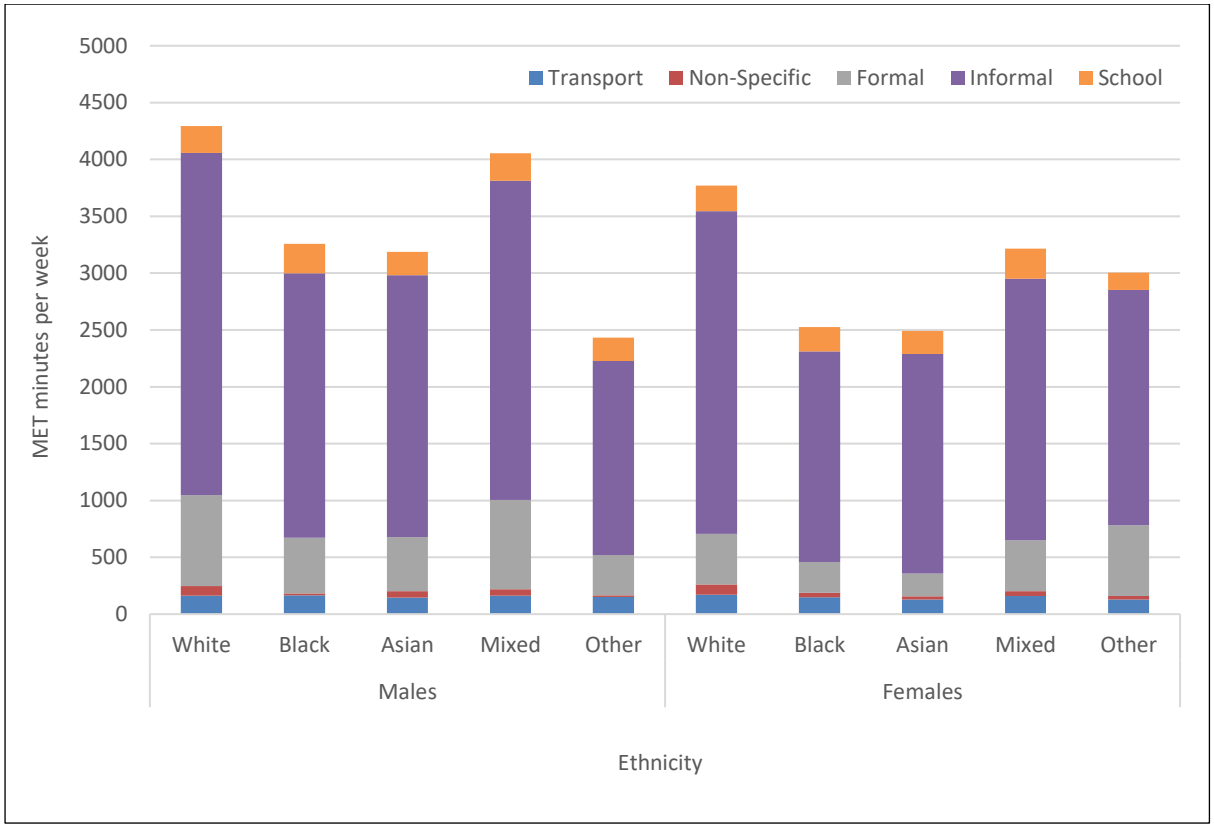
Appendix 10 - Table showing outcomes on total MET minutes per week and all domain specific physical activity by ethnicity, for the HSE 2012 on linear regressions controlling for age and sex



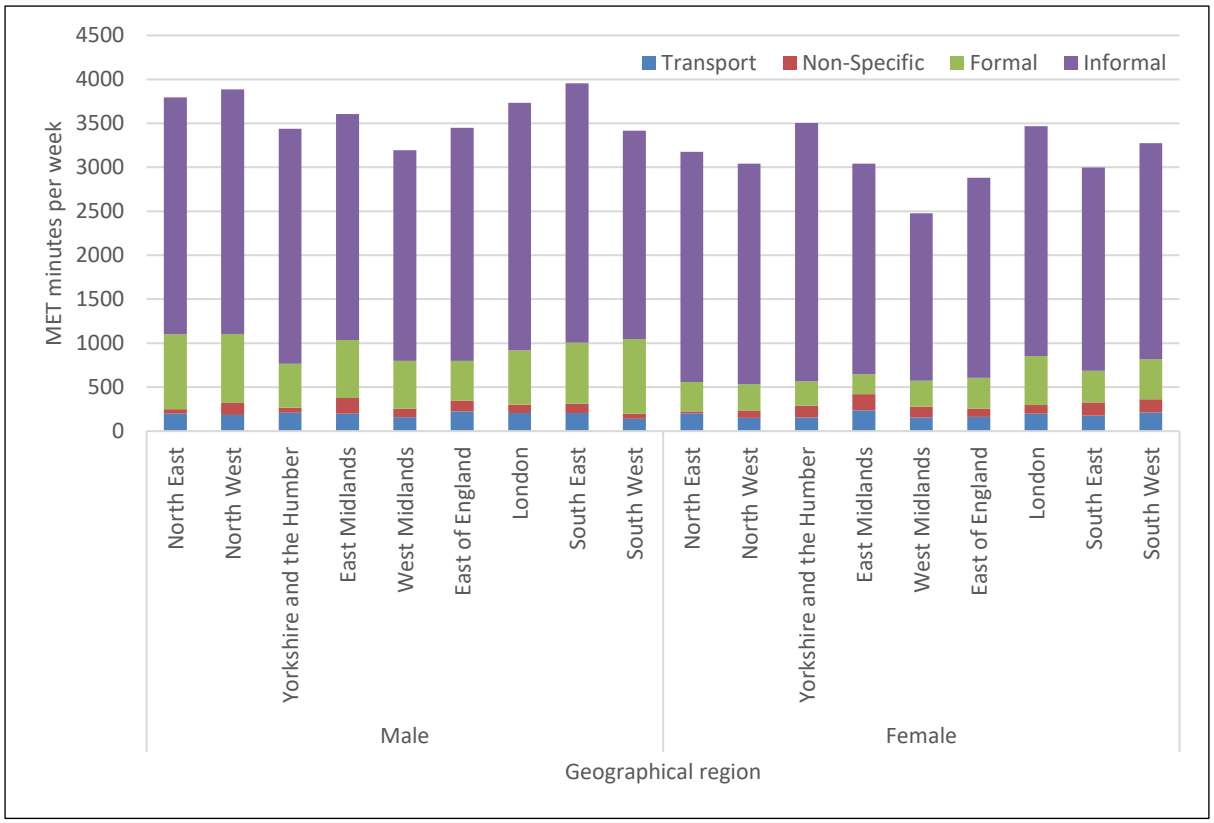
Appendix 11 - Stacked column graph showing domain contribution to mean total MET minutes per week for HSE 2012, by ethnicity and sex

	Df	SS	MS	F	p
By Ethnicity					
Total	4	1192000000	298100000	28.12	<0.001
Total Inc School	4	1236000000	309000000	28.97	<0.001
Active Travel	4	841476	210369	3.20	0.013
Non-Specific	4	3159533	789883	6.39	<0.001
Formal	4	74790651	18697663	14.72	<0.001
Informal	4	565200000	141300000	16.79	<0.001
School	4	1036698	259174	2.56	0.037
By Region					
Total	8	551500000	68935468	6.41	<0.001
Total Inc School	8	510200000	63770647	5.88	<0.001
Active Travel	8	822552	102819	1.56	0.131
Non-Specific	8	1922628	240329	1.94	0.050
Formal	8	50849990	6356249	4.66	<0.001
Informal	8	586400000	73304816	8.67	<0.001
School	8	2608866	326108	3.23	0.001

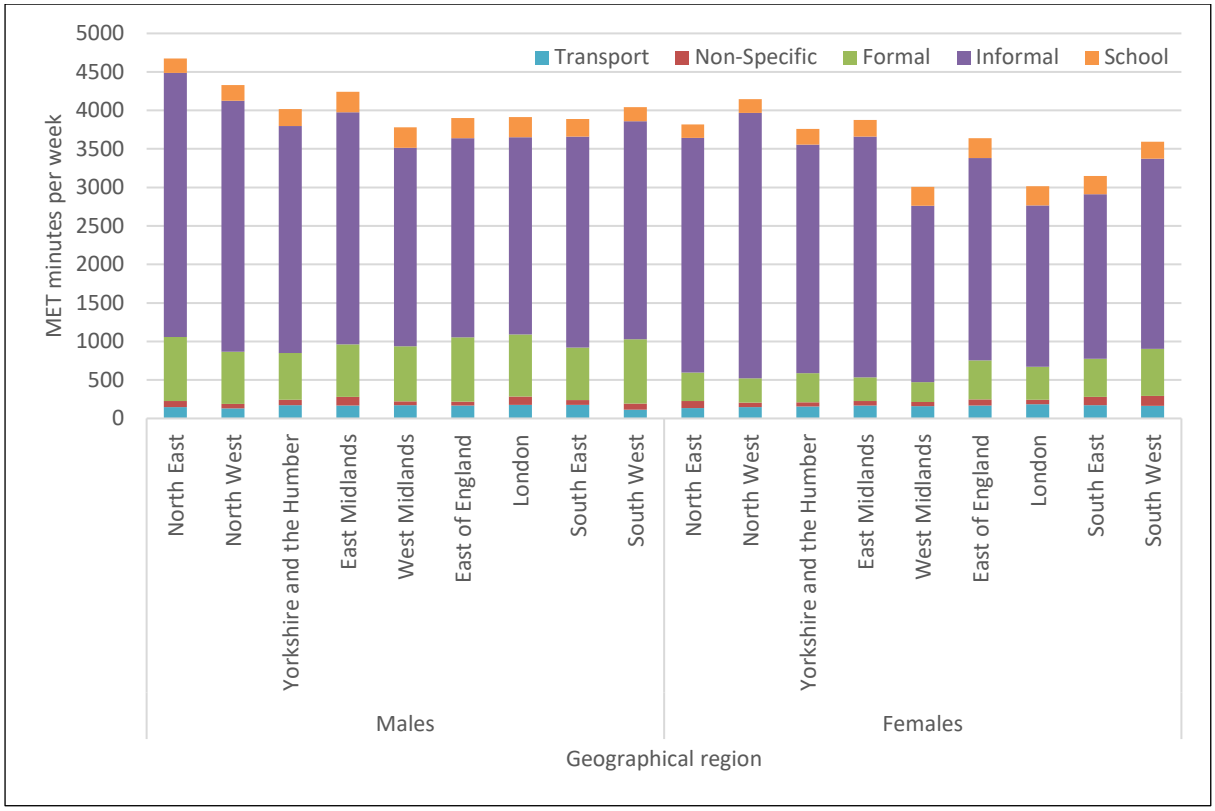
Appendix 12 - Table showing outcomes on total MET minutes per week and all domain specific physical activity by ethnicity, for the HSE 2015 on linear regressions controlling for age and sex



Appendix 13 - Stacked column graph showing domain contributions to mean MET minutes per week for HSE 2015, by ethnicity and sex



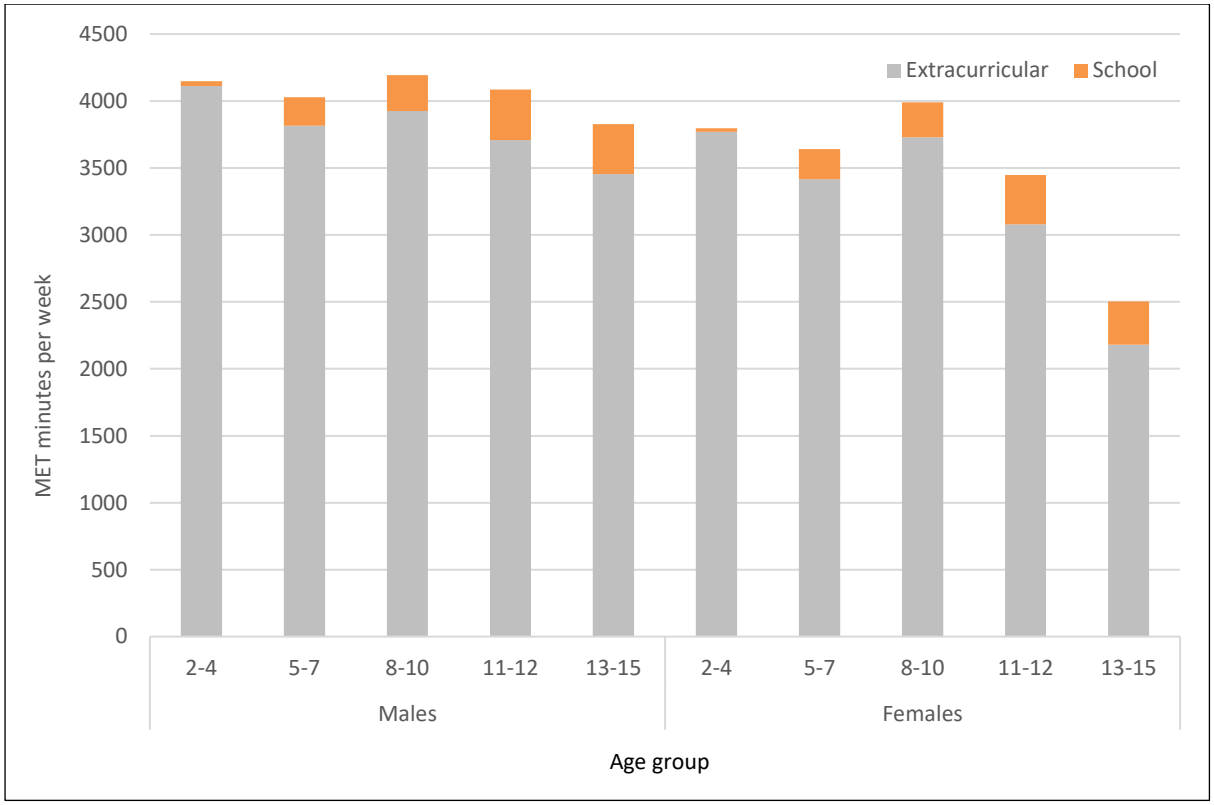
Appendix 14 - Stacked column graph showing the domain contribution to mean MET minutes per week for HSE 2012, by geographical region and sex



Appendix 15 - Stacked column graph showing the domain contribution to mean MET minutes per week for HSE 2015, by geographical region and sex

Activity	Boys		Girls		Gender Differences	
	Mean (SD)	Contribution (%)	Mean (SD)	Contribution (%)	t	*p*
2012						
Cycling	337.9 (994.2)	12.3	200.6 (676.1)	8.1	4.09**	<0.001
Walking	343.5 (683.6)	17.7	376.9 (680.4)	22.3	-3.17**	0.002
Housework & Gardening	35.4 (132.7)	3.5	28.2 (94.3)	3.6	-0.13	0.897
Hopscotch	2.2 (26.3)	0.1	16.8 (133.7)	1.0	-4.09**	<0.001
Trampolining	193.3 (571.9)	7.9	180.5 (487.4)	9.0	-1.16	0.247
Playing	1562.1 (2405.3)	47.4	1159.6 (2113.6)	35.2	6.73**	<0.001
Skating	244.3 (873.8)	8.4	119.2 (378.7)	5.3	3.51**	<0.001
Dancing	50.1 (230.4)	2.3	229.6 (528.7)	13.3	-11.50**	<0.001
Skipping	7.1 (66.5)	0.3	35.4 (143.9)	2.1	-5.18**	<0.001
2015						
Cycling	337.6 (994.2)	10.0†	172.7 (583.3)	6.2†	7.21**	<0.001
Walking	456.1 (742.1)	21.6†	469.9 (768.2)	25.7†	-4.87**	<0.001
Housework & Gardening	39.3 (172.2)	2.4†	45.6 (160.4)	3.7	-3.75**	<0.001
Hopscotch	6.5 (90.3)	0.2	8.1 (73.6)	0.4†	-2.65**	0.008
Trampolining	191.8 (589.8)	6.8	223.0 (732.0)	19.3	-3.18**	0.002
Playing	1733.1 (2435.9)	51.3†	1375.0 (2239.4)	34.9†	12.07**	<0.001
Skating	149.9 (534.4)	5.1†	103.9 (330.9)	13.0†	2.05**	0.041
Dancing	52.5 (235.8)	2.3	201.3 (466.2)	21.5†	-17.91**	<0.001
Skipping	3.9 (43.7)	0.3	23.5 (139.9)	5.4†	-5.57**	<0.001

Appendix 16 - Table showing means, standard deviations, and percentage contribution for each activity to domain total MET minutes per week, with comparisons across sex and survey year on the percentage contribution from each activity
*** p < 0.05* *† Significant difference (p < 0.05) between 2012 and 2015 data*



Appendix 17 - Stacked column graph showing the contribution of school physical activity to total physical activity for HSE 2015, by age and sex

	B	SE B	β	t	p	95% CI-	95% CI+
2012 Non-School PA							
Active Travel	11.37	4.63	0.06	2.46	0.014	2.29	20.45
Non-Specific	56.94	8.57	0.16	6.64	<0.001	40.12	73.75
Formal	265.43	16.50	0.35	16.09	<0.001	233.07	297.79
Informal	1499.33	29.53	0.76	50.77	<0.001	1441.40	1557.25
2015 Non-School PA							
Active Travel	20.87	2.57	0.11	8.13	<0.001	15.84	25.90
Non-Specific	35.42	3.49	0.14	10.16	<0.001	28.59	42.26
Formal	307.77	10.99	0.36	28.01	<0.001	286.23	329.31
Informal	1560.91	17.98	0.76	86.80	<0.001	1525.65	1596.16
2015 Including School PA							
Active Travel	23.98	2.56	0.13	9.37	<0.001	18.97	29.00
Non-Specific	36.10	3.48	0.14	10.37	<0.001	29.28	42.93
Formal	305.92	10.99	0.36	27.85	<0.001	284.38	327.46
Informal	1548.19	18.16	0.75	85.24	<0.001	1512.58	1583.79
School	35.55	3.21	0.15	11.09	<0.001	29.27	41.84

Appendix 18 – Table showing results from linear regressions of domain-specific MET minutes per week, by total physical activity quintile, controlling for age and sex

	Input					Output							
Age Group	**Incidence**	**Prevalence**	**Remission**	**Case Fatality**	**Mortality**	**Incidence**	**Prevalence**	**Remission**	**Case Fatality**	**Duration**	**Mortality**	**RR Mortality**	**Age of Onset**
0-4	0	0.0006	0	0	0	0	0.0006	0	0	68.27	0	1.0344	2.4994
5-9	0	0.0006	0	0	0	0	0.0007	0	0	63.33	0	1.0601	7.4984
10-14	0	0.0006	0	0	0	0	0.0007	0	0	58.36	0	1.059	12.4983
15-19	0	0.0006	0	0	0	0	0.0008	0	0	53.42	0	1.022	17.4983
20-24	0	0.0006	0	0	0	0	0.0008	0	0	48.52	0	1.0124	22.4983
25-29	0	0.0006	0	0	0	0	0.0009	0	0.230	43.44	0	6.2923	27.9083
30-34	0.0001	0.0006	0	0.138	0	0	0.001	0	1	40.09	0	13.229	32.5951
35-39	0.0003	0.0006	0	0.138	0	0	0.0011	0	0.0126	37.79	0	11.6238	37.1577
40-44	0.0006	0.0006	0	0.138	0	0.0001	0.0011	0	0.0116	34.51	0	7.861	43.6043
45-49	0.0012	0.0107	0	0.138	0	0.0006	0.0025	0	0.007	31.71	0	4.0419	48.1403
50-54	0.0019	0.0107	0	0.138	0	0.0017	0.0083	0	0.0024	28.16	0	1.7284	52.7325
55-59	0.0025	0.0337	0	0.142	0.0001	0.0026	0.019	0	0.0017	24.14	0	1.2829	57.5972
60-64	0.0031	0.0337	0	0.142	0.0001	0.0033	0.0331	0	0.0018	20.19	0.0001	1.1871	62.5699
65-69	0.0039	0.0675	0	0.195	0.0001	0.0041	0.0502	0	0.0021	16.43	0.0001	1.1462	67.593
70-74	0.0052	0.0675	0	0.195	0.0001	0.0055	0.072	0	0.2%	12.96	0.0002	1.0918	72.6024
75-79	0.0071	0.115	0	0.28	0.0003	0.0075	0.1006	0	0.0024	9.91	0.0002	1.0571	77.5848
80-84	0.01	0.115	0	0.28	0.0003	0.0098	0.1372	0	0.0029	7.36	0.0004	1.0385	82.5683
85-89	0.0145	0.115	0	0.379	0.0008	0.0118	0.1811	0	0.0035	5.73	0.0006	1.0283	87.4806
90-94	0.0169	0.115	0	0.379	0.0008	0.0114	0.2248	0	0.0036	4.43	0.0008	1.0205	92.424
95-99	0.0169	0.115	0	0.379	0.0008	0.0108	0.2632	0	0.0034	3.68	0.0009	1.0139	97.4512
100+	0.0169	0.115	0	0.379	0.0008	0.0107	0.2847	0	0.0032	3.49	0.0009	1.0112	103.0203

Appendix 19 – Table showing the input and output data for male myocardial infarction from DisMod II for the process of standardisation for internal consistency

	Input					Output							
Age Group	Incidence	Prevalence	Remission	Case Fatality	Mortality	Incidence	Prevalence	Remission	Case Fatality	Duration	Mortality	RR Mortality	Age of Onset
0-4	0	0.0001	0	0	0	0	0.0001	0	0	68.7289	0	1.0349	2.4969
5-9	0	0.0001	0	0	0	0	0.0001	0	0	63.7876	0	1.0587	7.4918
10-14	0	0.0001	0	0	0	0	0.0002	0	0	58.8216	0	1.0628	12.4916
15-19	0	0.0001	0	0	0	0	0.0002	0	0	53.8529	0	1.0588	17.4916
20-24	0	0.0001	0	0	0	0	0.0002	0	0	48.8928	0	1.0323	22.4917
25-29	0	0.0001	0	0	0	0	0.0002	0	0.0028	44.1107	0	14.1389	27.52
30-34	0	0.0001	0	0.133	0	0	0.0002	0	0.0122	40.7297	0	31.0408	32.49
35-39	0.0001	0.0001	0	0.133	0	0	0.0002	0	0.0164	38.8279	0	25.0591	37.4441
40-44	0.0002	0.0001	0	0.133	0	0	0.0002	0	0.0156	36.5894	0	16.6647	43.6959
45-49	0.0003	0.0026	0	0.133	0	0.0002	0.0005	0	0.0093	34.3295	0	7.3576	48.1624
50-54	0.0005	0.0026	0	0.133	0	0.0004	0.002	0	0.0027	30.9066	0	2.3201	52.7436
55-59	0.0007	0.0082	0	0.174	0	0.0007	0.0047	0	0.0017	26.7553	0	1.4294	57.6407
60-64	0.001	0.0082	0	0.174	0	0.001	0.0087	0	0.0019	22.5786	0	1.3011	62.6569
65-69	0.0016	0.0187	0	0.253	0.0001	0.0015	0.0147	0	0.0026	18.5672	0	1.2675	67.6847
70-74	0.0026	0.0187	0	0.253	0.0001	0.0024	0.024	0	0.0028	14.8436	0.0001	1.1736	72.6745
75-79	0.0042	0.0526	0	0.358	0.0002	0.0038	0.0385	0	0.0029	11.4552	0.0001	1.1012	77.6516
80-84	0.0065	0.0526	0	0.358	0.0002	0.0053	0.0595	0	0.0037	8.6011	0.0002	1.0668	82.5786
85-89	0.0098	0.0526	0	0.457	0.0006	0.0056	0.0843	0	0.0046	6.6741	0.0004	1.0486	87.4031
90-94	0.0133	0.0526	0	0.457	0.0006	0.0036	0.1034	0	0.0053	5.118	0.0005	1.0367	92.27
95-99	0.0133	0.0526	0	0.457	0.0006	0.0028	0.1144	0	0.0053	4.1311	0.0006	1.0253	97.507
100+	0.0133	0.0526	0	0.457	0.0006	0.0029	0.1203	0	0.0051	3.9046	0.0006	1.0203	103.4703

Appendix 20 - Table showing the input and output data for female myocardial infarction from DisMod II for the process of standardisation for internal consistency

	Input					Output							
Age Group	Incidence	Prevalence	Remission	Case Fatality	Mortality	Incidence	Prevalence	Remission	Case Fatality	Duration	Mortality	RR Mortality	Age of Onset
0-4	0	0.001	0	0.13	0.0002	0.0001	0.001	0	0.1367	7.3439	0.0001	767.2065	2.4974
5-9	0	0.001	0	0.13	0.0002	0.0001	0.001	0	0.1366	7.3722	0.0001	1331.844	7.495
10-14	0	0.001	0	0.13	0.0002	0.0001	0.001	0	0.1366	7.4203	0.0001	1318.81	12.5009
15-19	0	0.001	0	0.13	0.0001	0.0001	0.001	0	0.1366	7.5194	0.0001	492.4234	17.5
20-24	0	0.001	0	0.13	0.0002	0.0001	0.001	0	0.1366	7.728	0.0001	277.757	22.4999
25-29	0	0.001	0	0.13	0.0001	0.0001	0.001	0	0.1365	8.152	0.0001	227.56	27.5254
30-34	0	0.001	0	0.13	0.0002	0.0002	0.0011	0	0.1361	8.9989	0.0001	170.7041	32.5729
35-39	0.0004	0.001	0	0.13	0.0002	0.0002	0.0012	0	0.1331	10.6086	0.0002	112.8582	37.5964
40-44	0.0004	0.001	0	0.13	0.0002	0.0003	0.0015	0	0.1182	13.1733	0.0002	71.1606	42.6237
45-49	0.0008	0.0085	0	0.13	0.0002	0.0004	0.0022	0	0.0835	15.7581	0.0002	35.7696	47.7701
50-54	0.0008	0.0085	0	0.13	0.0002	0.0008	0.0043	0	0.0503	16.2333	0.0002	14.8465	52.7246
55-59	0.0021	0.026	0	0.13	0.0004	0.0014	0.0084	0	0.0395	15.0957	0.0003	7.7345	57.6829
60-64	0.0021	0.026	0	0.13	0.0004	0.0024	0.0154	0	0.0318	13.0788	0.0005	4.3146	62.776
65-69	0.0068	0.0608	0	0.1	0.0013	0.0048	0.0289	0	0.0372	10.7607	0.0011	3.5041	67.7321
70-74	0.0068	0.0608	0	0.1	0.0013	0.0072	0.0508	0	0.0394	8.5381	0.002	2.5964	72.5942
75-79	0.0109	0.1455	0	0.13	0.0087	0.0092	0.0748	0	0.063	6.317	0.0047	2.5153	77.5928
80-84	0.0109	0.1455	0	0.13	0.0087	0.0121	0.0912	0	0.0988	4.9114	0.009	2.3317	82.6056
85-89	0.0206	0.1455	0	0.31	0.0087	0.0155	0.1092	0	0.0941	4.2683	0.0103	1.7769	87.5689
90-94	0.0206	0.1455	0	0.31	0.0087	0.0178	0.1371	0	0.0764	3.6246	0.0105	1.4374	92.5149
95-99	0.0206	0.1455	0	0.31	0.0087	0.0182	0.1694	0	0.062	3.1618	0.0105	1.2565	97.4777
100+	0.0206	0.1455	0	0.31	0.0087	0.018	0.1882	0	0.0568	3.0294	0.0107	1.2	103.0203

Appendix 21 - Table showing the input and output data for male stroke from DisMod II for the process of standardisation for internal consistency

	Input					Output							
Age Group	Incidence	Prevalence	Remission	Case Fatality	Mortality	Incidence	Prevalence	Remission	Case Fatality	Duration	Mortality	RR Mortality	Age of Onset
0-4	0	0.0011	0	0.13	0.0001	0	0.0009	0	0.1262	7.5295	0.0001	723.7426	2.5048
5-9	0	0.0011	0	0.13	0.0001	0	0.0006	0	0.1327	7.327	0.0001	1249.147	7.5107
10-14	0	0.0011	0	0.13	0.0001	0	0.0004	0	0.1384	7.2923	0.0001	1417.349	12.5067
15-19	0	0.0011	0	0.13	0.0001	0	0.0003	0	0.1399	7.4086	0	1349.102	17.5036
20-24	0	0.0011	0	0.13	0.0001	0	0.0003	0	0.1401	7.6873	0	735.4979	22.5018
25-29	0	0.0011	0	0.13	0.0001	0	0.0003	0	0.14	8.257	0	471.8036	27.5069
30-34	0	0.0011	0	0.13	0.0001	0.0001	0.0003	0	0.1391	9.5512	0	341.6292	33.0041
35-39	0.0003	0.0011	0	0.13	0.0001	0.0002	0.0006	0	0.1317	11.6456	0.0001	188.7152	37.8207
40-44	0.0003	0.0011	0	0.13	0.0001	0.0003	0.0012	0	0.1099	14.4713	0.0001	111.1185	42.5454
45-49	0.0006	0.0075	0	0.13	0.0001	0.0004	0.002	0	0.0742	16.9674	0.0001	49.8265	47.723
50-54	0.0006	0.0075	0	0.13	0.0001	0.0007	0.0037	0	0.0453	17.1428	0.0002	19.5376	52.7046
55-59	0.0014	0.018	0	0.13	0.0003	0.001	0.0068	0	0.0356	15.7197	0.0002	10.0033	57.6466
60-64	0.0014	0.018	0	0.13	0.0003	0.0016	0.0117	0	0.0302	13.3786	0.0004	5.8992	62.763
65-69	0.0046	0.0416	0	0.1	0.001	0.0033	0.0206	0	0.0398	10.8742	0.0008	5.0953	67.7436
70-74	0.0046	0.0416	0	0.1	0.001	0.0051	0.0353	0	0.0441	8.5458	0.0016	3.7212	72.6325
75-79	0.0111	0.1217	0	0.13	0.0101	0.0082	0.0539	0	0.0746	6.1592	0.004	3.5835	77.7119
80-84	0.0111	0.1217	0	0.13	0.0101	0.0125	0.0721	0	0.1245	4.7697	0.009	3.2754	82.6093
85-89	0.0186	0.1217	0	0.31	0.0101	0.0151	0.088	0	0.1321	4.1462	0.0116	2.4097	87.5418
90-94	0.0186	0.1217	0	0.31	0.0101	0.0164	0.1048	0	0.1188	3.5619	0.0125	1.8374	92.508
95-99	0.0186	0.1217	0	0.31	0.0101	0.0166	0.1226	0	0.1031	3.1156	0.0126	1.4976	97.49
100+	0.0186	0.1217	0	0.31	0.0101	0.0166	0.1329	0	0.0967	2.9812	0.0128	1.3841	103.4703

Appendix 22 - Table showing the input and output data for female stroke from DisMod II for the process of standardisation for internal consistency

	Input				Output							
Age Group	Incidence	Prevalence	Remission	Mortality	Incidence	Prevalence	Remission	Case Fatality	Duration	Mortality	RR Mortality	Age of Onset
0-4	0.0004	0	0	0	0	0	0	0	47.8652	0	1	3.9942
5-9	0.0003	0	0	0	0.0001	0.0002	0	0	43.9791	0	1.0086	7.9039
10-14	0.0003	0	0	0	0.0002	0.0009	0	0.0011	39.2898	0	18.7759	12.6394
15-19	0.0005	0.013	0	0	0.0003	0.0019	0	0.0177	35.4801	0	59.525	17.8828
20-24	0.0006	0.0162	0	0.0002	0.0006	0.0039	0	0.0352	35.5431	0.0001	71.2308	22.661
25-29	0.0009	0.0162	0	0.0002	0.0009	0.0069	0	0.0284	36.5613	0.0002	48.8553	27.6508
30-34	0.0014	0.0162	0	0.0002	0.0014	0.0115	0	0.0197	35.9688	0.0002	25.8307	32.6707
35-39	0.0021	0.0846	0	0.0004	0.0021	0.0188	0	0.0167	34.2439	0.0003	14.9272	37.6627
40-44	0.0033	0.0846	0	0.0004	0.0032	0.0299	0	0.0131	31.9518	0.0004	8.8958	42.6641
45-49	0.0052	0.0846	0	0.0004	0.0049	0.0473	0	0.0083	28.8479	0.0004	4.4519	47.6464
50-54	0.0077	0.0846	0	0.0004	0.0069	0.073	0	0.0056	25.1651	0.0004	2.5484	52.6084
55-59	0.0099	0.0999	0	0.0005	0.0089	0.1068	0	0.0053	21.3077	0.0006	1.8871	57.5645
60-64	0.0123	0.0999	0	0.001	0.0106	0.1459	0	0.0071	17.5704	0.001	1.7319	62.5442
65-69	0.0149	0.1368	0	0.002	0.0123	0.1875	0	0.0103	14.0606	0.0019	1.6993	67.5304
70-74	0.0166	0.1368	0	0.0035	0.0132	0.2279	0	0.0155	10.8612	0.0035	1.6221	72.4844
75-79	0.0163	0.1431	0	0.0076	0.0128	0.2581	0	0.0274	8.0697	0.0071	1.6614	77.4632
80-84	0.0141	0.1431	0	0.0142	0.0117	0.2671	0	0.0479	5.8378	0.0128	1.6397	82.4612
85-89	0.0119	0.1431	0	0.0161	0.0098	0.2502	0	0.0702	4.4747	0.0176	1.5795	87.4001
90-94	0.0054	0.1431	0	0.0164	0.0066	0.212	0	0.0855	3.457	0.0181	1.4838	92.3564
95-99	0.0054	0.1431	0	0.0163	0.0054	0.165	0	0.0993	2.8192	0.0164	1.409	97.5231
100+	0.0054	0.1431	0	0.0166	0.0054	0.1386	0	0.1061	2.6638	0.0147	1.3736	103.0203

Appendix 23 - Table showing the input and output data for male type 2 diabetes from DisMod II for the process of standardisation for internal consistency

	Input				Output							
Age Group	Incidence	Prevalence	Remission	Mortality	Incidence	Prevalence	Remission	Case Fatality	Duration	Mortality	RR Mortality	Age of Onset
0-4	0.0004	0	0	0	0.0001	0.0003	0	0	72.6134	0	1.0001	2.3988
5-9	0.0003	0	0	0	0.0001	0.0009	0	0	67.8778	0	1.0073	7.1864
10-14	0.0004	0	0	0	0.0001	0.0012	0	0	62.0205	0	1.0366	13.0832
15-19	0.0009	0.0151	0	0	0.0005	0.0024	0	0	57.0561	0	1.055	18.0796
20-24	0.0013	0.0189	0	0	0.0012	0.0069	0	0	52.4902	0	1.0305	22.6852
25-29	0.0017	0.0189	0	0	0.0016	0.0141	0	0.001	47.75	0	5.3871	27.5543
30-34	0.0018	0.0189	0	0	0.0018	0.0223	0	0.004	43.3566	0.0001	10.7517	32.5511
35-39	0.0022	0.0594	0	0.0002	0.0022	0.0314	0	0.0053	39.41	0.0002	8.6608	37.5965
40-44	0.0029	0.0594	0	0.0002	0.0029	0.0427	0	0.0045	35.4685	0.0002	5.5776	42.6028
45-49	0.0043	0.0594	0	0.0002	0.0039	0.0577	0	0.0038	31.3306	0.0002	3.404	47.6121
50-54	0.006	0.0594	0	0.0004	0.005	0.0772	0	0.0037	27.1671	0.0003	2.4852	52.58
55-59	0.0074	0.072	0	0.0004	0.0061	0.1011	0	0.004	23.0224	0.0004	1.9954	57.5545
60-64	0.0092	0.072	0	0.0007	0.0072	0.128	0	0.0056	18.9653	0.0007	1.9051	62.5673
65-69	0.0114	0.1098	0	0.0014	0.009	0.1583	0	0.0085	15.1056	0.0013	1.8869	67.5693
70-74	0.0134	0.1098	0	0.0028	0.0103	0.1906	0	0.0143	11.5577	0.0027	1.8762	72.5091
75-79	0.0138	0.1188	0	0.0066	0.0105	0.2156	0	0.0286	8.4016	0.0062	2.0005	77.4856
80-84	0.0125	0.1188	0	0.0145	0.0101	0.2199	0	0.0587	5.8663	0.0129	2.0685	82.4843
85-89	0.0106	0.1188	0	0.0185	0.0088	0.1925	0	0.1007	4.2921	0.0194	2.0839	87.4122
90-94	0.0045	0.1188	0	0.0197	0.0059	0.1407	0	0.1365	3.1821	0.0192	1.9582	92.3499
95-99	0.0045	0.1188	0	0.0198	0.0047	0.0867	0	0.1744	2.4729	0.0151	1.843	97.5243
100+	0.0045	0.1188	0	0.02	0.0048	0.0613	0	0.1946	2.3025	0.0119	1.7733	103.4703

Appendix 24 - Table showing the input and output data for female type 2 diabetes from DisMod II for the process of standardisation for internal consistency

	Input			Output							
Age Group	Incidence	Remission	Mortality	Incidence	Prevalence	Remission	Case Fatality	Duration	Mortality	RR Mortality	Age of Onset
0-4	0	0	0	0	0	0	0	0	0	1014.37	2.365
5-9	0	0	0	0	0	0	0	0	0	0	6.8291
10-14	0	0	0	0	0	0	0.17	6.5886	0	1184.654	14.25
15-19	0	0	0	0	0	0	0.1698	7.2956	0	512.4142	18.1803
20-24	0	0	0	0	0	0	0.1625	8.8427	0	324.768	22.7279
25-29	0	0	0	0	0.0001	0	0.1338	11.4522	0	224.6628	27.7424
30-34	0.0001	0	0	0	0.0002	0	0.0848	13.2475	0	109.2996	32.7041
35-39	0.0001	0	0	0.0001	0.0003	0	0.0697	13.2957	0	58.7267	37.679
40-44	0.0001	0	0	0.0001	0.0006	0	0.0629	12.782	0	37.9238	42.715
45-49	0.0002	0	0.0001	0.0002	0.001	0	0.0641	11.6925	0.0001	26.1891	47.6748
50-54	0.0005	0	0.0001	0.0003	0.0018	0	0.0794	10.8632	0.0001	21.9449	52.8203
55-59	0.0009	0	0.0003	0.0007	0.0033	0	0.0828	10.5407	0.0003	14.8718	57.7443
60-64	0.0015	0	0.0003	0.0012	0.0061	0	0.0721	9.9215	0.0004	8.5221	62.6548
65-69	0.002	0	0.0008	0.0016	0.0101	0	0.076	8.879	0.0008	6.1894	67.6386
70-74	0.0031	0	0.0008	0.0025	0.0152	0	0.074	7.8424	0.0011	4.0531	72.6668
75-79	0.0037	0	0.0018	0.0033	0.0231	0	0.0681	6.5154	0.0016	2.6597	77.5785
80-84	0.0046	0	0.0018	0.004	0.0316	0	0.0729	5.0602	0.0023	1.9822	82.5716
85-89	0.005	0	0.0032	0.0046	0.0392	0	0.0843	4.0156	0.0033	1.6941	87.5256
90-94	0.0049	0	0.0039	0.0047	0.0431	0	0.102	3.1705	0.0044	1.5728	92.4888
95-99	0.0049	0	0.0039	0.0046	0.0431	0	0.1096	2.6914	0.0047	1.4504	97.5031
100+	0.0049	0	0.0039	0.0046	0.0429	0	0.1101	2.5685	0.0047	1.3876	103.0203

Appendix 25 - Table showing the input and output data for male bowel cancer from DisMod II for the process of standardisation for internal consistency

	Input			Output							
Age Group	Incidence	Remission	Mortality	Incidence	Prevalence	Remission	Case Fatality	Duration	Mortality	RR Mortality	Age of Onset
0-4	0	0	0	0	0	0	0.14	10.4027	0	815.4101	3.9943
5-9	0	0	0	0	0	0	0.14	12.8749	0	1416.461	7.9213
10-14	0	0	0	0	0	0	0.1367	18.1676	0	1396.91	12.603
15-19	0	0	0	0	0.0001	0	0.0833	25.8818	0	902.9489	17.6414
20-24	0	0	0	0	0.0002	0	0.0211	27.3492	0	133.9122	22.5733
25-29	0	0	0	0	0.0003	0	0.0261	25.1508	0	87.5669	27.7171
30-34	0.0001	0	0	0.0001	0.0005	0	0.0241	23.3716	0	60.3758	32.6606
35-39	0.0001	0	0	0.0001	0.0007	0	0.0261	21.1665	0	38.2393	37.5856
40-44	0.0001	0	0	0.0001	0.001	0	0.0284	18.9746	0	28.9173	42.6957
45-49	0.0002	0	0.0001	0.0002	0.0015	0	0.0337	16.7782	0.0001	21.6733	47.6825
50-54	0.0004	0	0.0001	0.0003	0.0022	0	0.0454	15.048	0.0001	18.7697	52.7397
55-59	0.0006	0	0.0002	0.0005	0.0035	0	0.0508	13.8142	0.0002	13.632	57.6933
60-64	0.0009	0	0.0002	0.0008	0.0056	0	0.0487	12.4159	0.0003	8.9163	62.6324
65-69	0.0012	0	0.0005	0.001	0.0083	0	0.0559	10.8269	0.0005	6.825	67.6286
70-74	0.0018	0	0.0005	0.0015	0.0117	0	0.0573	9.3322	0.0007	4.5972	72.6638
75-79	0.0024	0	0.0011	0.0021	0.0169	0	0.056	7.6209	0.0009	2.9733	77.5989
80-84	0.0031	0	0.0011	0.0027	0.023	0	0.0621	5.8704	0.0014	2.1461	82.5842
85-89	0.0034	0	0.0021	0.0031	0.0287	0	0.0752	4.5305	0.0022	1.805	87.5171
90-94	0.0031	0	0.0029	0.003	0.0307	0	0.1024	3.4423	0.0031	1.7092	92.4714
95-99	0.0031	0	0.0029	0.0029	0.0286	0	0.1209	2.8264	0.0035	1.5797	97.4998
100+	0.0031	0	0.0029	0.0029	0.027	0	0.1259	2.6727	0.0034	1.5005	103.4703

Appendix 26 - Table showing the input and output data for female bowel cancer from DisMod II for the process of standardisation for internal consistency

	Input			Output							
Age Group	Incidence	Remission	Mortality	Incidence	Prevalence	Remission	Case Fatality	Duration	Mortality	RR Mortality	Age of Onset
0-4	0	0	0	0	0	0	0.02	0	0	0	2.365
5-9	0	0	0	0	0	0	0.02	43.834	0	216.4708	9
10-14	0	0	0	0	0	0	0.0197	43.3257	0	201.8961	13.0339
15-19	0	0	0	0	0.0001	0	0.0168	42.4442	0	161.4855	17.5885
20-24	0	0	0	0	0.0001	0	0.0135	40.5571	0	69.9488	22.6851
25-29	0.0001	0	0	0.0001	0.0003	0	0.015	38.1162	0	49.9747	28.2143
30-34	0.0003	0	0	0.0003	0.001	0	0.0177	36.3597	0	42.4716	32.9356
35-39	0.0007	0	0.0001	0.0007	0.0032	0	0.0166	34.6074	0.0001	24.8229	37.796
40-44	0.0014	0	0.0001	0.0013	0.0077	0	0.0135	32.3159	0.0001	14.3888	42.7294
45-49	0.0027	0	0.0003	0.0022	0.0156	0	0.0119	29.4685	0.0002	8.3704	47.6664
50-54	0.0035	0	0.0003	0.0029	0.0269	0	0.0124	26.4713	0.0003	5.8982	52.5606
55-59	0.0033	0	0.0005	0.0033	0.0399	0	0.0128	23.4097	0.0005	4.2012	57.5485
60-64	0.0042	0	0.0005	0.0038	0.0541	0	0.0118	20.2435	0.0006	2.9409	62.5485
65-69	0.0049	0	0.0007	0.0042	0.0698	0	0.0113	16.9822	0.0008	2.1996	67.5074
70-74	0.004	0	0.0007	0.0042	0.0852	0	0.0112	13.7383	0.001	1.7036	72.4861
75-79	0.0043	0	0.0013	0.0042	0.0994	0	0.012	10.6508	0.0012	1.4238	77.5078
80-84	0.0045	0	0.0013	0.0044	0.1125	0	0.0143	7.9694	0.0016	1.264	82.5164
85-89	0.0047	0	0.0022	0.0046	0.1241	0	0.0189	6.0976	0.0023	1.2033	87.5043
90-94	0.0047	0	0.0035	0.0046	0.1315	0	0.0272	4.6387	0.0036	1.1879	92.4956
95-99	0.0047	0	0.0035	0.0046	0.1347	0	0.0302	3.8073	0.0041	1.1451	97.4998
100+	0.0047	0	0.0035	0.0046	0.1361	0	0.03	3.6027	0.0041	1.1194	103.4703

Appendix 27 - Table showing the input and output data for female breast cancer from DisMod II for the process of standardisation for internal consistency

	Input			Output							
Age Group	**Incidence**	**Remission**	**Mortality**	**Incidence**	**Prevalence**	**Remission**	**Case Fatality**	**Duration**	**Mortality**	**RR Mortality**	**Age of Onset**
0-4	0	0	0	0	0	0	0.04	0	0	0	2.3715
5-9	0	0	0	0	0	0	0.04	22.4155	0	431.8762	9
10-14	0	0	0	0	0	0	0.0397	21.9675	0	404.655	13.0112
15-19	0	0	0	0	0	0	0.0362	21.2325	0	344.5172	17.4441
20-24	0	0	0	0	0	0	0.0329	19.7483	0	169.7368	22.5258
25-29	0	0	0	0	0.0001	0	0.0371	17.8534	0	123.741	27.9961
30-34	0	0	0	0	0.0001	0	0.045	16.4656	0	108.0837	32.7712
35-39	0	0	0	0	0.0002	0	0.0525	15.38	0	75.5542	37.6555
40-44	0.0001	0	0	0.0001	0.0004	0	0.0677	14.9065	0	66.7892	42.7099
45-49	0.0001	0	0	0.0001	0.0006	0	0.0742	15.5251	0	47.4497	47.6888
50-54	0.0003	0	0	0.0002	0.001	0	0.0654	16.2656	0.0001	26.9749	52.8111
55-59	0.0006	0	0.0001	0.0004	0.0021	0	0.0551	16.529	0.0001	14.9271	57.7298
60-64	0.0007	0	0.0001	0.0006	0.004	0	0.0382	15.7579	0.0002	7.3972	62.6273
65-69	0.0009	0	0.0002	0.0008	0.0066	0	0.0334	13.9417	0.0002	4.5057	67.5573
70-74	0.001	0	0.0002	0.0009	0.0095	0	0.0315	11.8649	0.0003	2.9941	72.5304
75-79	0.0009	0	0.0004	0.0009	0.0123	0	0.0283	9.6278	0.0003	2.0144	77.4776
80-84	0.0008	0	0.0004	0.0008	0.0147	0	0.0281	7.4564	0.0004	1.5268	82.4424
85-89	0.0007	0	0.0005	0.0007	0.0161	0	0.0294	5.8765	0.0005	1.3136	87.4141
90-94	0.0005	0	0.0005	0.0005	0.0167	0	0.0306	4.5599	0.0005	1.2137	92.4262
95-99	0.0005	0	0.0005	0.0005	0.0167	0	0.0311	3.7452	0.0005	1.1491	97.4967
100+	0.0005	0	0.0005	0.0005	0.0166	0	0.0311	3.5429	0.0005	1.1238	103.4703

Appendix 28 - Table showing the input and output data for female uterine cancer from DisMod II for the process of standardisation for internal consistency

Age		Male					Female				
		Inactive	Barely	Some-what	Active	Highly	Inactive	Barely	Some-what	Active	Highly
5	Mean	376.15	752.79	1615.00	2582.46	5270.79	196.88	765.38	1497.81	2775.39	5510.82
	SD	190.92	102.22	233.57	395.61	1717.57	150.80	269.81	226.36	522.92	1942.68
6	Mean	237.12	870.69	1425.85	2597.31	4329.43	473.50	176.73	1871.00	2581.77	3962.92
	SD	162.81	200.27	268.00	424.27	1310.54	256.91	189.40	268.71	147.91	1004.35
7	Mean	383.32	834.86	1721.17	2943.18	6112.29	537.08	990.13	1559.17	2309.75	4506.58
	SD	195.65	127.39	248.40	491.90	2266.58	179.80	154.52	241.35	409.75	964.00
8	Mean	319.31	815.88	1334.69	2270.63	4295.96	463.12	764.50	1308.04	1985.68	4779.89
	SD	190.20	116.20	196.73	447.30	1257.57	145.77	83.61	226.60	392.16	2437.39
9	Mean	111.59	873.45	2126.64	3006.23	5911.09	348.96	989.29	1535.92	2680.63	5022.23
	SD	101.44	344.21	255.93	369.24	2751.74	256.12	221.43	240.63	434.92	1700.46
10	Mean	261.82	866.55	1706.50	2303.64	3949.63	277.33	818.46	1227.38	1937.63	4027.17
	SD	225.27	182.10	214.53	235.81	966.72	163.07	168.29	135.91	293.30	1684.95
11	Mean	98.82	669.50	1711.21	3225.09	6206.75	269.57	878.40	1269.46	1866.33	5027.00
	SD	114.50	215.58	414.22	754.45	1810.03	178.84	128.48	111.92	238.80	2311.09
12	Mean	124.19	707.31	1373.25	1994.19	5689.64	276.96	915.81	1590.46	2423.54	4118.39
	SD	111.85	264.37	159.88	150.55	3042.50	212.57	106.10	266.75	243.51	1352.12
13	Mean	252.22	980.38	1345.95	1969.11	4439.83	225.29	533.71	856.08	1416.16	2891.35
	SD	280.85	94.98	132.42	323.02	1092.29	114.44	66.11	158.46	210.89	1098.95
14	Mean	106.82	408.85	1348.60	2596.15	7232.68	26.25	297.95	730.56	1571.06	3532.22
	SD	95.24	120.70	227.07	360.25	4399.47	40.77	138.13	185.91	498.45	1018.68
15	Mean	149.55	539.62	1090.79	1650.64	4352.70	91.31	417.86	809.89	1565.81	3237.25
	SD	148.00	144.22	160.33	315.65	2285.46	70.04	172.24	104.26	405.28	909.47
16	Mean	77.48	580.41	1347.66	2502.02	8314.68	1.00	27.63	383.83	944.28	3212.18
	SD	114.48	187.50	279.22	669.01	4362.21	1.85	27.28	188.03	174.61	2176.29
17	Mean	21.56	1059.42	2536.59	4450.25	9306.61		108.96	687.59	1653.64	5996.41
	SD	40.96	271.99	327.24	1052.60	2638.45		169.81	238.53	316.34	2580.99
18	Mean	306.78	1174.88	3530.96	6943.08	12509.33	9.83	476.26	1584.18	3341.72	7875.42
	SD	262.56	359.00	882.42	1279.75	4649.09	28.03	422.15	285.85	629.99	5036.99
19	Mean	539.69	2528.64	4565.28	6863.86	13055.25	122.66	674.27	1863.05	3263.77	7590.12
	SD	466.42	727.29	605.29	1282.64	4754.11	95.67	286.63	560.68	381.76	2724.76
20	Mean	241.43	1519.82	3614.63	6886.82	13034.92	2.01	161.78	1542.03	3406.26	11496.58
	SD	302.42	652.15	888.33	1350.91	4372.57	5.12	150.35	620.03	808.27	6111.64
21	Mean	318.96	2054.19	3206.11	6527.66	15155.97	38.91	461.47	2211.19	4330.20	11169.64
	SD	336.60	480.50	584.01	1776.97	4458.65	40.33	404.13	482.90	1122.00	4008.74
22	Mean	386.28	2610.94	4660.49	8639.89	17827.04	93.95	742.60	2671.85	4794.28	11180.48
	SD	553.13	492.95	668.00	1339.53	7378.75	112.33	401.47	615.06	787.56	4024.33
23	Mean	723.58	3092.65	5845.33	9201.02	17219.29	104.59	1067.65	2894.32	4968.53	11527.41
	SD	802.57	626.29	952.69	1435.76	4492.54	119.90	584.35	492.56	875.87	6547.80
24	Mean	1008.89	3498.06	6303.27	9782.34	16256.41	210.07	1565.19	2887.19	4645.76	11028.79
	SD	417.40	992.36	747.69	1476.41	2744.59	287.98	300.49	542.17	763.69	5986.82
25	Mean	233.05	2293.03	4659.59	7547.28	15040.61	27.98	487.21	2197.96	4163.75	9986.27
	SD	301.99	960.47	763.27	744.15	5429.53	40.39	284.35	664.36	836.89	4532.25
26	Mean	696.88	3784.14	5417.88	7732.92	16043.97	133.17	2242.11	4112.71	6306.82	12242.70
	SD	661.93	798.44	372.55	1268.67	7174.58	226.64	990.08	455.99	817.30	5567.15
27	Mean	1185.23	3982.25	6152.23	8117.09	22255.75	330.63	1890.39	3434.52	5407.75	8630.71

	SD	1146.08	688.30	594.37	821.97	25557.66	300.38	586.44	361.52	893.39	1868.87
28	**Mean**	932.36	3707.44	5528.86	9322.39	16109.13	126.67	1300.12	2849.14	4488.76	9660.88
	SD	942.84	345.21	814.21	1869.71	3304.55	145.97	561.43	403.89	647.54	4234.16
29	**Mean**	978.03	2756.88	5457.45	9283.08	21024.70	75.56	786.99	2330.01	4705.43	7908.03
	SD	914.38	517.99	1084.16	1282.47	8782.17	109.85	345.78	664.64	635.18	1910.32
30	**Mean**	1397.23	3614.53	5457.39	8322.18	17024.51	18.15	692.19	2732.67	4753.19	9768.65
	SD	859.11	567.00	722.93	1190.37	6236.40	29.06	572.99	637.12	777.31	4590.92
31	**Mean**	1996.49	3855.38	6139.46	9301.61	19099.52	70.91	950.14	2475.06	3958.18	7993.30
	SD	932.65	694.68	946.04	1091.89	4381.51	74.40	448.73	368.24	537.18	3230.28
32	**Mean**	2033.12	3756.30	5135.04	6708.03	11983.23	211.86	1641.36	3108.86	4540.63	9679.42
	SD	990.17	322.04	355.81	810.99	4544.06	305.15	485.11	285.99	618.17	3333.26
33	**Mean**	1027.73	3437.58	5649.06	8147.98	14829.22	434.50	2040.55	3552.43	5083.60	8026.01
	SD	1011.07	548.46	901.35	813.13	4387.87	462.40	338.49	398.25	390.31	1701.97
34	**Mean**	681.35	2957.71	4703.71	8239.27	14489.09	69.90	1058.14	2712.80	4433.78	7856.71
	SD	870.59	389.49	856.43	1360.65	4976.07	77.02	585.83	396.94	776.94	1740.02
35	**Mean**	859.95	3808.61	5608.96	7845.48	11938.94	265.14	1600.14	2853.66	5362.93	14200.13
	SD	1185.68	458.42	647.83	886.50	2750.48	211.85	311.78	572.91	904.48	13210.84
36	**Mean**	1471.66	3053.80	4427.49	6104.53	14226.03	329.00	1870.04	2939.63	4478.63	7503.04
	SD	854.45	403.14	413.95	997.54	5818.81	372.90	406.92	244.72	737.95	1401.31
37	**Mean**	1323.11	3608.55	5287.21	8088.36	13072.22	142.69	1346.78	3200.77	4694.17	9535.40
	SD	968.33	360.48	614.08	827.39	2705.57	147.19	414.96	656.64	550.09	3933.50
38	**Mean**	483.42	3346.72	5317.67	8133.25	15118.80	532.04	1805.98	3319.06	5409.69	10023.44
	SD	672.72	736.74	689.03	1214.17	3264.62	386.17	435.56	513.12	668.06	2730.28
39	**Mean**	1453.46	4379.35	6292.24	9947.22	14306.16	248.56	1482.43	2891.34	4610.35	8538.69
	SD	1538.74	364.85	945.07	1249.53	2358.96	272.54	335.50	551.55	651.36	2430.78
40	**Mean**	1165.33	3159.21	4622.48	6567.61	11923.68	247.63	1793.84	2917.21	4347.08	8119.63
	SD	1132.86	317.16	593.55	644.97	2739.04	296.46	476.40	397.01	413.66	3039.77
41	**Mean**	856.35	4295.22	5742.69	7936.57	15232.17	228.04	1439.39	2628.38	4218.42	9176.61
	SD	1163.13	403.44	539.38	752.45	8109.67	245.00	459.22	372.59	754.94	2564.60
42	**Mean**	216.71	3123.75	5111.20	6948.01	11859.47	412.07	2129.43	3391.32	4957.86	10429.14
	SD	359.28	904.92	523.14	593.93	3277.97	408.33	544.13	350.89	627.62	4549.31
43	**Mean**	461.29	2366.14	4432.90	6908.66	12740.04	158.10	1536.22	3817.24	5558.35	9628.89
	SD	524.43	654.63	563.22	787.63	4230.68	243.85	504.21	683.48	456.45	3711.91
44	**Mean**	527.57	3435.64	4896.97	7431.79	12884.11	431.55	2269.33	3992.58	5419.76	10663.73
	SD	793.46	409.48	583.64	1055.31	3260.39	461.37	526.66	526.66	565.38	3987.65
45	**Mean**	1312.28	3327.34	5362.60	8145.81	13279.36	149.72	1929.45	3485.20	5027.56	9918.02
	SD	1120.24	375.21	859.41	888.52	2988.13	204.70	576.93	543.51	519.20	4195.21
46	**Mean**	1018.91	3547.19	5026.50	7002.66	12087.15	483.29	2086.44	3662.41	5073.94	8697.95
	SD	888.22	481.57	589.42	916.91	3383.23	473.96	515.48	371.25	587.54	2166.05
47	**Mean**	1061.48	3780.30	5284.39	7259.11	12194.49	192.92	2220.83	3701.30	5310.23	9541.61
	SD	997.59	586.48	576.96	708.20	2904.92	253.03	574.49	484.41	685.84	1979.51
48	**Mean**	871.05	3247.23	5776.08	9044.68	14108.84	202.44	1933.91	3455.03	5270.96	10506.58
	SD	607.41	639.53	1073.65	1206.12	2784.54	331.44	448.51	484.55	565.31	6643.94
49	**Mean**	796.65	3698.80	5074.19	7776.91	13368.56	251.08	1910.90	3358.17	5294.81	10523.94
	SD	1094.56	481.84	579.79	1199.97	3807.86	344.42	499.35	406.59	772.64	3729.47
50	**Mean**	1118.41	3092.19	4305.61	6547.29	14640.75	533.97	2626.43	4554.65	6869.47	12714.93
	SD	877.44	274.62	421.77	1022.41	5026.14	571.95	601.70	626.15	873.69	7606.30

51	**Mean**	492.75	2833.25	4518.05	6865.85	13804.09	285.13	1692.06	3176.69	5261.80	10500.41
	SD	619.38	600.35	452.60	987.03	4604.18	336.69	505.41	408.67	703.17	5778.27
52	**Mean**	2.33	1505.90	4570.43	7509.45	14873.85	46.81	1754.93	4249.38	6092.18	9968.60
	SD	4.33	1017.60	640.28	1374.43	5617.11	95.88	865.21	722.66	574.18	2602.07
53	**Mean**	30.48	1947.08	4594.99	7362.38	12314.47	127.95	1712.02	3246.93	5597.83	15232.16
	SD	50.40	1066.56	738.29	773.03	3608.08	220.15	558.27	598.86	849.90	15790.29
54	**Mean**	273.67	2475.58	4343.96	6787.15	16270.52	63.29	1514.20	3538.90	5116.50	10758.04
	SD	336.18	685.15	651.03	888.58	5912.30	132.16	786.23	415.75	806.65	4186.57
55	**Mean**	86.16	1913.88	3472.38	5532.76	11246.16	400.74	1544.16	3474.70	5932.93	8417.61
	SD	140.48	452.31	496.98	1059.53	4042.40	314.05	339.98	918.00	503.54	1616.03
56	**Mean**	250.24	2042.88	4003.89	5298.04	10738.20	68.25	1507.29	3100.09	4742.42	9102.27
	SD	291.43	814.34	303.35	573.12	3180.24	131.94	536.02	615.19	515.98	3325.56
57	**Mean**	33.15	1426.21	3769.83	6533.12	14990.66	14.46	999.77	3264.88	5149.27	9529.56
	SD	80.41	624.71	801.24	986.94	7968.85	38.08	571.44	589.76	663.23	4268.29
58	**Mean**	0.00	1879.49	4699.32	7436.44	15534.29		220.40	2194.96	3910.89	8521.07
	SD	0.00	1135.78	766.19	1125.85	5645.30		355.92	521.36	720.23	3463.02
59	**Mean**	273.52	2784.08	4899.58	7670.55	12098.61	30.63	442.55	1701.79	3551.89	8209.79
	SD	399.74	652.87	444.19	1390.31	1944.35	56.20	246.50	443.22	743.29	5883.80
60	**Mean**	1.33	293.13	2230.45	4288.44	10104.94	0.00	385.19	1521.96	3584.19	6909.01
	SD	3.55	196.31	575.80	725.66	4807.34	0.00	291.92	576.44	454.44	4745.58
61	**Mean**	76.72	779.21	2825.39	5269.61	12724.78	56.88	701.54	1738.48	2955.47	9039.25
	SD	98.23	457.39	435.06	776.15	5395.06	117.90	260.57	443.21	367.35	5119.61
62	**Mean**	6.23	722.55	2606.12	4464.62	12538.81	5.88	343.00	1461.76	3371.02	7318.84
	SD	19.36	507.47	307.08	841.93	7569.39	17.92	237.81	345.83	897.65	2699.90
63	**Mean**		137.88	1154.35	2889.38	7529.19	0.33	189.84	836.95	1852.34	4854.18
	SD		203.99	521.89	590.87	2757.18	1.30	138.66	334.84	394.50	2496.63
64	**Mean**		171.73	1407.52	4040.63	11325.13	0.00	169.87	785.79	1875.35	4797.80
	SD		273.08	554.29	1055.71	3322.17	0.00	123.05	152.05	587.69	2463.77
65	**Mean**	3.56	478.64	1726.07	3895.10	8453.79	0.00	184.87	879.64	2297.15	6923.58
	SD	7.13	272.49	538.82	879.30	2953.41	0.00	133.23	332.94	594.95	4052.81
66	**Mean**		63.65	909.77	2431.62	7746.38		36.44	516.04	1950.32	5074.73
	SD		98.51	319.33	819.35	6121.40		64.73	181.09	489.61	2399.45
67	**Mean**		51.33	569.71	1743.41	7030.97	0.00	156.83	824.52	1878.60	7930.77
	SD		86.35	254.11	530.36	9005.97	0.00	130.52	306.42	380.66	5018.88
68	**Mean**		44.12	552.39	1791.66	6915.18		30.80	461.06	1615.24	6180.13
	SD		77.04	215.43	650.58	3705.83		62.70	256.22	381.74	3442.25
69	**Mean**		54.78	602.52	2186.81	7546.33	0.36	215.53	751.45	1992.48	4072.66
	SD		80.79	276.77	887.13	3458.83	1.21	157.59	148.14	629.90	970.55
70	**Mean**		6.88	286.63	2060.10	7518.98		15.09	243.25	621.48	2019.45
	SD		19.87	198.46	740.90	4453.72		29.21	80.44	178.74	1563.14
71	**Mean**		1.47	114.25	1345.18	4831.21		24.67	317.25	779.63	3878.41
	SD		6.88	66.12	769.27	1744.96		49.15	77.03	307.21	3002.10
72	**Mean**		4.02	222.03	905.01	4656.76			16.58	698.36	3795.00
	SD		11.10	124.22	415.21	1841.61			44.80	275.66	3320.23
73	**Mean**		0.36	356.25	1147.90	5022.23			35.76	700.58	2468.79
	SD		1.71	246.64	348.93	2181.24			69.50	278.76	1548.33
74	**Mean**		19.98	176.66	1110.98	4429.47		3.20	162.73	562.29	2493.00

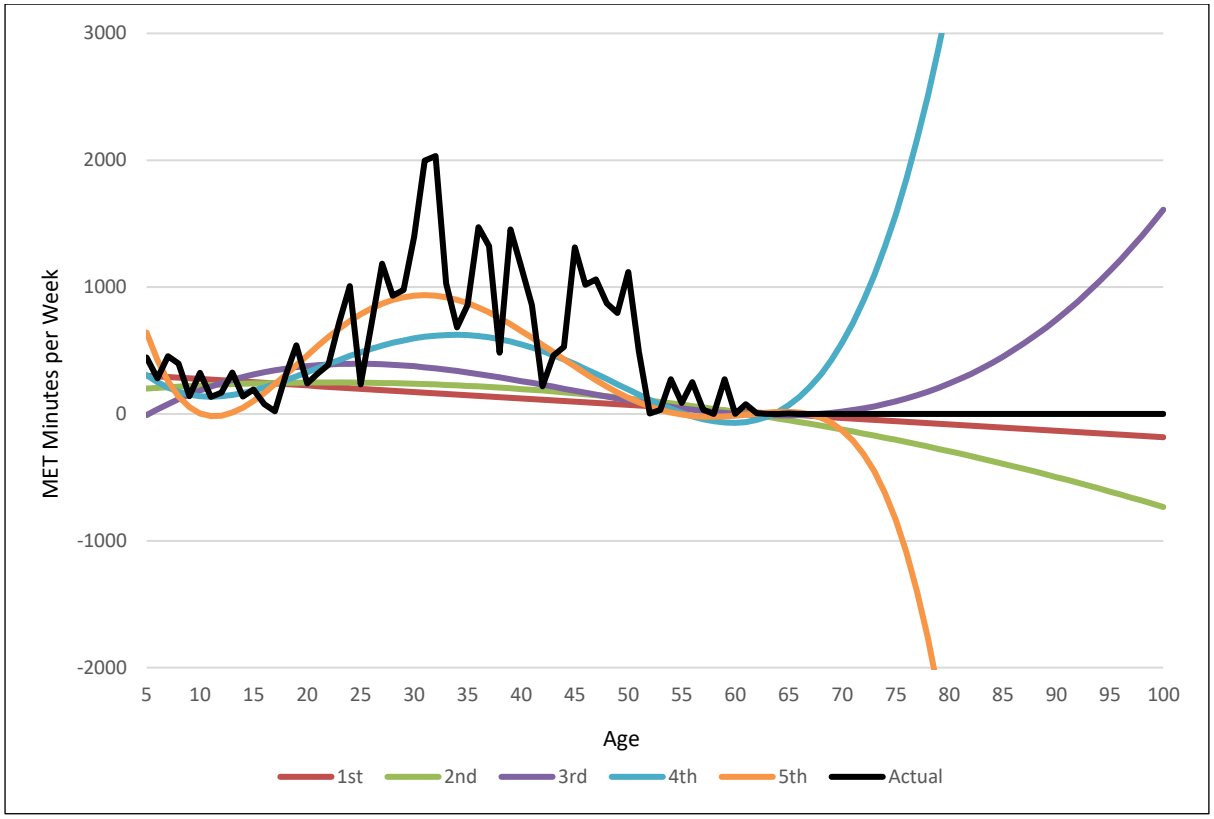
	SD	39.59	64.72	672.86	2594.49	9.90	92.46	242.19	1293.24
75	**Mean**	5.25	218.59	1075.94	8737.08	2.26	180.95	788.92	3127.29
	SD	13.87	110.62	418.75	17929.36	6.89	130.41	282.96	1284.30
76	**Mean**	3.11	261.81	933.95	4284.15		18.66	577.39	3328.08
	SD	13.54	165.15	379.38	1683.48		36.38	326.78	2632.14
77	**Mean**	4.99	196.91	801.07	3112.99			43.58	2918.97
	SD	13.29	115.53	144.42	2828.76			107.35	3099.97
78	**Mean**	8.94	204.70	789.75	2833.55		0.17	130.05	1588.63
	SD	22.68	75.93	312.53	1753.64		0.82	83.65	1362.68
79	**Mean**	2.48	191.75	782.00	3149.46		18.26	345.85	1533.78
	SD	8.94	128.02	260.61	2041.62		40.10	142.93	479.89
80	**Mean**		0.50	188.30	4856.96		0.00	63.17	834.77
	SD		2.00	170.94	7244.99		0.00	51.33	879.32
81	**Mean**	1.00	426.13	1207.94	3762.82		0.48	179.42	1541.83
	SD	3.46	181.71	205.72	4286.42		2.40	98.08	1458.98
82	**Mean**		27.98	610.88	3229.81		0.00	128.66	1235.19
	SD		59.77	258.69	2904.74		0.00	59.18	1441.79
83	**Mean**			5.38	1172.13			9.62	771.75
	SD			18.62	1199.31			26.34	1144.98
84	**Mean**		0.00	100.33	745.25			0.85	1056.21
	SD		0.00	49.65	442.38			2.79	2171.89
85	**Mean**		2.15	521.90	2116.40			10.36	513.00
	SD		8.33	407.35	1616.36			47.46	423.59
86	**Mean**		0.00	56.25	611.25			1.45	645.00
	SD		0.00	67.53	295.57			4.63	1173.25
87	**Mean**			0.00	41.25				20.15
	SD			0.00					71.47
88	**Mean**			0.33	153.19				28.38
	SD			1.15	160.98				76.10
89	**Mean**			0.00	64.50				85.25
	SD			0.00					306.73
90	**Mean**		0.00		700.00			0.00	548.50
	SD							0.00	75.66
91	**Mean**				10.75				27.64
	SD				26.33				103.43
92	**Mean**				0.00			0.00	610.17
	SD				0.00			0.00	914.68
93	**Mean**								877.00
	SD								2148.20
94	**Mean**		0.00		48.75				0.00
	SD								0.00
95	**Mean**				0.00				
	SD				0.00				
96	**Mean**			0.00	403.50				
	SD			0.00					
97	**Mean**						0.00		132.00
	SD								

98	**Mean**	0.00
	SD	
99	**Mean**	
	SD	
100	**Mean**	
	SD	

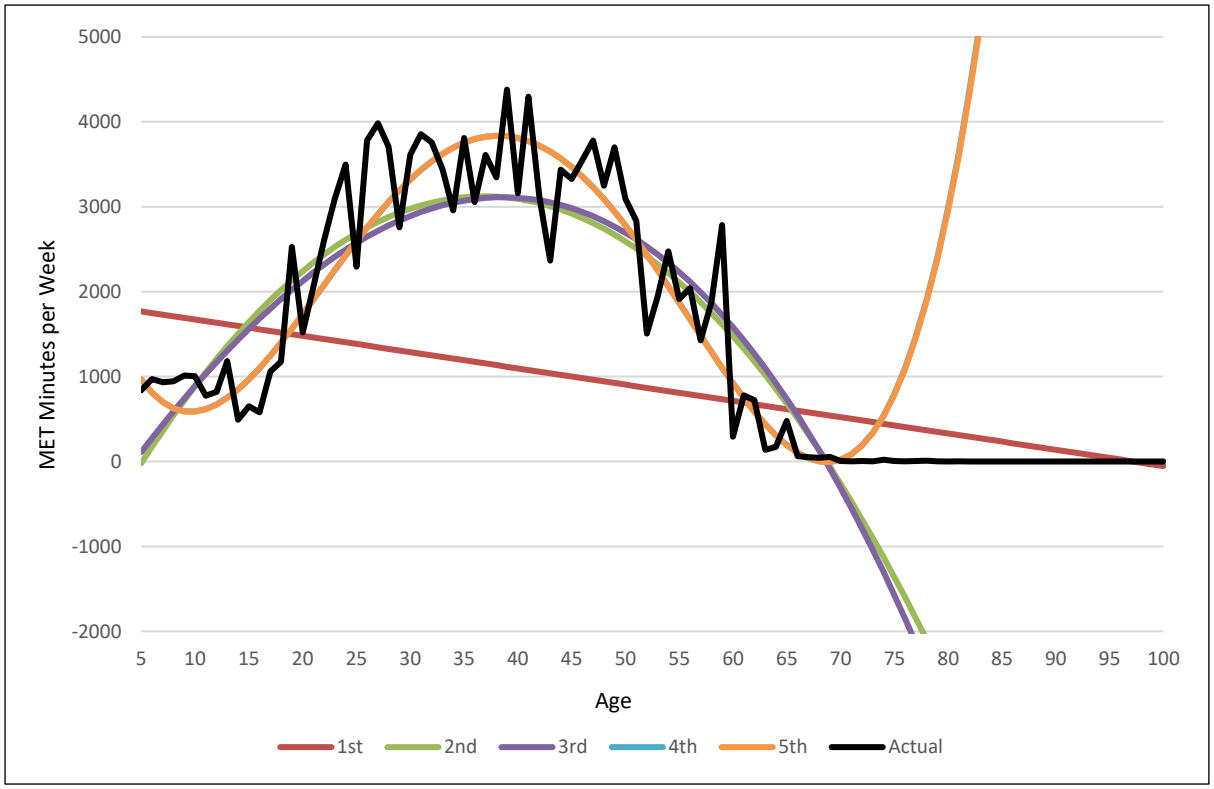
Appendix 29 - Table showing raw MET minutes per week scores for each quintile imported into the core model derived from Health Survey for England 2012 data, by age and sex

Age	Male					Female				
	Inactive	Barely	Some-what	Active	Highly	Inactive	Barely	Some-what	Active	Highly
5	445.7981	840.271	1728.935	2712.61	5417.714	249.2935	870.3201	1620.12	2977.596	5669.334
6	281.017	971.8802	1526.437	2728.202	4450.116	599.5415	200.9566	2023.787	2769.878	4076.906
7	454.289	931.8876	1842.592	3091.507	6282.678	680.0501	1125.873	1686.49	2478.035	4636.204
8	396.2426	944.3092	1441.622	2431.528	4444.09	586.6016	897.6632	1430.036	2096.634	4930.131
9	138.4779	1010.941	2297.013	3219.248	6114.912	442.0054	1161.61	1679.178	2830.411	5180.086
10	324.9014	1002.944	1843.217	2466.871	4085.812	351.2821	961.0201	1341.852	2045.894	4153.746
11	133.5666	775.1466	1950.804	3484.964	6542.832	346.1997	1101.791	1465.196	2060.936	5305.122
12	167.8633	818.9204	1565.527	2154.881	5997.725	355.6864	1148.712	1835.682	2676.242	4346.237
13	326.2133	1180.891	1489.315	2205.037	4691.029	297.2336	668.1863	1023.695	1593.142	3153.631
14	138.1564	492.4722	1492.247	2907.203	7641.892	34.63236	373.0242	873.5902	1767.395	3852.643
15	193.4157	649.9865	1206.979	1848.404	4598.967	120.4711	523.1442	968.4562	1761.497	3530.913

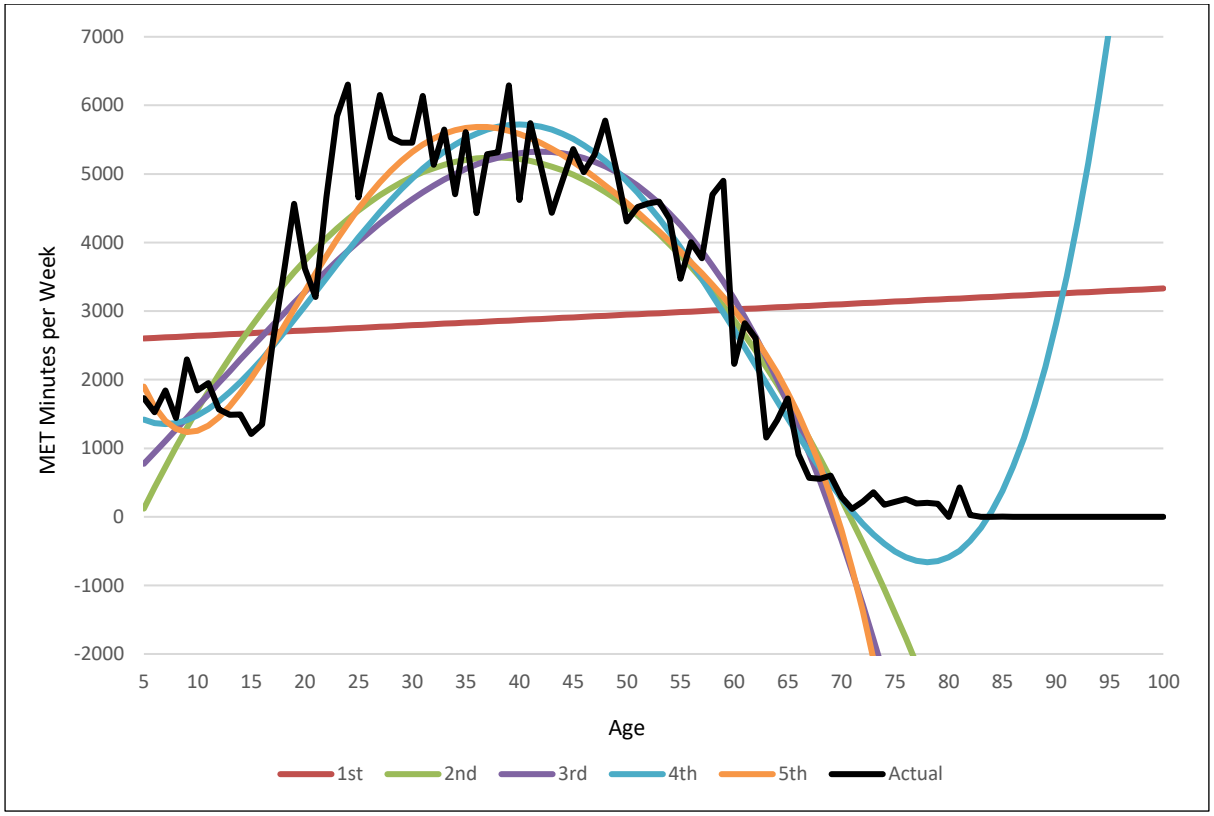
Appendix 30 - Table showing the updated childhood point estimates for each quintile used in the model, drawn from Health Survey for England 2012 data, following addition of school physical activity weightings derived from Health Survey for England 2015 data, by age and sex



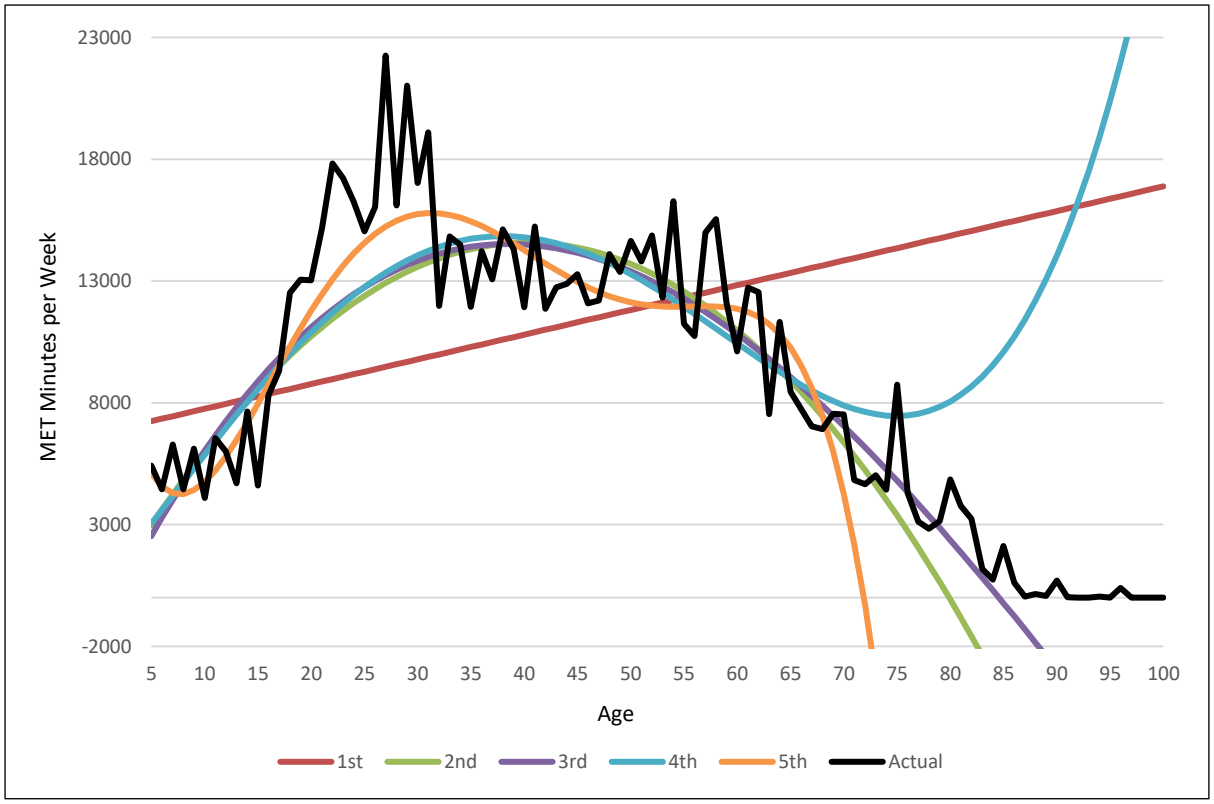
Appendix 31 - Line graph showing the relative fit of degrees of polynomial compared to raw data for the Male Inactive stratum



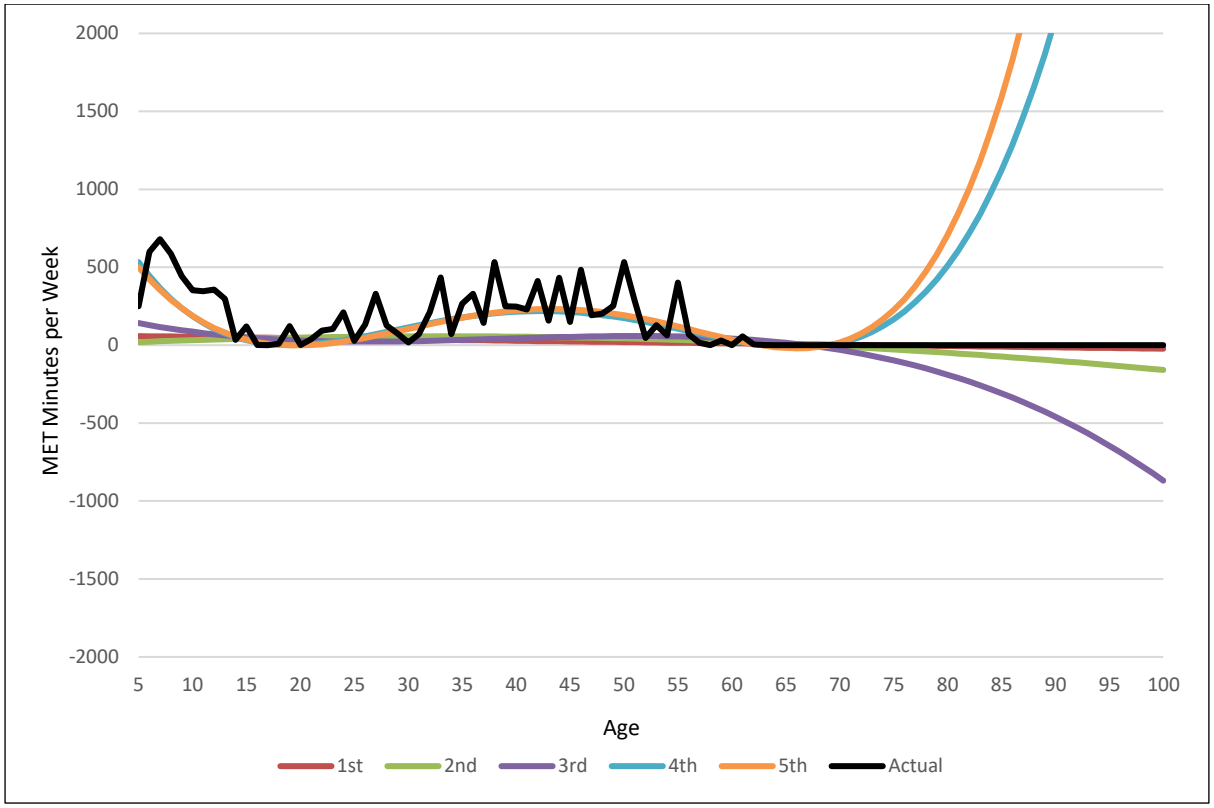
Appendix 32 - Line graph showing the relative fit of degrees of polynomial compared to raw data for the Male Barely Active stratum



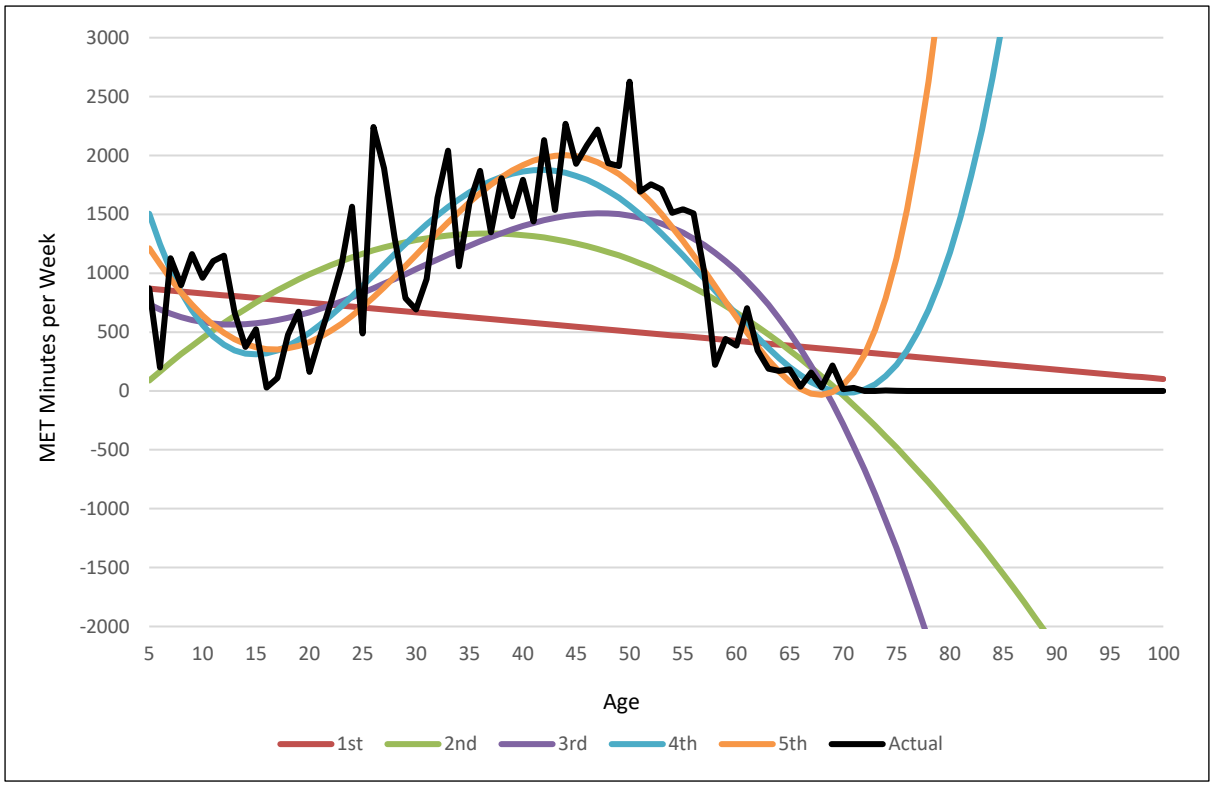
Appendix 33 - Line graph showing the relative fit of degrees of polynomial compared to raw data for the Male Somewhat Active stratum



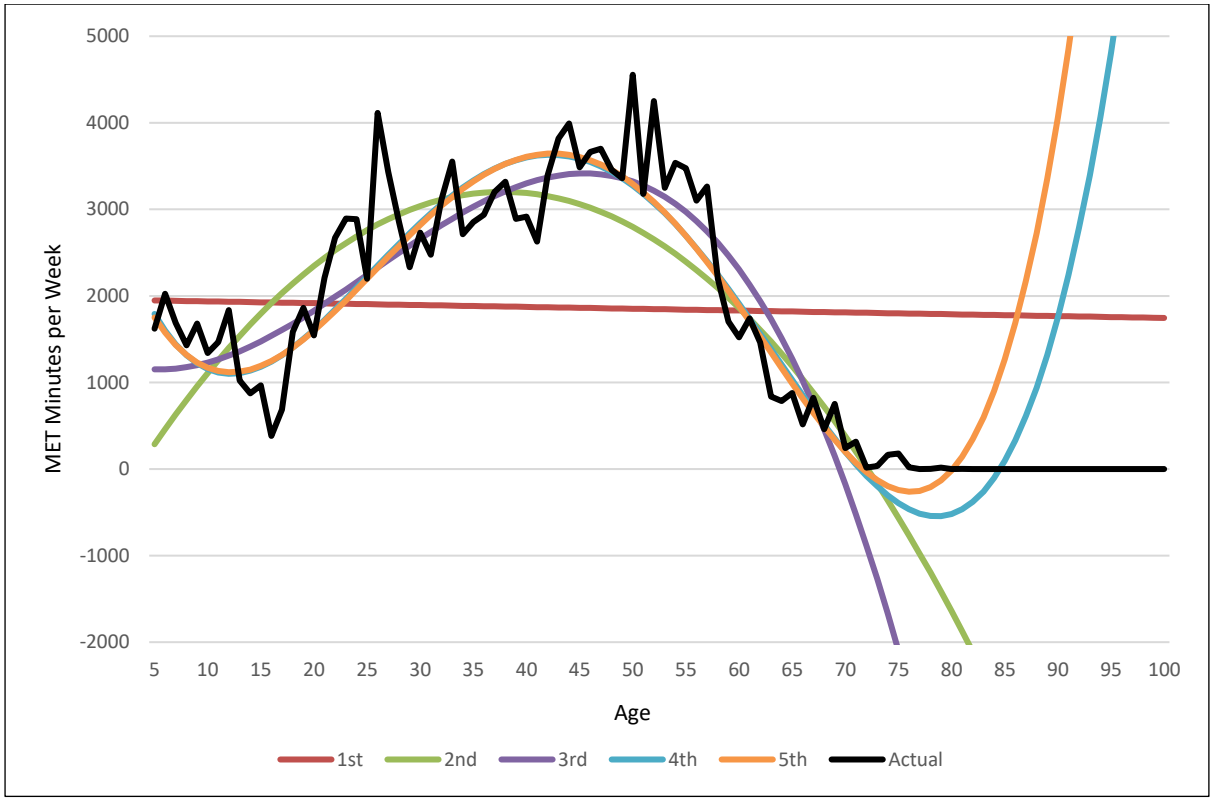
Appendix 34 - Line graph showing the relative fit of degrees of polynomial compared to raw data for the Male Highly Active stratum



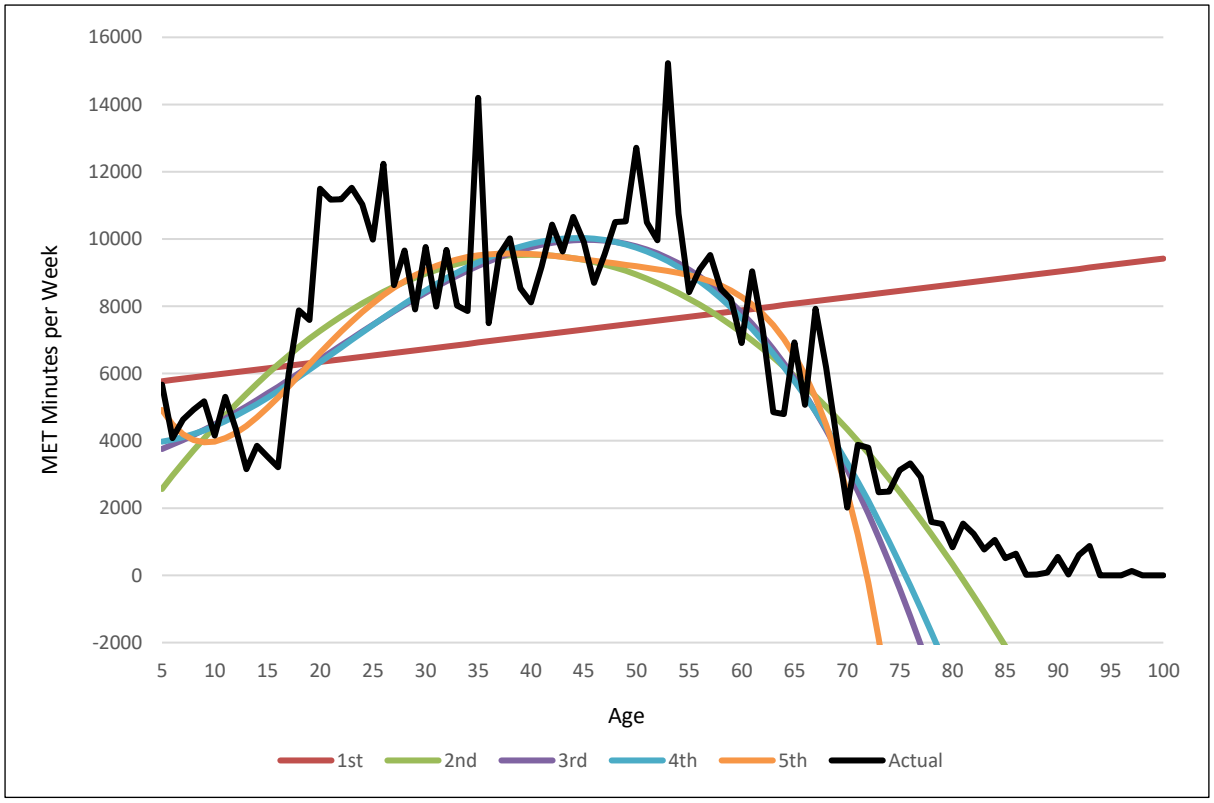
Appendix 35 - Line graph showing the relative fit of degrees of polynomial compared to raw data for the Female Inactive stratum



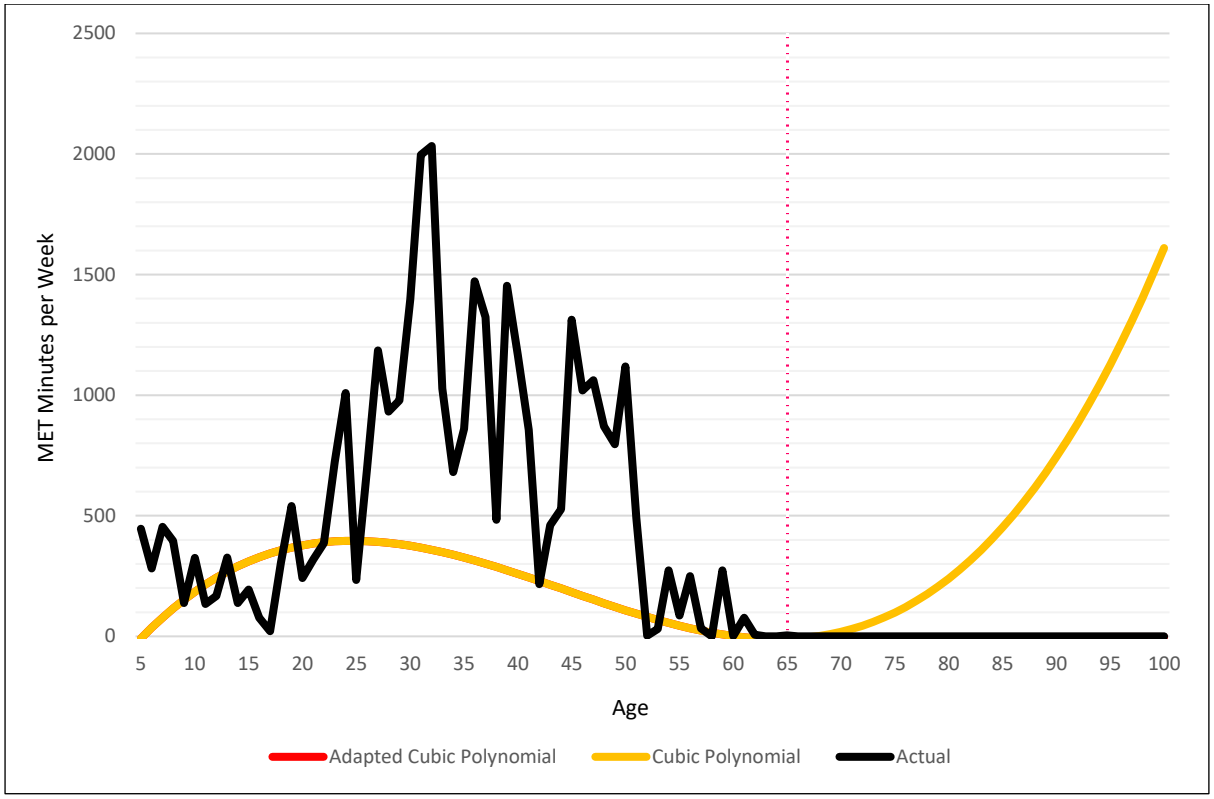
Appendix 36 - Line graph showing the relative fit of degrees of polynomial compared to raw data for the Female Barely Active stratum



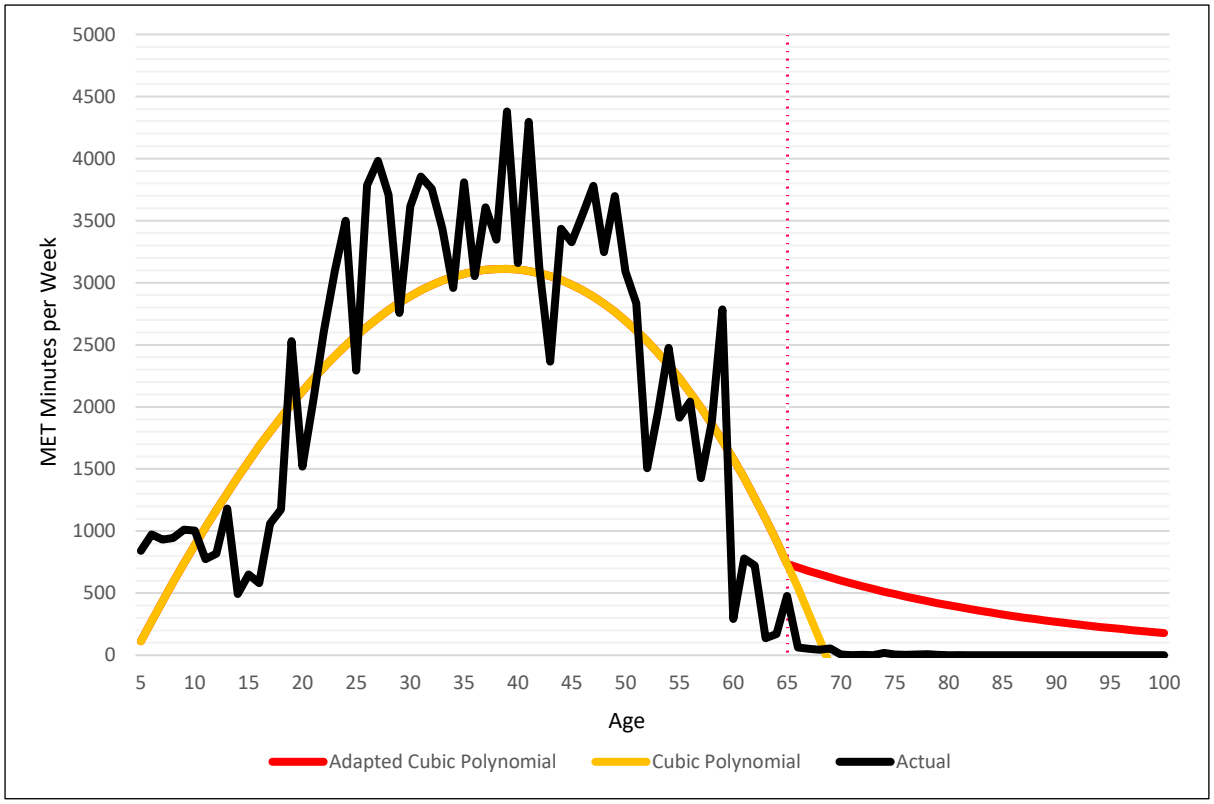
Appendix 37 - Line graph showing the relative fit of degrees of polynomial compared to raw data for the Female Somewhat Active stratum



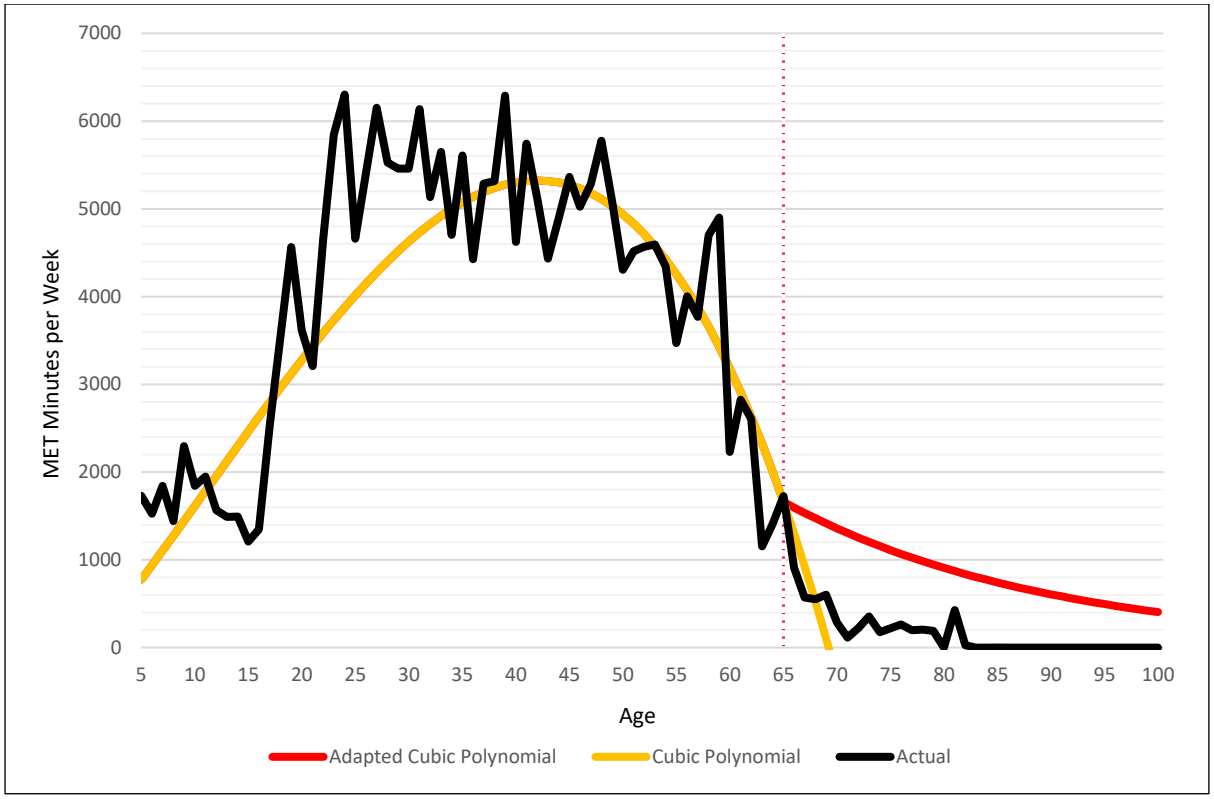
Appendix 38 - Line graph showing the relative fit of degrees of polynomial compared to raw data for the Female Highly Active stratum



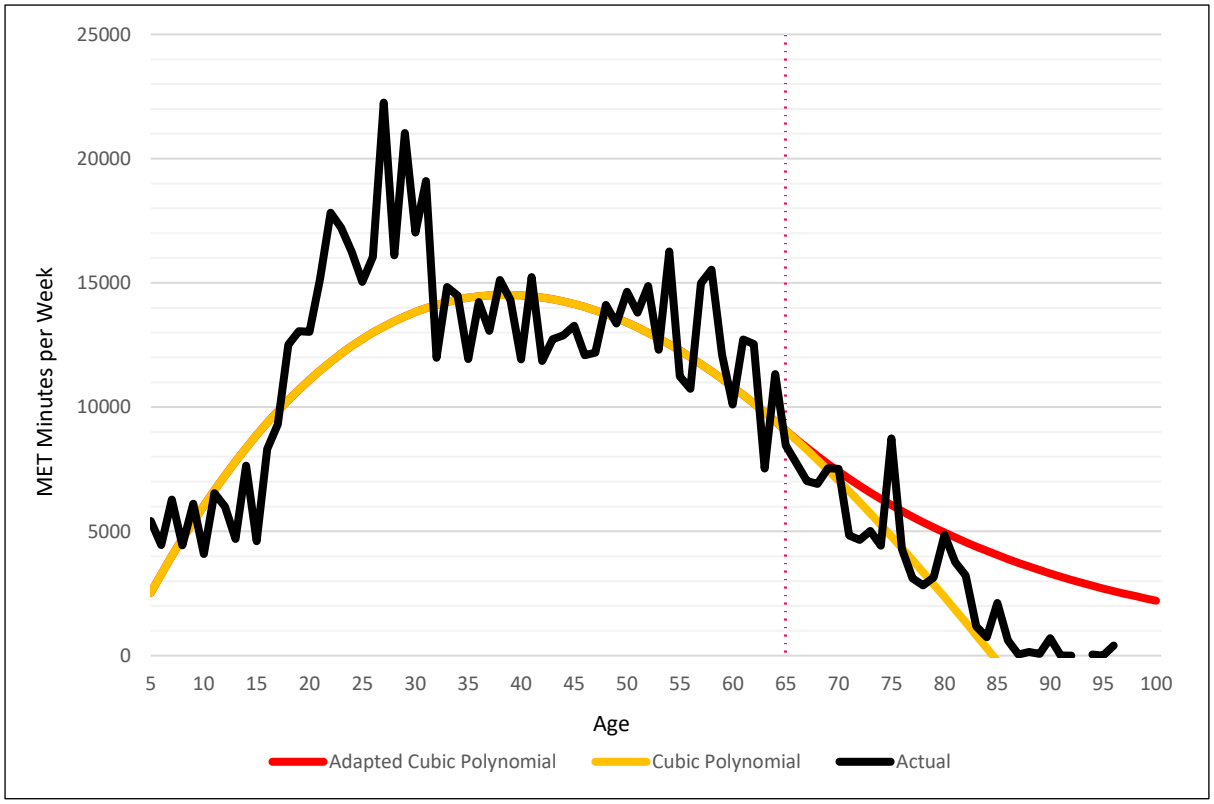
Appendix 39 - Line graph showing actual data, cubic polynomial, and cubic polynomial with forced exponential decay after 65 years for Male Inactive stratum



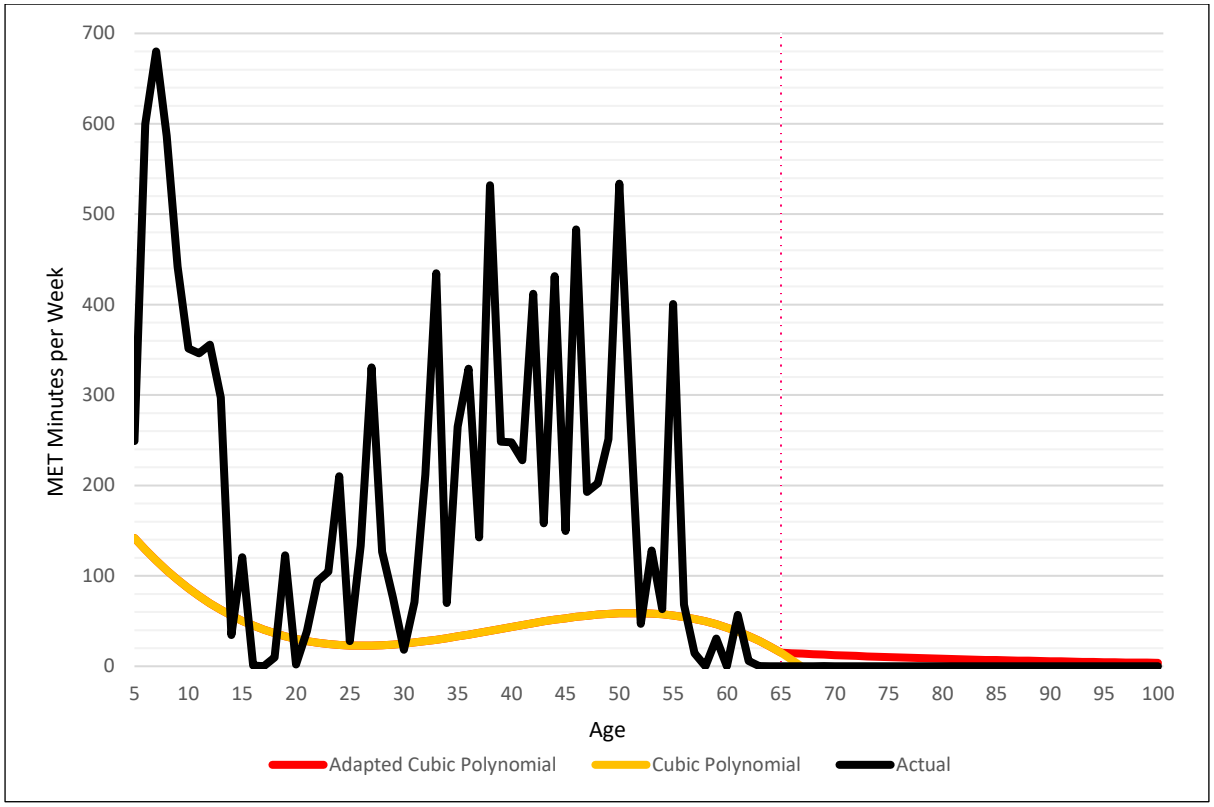
Appendix 40 - Line graph showing actual data, cubic polynomial, and cubic polynomial with forced exponential decay after 65 years for Male Barely Active stratum



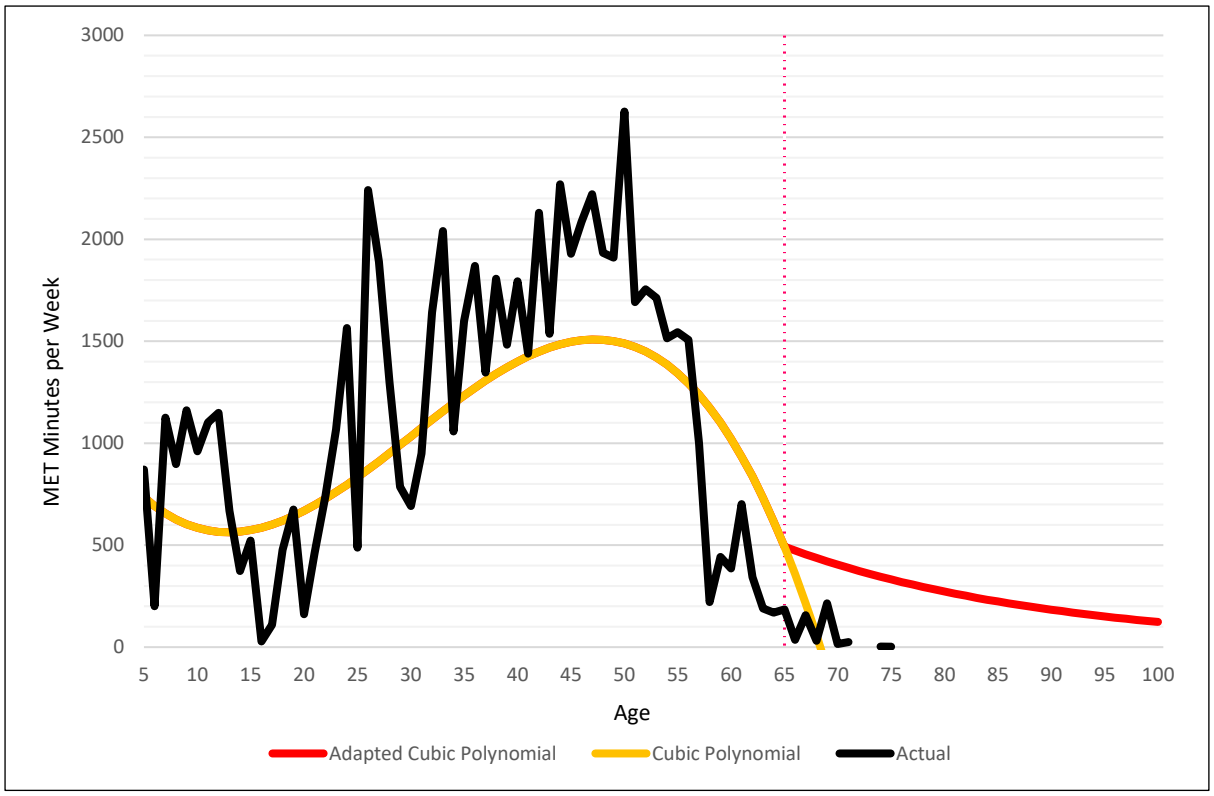
Appendix 41 - Line graph showing actual data, cubic polynomial, and cubic polynomial with forced exponential decay after 65 years for Male Somewhat Active stratum



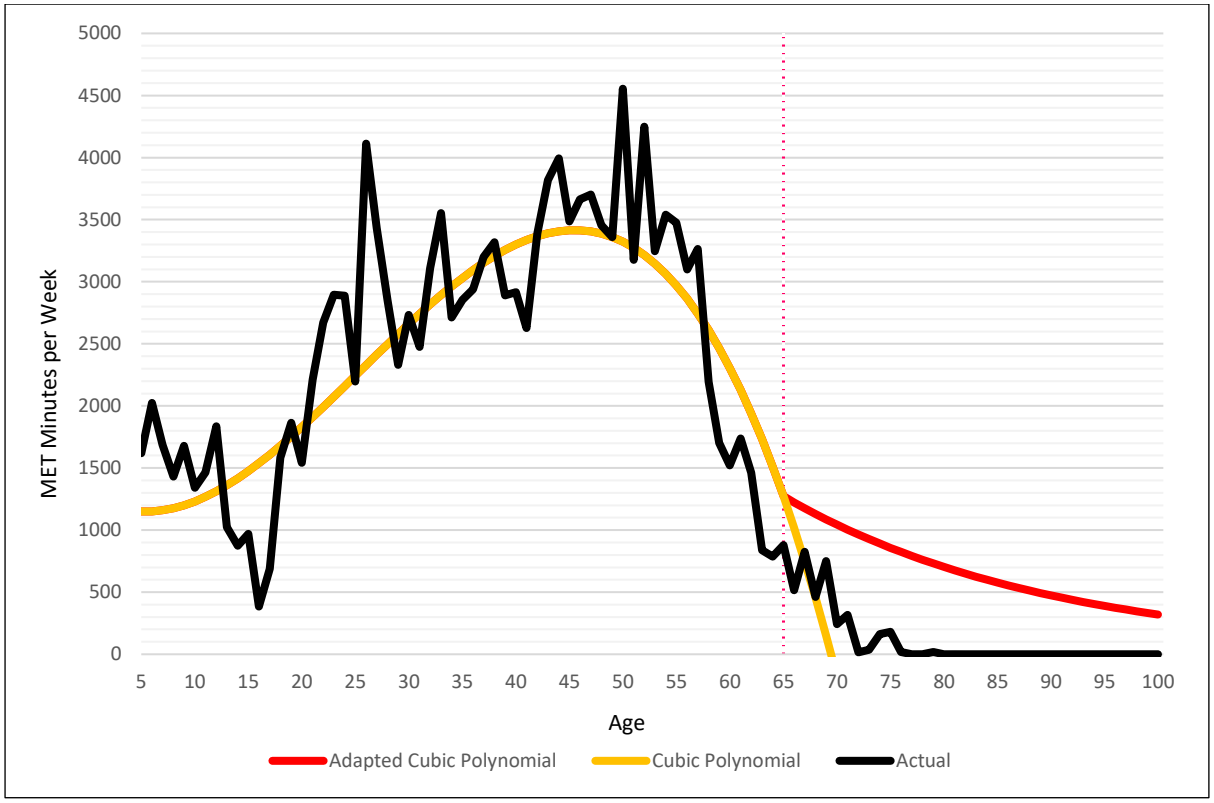
Appendix 42 - Line graph showing actual data, cubic polynomial, and cubic polynomial with forced exponential decay after 65 years for Male Highly Active stratum



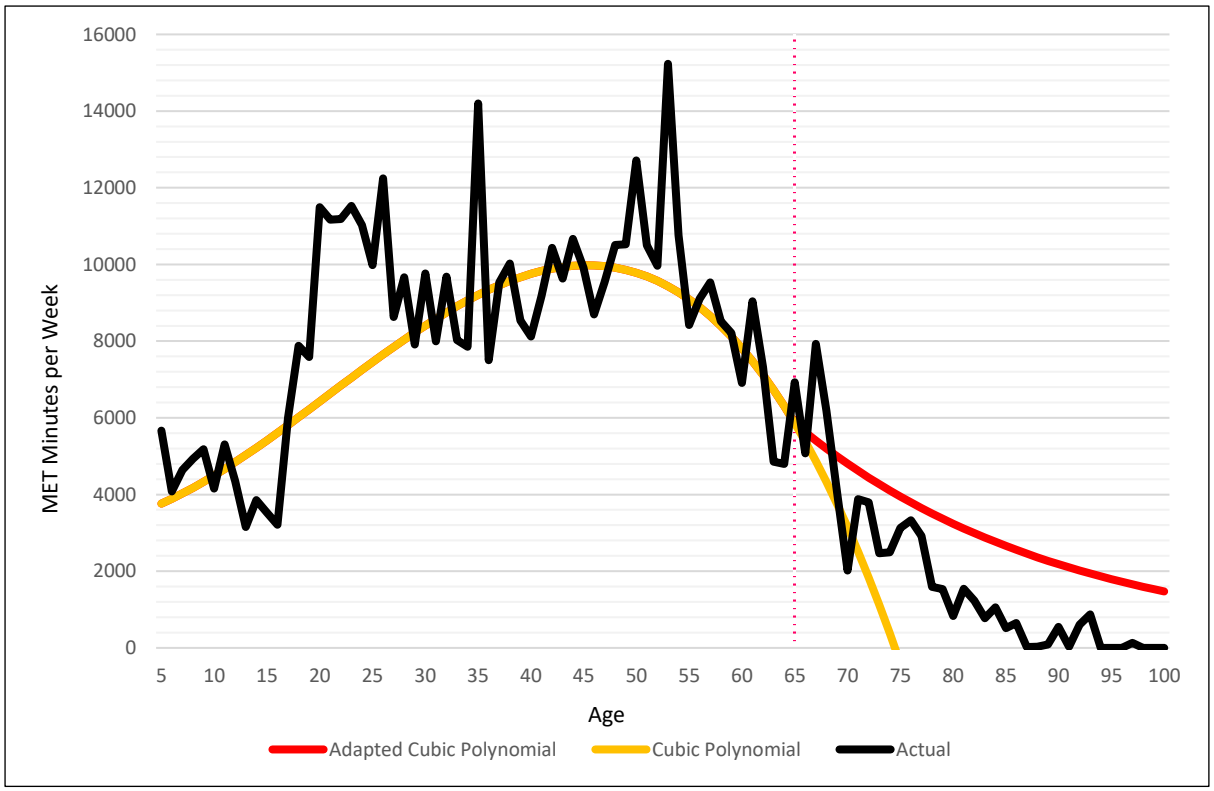
Appendix 43 - Line graph showing actual data, cubic polynomial, and cubic polynomial with forced exponential decay after 65 years for Female Inactive stratum



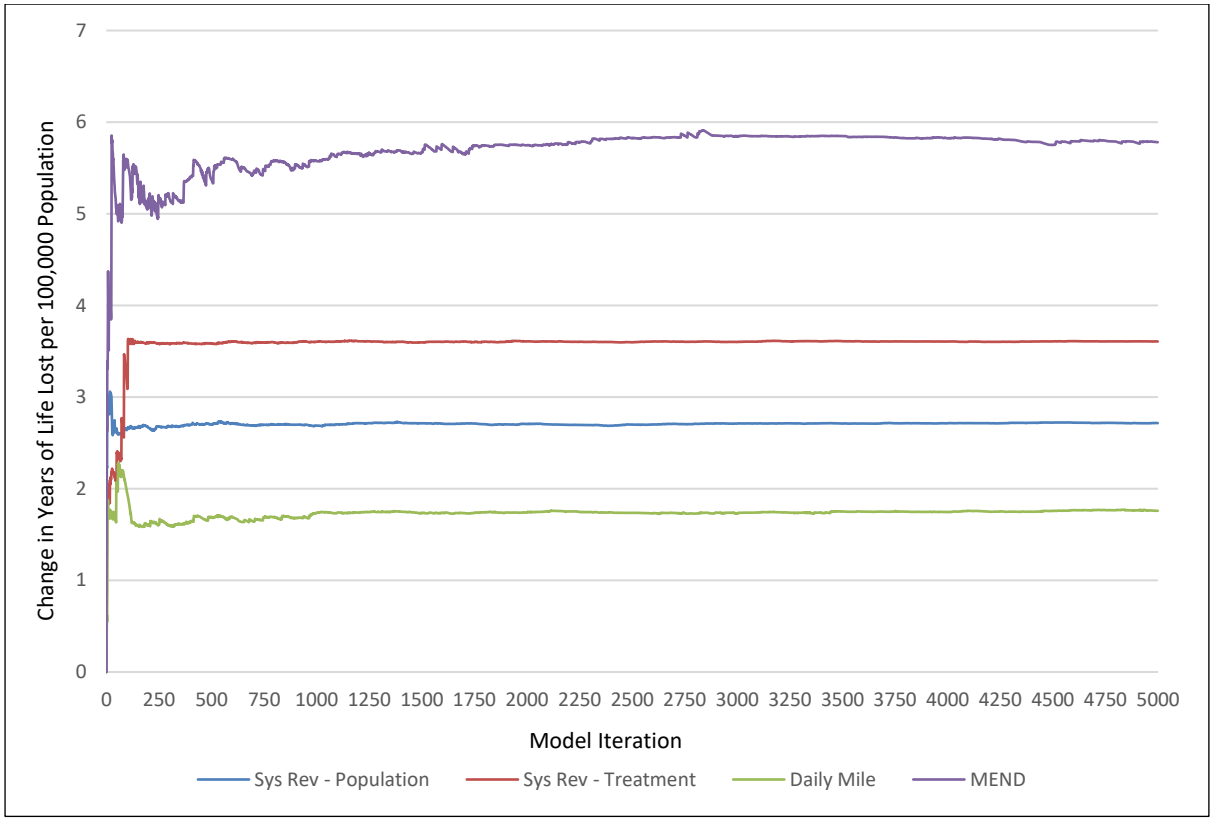
Appendix 44 - Line graph showing actual data, cubic polynomial, and cubic polynomial with forced exponential decay after 65 years for Female Barely Active stratum



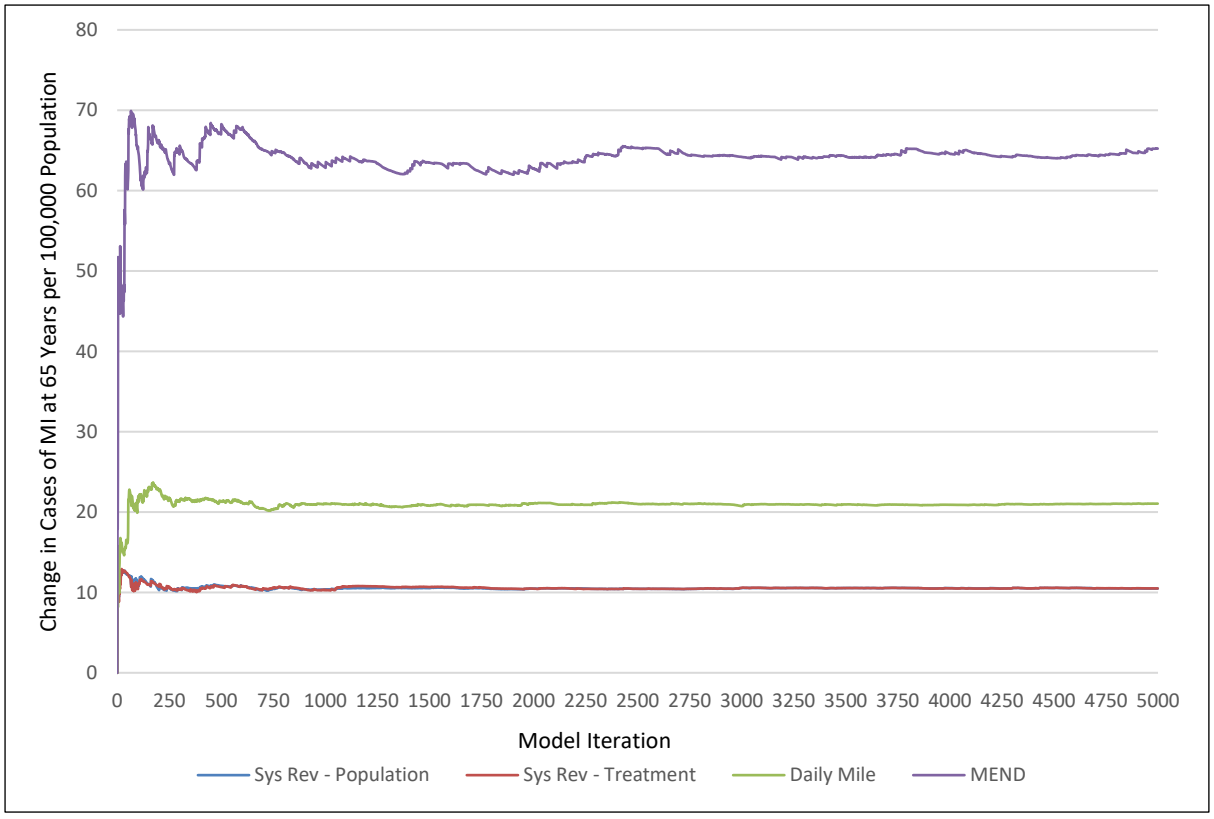
Appendix 45 - Line graph showing actual data, cubic polynomial, and cubic polynomial with forced exponential decay after 65 years for Female Somewhat Active stratum



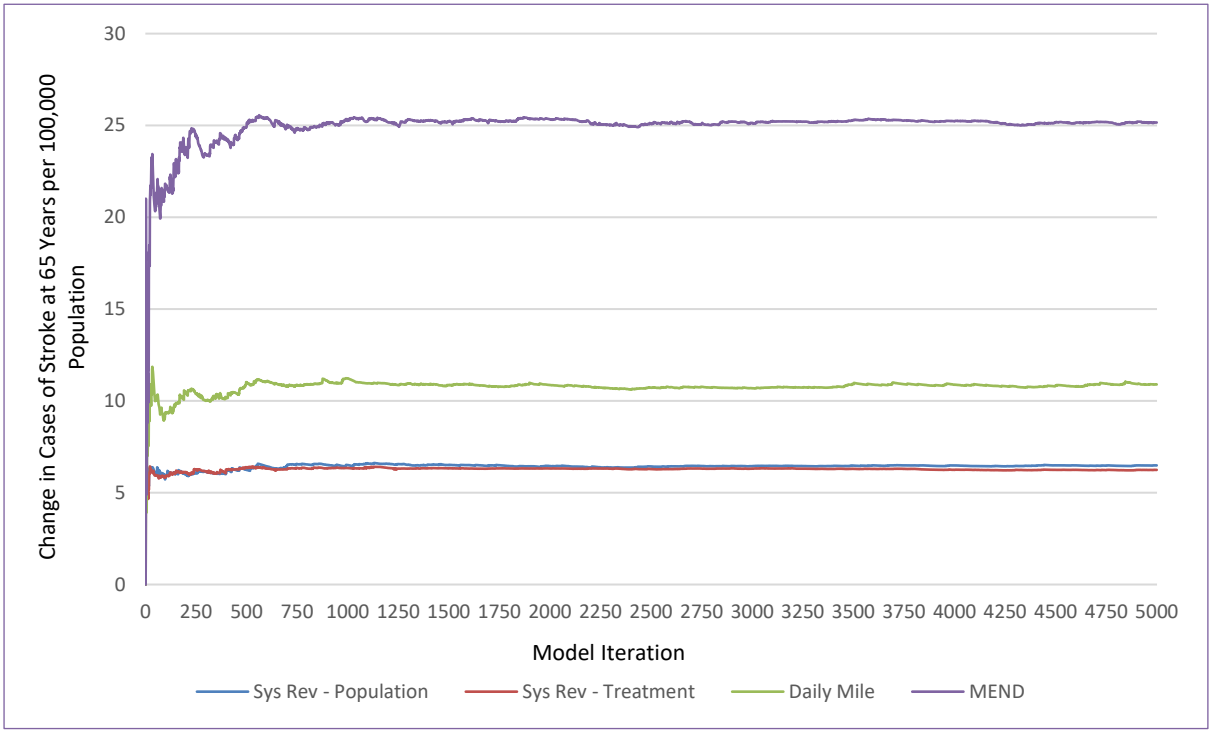
Appendix 46 - Line graph showing actual data, cubic polynomial, and cubic polynomial with forced exponential decay after 65 years for Female Highly Active stratum



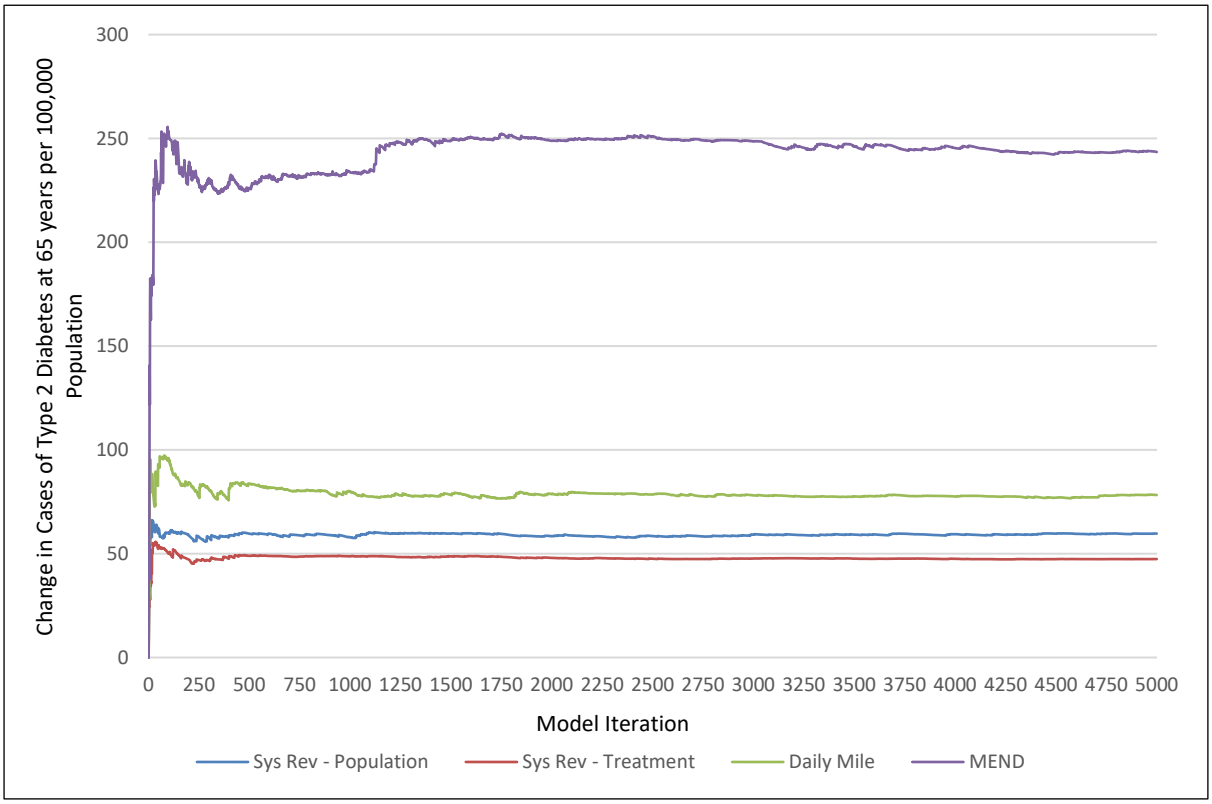
Appendix 47 - Line graph showing stability of confidence interval for years of life lost per 100,000 population against number of iterations for each counterfactual scenario



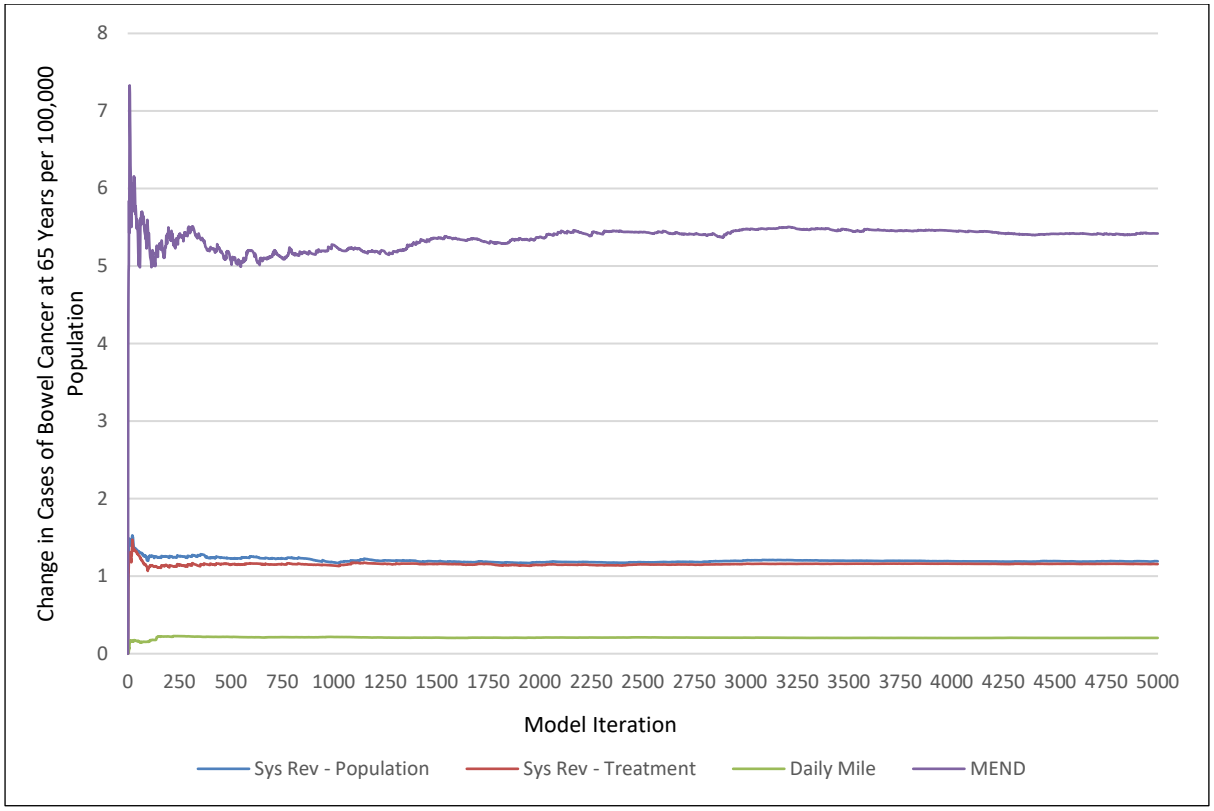
Appendix 48 - Line graph showing stability of confidence interval for change in prevalent cases of myocardial infarction at 65 years of age per 100,000 population against number of iterations for each counterfactual scenario



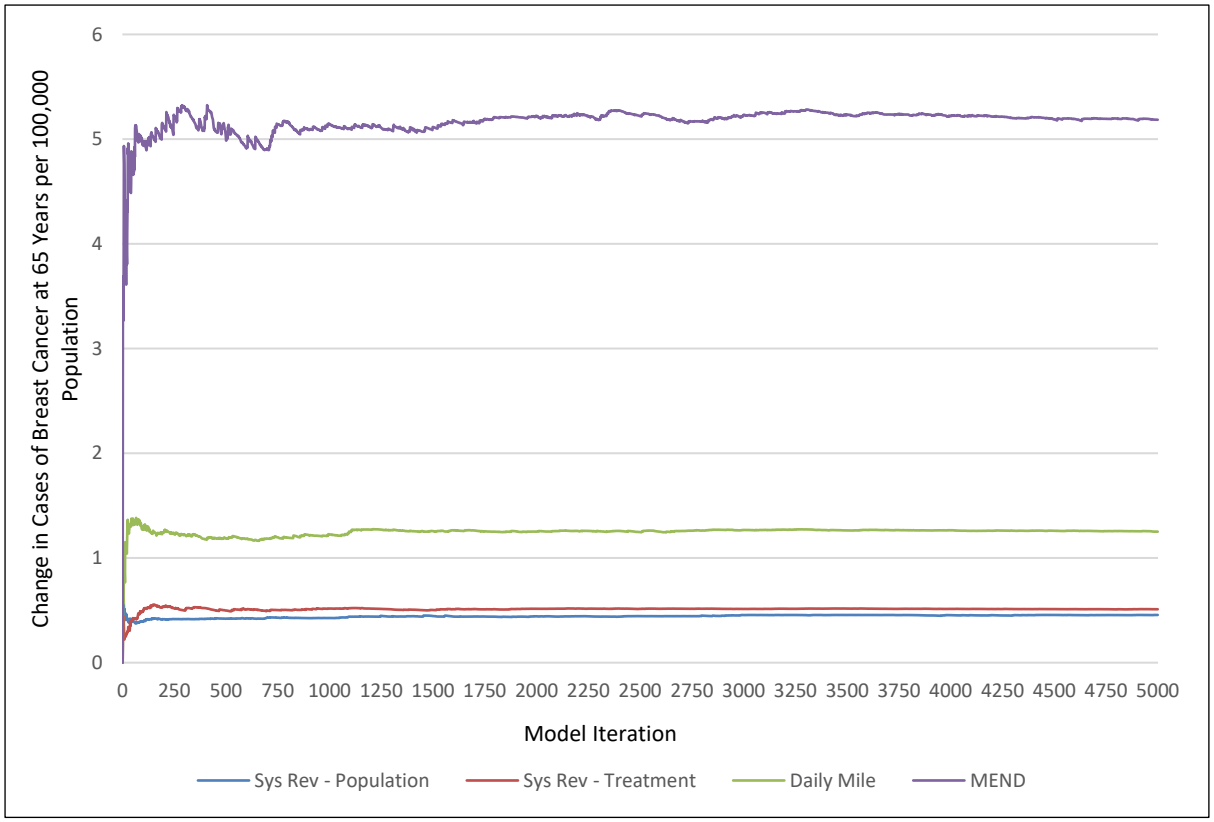
Appendix 49 - Line graph showing stability of confidence interval for change in prevalent cases of stroke at 65 years of age per 100,000 population against number of iterations for each counterfactual scenario



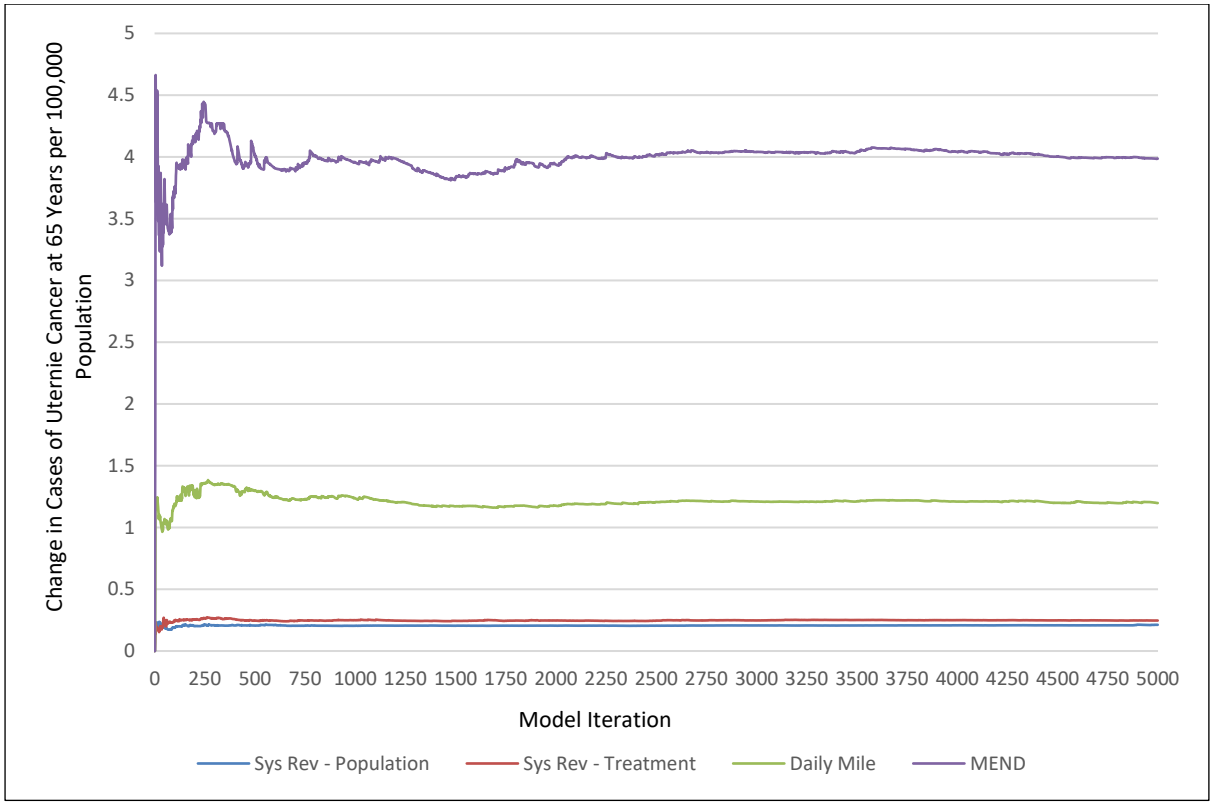
Appendix 50 - Line graph showing stability of confidence interval for change in prevalent cases of type 2 diabetes at 65 years of age per 100,000 population against number of iterations for each counterfactual scenario



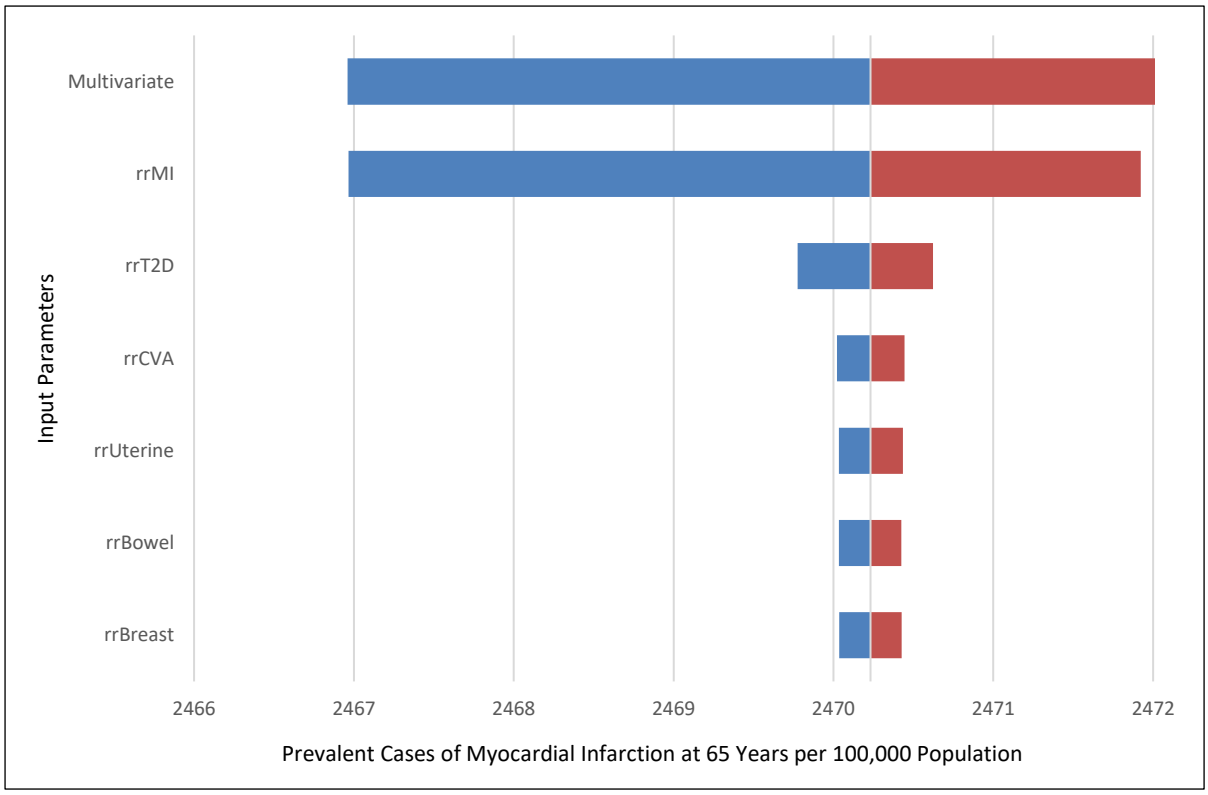
Appendix 51 - Line graph showing stability of confidence interval for change in prevalent cases of bowel cancer at 65 years of age per 100,000 population against number of iterations for each counterfactual scenario



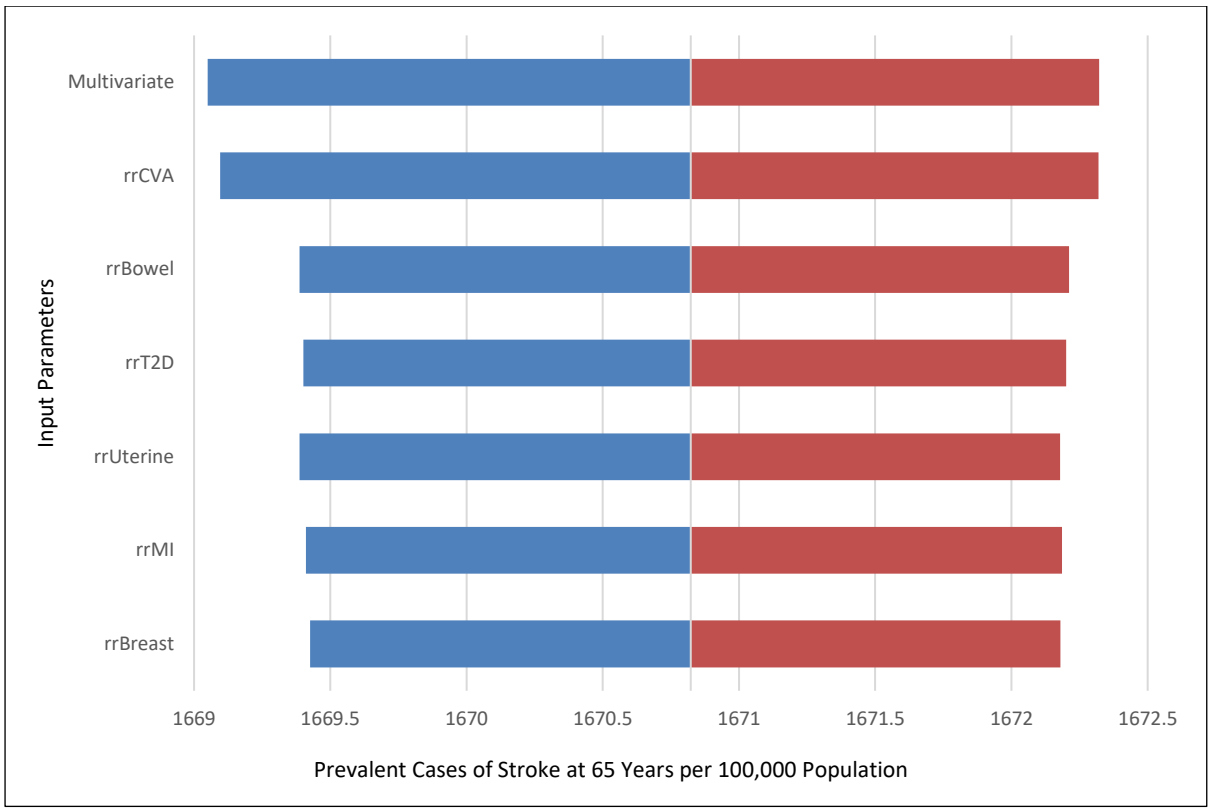
Appendix 52 - Line graph showing stability of confidence interval for change in prevalent cases of breast cancer at 65 years of age per 100,000 population against number of iterations for each counterfactual scenario



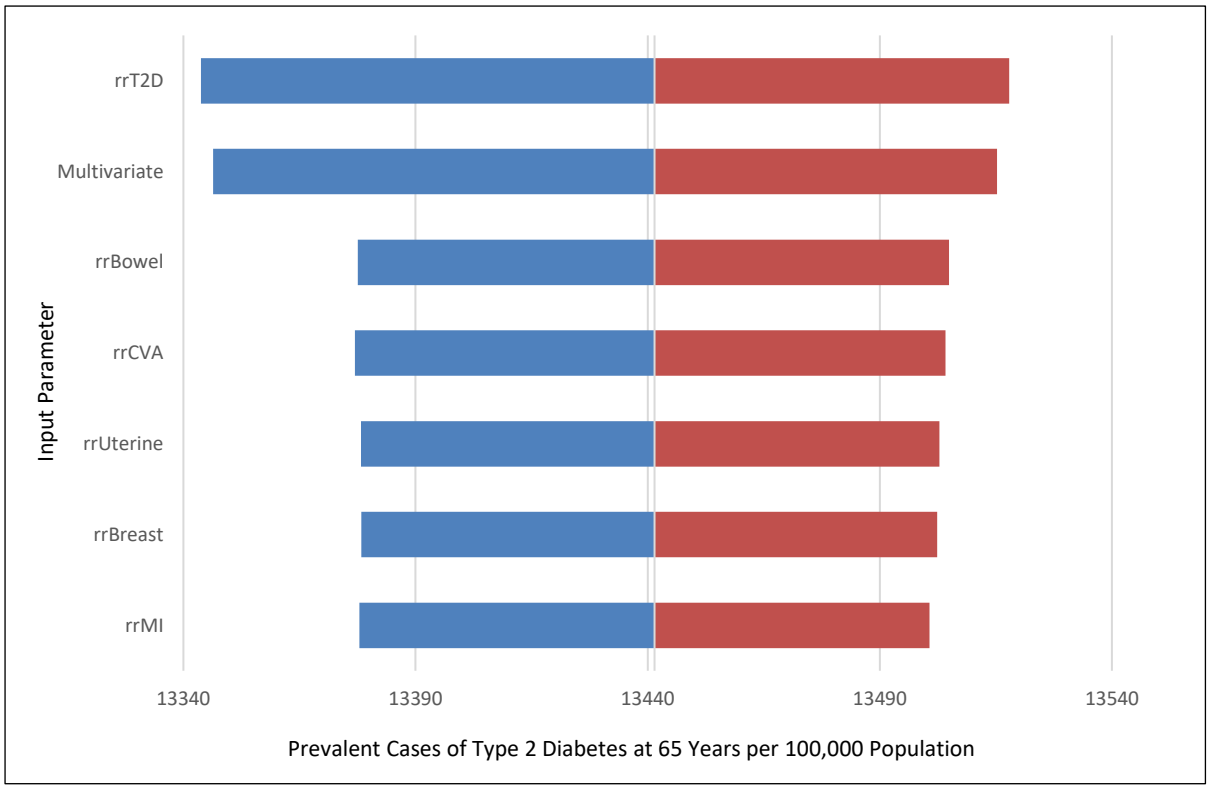
Appendix 53 - Line graph showing stability of confidence interval for prevalent cases of uterine cancer at 65 years of age per 100,000 population against number of iterations for each counterfactual scenario



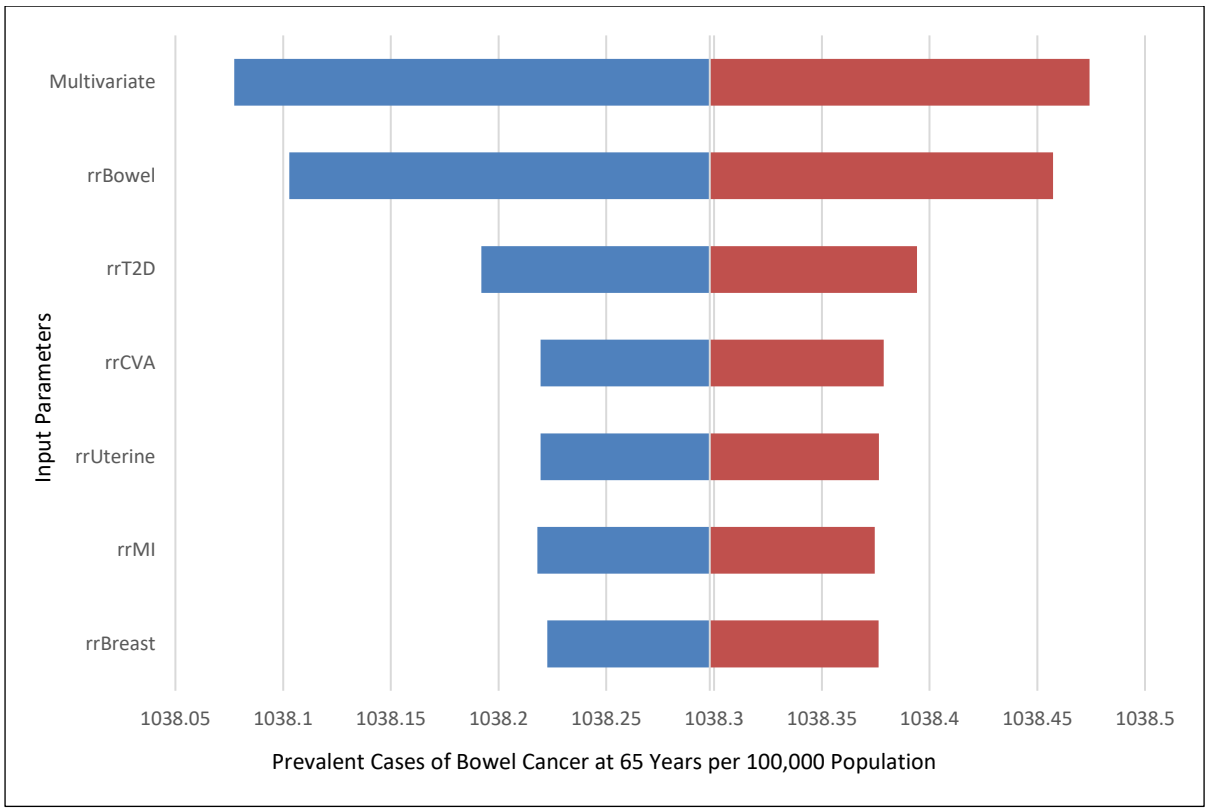
Appendix 54 - Tornado plot showing the sensitivity of the estimate for prevalent cases of myocardial infarction at 65 years of age (2470.23) per 100,000 population due to uncertainty within specific input parameters within the baseline model



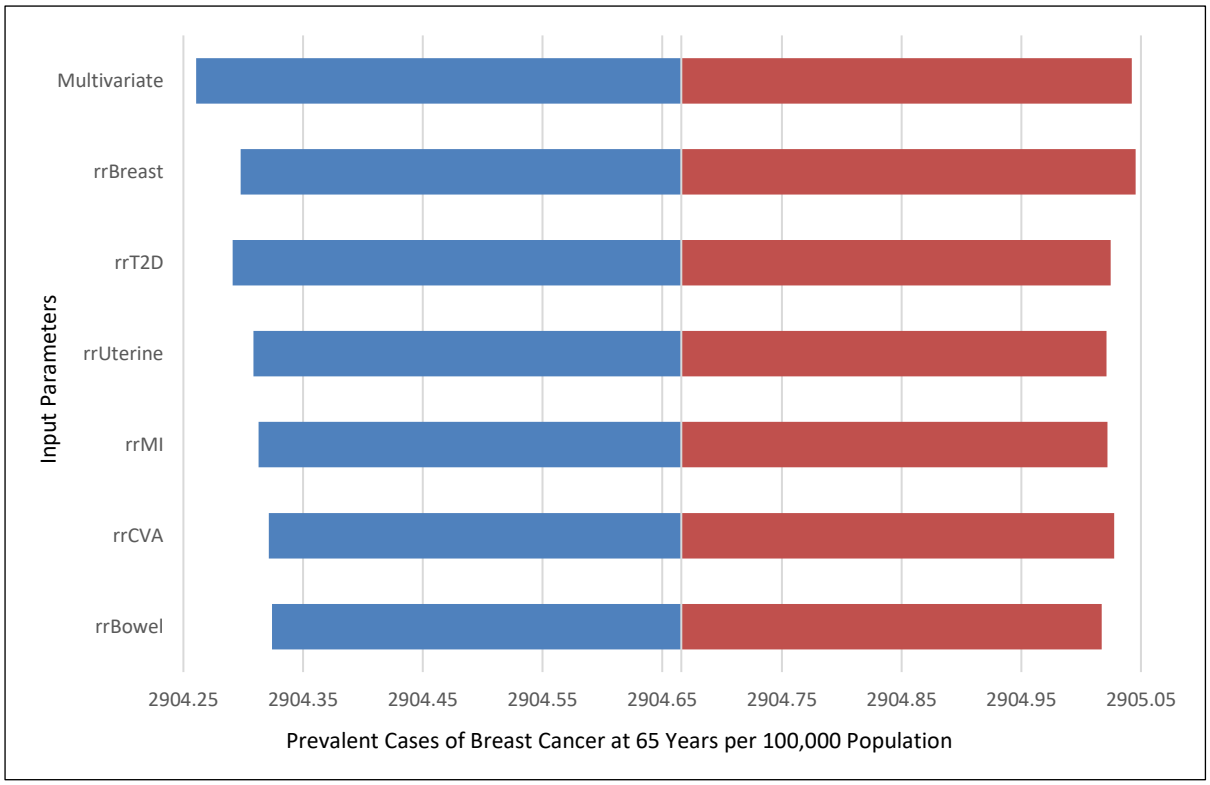
Appendix 55 - Tornado plot showing the sensitivity of the estimate for prevalent cases of stroke at 65 years of age (1670.82) per 100,000 population due to uncertainty within specific input parameters within the baseline model



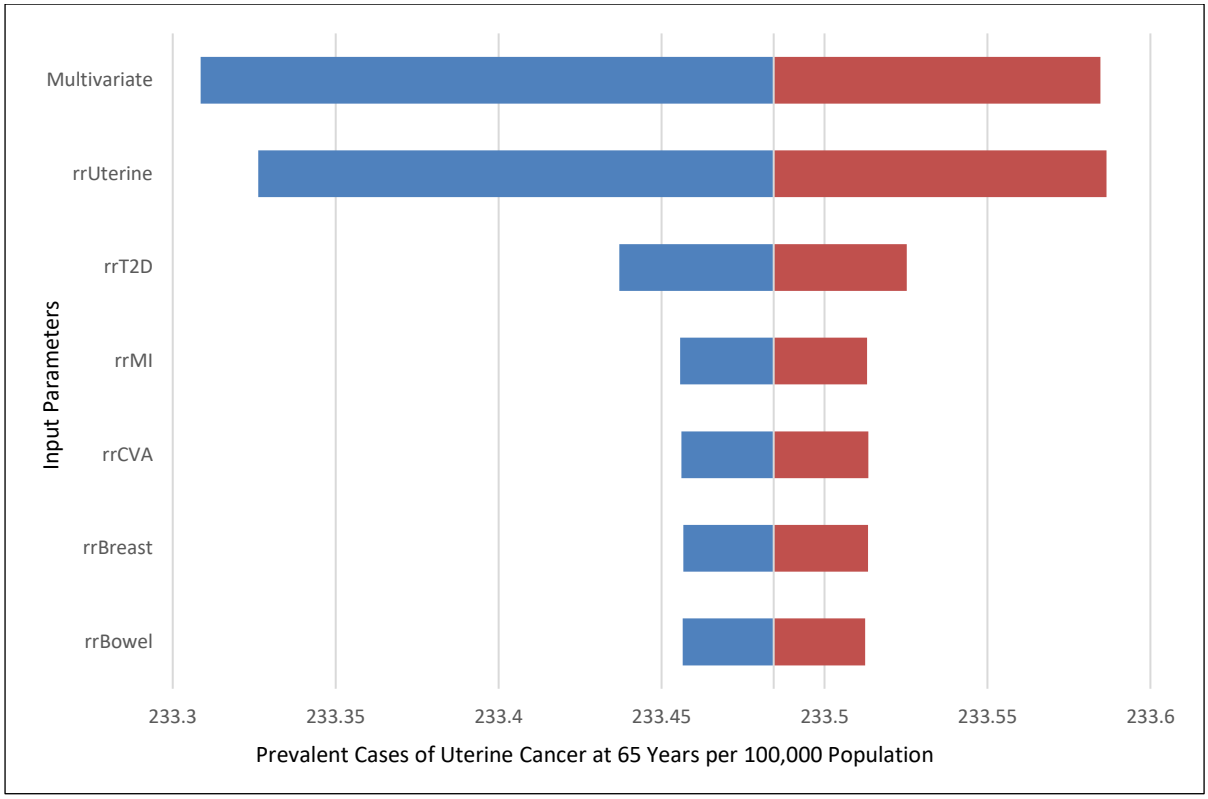
Appendix 56 - Tornado plot showing the sensitivity of the estimate for prevalent cases of type 2 diabetes at 65 years of age (13441.48) per 100,000 population due to uncertainty within specific input parameters within the baseline model



Appendix 57 - Tornado plot showing the sensitivity of the estimate for prevalent cases of bowel cancer at 65 years of age (1038.29) per 100,000 population due to uncertainty within specific input parameters within the baseline model



Appendix 58 - Tornado plot showing the sensitivity of the estimate for prevalent cases of breast cancer at 65 years of age (2904.67) per 100,000 population due to uncertainty within specific input parameters within the baseline model



Appendix 59 - Tornado plot showing the sensitivity of the estimate for prevalent cases of uterine cancer at 65 years of age (233.48) per 100,000 population due to uncertainty within specific input parameters within the baseline model

PubMed, MEDLINE, SportDiscus, Google Scholar	*child* OR adolescen* OR "young people"* *AND* *"physical activity" OR sport* OR cycl* OR walk* OR "physical education" OR "television view*" OR "tv view*" OR sedentary OR danc* OR "physical inactivity" OR "physical fitness" OR lifestyle OR exercise OR screen time OR "active travel*" OR commut** *AND* *clinical trial OR control* trial OR random* OR trial OR evaluation OR effect* OR random* sample OR control**
EMBASE, ScienceDirect, PsychINFO	1. child* 2. adolecen* 3. "young people" 4. 1 OR 2 OR 3 5. "physical activity" 6. sport* 7. cycl* 8. walk* 9. "physical education" 10. "television view*" 11. "tv view*" 12. sedentary 13. danc* 14. "physical inactivity" 15. "physical fitness" 16. lifestyle 17. exercise 18. screen time 19. "active travel" 20. commut* 21. 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 22. clinical trial 23. control* trial 24. random* 25. trial 26. evaluation 27. effect* 28. random* sample 29. control* 30. 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 31. 4 AND 21 AND 30

Appendix 60 - Table of search terms for the searching of databases: PubMed, MEDLINE, EMBASE, PsychINFO, ScienceDirect, SportDiscus and Google Scholar)

PA – Physical Activity, MPA – Moderate Physical Activity, VPA – Vigorous Physical Activity, MVPA – Moderate to Vigorous Physical Activity, FU – Follow-Up

Basics	Lead Author
	Year
	Country
	Study
Participants	Baseline n
Primary Intervention	n
	% Female
	Baseline Age Non-Stratified
	Baseline Age Boys
	Baseline Age Girls
	Baseline BMI Non-Stratified
	Baseline BMI Boys
	Baseline BMI Girls
	Baseline BMI SD
	Baseline BMI %ile Boys
	Baseline BMI %ile Girls
	% Overweight
	% Overweight Boys
	% Overweight Girls
	% Obese Non-Stratified
	% Obese Boys
	% Obese Girls
	Baseline zBMI Non-Stratified
	Baseline zBMI Boys

	Baseline zBMI Girls
	Baseline Global PA Non-Stratified
	Baseline Global PA Boys
	Baseline Global PA Girls
	Of What
	Baseline Global PA SD
	Baseline MVPA Non-Stratified
	Baseline MVPA Boys
	Baseline MVPA Girls
	Baseline MPA Non-Stratified
	Baseline MPA Boys
	Baseline MPA Girls
	Baseline VPA Non-Stratified
	Baseline VPA Boys
	Baseline VPA Girls
	Of What
	Baseline MVPA SD
Secondary Intervention	n
	% Female
	Baseline Age Non-Stratified
	Baseline Age Boys
	Baseline Age Girls
	Baseline BMI Non-stratified
	Baseline BMI Boys
	Baseline BMI Girls
	Baseline BMI SD
	% Overweight

	% Overweight Boys
	% Overweight Girls
	% Obese
	% Obese Boys
	% Obese Girls
	Baseline zBMI
	Baseline Global PA Non-Stratified
	Baseline Global PA Boys
	Baseline Global PA Girls
	Baseline MVPA
	Baseline MVPA Boys
	Baseline MVPA SD
	Baseline MPA Non-Stratified
	Baseline MPA Boys
	Baseline MPA Girls
	Baseline VPA Boys
	Baseline VPA Girls
Tertiary Intervention	n
	% Female
	Baseline Age
	Baseline BMI
	% Overweight
	% Obese
	% Obese Boys
	% Obese Girls
	Baseline zBMI
	Baseline Global PA Non-Stratified

	Baseline Global PA Boys
	Baseline Global PA Girls
	Baseline MVPA
	Baseline MVPA Boys
	Baseline MVPA Girls
	Baseline MPA Boys
	Baseline MPA Girls
	Baseline VPA Non-Stratified
	Baseline VPA Boys
	Baseline VPA Girls
Control	n
	% Female
	Baseline Age Non-Stratified
	Baseline Age Boys
	Baseline Age Girls
	Baseline BMI Non-Stratified
	Baseline BMI Boys
	Baseline BMI Girls
	Baseline BMI SD
	Baseline BMI %ile Boys
	Baseline BMI %ile Girls
	% Overweight
	% Overweight Boys
	% Overweight Girls
	% Obese
	% Obese Boys
	% Obese Girls

	Baseline zBMI Non-Stratified
	Baseline zBMI Boys
	Baseline zBMI Girls
	Baseline Global PA Non-Stratified
	Baseline Global PA Boys
	Baseline Global PA Girls
	Of What
	Baseline Global PA SD
	Baseline MVPA Non-Stratified
	Baseline MVPA Boys
	Baseline MVPA Girls
	Baseline MPA Non-Stratified
	Baseline MPA Boys
	Baseline MPA Girls
	Baseline VPA Non-Stratified
	Baseline VPA Boys
	Baseline VPA Girls
	Of What
	Baseline MVPA SD
Secondary Control	n
	% Female
	Baseline Age
	Baseline BMI
	Baseline BMI SD
	Baseline Global PA Boys
	Baseline Global PA SD
	Baseline MVPA Boys

	Baseline MVPA SD
Supplemental	SES
	Ethnic
Study	Duration of Intervention (Months)
	Intervention Setting
	Intervention Type
	Frequency of Contact
	Theory
	Prevent Treat
Quality	Design
	Control
	Unit of Randomisation
Measures	Primary Type
	Actual Measure
	Primary Duration (Days)
Post-Intervention Measurement/Intervention	Post-Intervention (Months)
	Post-Intervention n
	% lost to Post-Intervention
	PI Global PA
	PI Global PA Change
	PI Global PA Boys
	PI Global PA Change Boys
	PI Global PA Girls
	PI Global PA Girls Change
	PI MVPA
	PI MVPA Change
	PI MVPA Boys

	PI MVPA Boys Change
	PI MVPA Girls
	PI MVPA Girls Change
	PI VPA
	PI VPA Boys
	PI VPA Girls
	PI BMI
	PI BMI Boys
	PI BMI Girls
	PI zBMI
	PI zBMI Boys
	PI zBMI Girls
	Secondary Type
	Secondary Duration
	Secondary FU Time
Post-Intervention Measurement/Seconday Intervention	PI n
	% lost to FU
	PI Global PA Boys
	PI MVPA Boys
	PI BMI Boys
	Secondary MVPA
Post-Intervention Measurement/Secondary Intervention	PI n
	% to follow-up
	PI Global PA
	PI MVPA
Post-Intervention Measurement/Control	Post-Intervention (Months)

	Post-Intervention n
	% lost to Post-Intervention
	PI Global PA
	PI Global PA Change
	PI Global PA Boys
	PI Global PA Girls
	PI MVPA
	PI MVPA Change
	PI MVPA Boys
	PI MVPA Girls
	PI VPA
	PI VPA Boys
	PI VPA Girls
	PI BMI
	PI BMI Boys
	PI BMI Girls
	PI zBMI
	PI zBMI Boys
	PI zBMI Girls
	Secondary Type
	Secondary Duration
	Secondary FU Time
Post-Intervention Measurement/Secondary Control	PI n
	% lost to FU
	PI Global PA Boys
	PI MVPA Boys

	PI BMI Boys
Follow-Up Measurement/Intervention	Interim FU (Months)
	Interim FU n
	% lost to Interim FU
	PI Global PA
	PI MVPA
	PI VPA Non-Stratified
	PI VPA Boys
	PI VPA Girls
	PI BMI
	PI zBMI
	Interim2 FU (months)
	Interim2 FU n
	% lost to FU
	PI Global PA
	PI Global VPA
	Final FU (months)
	Final FU n
	% lost to Final FU
	PI Global PA
	PI Global PA Change
	PI Global PA Boys
	PI Global PA Girls
	PI MVPA
	PI MPA
	PI VPA

	PI MVPA Boys
	PI MVPA Boys Change
	PI MVPA Girls
	PI MVPA Girls Change
	PI MPA Non-Stratified
	PI VPA Non-Stratified
	PI VPA Boys
	PI VPA Girls
	PI BMI
	PI BMI Boys
	PI BMI Boys Change
	PI BMI Girls
	PI BMI Girls Change
	PI zBMI Non-Stratified
	PI zBMI Boys
	PI zBMI Boys Change
	PI zBMI Girls
	PI zBMI Girls Change
Final Follow-Up Measurement/Secondary Intervention	FU n
	% lost to FU
	PI BMI FU Non-Stratified
	PI BMI FU Boys
	PI Global PA Boys
	PI MVPA FU Non-Stratified
	PI MVPA Boys
	PI MPA FU Non-Stratified

	PI VPA FU Non-Stratified
	Secondary
Follow-Up Measurement/Control	Interim FU (Months)
	Interim FU n
	% lost to Interim FU
	PI Global PA
	PI MVPA
	PI VPA Non-Stratified
	PI VPA Boys
	PI VPA Girls
	PI BMI
	PI zBMI
	Interim2 FU (months)
	Interim2 FU n
	% lost to FU
	PI Global PA
	PI Global VPA
	Final FU (months)
	Final FU n
	% lost to Final FU
	PI Global PA
	PI Global PA Boys
	PI Global PA Girls
	PI MVPA
	PI MVPA Boys
	PI MVPA Boys Change
	PI MVPA Girls

	PI MVPA Girls Change
	PI MPA FU Non-Stratified
	PI VPA FU Non-Stratified
	PI VPA Boys
	PI VPA Girls
	PI BMI Non-Stratified
	PI BMI Boys
	PI BMI Boys Changes
	PI BMI Girls
	PI BMI Girls Changes
	PI zBMI
	PI zBMI Boys
	PI zBMI Boys Change
	PI zBMI Girls
	PI zBMI Girls Change
Final Follow-Up Measurement/Secondary Control	FU n
	% lost to FU
	PI BMI FU Boys
	PI Global PA Boys
	PI MVPA Boys
	Secondary

Appendix 61 - Study-level data extraction form

NICE National Institute for Health and Care Excellence

Process and methods guides

The guidelines manual: appendices B–I

http://publications.nice.org.uk/pmg6b

Published: 30 November 2012

Appendix C: Methodology checklist: randomised controlled trials

Checklist

Study identification Include author, title, reference, year of publication		
Guideline topic:	**Review question no:**	
Checklist completed by:		
		Circle or highlight one option for each question
A. Selection bias (systematic differences between the comparison groups)		

This is an extract from a NICE publication. The complete publication is available at http://publications.nice.org.uk/PMG6B

A1	An appropriate method of randomisation was used to allocate participants to treatment groups (which would have balanced any confounding factors equally across groups)	Yes	No	Unclear	N/A
A2	There was adequate concealment of allocation (such that investigators, clinicians and participants cannot influence enrolment or treatment allocation)	Yes	No	Unclear	N/A
A3	The groups were comparable at baseline, including all major confounding and prognostic factors	Yes	No	Unclear	N/A

Based on your answers to the above, in your opinion was selection bias present? If so, what is the likely direction of its effect?

Low risk of bias	Unclear/unknown risk	High risk of bias

Likely direction of effect:

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B. Performance bias (systematic differences between groups in the care provided, apart from the intervention under investigation)

B1	The comparison groups received the same care apart from the intervention(s) studied	Yes	No	Unclear	N/A
B2	Participants receiving care were kept 'blind' to treatment allocation	Yes	No	Unclear	N/A
B3	Individuals administering care were kept 'blind' to treatment allocation	Yes	No	Unclear	N/A

Based on your answers to the above, in your opinion was performance bias present? If so, what is the likely direction of its effect?

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Low risk of bias	Unclear/unknown risk	High risk of bias

Likely direction of effect:

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C. Attrition bias (systematic differences between the comparison groups with respect to loss of participants)					
C1	All groups were followed up for an equal length of time (or analysis was adjusted to allow for differences in length of follow-up)	Yes	No	Unclear	N/A
C2	a. How many participants did not complete treatment in each group?				
	b. The groups were comparable for treatment completion (that is, there were no important or systematic differences between groups in terms of those who did not complete treatment)	Yes	No	Unclear	N/A
C3	a. For how many participants in each group were no outcome data available? .				
	b. The groups were comparable with respect to the availability of outcome data (that is, there were no important or systematic differences between groups in terms of those for whom	Yes	No	Unclear	N/A

	outcome data were not available).				
Based on your answers to the above, in your opinion was attrition bias present? If so, what is the likely direction of its effect?					
Low risk of bias	Unclear/unknown risk	High risk of bias			
Likely direction of effect:					
D. Detection bias (bias in how outcomes are ascertained, diagnosed or verified)					
D1	The study had an appropriate length of follow-up	Yes	No	Unclear	N/A
D2	The study used a precise definition of outcome	Yes	No	Unclear	N/A
D3	A valid and reliable method was used to	Yes	No	Unclear	N/A

	determine the outcome				
D4	Investigators were kept 'blind' to participants' exposure to the intervention	Yes	No	Unclear	N/A
D5	Investigators were kept 'blind' to other important confounding and prognostic factors	Yes	No	Unclear	N/A

Based on your answers to the above, in your opinion was detection bias present? If so, what is the likely direction of its effect?

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Low risk of bias	Unclear/unknown risk	High risk of bias

Likely direction of effect:

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Notes on use of Methodology checklist: randomised controlled trials

The studies covered by this checklist are designed to answer questions about the relative effects of interventions such as drugs, psychological therapies, operations or placebos. Such studies can include comparisons of 'test and treat strategies' involving a diagnostic test and subsequent management. The checklist does not cover comparisons of diagnostic test accuracy or questions about prognosis.

Some of the items on this checklist may need to be filled in individually for different outcomes reported by the study. It is therefore important that the systematic reviewer has a clear idea of what the important outcomes are **before** appraising a study. You are likely to need input from the Guideline Development Group in defining the important outcomes.

Checklist items are worded so that a 'yes' response always indicates that the study has been designed/conducted in such a way as to minimise the risk of bias for that item. An 'unclear' response to a question may arise when the item is not reported or not clearly reported. 'N/A' should be used when a randomised controlled trial cannot give an answer of 'yes' no matter how well it has been done.

This checklist is designed to assess the internal validity of the study; that is, whether the study provides an unbiased estimate of what it claims to show. Internal validity implies that the differences observed between groups of participants allocated to different interventions may (apart from the possibility of random error) be attributed to the intervention under investigation. Biases are characteristics that are likely to make estimates of effect differ systematically from the truth.

Recording the presence and direction of bias

The checklist contains four sections (A–D), each of which addresses a potential source of bias relating to internal validity. At the end of each section you are asked to give your opinion on whether bias is present and to estimate the likely direction of this bias – that is, whether you think it will have increased or decreased the effect size reported by the study. It will not always be possible to determine the direction of bias, but thinking this through can help greatly in interpreting results.

A: Selection bias

Selection bias may be introduced into a study when there are systematic differences between the participants in the different treatment groups. As a result, the differences in the outcome observed may be explained by pre-existing differences between the groups rather than because of the treatment itself. For example, if the people in one group are in poorer health, then they are more likely to have a bad outcome than those in the other group, regardless of the effect of the treatment. The treatment groups should be similar at the start of the study – the only difference between the groups should be the intervention received.

Randomisation

There are two aspects to randomisation:

- generation of the random allocation sequence that results in groups that differ only randomly
- allocation concealment, so that both the participant and the investigator are unaware of which group the next participant will be allocated to when entering the study.

A1. An appropriate method of randomisation was used to allocate participants to treatment groups

If an appropriate method of randomisation has been used, each participant should have an equal chance of ending up in any of the treatment groups. Examples of random allocation sequences include random numbers generated by computer, tables of random numbers, and drawing of lots or envelopes. The allocation sequence should not be related to outcome or prognosis, or be predictable, such as date of birth or admission date.

There are some more complicated ways of allocating people to treatment groups that minimise the differences between groups, such as block randomisation and minimisation. Although these are not truly random, they are usually considered to be adequate for the purpose. If a study does not report the method of randomisation used, this should be scored as 'unclear'.

A2. There was adequate concealment of allocation

If investigators are aware of the allocation group for the next participant being enrolled in the study, there is potential for participants to be enrolled in an order that results in imbalances in important characteristics. For example, a clinician might feel that participants who are more unwell are likely to do better on a new, experimental, treatment and be tempted to enrol such

participants when they know they will be allocated to that group. This would result in the participants in the intervention group being, on average, more unwell. Concealment of treatment group may not always be feasible (as in, for example, a comparison of a surgical with a medical intervention), but concealment of allocation up until the point of enrolment in the study should always be possible.

The information presented within the paper should provide some assurance that allocations were not known until at least the point of enrolment. Centralised allocation, computerised allocation systems and the use of coded identical containers are all regarded as adequate methods of concealment. Sealed envelopes can be considered as adequate concealment if the envelopes are serially numbered and opaque, and allocation is performed by a third party. Poor methods of allocation concealment include alternation, or the use of case record numbers, date of birth or day of the week.

If the method of allocation concealment used is regarded as poor, or relatively easy to subvert, the study must be given a lower quality rating. If a study does not report any concealment approach, this should be scored as 'unclear'.

A3. The groups were comparable at baseline, including all major confounding and prognostic factors

Studies may report the distributions of potential prognostic and confounding factors in the comparison groups, or important differences in the distribution of these factors may be noted.

Formal tests comparing the groups are problematic – failure to detect a difference does not mean that a difference does not exist, and multiple comparisons of factors may falsely detect some differences that are not real.

Clinical input may be required to determine whether all likely confounders have been considered. Confounding factors may differ according to outcome, so you will need to consider potential confounding factors for all of the outcomes that are of interest to your review.

B: Performance bias

Performance bias refers to systematic differences between the comparison groups in the care provided to the participants, other than the intervention under investigation.

This may consist of additional treatment, advice or counselling, rather than a physical intervention, or even simply a belief about the effects of an intervention. If performance bias is present, it can be difficult to attribute any observed effect to the experimental treatment rather than to the other factors.

B1. The comparison groups received the same care apart from the intervention(s) studied

There should be no differences between the treatment groups apart from the intervention received. If some participants received additional treatment (known as 'co-intervention'), this treatment is a potential confounding factor that may compromise the results.

Blinding (also known as masking) refers to the process of withholding information about treatment allocation or exposure status from those involved in the study who could potentially be influenced by this information. This can include participants, investigators, those administering care and those involved in data collection and analysis. If people are aware of the treatment allocation or exposure status ('unblinded'), this can bias the results of studies, either intentionally or unintentionally, through the use of other effective co-interventions, decisions about withdrawal, differential reporting of symptoms or influencing concordance with treatment. Blinding of those assessing outcomes is covered in section D on detection bias.

Blinding of participants and carers is not always possible, particularly in studies of non-drug interventions, and so performance bias may be a particular issue in these studies. It is important to think about the likely size and direction of bias caused by failure to blind.

The terms 'single blind', 'double blind' and even 'triple blind' are sometimes used in studies. Unfortunately, they are not always used consistently. Commonly, when a study is described as 'single blind', only the participants are blind to their group allocation. When both participants and investigators are blind to group allocation, the study is often described as 'double blind'. It is preferable to record exactly who was blinded, if reported, to avoid misunderstanding.

B2. Participants receiving care were kept 'blind' to treatment allocation

The knowledge of assignment to a particular treatment group may affect outcomes, such as a study participant's reporting of symptoms, self-use of other known interventions or even dropping out of the study.

B3. Individuals administering care were kept 'blind' to treatment allocation

If individuals who are administering the intervention and/or other care to the participant are aware of treatment allocation, they may treat participants receiving one treatment differently from those receiving the comparison treatment; for example, by offering additional co-interventions.

C: Attrition bias

Attrition refers to the loss of participants during the course of a study. Attrition bias occurs when there are systematic differences between the comparison groups with respect to participants lost, or differences between participants lost to the study and those who remain. Attrition can occur at any point after participants have been allocated to their treatment groups. As such, it includes participants who are excluded after allocation (and may indicate a violation of eligibility criteria), those who do not complete treatment (whether or not they continue measurement) and those who do not complete outcome measurement (regardless of whether or not treatment was completed). Consideration should be given to why participants dropped out, as well as how many. Participants who dropped out of a study may differ in some significant way from those who remained as part of the study throughout. Drop-out rates and reasons for dropping out should be similar across all treatment groups. The proportion of participants excluded after allocation should be stated in the study report, and the possibility of attrition bias considered within the analysis; however, these are not always reported.

C1. All groups were followed up for an equal length of time (or analysis was adjusted to allow for differences in length of follow-up)

If the comparison groups are followed up for different lengths of time, then more events are likely to occur in the group followed up for longer, distorting the comparison. This may be overcome by adjusting the denominator to take the time into account; for example by using person-years.

C2a. How many participants did not complete treatment in each group?

A very high number of participants dropping out of a study should give concern. The drop-out rate may be expected to be higher in studies conducted over a longer period of time. The drop-out rate includes people who did not even start treatment; that is, they were excluded from the study after allocation to treatment groups.

C2b. The groups were comparable for treatment completion (that is, there were no important or systematic differences between groups in terms of those who did not complete treatment)

If there are systematic differences between groups in terms of those who did not complete treatment, consider both why participants dropped out and whether any systematic differences in those who dropped out may be related to the outcome under study, such as potential confounders. Systematic differences between groups in terms of those who dropped out may also result in treatment groups that are no longer comparable with respect to potential confounding factors.

C3a. For how many participants in each group were no outcome data available?

A very high number of participants for whom no outcome data were available should give concern.

C3b. The groups were comparable with respect to the availability of outcome data (that is, there were no important or systematic differences between groups in terms of those for whom outcome data were not available)

If there are systematic differences between groups in terms of those for whom no outcome data were available, consider both why the outcome data were not available and whether there are any systematic differences between participants for whom outcome data were and were not available.

D: Detection bias (this section should be completed individually for each important relevant outcome)

The way outcomes are assessed needs to be standardised for the comparison groups; failure to 'blind' people who are assessing outcomes can also lead to bias, particularly with subjective outcomes. Most studies report results for more than one outcome, and it is possible that detection bias may be present in a study for some, but not all, outcomes. It is therefore recommended that this section is completed individually for each important outcome that is relevant to the guideline review question under study. To avoid biasing your review, you should identify the relevant outcomes **before** considering the results of the study. Clinical input may be required to identify the most important outcomes for a review.

D1. The study had an appropriate length of follow-up

The follow-up of participants after treatment should be of an adequate length to identify the outcome of interest. This is particularly important when different outcomes of interest occur early and late after an intervention. For example, after surgical interventions there is usually an early harm because of side effects, with benefits apparent later on. A study that is too short will give an unbalanced assessment of the intervention.

For events occurring later, a short study will give an imprecise estimate of the effect, which may or may not also be biased. For example, a late-occurring side effect will not be detected in the treatment arm if the study is too short.

D2. The study used a precise definition of outcome

D3. A valid and reliable method was used to determine the outcome

The outcome under study should be well defined. It should be clear how the investigators determined whether participants experienced, or did not experience, the outcome. The same methods for defining and measuring outcomes should be used for all participants in the study. Often there may be more than one way of measuring an outcome (for example, physical or laboratory tests, questionnaire, reporting of symptoms). The method of measurement should be valid (that is, it measures what it claims to measure) and reliable (that is, it measures something consistently).

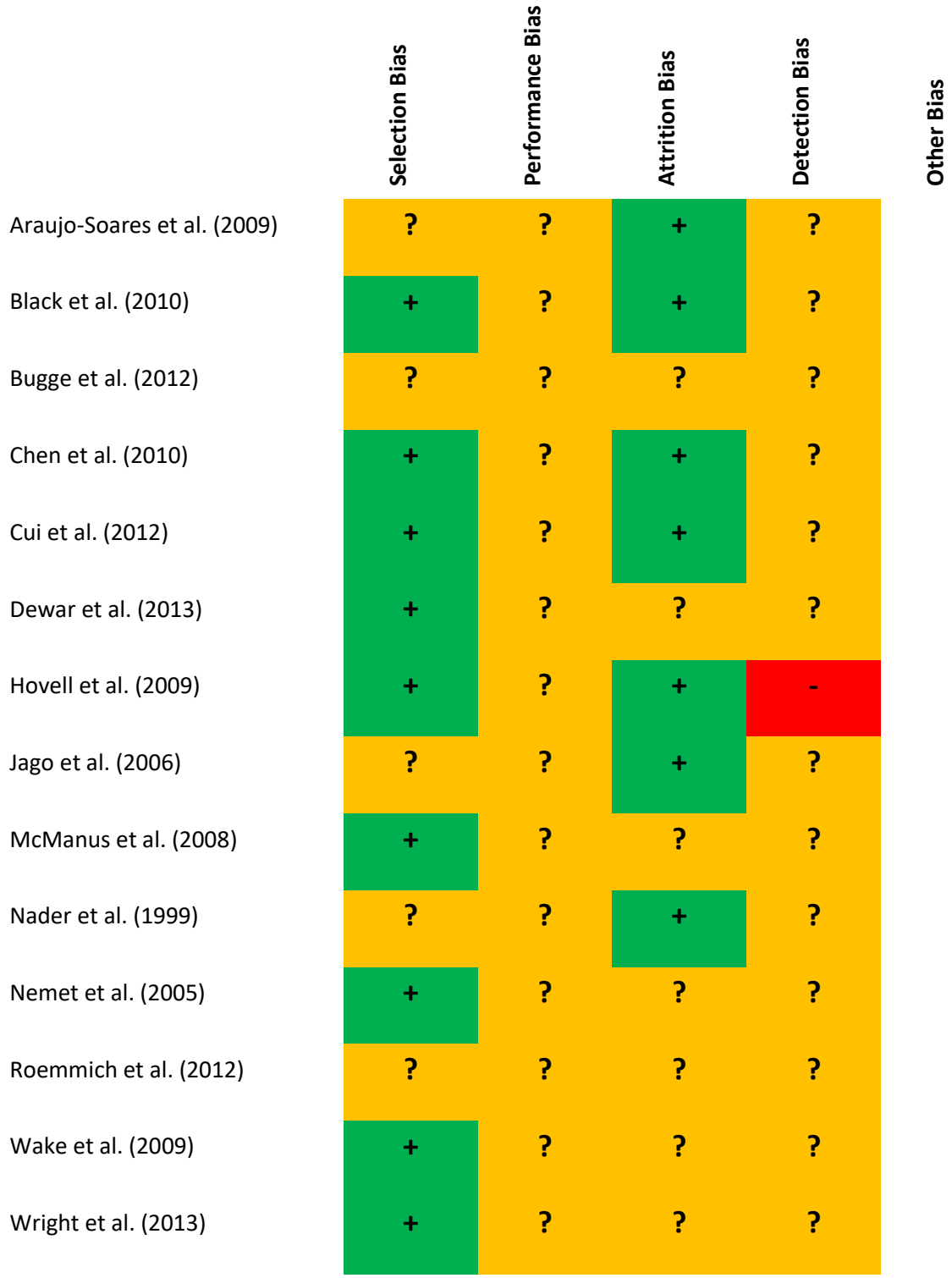
D4. Investigators were kept 'blind' to participants' exposure to the intervention

D5. Investigators were kept 'blind' to other important confounding and prognostic factors

In this context the 'investigators' are the individuals who are involved in making the decision about whether a participant has experienced the outcome under study. This can include those responsible for taking physical measurements and recording symptoms, even if they are not ultimately responsible for determining the outcome. Investigators can introduce bias through differences in measurement and recording of outcomes, and making biased assessments of a participant's outcome based on the collected data. The degree to which lack of blinding can introduce bias will vary depending on the method of measuring an outcome, but will be greater for more subjective outcomes, such as reporting of pain.

Physical separation of the assessment from the participant (for example, sending samples off to a laboratory) can often be considered as blind if it can be assumed that the laboratory staff are unaware of the treatment assignment.

Appendix 62 - Example Methodology Checklist for Randomised Controlled Trials (NICE, 2012)



Appendix 63 - Risk of bias summary for included studies

Study	Araujo-Soares et al. (2009)
Methods	Study Design: Cluster-randomised controlled trial Unit of Allocation: Class Intervention Period: 12 weeks Post-Intervention Follow-Up Period: 3 months and 9 months Differences in Baseline Characteristics: Reported Unit of Analysis: Child Control Strategy: Intention to treat
Participants	Control *n*: Baseline = 157; Post-Intervention = 157; 3 Month Follow-Up = 157, 9 Month Follow-Up = 102* Intervention *n*: Baseline = 134; Post-Intervention = 134; 3 Month Follow-Up = 134, 9 Month Follow-Up = 90* Setting: School Recruitment: Not reported Location: Northern Portugal Percentage of Eligible Population Included: 100% Mean Age at Baseline: Intervention = 12.19 ± 1.1, Control = 12.05 ± 0.9 Baseline Weight Status: Not reported Gender: Females = 52.6% *data entered into meta-analysis
Interventions	• Manualised delivery by trained psychologist and physical education teacher • Children and parent problem-solving groups • Action planning and coping planning • Behavioural contracts Theoretical Grounding: Social cognitive theory, self-regulation theory
Outcomes	Moderate to Vigorous Physical Activity: Self Report (International Physical Activity Questionnaire)
Study	Black et al. (2010)
Methods	Study Design: Randomised controlled trial Unit of Allocation: Individual

	Intervention Period: 3-6 months Post-Intervention Follow-Up Period: 18-21 months Differences in Baseline Characteristics: Reported Unit of Analysis: Child Control Strategy: Intention to treat
Participants	Control *n*: Baseline = 114; Post-Intervention = 93; 24 Month Follow-Up = 90* Intervention *n*: Baseline = 121; Post-Intervention = 91; 9 Month Follow-Up = 89* Setting: Community Recruitment: Not reported Location: Baltimore, USA Percentage of Eligible Population Included: 100% Mean Age at Baseline: Intervention = 13.3 ± 1.0, Control = 13.3 ± 1.0 Baseline Weight Status: Intervention = 44.6%, Control = 31.6% Gender: Intervention = 51.2%, Control = 47.4% *data entered into meta-analysis
Interventions	• Manualised, twelve session intervention for urban, black adolescents • Each session incorporates a challenge/goal related to diet/physical activity • Participants engage in physical activity classes and sample healthy foods • Classes and contact is delivered by mentors from a similar background Theoretical Grounding: Social cognitive theory
Outcomes	Anthropometry: zBMI Body Composition: Dual-Energy Radiograph Absorptiometry Total Physical Activity: Objective (Actiwatch Accelerometer) Play-Equivalent Physical Activity: Objective (Actiwatch Accelerometer) Diet: Self-Report (Youth Adolescent Food Frequency Questionnaire)
Study	Bugge et al. (2012)
Methods	Study Design: Controlled longitudinal trial Unit of Allocation: School

	Intervention Period: 3 years
	Post-Intervention Follow-Up Period: 4 years
	Differenced in Baseline Characteristics: Reported
	Unit of Analysis: Child
	Control Strategy: Match groups for socio-demographic characteristics
Participants	Control *n*: Baseline = 225; Post-Intervention = 186; 4 Year Follow-Up = 125*
	Intervention *n*: Baseline = 334; Post-Intervention = 289; 4 Year Follow-Up = 175*
	Setting: School
	Recruitment: Children volunteered from within all schools in two local authority areas
	Location: Copenhagen, Denmark
	Percentage of Eligible Population Included: 100%
	Mean Age at Baseline: Intervention = 6.8 ± 0.4, Control = 6.7 ± 0.4
	Baseline Weight Status (BMI): Intervention = 16.1 ± 1.8, Control = 16.1 ± 1.8
	Gender: 52.45% Female
	*data entered into meta-analysis
Interventions	Double PE curriculum content
Outcomes	Anthropometry: BMI, zBMI, Skinfold, Waist Circumference
	Total Physical Activity: Objective (Actigraph 7164 Accelerometer)
	Moderate to Vigorous Physical Activity: Objective (Actigraph 7164 Accelerometer)
	Cardiovascular Fitness: VO_2max
Study	Chen et al. (2010)
Methods	Study Design: Randomised controlled trial
	Unit of Allocation: Individual
	Intervention Period: 8 weeks
	Post-Intervention Follow-Up Period: 6 months and 8 months

	Differenced in Baseline Characteristics: Reported Unit of Analysis: Child Control Strategy: Waiting list
Participants	Control *n*: Baseline = 32; Post-Intervention = not reported; 6 Month Follow-Up = 24* Intervention *n*: Baseline = 35; Post-Intervention = not reported; 6 Month Follow-Up = not reported; 8 Month Follow-Up = 33* Setting: School Recruitment: Invited volunteer parents from Chinese-language sources in local area Location: San Francisco, USA Percentage of Eligible Population Included: 93% Mean Age at Baseline: Intervention = 9.14 ± 0.85, Control = 8.78 ± 0.91 Baseline Weight Status: 81% > 85th percentile Gender: 43% Female *data entered into meta-analysis
Interventions	Play-based workshops for children that developed problem-solving towards food choice and physical activity. Empower children to develop self-efficacy regarding meal selection and alternatives to sedentary travel and activity. Reinforced with family-based meeting to develop social support. Theoretical Grounding: Social Cognitive Theory
Outcomes	Anthropometry: BMI, Wait-to-Hip Ratio Total Physical Activity: Objective (Caltrac Accelerometer) Diet: Fat, Sugar and Vegetable Consumption Dietary Knowledge: Adapted from CATCH Health Behaviour Questionnaire Physical Activity Knowledge: Adapted from CATCH Health Behaviour Questionnaire Physical Activity Self-Efficacy: Sub-scale from Health Behaviour Questionnaire
Study	Cui et al. (2012)
Methods	Study Design: Cluster randomised controlled trial

	Unit of Allocation: School
	Intervention Period: 4 weeks
	Post-Intervention Follow-Up Period: 6 months
	Differenced in Baseline Characteristics: Reported
	Unit of Analysis: Child
	Control Strategy: Matched School
Participants	Control *n*: Baseline = 371; Post-Intervention = not reported; 6 Month Follow-Up = 336*
	Intervention *n*: Baseline = 358; Post-Intervention = not reported; 6 Month Follow-Up = 346*
	Setting: School
	Recruitment: Not reported
	Location: Beijing, China
	Percentage of Eligible Population Included: 100%
	Mean Age at Baseline: Intervention = 12.7 ± , Control = ± 12.7
	Baseline Weight Status: Intervention = 36.2%, Control = 29.4% Overweight or Obese
	Gender: Female = 48%
	*data entered into meta-analysis
Interventions	Four-component intervention adapted from Shah et al. (2011), comprising food choice, physical activity, sedentary behaviour and carbonated drink consumption. This was achieved through a peer-led information provision and goal setting programme.
	Theoretical Grounding: Social cognitive theory
Outcomes	Moderate to Vigorous Physical Activity: Validated 7-Day Physical Activity Questionnaire (Liu, Ma, Zhang, & Ma, 2003)
	Physiological: Height, Weight and BMI
Study	Dewar et al. (2013)
Methods	Study Design: Cluster randomised controlled trial
	Unit of Allocation: School

	Intervention Period: 12 months Post-Intervention Follow-Up Period: 12 months Differences in Baseline Characteristics: Reported Unit of Analysis: Child Control Strategy: Waiting list
Participants	Control *n*: Baseline = 179; Post-Intervention = 153; 12 Month Follow-Up = 153* Intervention *n*: Baseline = 178; Post-Intervention = 141; 6 Month Follow-Up = 141* Setting: School Recruitment: Invitation to schools randomly selected from within area Location: NSW, Australia Percentage of Eligible Population Included: 100% Mean Age at Baseline: 13.2 ± 0.5 Baseline Weight Status: 42.9% Overweight or Obese Gender: Female = 100% *data entered into meta-analysis
Interventions	• Enhanced school sport and lunchtime physical activity sessions, nutrition workshops • Mediators targeted with additional physical activity sessions, seminars, student handbooks, parent newsletters & text messages Theoretical Grounding: Social Cognitive Theory
Outcomes	Moderate to Vigorous Physical Activity: Objective (Actigraph Accelerometer) Sedentary Behaviour: Objective (Accelerometer); Self-Report (Adolescent Sedentary Activity Questionnaire) Psychosocial Variables: Self-Report scale constructed for measurement
Study	Hovell et al. (2009)
Methods	Study Design: Randomised controlled trial Unit of Allocation: Individual Intervention Period: 8 weeks

	Post-Intervention Follow-Up Period: 6 months & 10 months Differences in Baseline Characteristics: Reported and adjusted; male and female data analysed separately due to significant difference at baseline Unit of Analysis: Child Control Strategy: Child safety intervention replaced diet and physical activity intervention
Participants	Control *n*: Baseline = 60; Post-Intervention = 49; 6 Month Follow-Up = 49, 10 Month Follow-Up = 44* Intervention *n*: Baseline = 78; Post-Intervention = 68; 6 Month Follow-Up = 66, 10 Month Follow-Up = 62* Setting: Outpatient Recruitment: Sequential over three years, recruited from advertisements and agency referrals Location: San Diego, USA Percentage of Eligible Population Included: 100% Mean Age at Baseline: Cohort = 11.48 ± 0.96 Baseline Weight Status: Not reported Gender: Females = 58.1% Female *data entered into meta-analysis
Interventions	• Outpatient-based weekly sessions for 90 minutes with separate parent and child classes • Parent training classes focussed on behaviour management, bone health, diet and physical activity • Telephone support for parents throughout the intervention period to support behaviour management • Child classes focussed on high impact physical activity participation and importance of calcium rich food Theoretical Grounding: None reported
Outcomes	Diet: Calcium intake & total energy intake using 24-hour recall conducted by telephone Moderate to Vigorous Physical Activity: 24-hour recall of specific high impact activities conducted by telephone Physiological: Bone mineral density, bone mineral content & body composition

Study	Jago et al. (2006)
Methods	Study Design: Cluster randomised controlled trial Unit of Allocation: Scout troop Intervention Period: 9 weeks Post-Intervention Follow-Up Period: 6 months Differenced in Baseline Characteristics: Reported Unit of Analysis: Child Control Strategy: Non-physical activity Fruit & Vegetables Guidance
Participants	Control *n*: Baseline = 233; 6 Month Follow-Up = 233* Intervention *n*: Baseline = 240; 6 Month Follow-Up = 240* Setting: Scout Troop Recruitment: Not reported Location: Houston, USA Percentage of Eligible Population Included: 100% Mean Age at Baseline: Cohort = 13 ± 0.1 Baseline Weight Status: Not reported Gender: Females = 0% Female *data entered into meta-analysis
Interventions	• Badge-based engagement in physical activity goal-setting intervention within Scout Troops • Badge intervention included goal setting, scout booklet & physical activity sessions • Web-based tracking of behaviour and goal-setting, participants logged on twice weekly Theoretical Grounding: None reported
Outcomes	Physiological: Height, Weight, BMI, Triceps Skinfold Total and Moderate to Vigorous Physical Activity: Objective (MTI Accelerometer)
Study	McManus et al. (2008)
Methods	Study Design: Cluster randomised controlled trial

	Unit of Allocation: School Intervention Period: 6 weeks Post-Intervention Follow-Up Period: 6 months Differences in Baseline Characteristics: Reported Unit of Analysis: Child Control Strategy: As intervention without healthy heart education or extra physical activity
Participants	Control *n*: Baseline = 69; 6 Month Follow-Up = 66* Intervention *n*: Baseline = 67 6 Month Follow-Up = 63* Setting: School Recruitment: Random selection from local school list Location: Hong Kong, Republic of China Percentage of Eligible Population Included: 100% Mean Age at Baseline: Cohort = 10.44 ± 0.85 Baseline Weight Status: Not reported Gender: Females = 50% Female *data entered into meta-analysis
Interventions	• Healthy heart training and additional PE sessions • Two-week educational programme incorporated within PE classes • Explicit heart-rate monitors and goal setting process Theoretical Grounding: Health Belief Model; Social Cognitive Theory; Diffusion of Innovation Theory
Outcomes	Moderate to Vigorous Physical Activity: Continuous heart rate telemetry Attraction to physical activity: Self-Report (Children's Attraction to Physical Activity Scale) Physiological: Weight, height, hip circumference, resting and exercise cardiopulmonary rate
Study	Nader et al. (1999)
Methods	Study Design: Cluster randomised prospective study Unit of Allocation: School

	Intervention Period: 3 Years Post-Intervention Follow-Up Period: 3 Years Differences in Baseline Characteristics: Reported (not for physical activity) Unit of Analysis: Child Control Strategy: Outpatient monitoring and ambulatory/dietary given, physical activity levels recommended
Participants	Control *n*: Baseline = 2117 (full cohort); 3 Year Follow-Up = 1400* (physical activity measurement sub-section) Intervention *n*: Baseline = 2989 (full cohort); 3 Year Follow-Up = 1996* (physical activity measurement sub-section) Note - No physical activity measurement occurred at baseline Setting: School Recruitment: All schools from 4 geographical centres invited to participate, 96 schools included Location: San Diego, Minnesota, Austin & New Orleans, USA. Percentage of Eligible Population Included: 100% Mean Age at Baseline: Cohort = 8.76 Baseline Weight Status: Not reported Gender: Females = 49% Female *data entered into meta-analysis
Interventions	• Comprehensive programme of curricular and extra-curricular physical activity and Nutrition intervention, comprising: • Eat Smart - School meals provided with lower fat and sodium content • CATCH PE - Trained PE staff to deliver enjoyable and engaging MVPA participation • Numerous classroom-based problem-solving and content aimed at inspiring greater levels of physical activity • 19 Home-delivery packets encouraging whole-family activity and family fun nights Theoretical Grounding: None reported
Outcomes	Total and Moderate to Vigorous Physical Activity: Self-Administered Physical Activity Checklist (SAPAC) Nutrition: 24-Hour Dietary Recall; Food Checklist

	Health Behaviour: Health Behaviour Survey (HBS) Physiological: Blood Cholesterol; HDL Cholesterol; Apolipoprotein B Levels; Height, Weight, Skinfold Thickness, Blood Pressure
Study	Nemet et al. (2005)
Methods	Study Design: Randomised prospective study Unit of Allocation: Individual Intervention Period: 3 months Post-Intervention Follow-Up Period: 9 months Differences in Baseline Characteristics: Reported Unit of Analysis: Child Control Strategy: Outpatient monitoring and ambulatory/dietary given, physical activity levels recommended
Participants	Control *n*: Baseline = 22; 9 Month Follow-Up = 20* Intervention *n*: Baseline = 24; 9 Month Follow-Up = 20* Setting: Outpatient clinic Recruitment: Self-referral Location: Tel Aviv, Israel Percentage of Eligible Population Included: 100% Mean Age at Baseline: Control = 11.3 ± 2.8, Intervention = 10.9 ± 1.9 Baseline Weight Status: 100% Obese Gender: Females = 45% Female *data entered into meta-analysis
Interventions	• Dietary intervention for parents and children focusing on nutritional education • Exercise programme occurred twice weekly for children focusing on a variety of activities, including walking Theoretical Grounding: None reported
Outcomes	Anthropomorphic: Height, Weight, BMI, Triceps & Subscapular Skinfolds Nutrition: Self-Report (2-Day Food Intake Diary) Total Physical Activity: Self-Report (see Godin & Shephard, 1985)

	Fitness: Progressive Treadmill Test Physiological: Triglycerides, Cholesterol, High-Density Lipoprotein
Study	Roemmich et al. (2012)
Methods	Study Design: Randomised prospective study Unit of Allocation: Individual Intervention Period: 4 months Post-Intervention Follow-Up Period: 8 months Differences in Baseline Characteristics: Reported Unit of Analysis: Child Control Strategy: No intervention group, accelerometer display turned off, limited screen time
Participants	Control *n*: Baseline = 21; 8 Month Follow-Up = 21* Intervention *n*: Baseline = 20; 8 Month Follow-Up = 20* Setting: Community Recruitment: Stratified random invitation to families, only one child per household Location: New York, USA Percentage of Eligible Population Included: 100% Mean Age at Baseline: Control Males = 11.3 ± 1.8, Females = 10.5 ± 1.6; Intervention Males = 10.5 ± 1.5, Females = 11.2 ± 1.1 Baseline Weight Status: 0% Overweight Gender: Females = 50% Female *data entered into meta-analysis
Interventions	• Family-based intervention involving conditional screen time • Problem solving opportunities to participate in physical activity • Provision of accelerometer with visible display in order to 'purchase' screen-based activities Theoretical Grounding: None reported
Outcomes	Anthropomorphic: Height, Weight, z-BMI

	Total and Moderate to Vigorous Physical Activity: Objective (BioTrainer-Pro Accelerometry) Sedentary Time: Self-Report (Habit Book)
Study	Wake et al. (2009)
Methods	Study Design: Nested randomised controlled trial Unit of Allocation: Individual Intervention Period: 12 weeks Post-Intervention Follow-Up Period: 9 months Differences in Baseline Characteristics: Reported Unit of Analysis: Child/Family Control Strategy: Non-intervention group within GP practices
Participants	Control *n*: Baseline = 119; 3 Month Follow-Up = 109; 9 Month Follow-Up = 91* Intervention *n*: Baseline = 139; 3 Month Follow-Up = 122; 9 Month Follow-Up = 110* Setting: Community/Primary Care Recruitment: Participants invited into over-arching survey by practice staff, random sample invited to join trial Location: Melbourne, Australia Percentage of Eligible Population Included: 100% Mean Age at Baseline: Control = 7.6 ± 1.4; Intervention = 7.4 ± 1.4 Baseline Weight Status: 100% Overweight Gender: Females = 60% Female *data entered into meta-analysis
Interventions	Incorporating existing intervention into current study from LEAP trial (McCallum et al., 2005), comprising brief solution-focused conducted by GP. A folder is provided to the child to consolidate therapy sessions, consisting of healthy lifestyle goals related to healthy family eating, physical activity, sedentary time, water consumption and lower fat food options. Theoretical Grounding: None reported

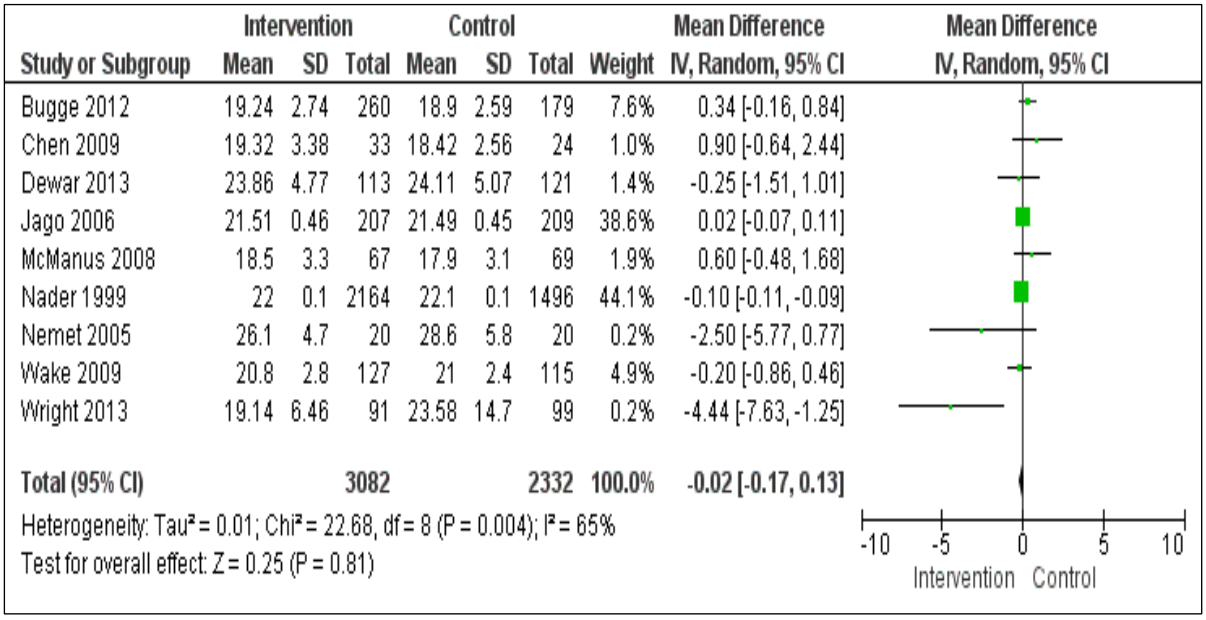
Outcomes	Total and Moderate to Vigorous Physical Activity: Objective (Actical Mini-Mitter Accelerometer), 4-Day Parent Report (non-validated) Physiological: Height, Weight, BMI, Waist Circumference, Maternal and Paternal BMI Nutrition: 4-Day Food Report Diary; Parental Report Health Status: Pediatric quality of life inventory (PedsQL 4.0) Psychological: Body Dissatisfaction (Body Figure Perception Questionnaire); Physical Appearance and Self-Worth (Harter's Perceived Competence Scale)
Study	Wright et al. (2013)
Methods	Study Design: Cluster randomised controlled trial Unit of Allocation: School Intervention Period: 6 weeks Post-Intervention Follow-Up Period: 12 months Differences in Baseline Characteristics: Reported Unit of Analysis: School Control Strategy: Standard education
Participants	Control *n*: Baseline = 130; 12 Month Follow-Up = 90* Intervention *n*: Baseline = 121; 12 Month Follow-Up = 91* Setting: School Recruitment: Drawn specifically from low SES schools Location: Los Angeles, USA Percentage of Eligible Population Included: 82% Mean Age at Baseline: Control = 8.3 ± 1.1; Intervention = 9.0 ± 1.6 Baseline Weight Status: Not reported Gender: Females = 50% Female *data entered into meta-analysis
Interventions	The Kids N Fitness (Monzavi et al., 2006) comprises nurse-led group meetings focusing on engaging in physical activity, nutrition education/behaviour modification and family support. The meetings contained a participation

	component, an educational component and a goal-setting and problem solving component. Theoretical Grounding: None reported
Outcomes	Moderate to Vigorous Physical Activity: Self-Report Child and Adolescent Trial for Cardiovasular Health (CATCH) School Physical Activity and Nutrition (SPAN) Student Questionnaire Anthropomorphic: Height, Weight, BMI, zBMI, Resting Blood Pressure, Waist Circumference

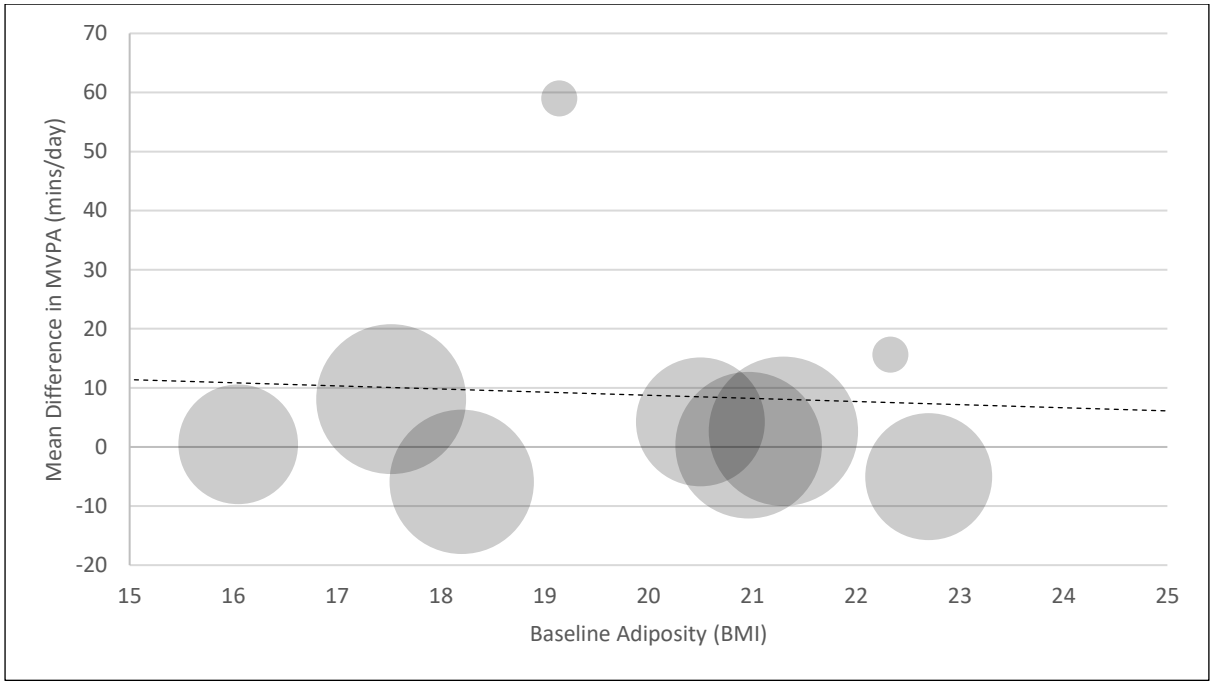
Appendix 64 - Table showing study-level summaries

The results from the nine studies reporting BMI measurement showed no effect of intervention, with a mean difference of -0.02 (95% CI: -0.17, 0.13; p = 0.81) (Appendix 66). The I^2 value of 65% revealed moderate statistical heterogeneity between the studies. Based on these results it was concluded that interventions to increase physical activity possessed negligible effect of BMI outcome at follow-up measurement. Meta-regression of the mean difference in MVPA and standardised mean difference in TPA by baseline BMI revealed no significant relationships; respective bubble plots are provided in Appendix 67 and Appendix 68.

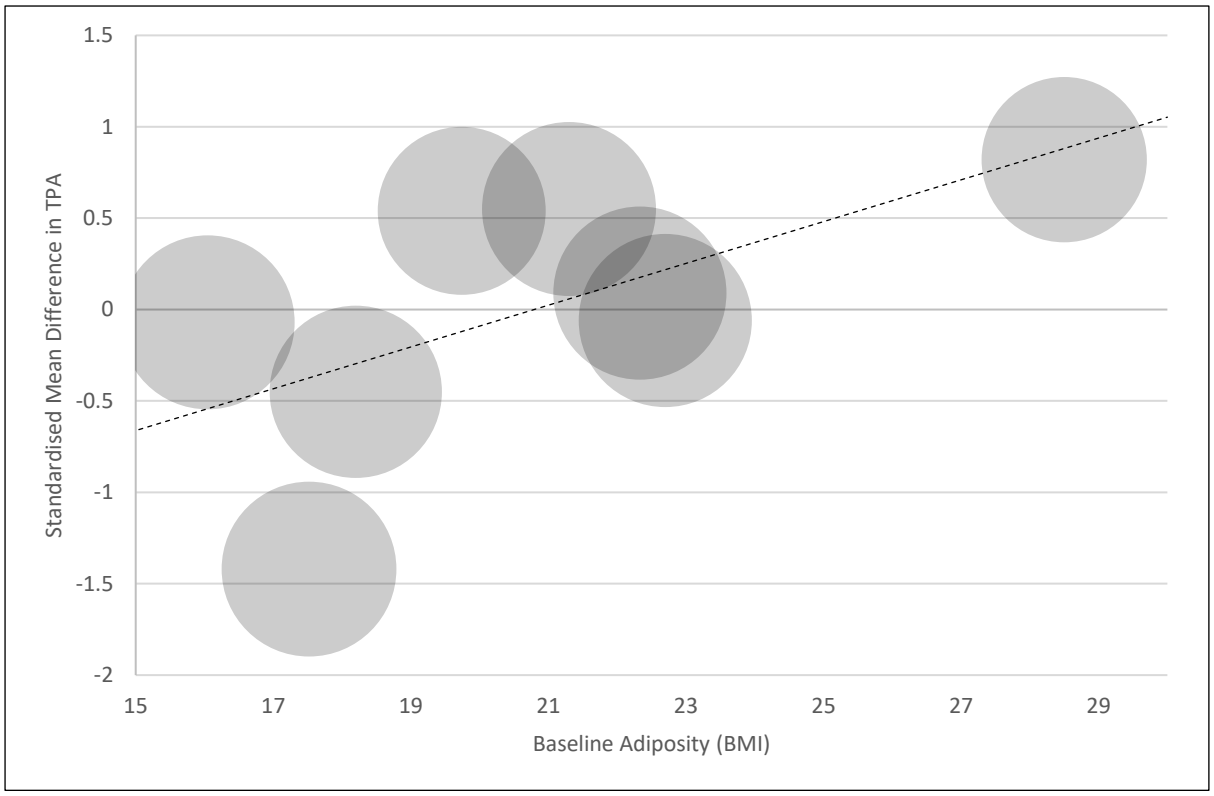
Appendix 65 – Exploration of effect of intervention on Body Mass Index



Appendix 66 - Forest plot showing mean difference in change in BMI between intervention (n = 3082) and control (n = 2332) groups across the 9 included studies reporting BMI data



Appendix 67 - Bubble plot showing regression of mean difference in MVPA (mins/day) by baseline adiposity (BMI) for 9 Studies with a coefficient of -0.483 (r^2 = -0.017; p = 0.74)



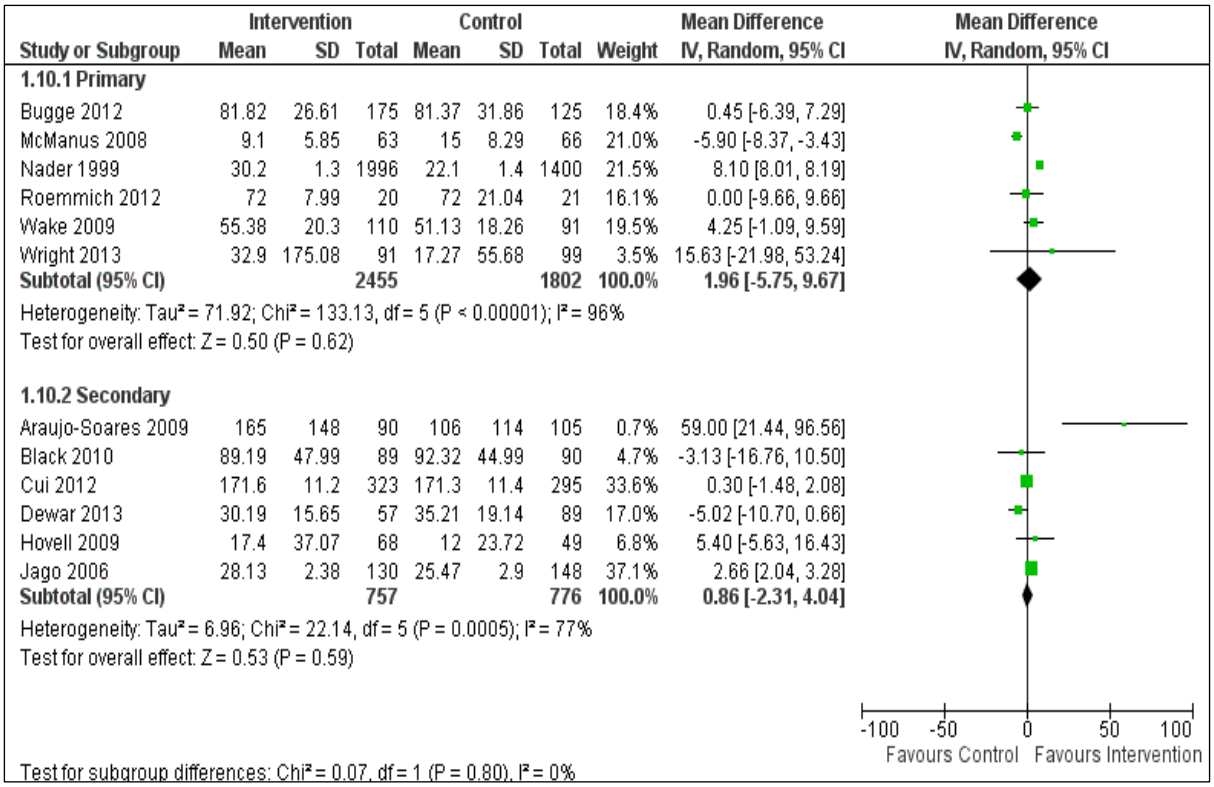
Appendix 68 - Bubble plot showing regression of standardised mean difference in TPA by baseline adiposity (BMI) for 8 studies with a coefficient of 0.121 (r^2 = 0.285; p = 0.10)

In the absence of access to the raw data, MVPA was stratified according to the nearest integer to the median age of the participant group at baseline. This median age of 11 years also dichotomised this variable according to the age at which children move from primary to secondary school in within the UK education system. Where participants were aged below eleven ($\bar{x}$ = 8.94) at baseline they were considered to be a primary education cohort and if over eleven were considered to be a secondary education cohort ($\bar{x}$ = 12.64). The oldest cohort ($\bar{x}$ = 13.3 years) was recruited by Black et al. (2010), therefore it was assumed that no participants were tertiary educational age (i.e. over 16) across the studies.

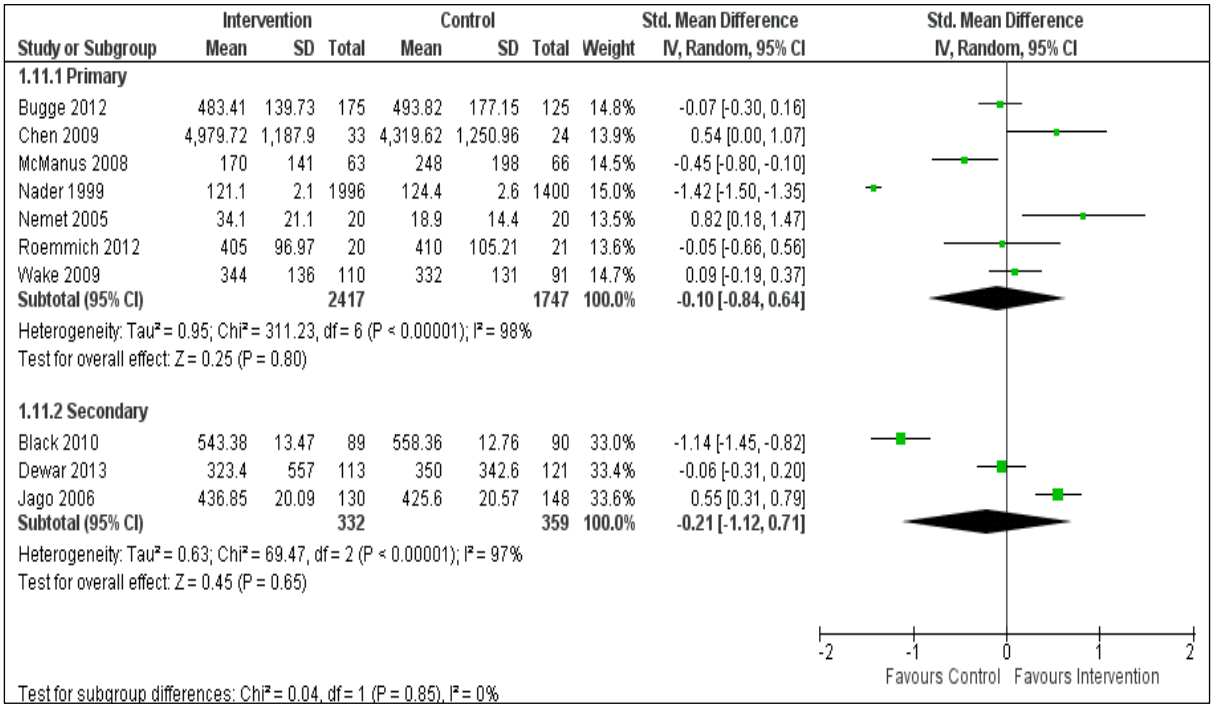
Analysis of the six studies that reported MVPA for a primary age sample revealed a mean difference of 1.96 minutes per day (95% CI: -5.75, 9.67; *p* = 0.62) (Appendix 70). The six studies reporting MVPA for secondary aged children returned a mean difference of 0.86 (95% CI: -2.31, 4.04; *p* = 0.59). The difference between the sub-groups was statistically non-significant (χ^2 = 0.07, *p* = 0.80). Meta-regression using mean age at baseline as a non-stratified covariant revealed no significant relationship for MVPA (Appendix 72).

Seven studies reported TPA for participants of primary educational age, with a further three studies reporting TPA for secondary educational aged participants. The standardised mean difference for the studies incorporating primary educational age children was -0.10 (95% CI: -0.84, 0.64, *p* = 0.80) (Appendix 71). For children of secondary educational age, the standardised mean difference was -0.21 (95% CI: -1.12, 0.71; *p* = 0.65). The difference between the sub-groups was non-significant (χ^2 = 0.04, *p* = 0.85). Meta-regression of standardised mean difference by baseline age as a non-stratified covariant revealed no significant relationship for TPA (Appendix 73).

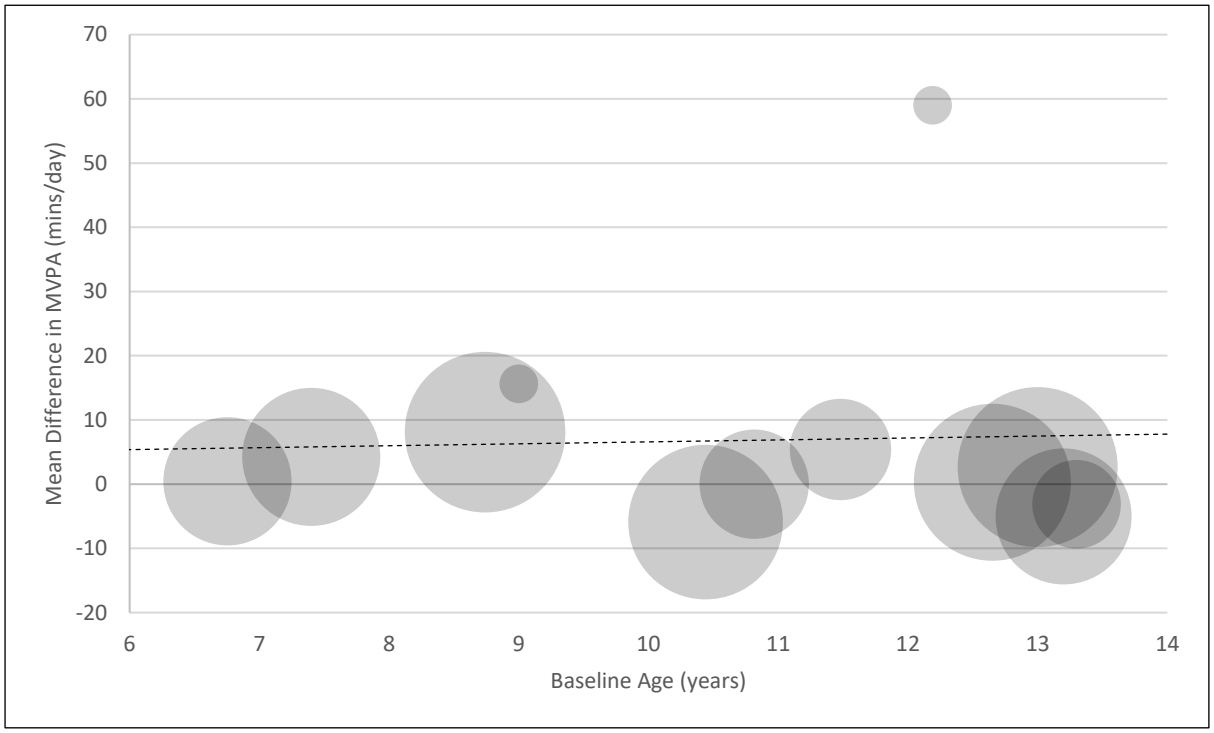
Appendix 69 – Additional sub-group analysis exploring the effect of intervention by age



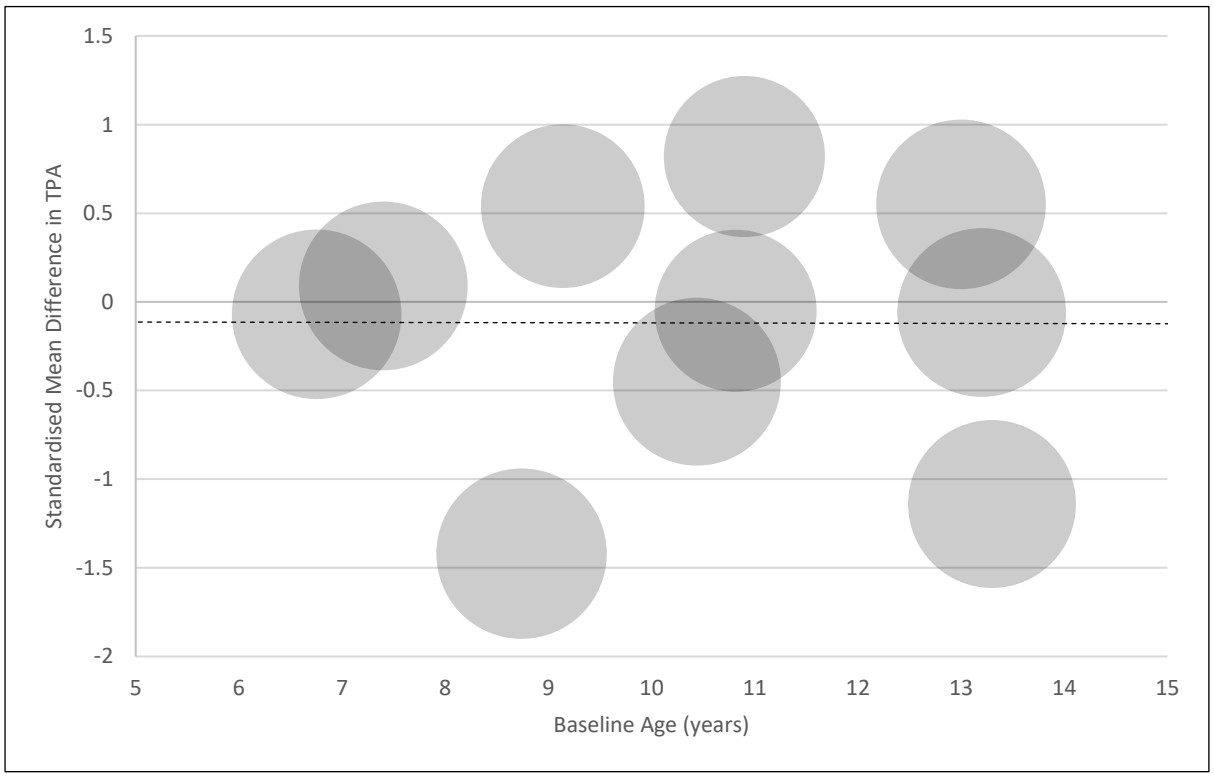
Appendix 70 - Forest plot showing the mean difference in change in MVPA between intervention (n = 3212) and control (n = 2578) groups stratified by age (primary: intervention n = 2455, control n = 1802 across 6 studies; secondary: intervention n = 757, control n =776 across 6 studies)



Appendix 71 - Forest plot showing the standardised mean difference in change in TPA between intervention (n = 2749) and control (n = 2106) groups stratified by age (primary: intervention n = 2417, control n = 1747 across 7 studies; secondary: intervention n = 332, control n = 359 across 3 studies)



Appendix 72 - Bubble plot showing the regression of mean difference in MVPA (mins/day) by baseline age (years) for 12 studies with a coefficient of -0.681 (r^2 = 0.019; p = 0.47)

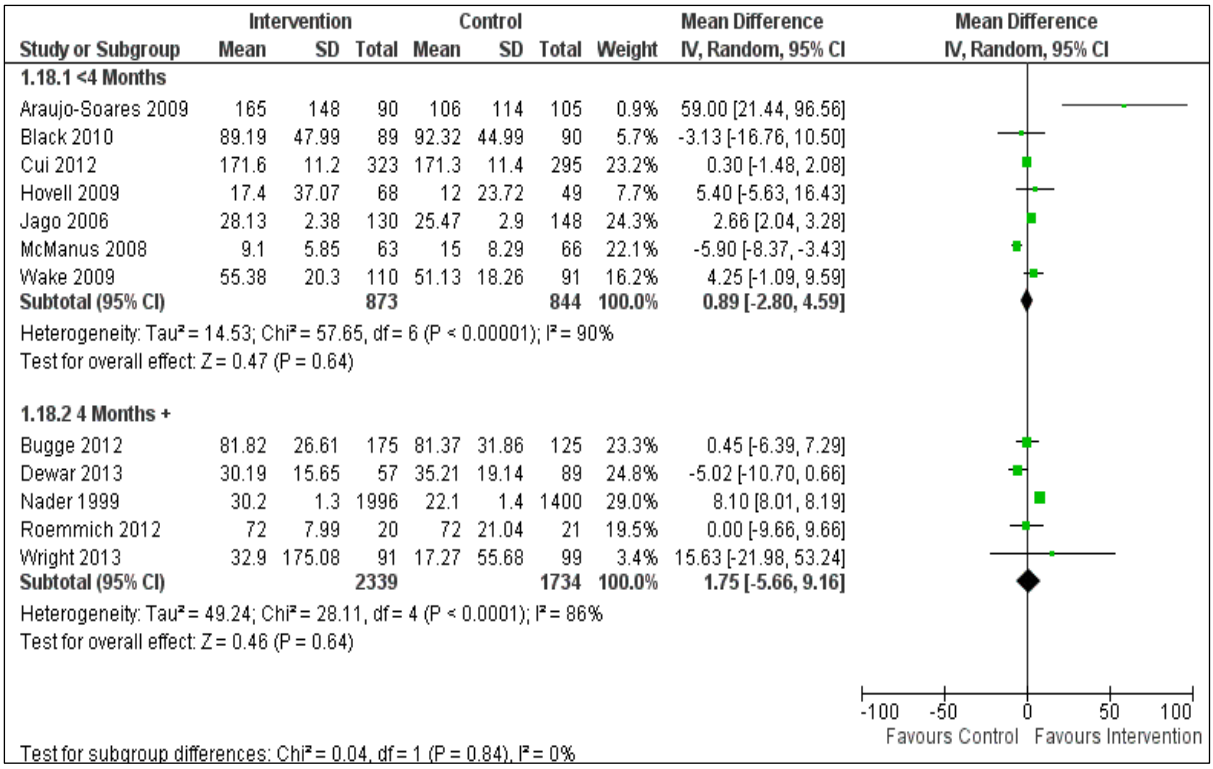


Appendix 73 - Bubble plot showing the regression of standardised mean difference in TPA by baseline age (years) for 10 studies with a coefficient of 0.001 (r^2 = -0.136; p = 0.99)

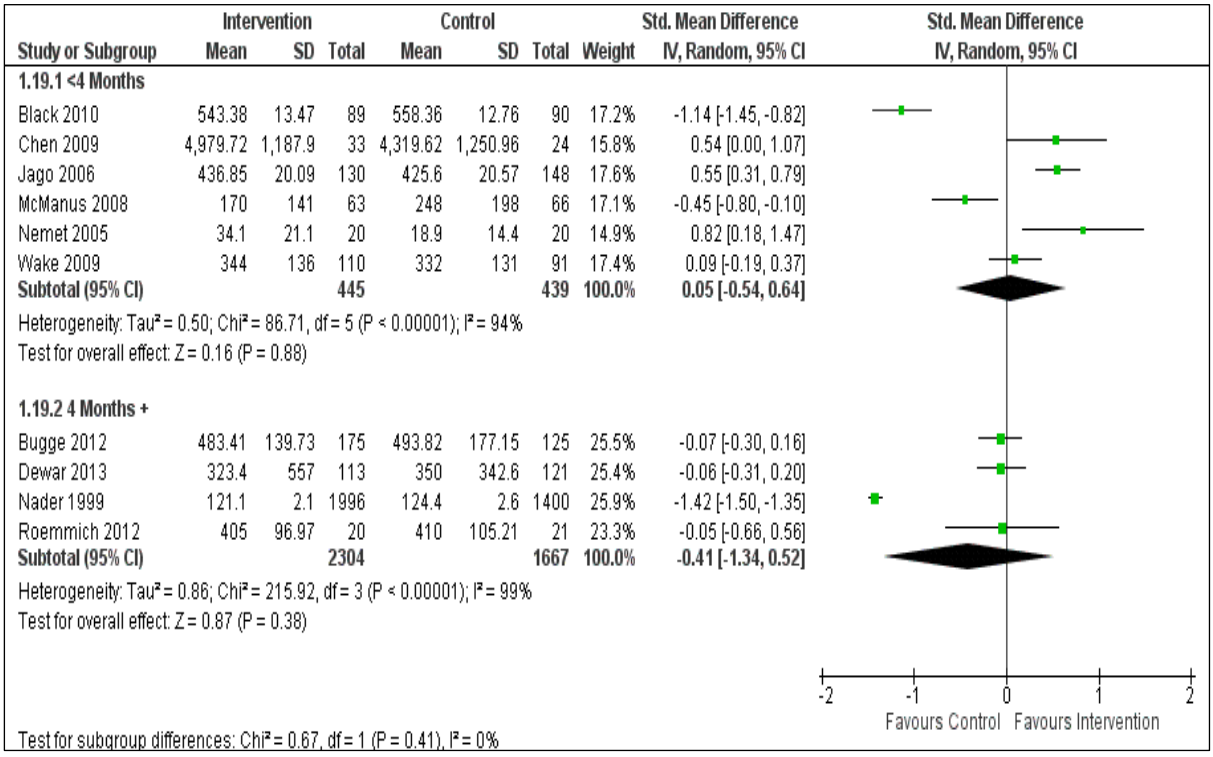
Seven studies implemented an intervention that lasted less than four months, with duration ranging from eight week interventions (Cui et al., 2012; Hovell et al., 2009; McManus et al., 2008), a nine week intervention (Jago et al., 2006), to three month interventions (Araujo-Soares et al., 2009; Black et al., 2010; Wake et al., 2009). Analysis revealed a non-significant mean difference of 0.89 (95% CI: 2.80, 4.59; $p = 0.64$). Five studies implemented an intervention over four months or longer, ranging from four months (Roemmich et al., 2012; Wright et al., 2013), twelve months (Dewar et al., 2013), thirty months (Nader et al., 1999) to thirty-six months (Bugge et al., 2012). There was a non-significant mean difference of 1.75 (95% CI: -5.66, 9.16; $p = 0.64$) (Appendix 75). There was no statistically significant difference between the groups ($\chi^2 = 0.04$; $p = 0.84$). Meta-regression of standardised mean difference in MVPA by intervention duration did not reveal a significant relationship (Appendix 77).

Six of the ten studies reporting TPA data incorporated an intervention lasting less than four months Interventions ranged from eight weeks (Chen et al., 2010; McManus et al., 2008), nine weeks (Jago et al., 2006), to three-month interventions (Black et al., 2010; Nemet et al., 2005; Wake et al., 2009). These studies provided a standardised mean difference of 0.05 (95% CI: -0.54, 0.64; $p = 0.88$) (Appendix 76). The remaining four studies ranged from an intervention duration of four months (Roemmich et al., 2012), twelve months (Dewar et al., 2013), thirty months (Nader et al., 1999) to thirty-six months (Bugge et al., 2012). Analysis of these studies provided a standardised mean difference of -0.41 (95% CI: -1.34, 0.52; $p = 0.38$). The difference between the groups was not significant ($\chi^2 = 0.67$; $p = 0.41$). Meta-regression of standardised mean difference in TPA by intervention duration did not reveal a significant relationship (Appendix 78).

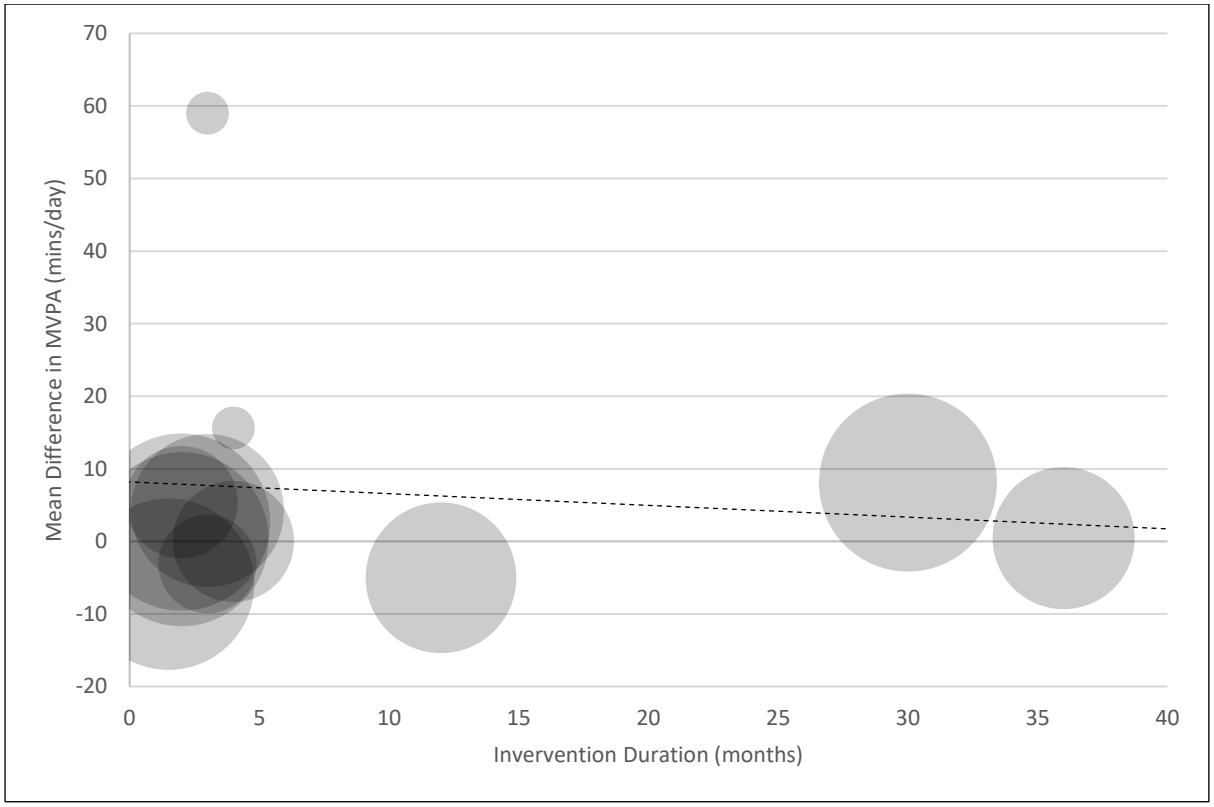
Appendix 74 – Additional sub-group analysis of effect by intervention duration



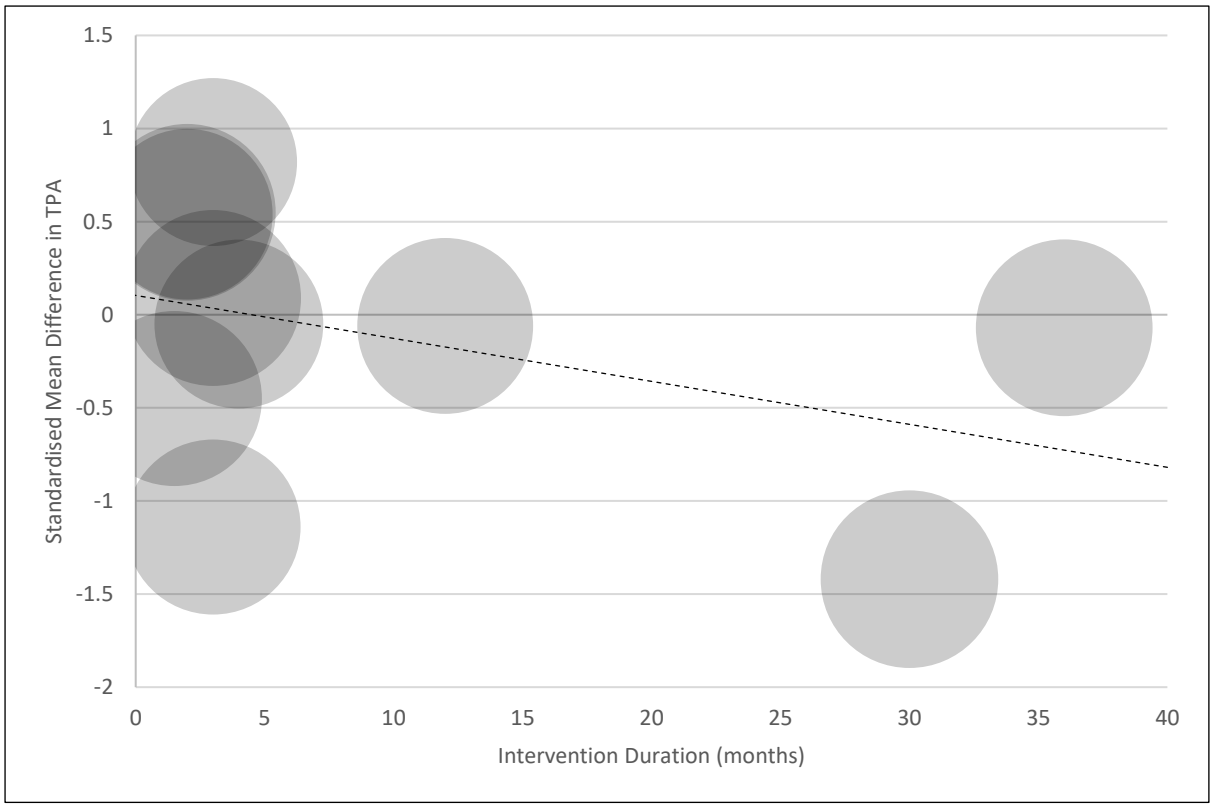
Appendix 75 - Forest plot showing the mean difference in change in MPVA between intervention (n = 3212) and control (n = 2578) groups stratified by intervention duration (under 4 months: intervention n = 873, control n = 844 across 7 studies; 4 months and over: intervention n = 2339, control n = 1734 across 5 studies)



Appendix 76 - Forest plot showing the standardised mean difference in change in TPA between intervention (n = 2750) and control (n = 2106) groups stratified by intervention duration (under 4 months: intervention n = 445, control n = 439 across 6 studies; 4 months and over: intervention n = 2304, control n = 1667 across 4 studies)



Appendix 77 - Bubble plot showing a meta-regression of the mean difference in MPVA by intervention duration (months) of 12 studies with a coefficient of -0.1.19 (r^2 = 0.024; p = 0.625)

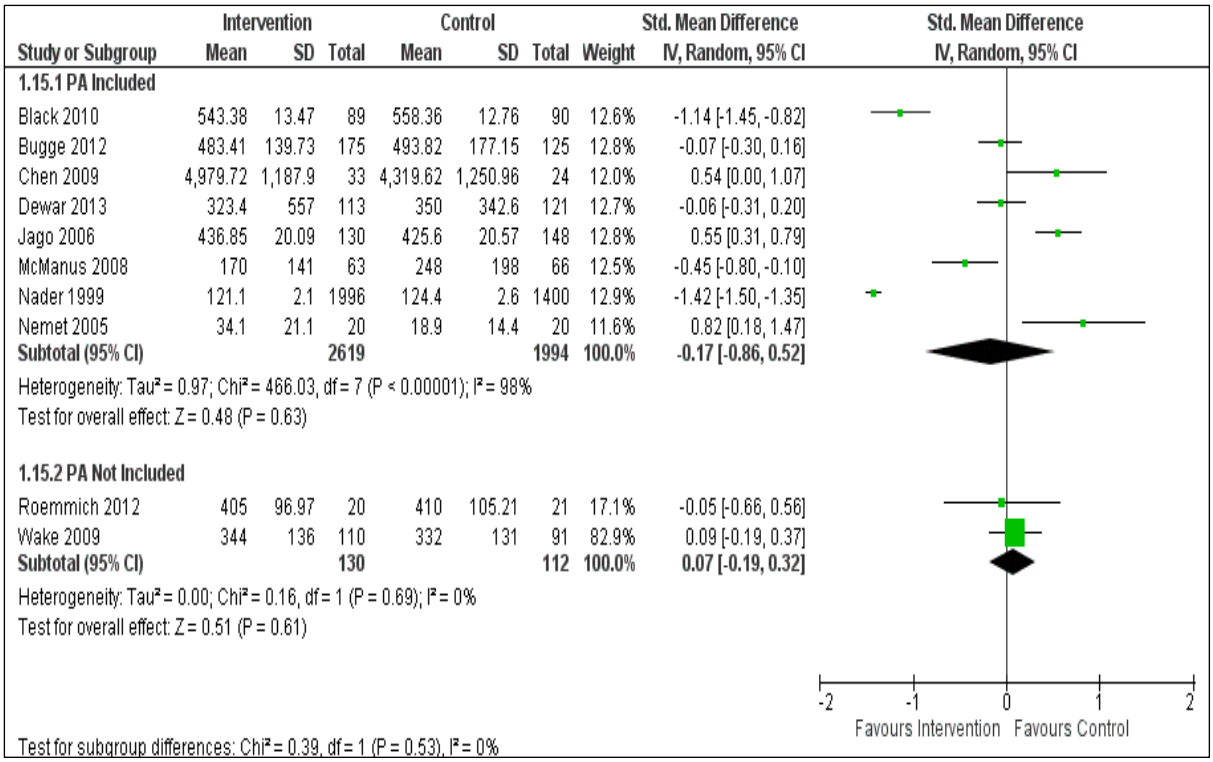


Appendix 78 - Bubble plot showing a meta-regression of the standardised mean difference in TPA by intervention duration (months) of 10 studies with a coefficient of -0.228 (r^2 = 0.061; p = 0.246)

Only one (Roemmich et al., 2012) of the ten studies that reported MVPA did not include an active physical activity element within the intervention delivery. A between group comparison by intervention strategy was therefore not performed. However, a one-study removal of Roemmich et al. (2012) from the combined MVPA analysis revealed no notable change in the overall mean difference, from 1.47 (95% CI: -1.88, 4.82; $p = 0.39$) to 1.57 (95% CI: -1.89, 5.04; $p = 0.37$). Roemmich et al. (2012) reported non-significant effects at eight months post-intervention and therefore did not represent a departure from the overall findings.

Two (Roemmich et al., 2012; Wake et al., 2009) of the ten studies that reported TPA did not include a physical activity delivery element within the intervention. The standardised mean difference for those two studies was 0.07 (95% CI: -0.19, 0.32; $p = 0.61$), a statistically non-significant effect negligibly favouring intervention. For the remaining studies that included physical activity delivery within the intervention the standardised mean difference of -0.17 (95% CI: -0.86, 0.52; $p = 0.63$) was non-significant (Appendix 80). The between group difference was not statistically significance ($\chi^2 = 0.39$; $p = 0.53$).

Appendix 79 – Additional sub-group analysis by inclusion or non-inclusion of a physical activity element within the intervention

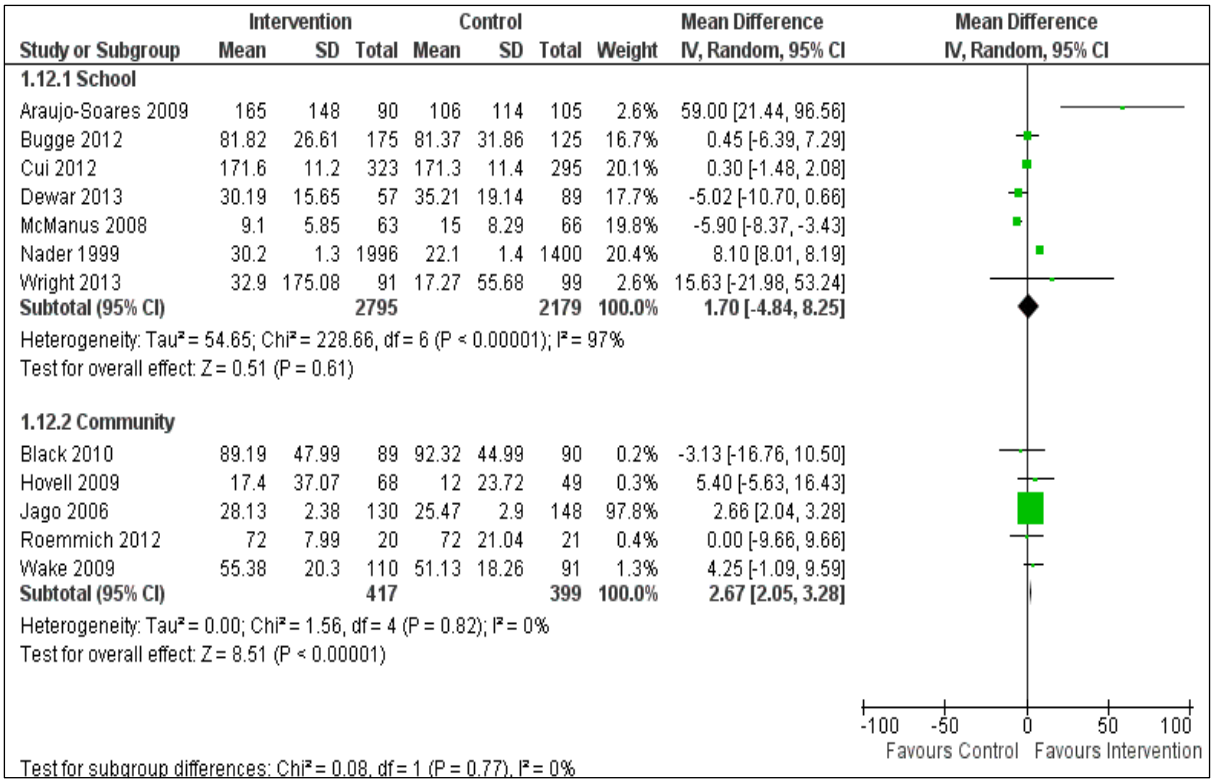


Appendix 80 - Forest plot showing standardised mean difference in change in TPA between intervention (n = 2479) and control (n = 1306) groups stratified by inclusion or absence of a physical activity component (physical activity included: intervention n = 2619, control n = 1994 across 8 studies; physical activity not included: intervention n = 130, control n = 112 across 2 studies)

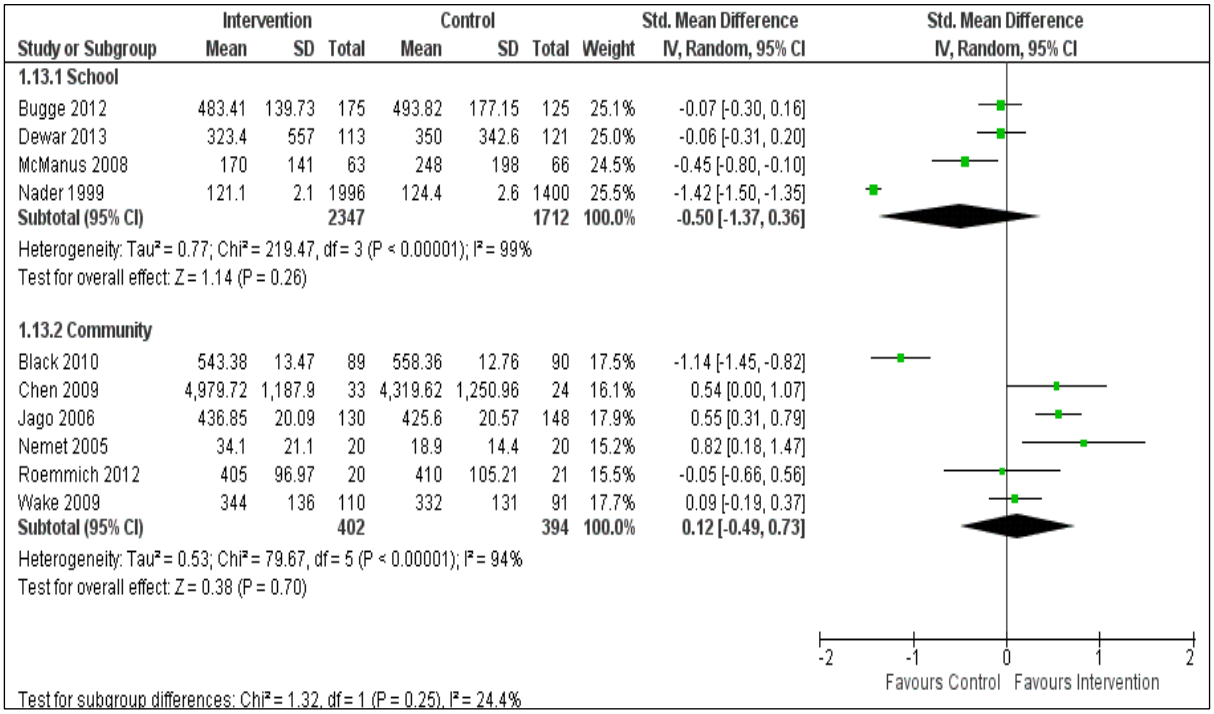
Seven of the twelve studies reporting MVPA took place either partially or fully in a school setting (Araujo-Soares et al., 2009; Bugge et al., 2012; Cui et al., 2012; Dewar et al., 2013; McManus et al., 2008; Nader et al., 1999; Wright et al., 2013) with the remaining seven studies based in the community and involving no delivery within a school setting (Black et al., 2010; Hovell et al., 2009; Jago et al., 2006; Roemmich et al., 2012; Wake et al., 2009). Analysis of the reported effects from the studies involving delivery within a school setting revealed a mean difference of 1.70 (95% CI: -4.84, 8.25; $p = 0.61$), while the mean difference from those studies incorporating community-based delivery produced a statistically significant mean difference of 2.67 (95% CI: 2.05, 3.28; $p < 0.001$) (Appendix 82). The difference between the groups was not statistically significant ($\chi^2 = 0.08$; $p = 0.77$). Within the community-based intervention sub-group the Jago et al. (2006) study accounted for 97.8% of the weighting; removal of this study from the analysis changed the effect to a non-significant mean effect of 2.97 minutes per day (95% CI: -1.13, 7.08; $p = 0.16$) in favour of intervention.

Of the ten studies reporting TPA, four (Bugge et al., 2012; Dewar et al., 2013; McManus et al., 2008; Nader et al., 1999) involved the delivery of an intervention in a school setting with the remainder (Black et al., 2010; Chen et al., 2010; Jago et al., 2006; Nemet et al., 2005; Roemmich et al., 2012; Wake et al., 2009) involving no element of delivery in the school setting. Analysis of the studies that incorporated at least an element of delivery within the school setting revealed a standardised mean difference of -0.50 (95% CI: -1.37, 0.36; $p = 0.16$). Those studies that did not include an element of delivery within the school setting also produced a non-significant standardised mean difference of 0.12 (95% CI: -0.49, 0.73; $p = 0.70$) (Appendix 83). There difference between the groups was not significant ($\chi^2 = 1.32$; $p = 0.25$).

Appendix 81 – Additional sub-group analysis of effects by intervention setting



Appendix 82 - Forest plot showing mean difference in change in MVPA between intervention (n = 3212) and control (n = 2578) groups stratified by intervention setting (school: intervention n = 2795, control n = 2179 across 7 studies; community: intervention n = 417, control n = 399 across 5 studies)

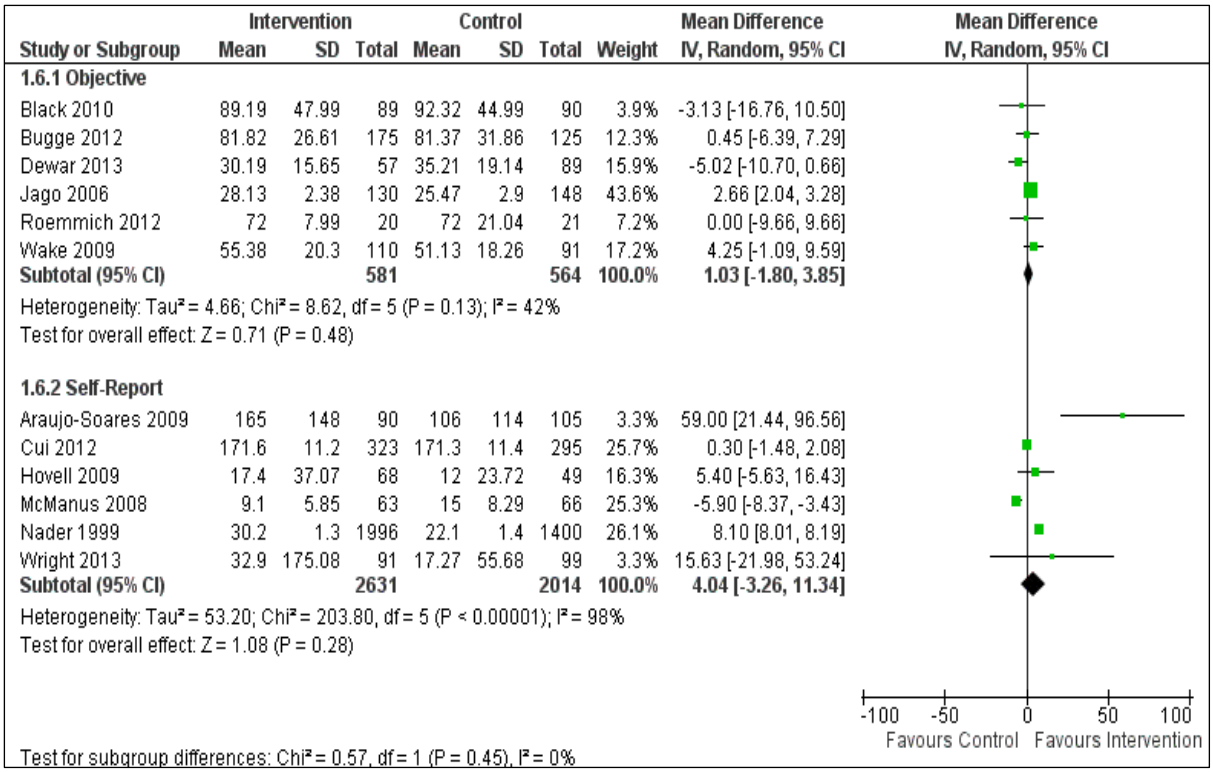


Appendix 83 - Forest plot showing standardised mean difference in change in TPA between intervention (n = 2749) and control (n = 2106) groups stratified by intervention setting (school: intervention n = 2347, control n = 1712 across 4 studies; community: intervention n = 402, control n = 394 across 5 studies)

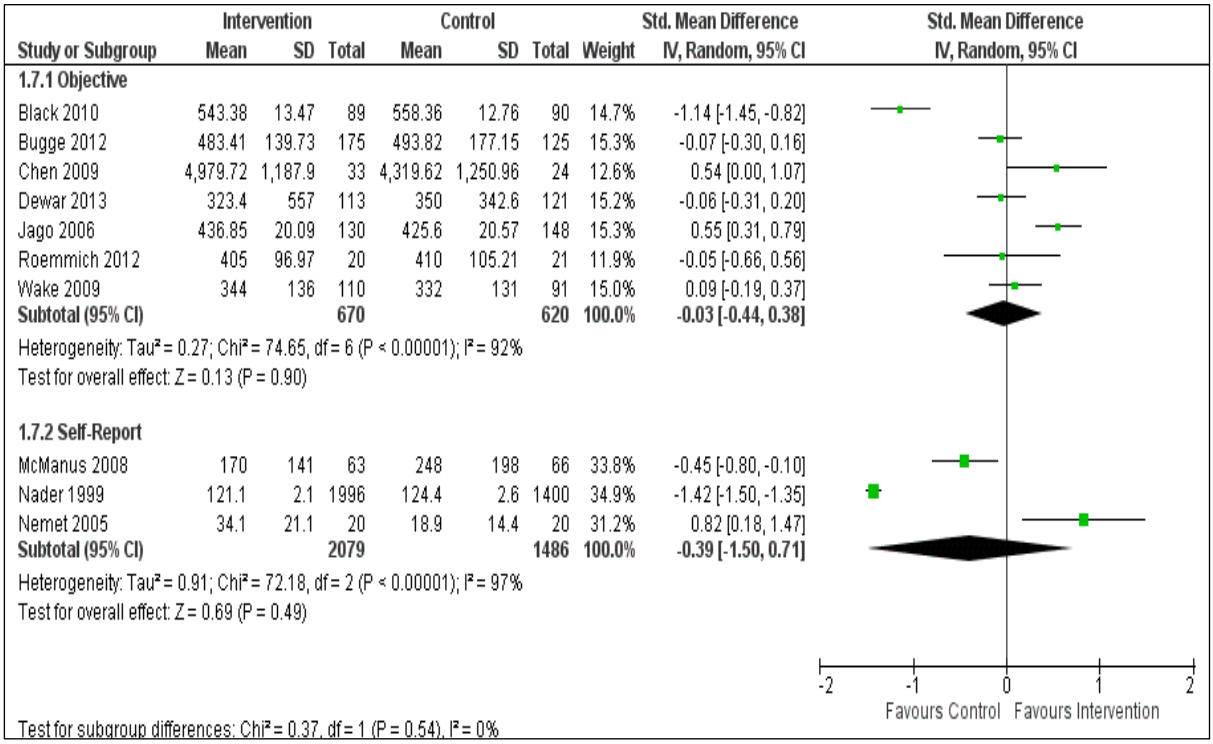
Of the twelve studies reporting MVPA outcome data six utilised objective measurements (Black et al., 2010; Bugge et al., 2012; Dewar et al., 2013; Jago et al., 2006; Roemmich et al., 2012; Wake et al., 2009) and six used self-report measures (Araujo-Soares et al., 2009; Cui et al., 2012; Hovell et al., 2009; McManus et al., 2008; Nader et al., 1999; Wright et al., 2013). Of those using objective measures there was a mean difference of 1.03 (95% CI -1.80, 3.85: p = 0.48) (Appendix 85). The studies utilising self-report measures also returned a mean difference of 4.04 (95% CI: -3.26, 11.34; p = 0.28). There was a statistically non-significant between group difference (χ^2 = 0.57, p = 0.45).

Of the ten studies reporting TPA seven utilised objective measurement (Black et al., 2010; Bugge et al., 2012; Chen et al., 2010; Dewar et al., 2013; Jago et al., 2006; Roemmich et al., 2012; Wake et al., 2009) and three used self-report measures (McManus et al., 2008; Nader et al., 1999; Wake et al., 2009). Analysis of the studies that utilised objective measurement revealed a non-significant standardised mean difference of -0.03 (95% CI: -0.44, 0.38; p = 0.90), while the studies that used self-report measures provided a standardised mean difference of -0.39 (95% CI: -1.50, 0.71; p = 0.49) (Appendix 86). There was no significant difference between the groups by measurement strategy (χ^2 = 0.37; p = 0.54).

Appendix 84 – Additional sub-group analysis of effects by report measure



Appendix 85 - Forest plot showing the mean difference in change in MVPA between intervention (n = 3212) and control (n = 2578) groups stratified by type of outcome measure (objective: intervention n = 581, control n = 564 across 6 studies; self-report: intervention n = 2631, control n = 2014 across 6 studies)



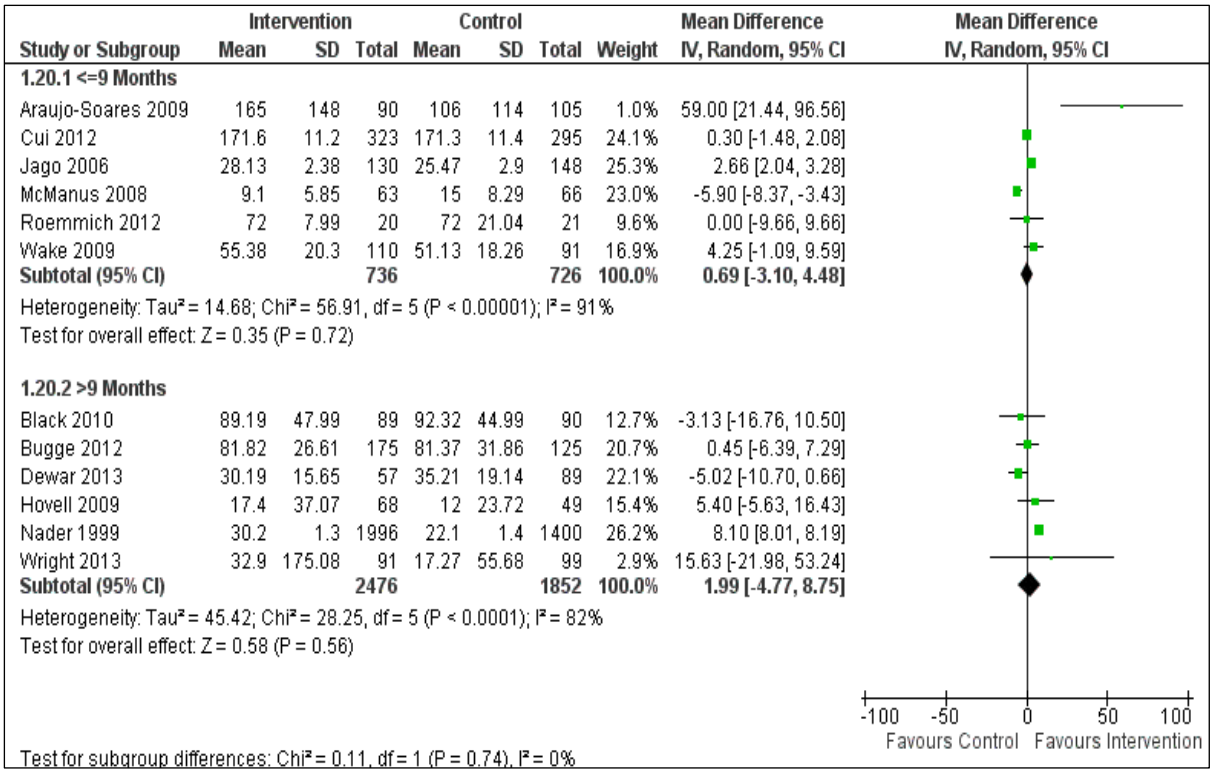
Appendix 86 - Forest plot showing the standardised mean difference in change in TPA between intervention (n = 2749) and control (n = 2106) groups stratified by type of outcome measure (objective: intervention n = 670, control n = 620 across 7 studies; self-report: intervention n = 2079, control n = 1486 across 3 studies)

The median length of post-intervention follow-up measurement for the twelve studies reporting MVPA data was 9.5 months. Of the six studies incorporating a follow-up measurement less than or equal to nine months the time varied between six months (Cui et al., 2012; Jago et al., 2006; McManus et al., 2008), eight months (Roemmich et al., 2012), and nine months (Araujo-Soares et al., 2009; Wake et al., 2009). Analysis of these studies revealed a non-significant mean difference of 0.69 minutes per day of MVPA (95% CI: -3.10, 4.48; p = 0.72) (Appendix 88). The remaining six studies utilised a follow-up duration over nine months, ranging from ten months (Hovell et al., 2009) ten-and-a-half months (Wright et al., 2013), twelve months (Dewar et al., 2013), thirteen months (Black et al., 2010), twenty-four months (Nader et al., 1999), to forty-eight months (Bugge et al., 2012). Analysis revealed a non-significant mean difference of 1.99 minutes per day (95% CI: -4.77, 8.75; p = 0.56) for these studies. There was a statistically non-significant difference between these groups (χ^2 = 0.11; p = 0.74). Meta-regression of standardised mean difference in MVPA by duration of post-intervention follow-up measurement revealed no significant relationship (Appendix 90).

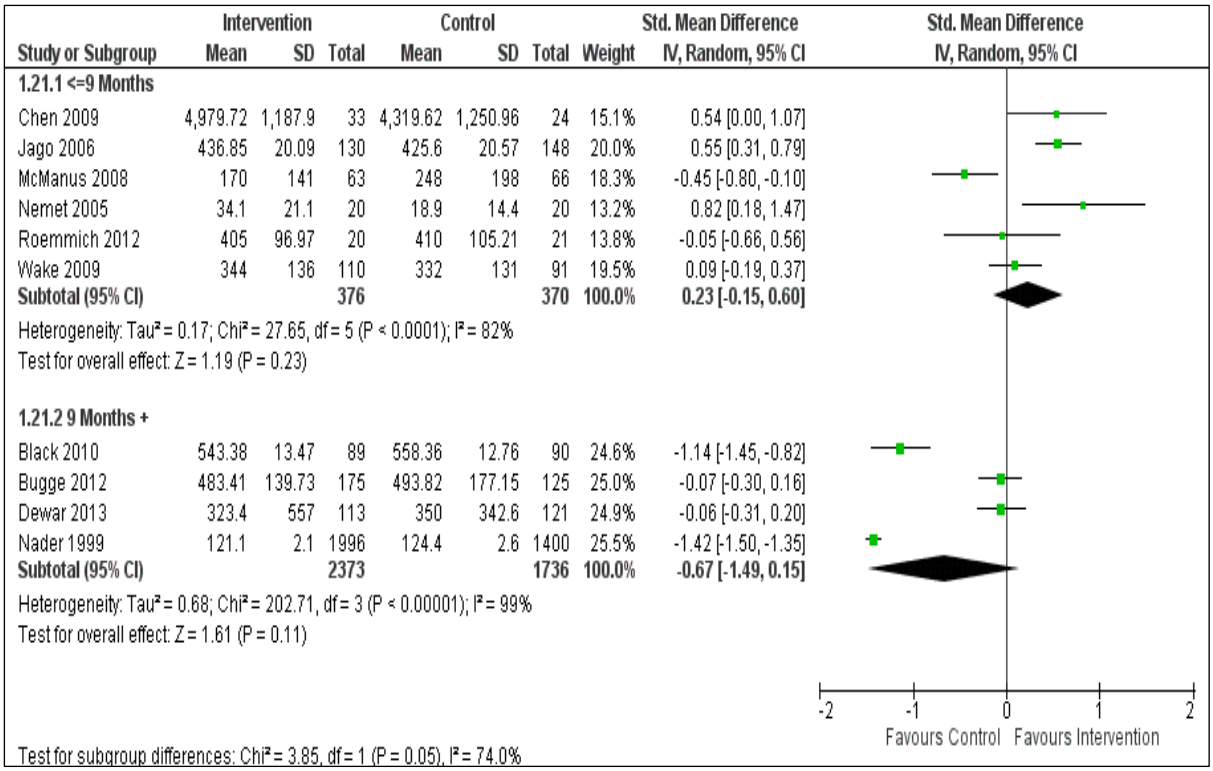
The median length of post intervention follow-up measurement for the ten studies reporting TPA data was nine months. Six studies incorporated a follow-up measurement time less than or equal to nine months, ranging from six months (Chen et al., 2010; Jago et al., 2006; McManus et al., 2008), eight months (Roemmich et al., 2012), to nine months (Nemet et al., 2005; Wake et al., 2009). These studies showed a non-significant standardised mean difference of 0.23 (95% CI: -0.15, 0.60; p = 0.23) (Appendix 89). The remaining four studies incorporated a follow-up delay of over nine months, ranging from twelve months (Dewar et al., 2013), thirteen months (Black et al., 2010), twenty-four months (Nader et al., 1999), to forty-eight months (Bugge et al., 2012). Analysis of these studies revealed a standardised mean difference of -0.67 (95% CI: -1.49, 0.15; p = 0.11) which approached statistical significance. There was a statistically significant difference between the groups in favour of the shorter follow-up duration (χ^2 = 3.85; p 0.05). Meta-regression of

standardised mean difference in TPA by duration of post-intervention follow-up measurement as a non-stratified covariate revealed no significant relationship (Appendix 91).

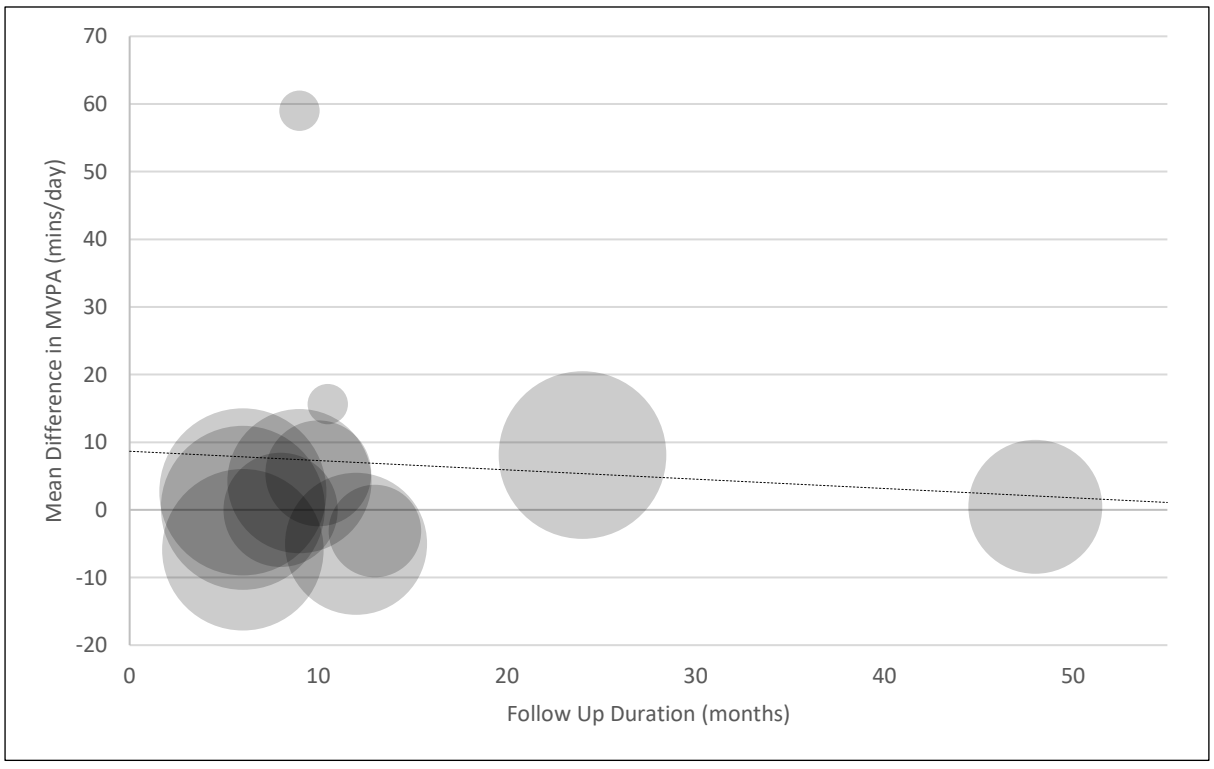
Appendix 87 – Additional sub-group analysis of effects by post-intervention follow-up duration



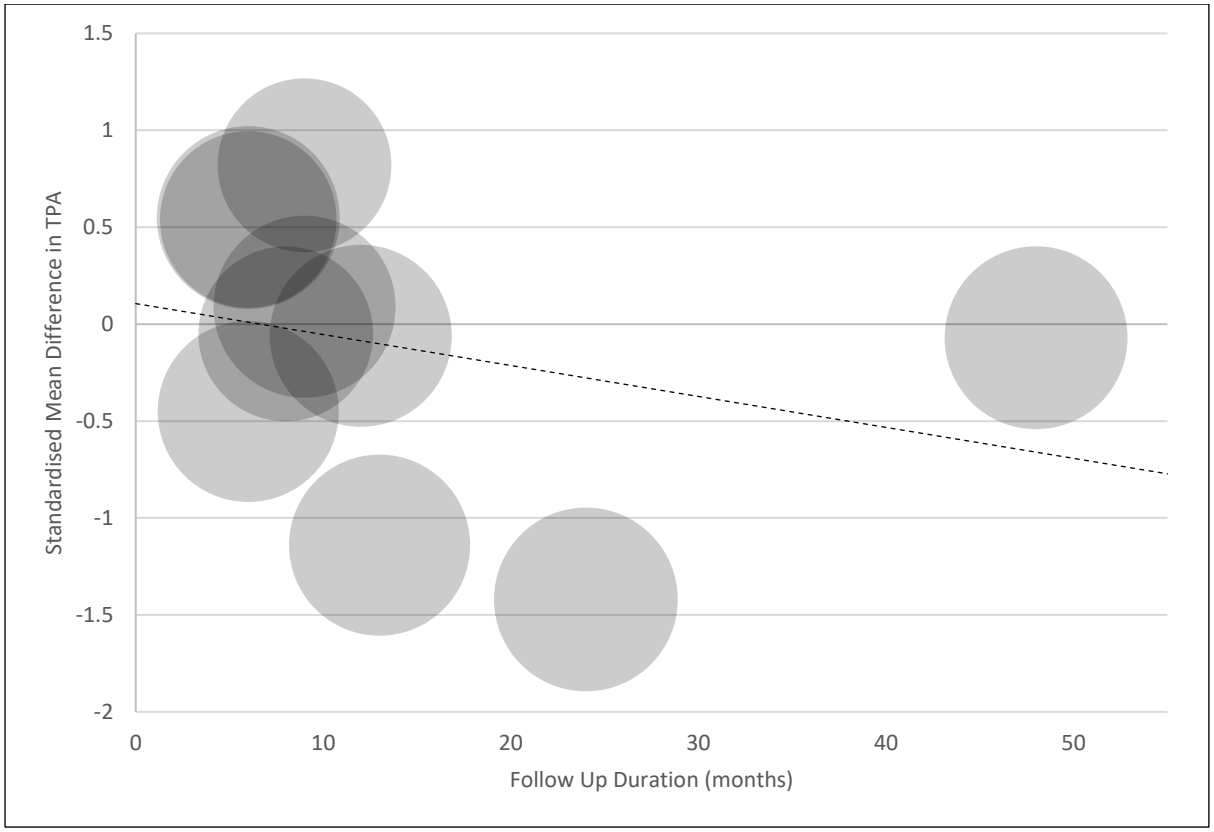
Appendix 88 - Forest plot showing the mean difference in change in MVPA between intervention (n = 3212) and control (n = 2578) groups stratified by follow-up duration (6 to 9 months: intervention n = 736, control n = 726 across 6 studies; over 9 months: intervention n = 2476, control n = 1852 across 6 studies)



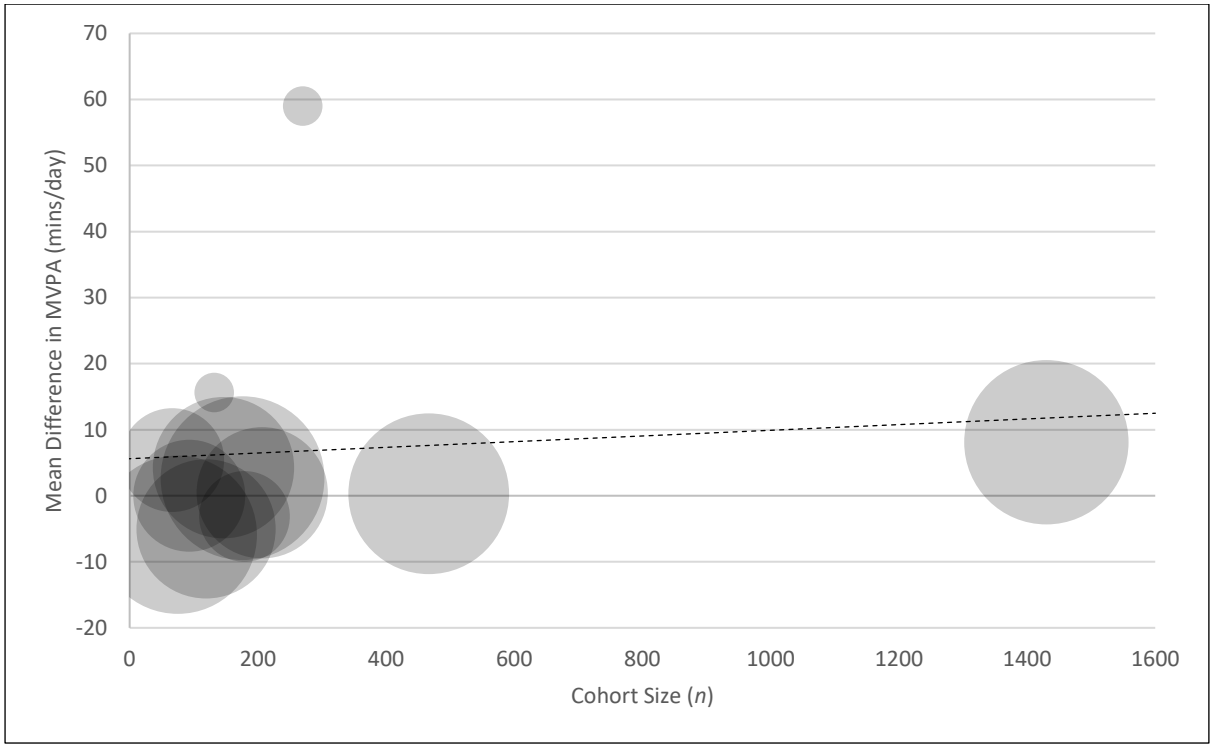
Appendix 89 - Forest plot showing the standardised mean difference in change in TPA between intervention (n = 2749) and control (n = 2106) groups stratified by follow-up duration (6 to 9 months: intervention n = 376, control n = 370 across 6 studies; over 9 months: intervention n = 2373, control n = 1736 across 4 studies)



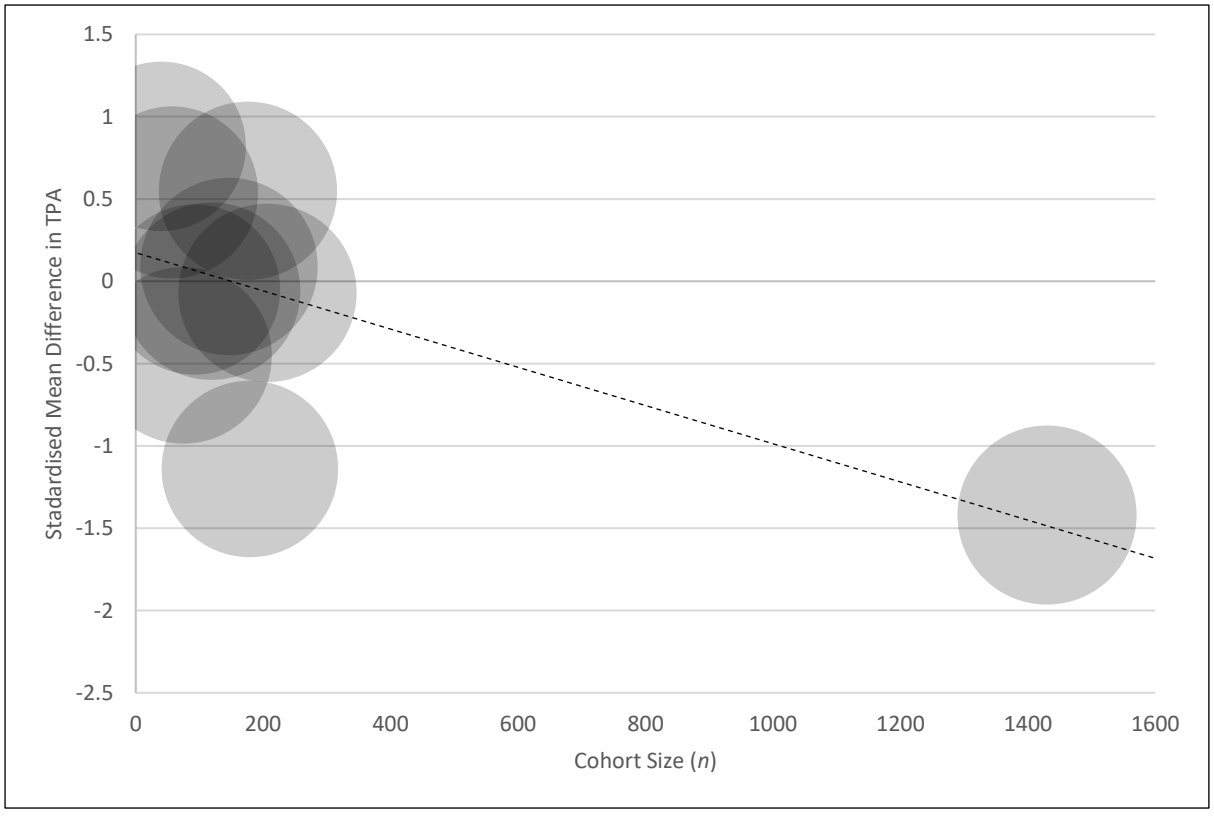
Appendix 90 - Bubble plot showing a meta-regression of mean difference in MVPA by follow-up duration (months) in 12 studies with a coefficient of -1.112 (r^2 = 0.204; p = 0.260)



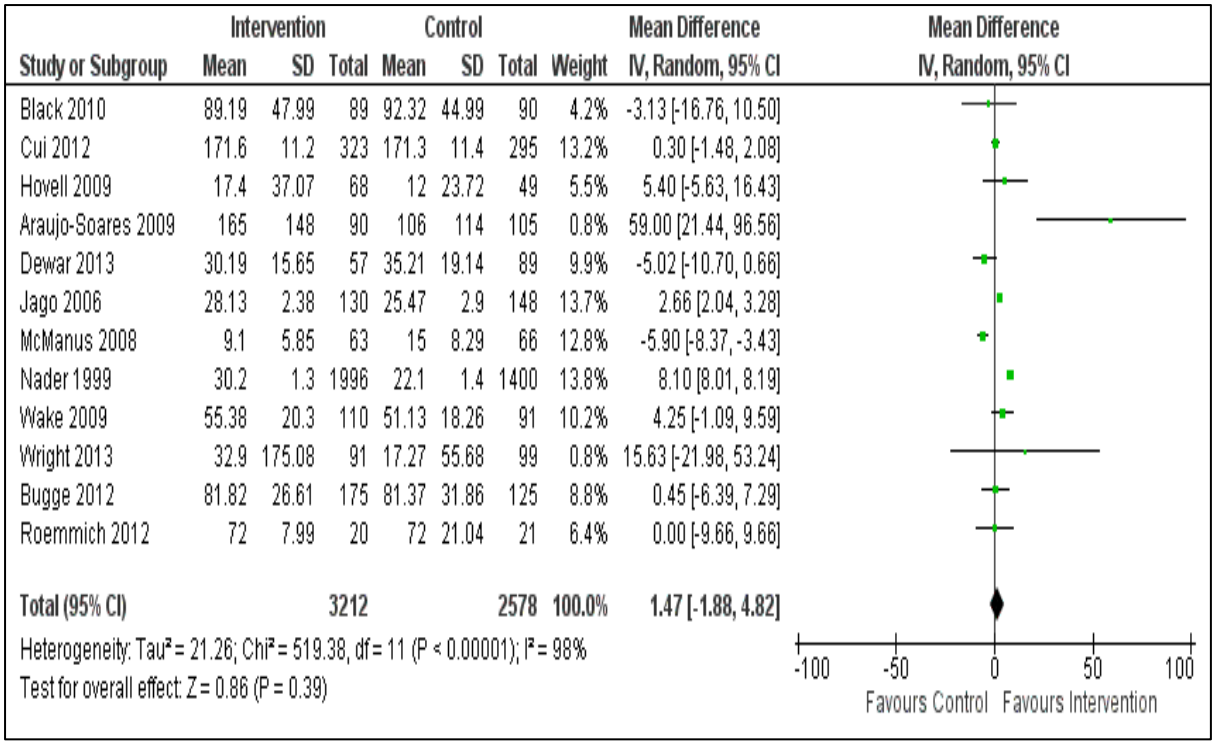
Appendix 91 - Bubble plot showing a meta-regression of standardised mean difference in TPA by follow-up duration (months) in 10 studies with a coefficient of -0.016 (r^2 = 0.044; p = 0.431)



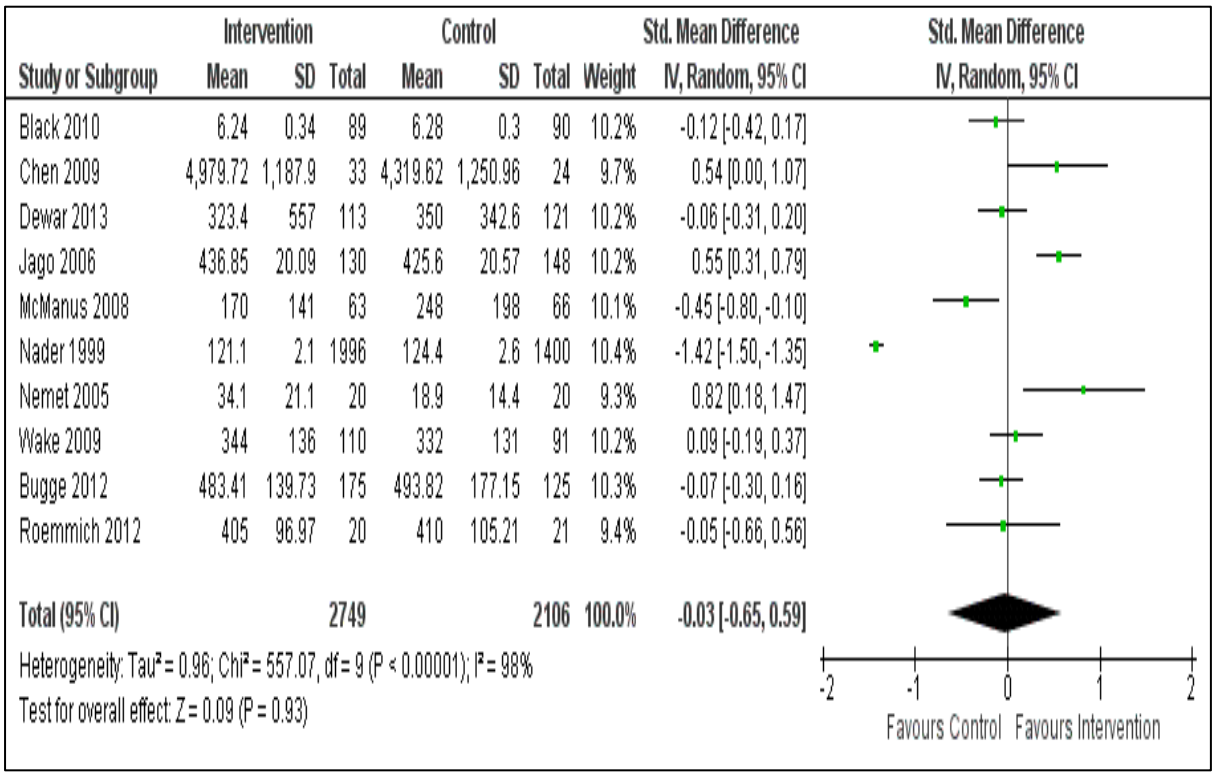
Appendix 92 - Bubble plot showing a meta-regression of the mean difference in MVPA by cohort size of 12 studies with a coefficient of 0.142 (r^2 = 0.326; p = 0.091)



Appendix 93 - Bubble plot showing a meta-regression of the standardised mean difference in TPA by cohort size of 10 studies with a coefficient of -0.001 (r^2 = 0.43; p = 0.03)



Appendix 94 - Forest plot showing the mean difference in change in MVPA between intervention (n = 3212) and control (n = 2578) ranked by study quality assessed using the NICE (2012) methodology checklist



Appendix 95 - Forest plot showing the standardised mean difference in chance between intervention (n = 2749) and control (n = 2106) ranked by study quality using the NICE (2012) methodology checklist