# Socioeconomic position, growth and physical activity: associations with adult fat and lean mass in the MRC National Survey of Health and Development

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Thesis submitted for the Degree of Doctor of Philosophy
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2013

I, David Anthony Bann, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

## Abstract

Fat and lean mass have important implications for adult health and physical functioning, but few studies have examined their determinants. This thesis used a life course perspective to examine how explanatory factors across life relate to adult measures of fat and lean mass.

The MRC National Survey of Health and Development was used—a British birth cohort study originally comprised of 5362 babies born in March 1946. At 60–64 years, 746 males and 812 females had fat and lean mass measures taken using dual energy X-ray absorptiometry. Linear regression was used to examine associations between prospectively ascertained explanatory variables (socioeconomic position, measures of growth, and physical activity) with these masses.

Lower childhood and adult socioeconomic position, greater weight gains in childhood and adolescence (7-20 years), and lower current physical activity levels (measured objectively and by self-report) were all associated with higher fat mass, with evidence in females of cumulative benefits of leisure time physical activity across adulthood (36 to 60–64 years) in leading to lower fat mass. Higher childhood (females only) and adult (both sexes) socioeconomic position, higher birth weight, greater weight gain from birth to 20 years, and physical activity participation across adulthood were all associated with higher lean mass; associations with socioeconomic position and physical activity were found after adjustment for fat mass. Associations between lower childhood socioeconomic position and higher fat mass were partly mediated by weight gain from 7–20 years; associations with higher fat and lower lean mass were partly mediated by leisure time physical activity measures.

Factors operating in both early and adult life were associated with adult fat and lean mass. These factors could be potential targets for public health strategies which seek to reduce fat mass and increase lean mass in the population.

## Acknowledgements

I thank my first supervisor Professor Diana Kuh, and second supervisors Dr Rachel Cooper and Dr Andrew Wills. I have learned an enormous amount under their supervision and am extremely grateful; the completion of this work was made possible with their guidance, feedback and encouragement.

For their support I wish to thank my colleagues in the MRC unit for Lifelong Health and Ageing and the Department of Epidemiology and Public Health (University College London), especially Peijue (Peggie) Huangfu, Dorina Cadar, Ayako Hiyoshi, Manu Mathur, and Shaun Scholes. For helpful feedback on my work I'm grateful to those in the Bone and Muscle Ageing Project Management Group (Dr Ann Prentice, Dr Kate Ward, Professor Judith Adams, Professor Avan Aihie Sayer, Professor Cyrus Cooper), particularly Professor Judith Adams who, along with Mike Machin, played a major role in deriving the body composition data used in this thesis. Colleagues in the MRC Epidemiology Unit in Cambridge derived the Actiheart data used in this thesis, and I'm grateful for their work. I also thank the study members of the MRC National Survey of Health and Development for their continued contribution to this outstanding scientific resource.

I thank all those who across my life have helped me—my friends and particularly my family (especially my Dad (Trev), Mother, Susan, Chris and Jenny) for encouraging me, supporting my growth and education, and steering me away from at one stage almost certain high school failure.

Finally, I thank the MRC for providing financial support.

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## Abbreviations

BIA=bioelectrical impedance analysis
BMI=body mass index
DXA=dual-energy X-ray absorptiometry
MET=metabolic equivalents
NS-SEC=The National Statistics Socio-economic Classification
NSHD=the MRC National Survey of Health and Development
SEP=socioeconomic position
SFT=skinfold thickness

# 1. Chapter 1: Introduction

The amount of fat and lean mass in our bodies (our body composition) has important implications for our health and physical functioning. Obesity—excess fat mass—is associated with numerous measures of ill health (type 2 diabetes, stroke, and cancer)[1] and increased rates of mortality.[2] Low lean mass is an indicator of low skeletal muscle mass and relates to worse physical functioning,[3;4] low bone mineral content,[5;6] and adverse glucose metabolism.[7]

Understanding the factors that influence the amount of fat and lean mass we have as adults is key to reducing the burdens associated with obesity and low lean mass in old age. The overall aim of this thesis is to use a life course perspective to examine the associations between factors across life with fat and lean mass in early old age, using data from the MRC National Survey of Health and Development (NSHD)—a British cohort of 5362 males and females followed up since birth in March 1946.

This chapter presents a broad overview of the research area investigated in this thesis, including evidence for the importance of fat and lean mass for health and physical functioning. An introduction to life course epidemiology is then presented, followed by an overview of previous research investigating the factors across life associated with adult fat and lean mass. The limitations of previous research are then briefly described along with the overall aim of this thesis.

## 1.1 Historical background: body weight, body shape and health

Interest in the weight and shape of the body has been recorded in human history for thousands of years. The first known artistic representation of obesity was created around 30 000 years ago, in the form of an obese statuette: the Venus of Willendorf.[8;9] However, it was not until 400 BC that the relationship between obesity and health was first documented, with physicians linking obesity with increased risk of infertility and mortality.[8] Since then, more robust epidemiological evidence has been published linking aspects of the weight and shape of the body with a wide range of health outcomes.

In the early 1920s, researchers such as Raymond Pearl (1879–1940) began compiling detailed measurements of human subjects and examining their

relationship with disease risk.[10;11] In 1934, Pearl and Ciocco[12] examined and compared two groups of people: those with heart disease, and those without (termed cardiac and non-cardiac individuals, respectively). A series of detailed measurements were taken from each participant, including height and weight, and measures from the head and chest. Comparison of these variables between the two groups showed that cardiac individuals were heavier (by around 10%) than their leaner 'non-cardiac' counterparts, with no notable differences in height.[12] Although the authors were wary of asserting causation in the associations found, they suggested that differences were likely due to the "accumulation of body fat from relative over-eating and lack of physical exercise" (p.711) in the cardiac group.[12] At a similar time to this study, the importance of weight and height were also being explored using life insurance data; shorter and heavier individuals were found to have higher risk of mortality and morbidity from chronic disease than taller, lighter individuals.[10]

In 1948, US researchers established the Framingham study: 5209 adult residents of Framingham, Massachusetts (USA) were enrolled to allow investigation of risk factors for the increasingly prevalent cardiovascular disease. The continued follow-up of this cohort and its offspring has provided a wealth of evidence on associations of body weight and shape with ill health. Findings published in 1969 showed study members who were heavier and more endomorphic (a specific body shape characterised by higher fat mass and abdominal fat distribution) were more likely to develop coronary heart disease than those of other body shapes.[13] Further work in 1988 showed that obesity—assessed using either waist circumference or measures of skinfold thickness (SFT)—was associated with increased risk of all-cause mortality.[14] This suggested that fat mass, and not weight per se, was related to poor health and subsequent mortality. Later work confirmed the importance of fat mass and its distribution, with analysis showing that greater abdominal fat mass was associated with increased risk of cardiovascular disease.[15]

Abraham et al (1971),[10;16] in a 30–40 year follow-up of the Hagerstown population study in Maryland (USA), showed that heavier adults tended to have higher blood pressure and higher serum cholesterol. In this study measured childhood height and weight data were available; analyses using these data showed that subjects who were underweight in childhood and heavier in adulthood had the highest number of risk factors for cardiovascular disease. This suggested that weight in both early and adult life were important in influencing health in adulthood.

A substantial body of epidemiological research—comprising prospective and retrospective studies, as well as systematic reviews and meta-analyses—have confirmed relationships between the weight and shape of the body and a number of health outcomes.[1;2;17] The composition of the body has also received research attention. Over time, a number of overlapping terms have been used to describe the dimensions and contents of the human body—for example, the body has been described in terms of constitution, form, somatotype, composition, shape, and anthropometrics. In this thesis, the term body composition will be used to refer to the content of the body as divided into fat and lean mass (total body weight excluding fat and bone mass).[18] In the following sections, the roles of fat and lean mass in normal bodily functioning will be briefly described, followed by the importance of fat and lean mass for both health and physical functioning.

## 1.2 **Fat mass: importance for health and physical functioning**

Fat mass is comprised of adipocytes (fat cells) and is known to be involved in energy metabolism,[19] heat insulation,[20] and various endocrine processes.[21] Both high and low levels of fat mass (overweight/obesity and lipodystrophy, respectively) are thought to be detrimental for health.[2;17;22]

Fat tissue can undergo considerable changes in size in adulthood, and the scope for variation is substantial—recorded percentage values have been as low as 2% and as high as 70%.[23] Average values of fat mass in adulthood have been estimated to be 18–24% for males and 25–31% for females.[24] Associations between fat mass and ill health have typically been deduced from studies using body mass index (BMI; weight (kg)/height $(m)^2$), a proxy measure of fat mass.[25] Overweight and obesity are defined as "abnormal or excessive fat accumulation that may impair health"[26] and reflect the upper distribution of fat mass. Standard BMI cut-off points have been developed—formed on the basis of non-communicable disease risk[27;28]—to enable simple categorisation of overweight and obesity. According to World Health Organization criteria, a BMI ≥25–30 is considered overweight, and ≥30 obese;[26] 'normal' BMI ranges have been defined as between 18.5–24.9, and underweight <18.5.[17] Aside from BMI, there are a number of other ways of measuring fat mass directly, from highly refined and relatively expensive measures generally only suitable for small clinical studies, to less refined measures more feasible for use in larger population-based studies. While cut points of obesity using direct measures of fat mass have been proposed (body fat percent >25% in males and >35% in females),[29;30] BMI classifications are more commonly used. The

limitations of using BMI as a measure of fat mass are described later in this chapter.

Plausible biological mechanisms have been suggested which may explain how high fat mass leads to ill health. For example, fat cells are now known to secrete multiple hormones, many of which are known to have wide-ranging effects on the immune, cardiovascular, reproductive, and inflammatory systems,[21;31] although the specific chain of events that lead to ill health is an area of on-going research. The most widely researched of these hormones are adipokines, cell-cell signalling proteins secreted by adipose tissue. For example, leptin (a cell-cell signalling protein) is known to correlate positively with fat mass,[32] and leptin is thought to be involved in reproductive and immune functioning.[33;34]

As well as affecting endocrine processes, high fat mass also causes increased load on the bodily systems. Since fat mass is served by a regular blood supply, an increase in fat tissue leads to an increase in cardiac load. The blood supply to adipose tissue accounts for around 3–7% of cardiac output in non-obese, and 15–30% in obese individuals.[23] High fat mass also affects the musculoskeletal system by impairing the joints (leading to increased risk of osteoarthritis[35]) and leading to fat infiltration of muscles.[36] These processes and others may impact on physical functioning, as studies have consistently found high fat mass is associated with concurrent and future measures of worse physical functioning.[4;37-39]

Recent systematic reviews and meta-analyses have confirmed that obesity, defined using the standard BMI cut-offs, is a significant risk factor for a number of health outcomes (including chronic diseases) and increased mortality.[1;2;17] For example, a recent narrative review in which systematic reviews were synthesised concluded that the relative risk ratios when comparing obese versus non-obese persons are approximately ≥5 for type 2 diabetes, dyslipidaemia, and non-alcoholic steatohepatitis; 2–5 for all-cause mortality, hypertension, myocardial infarction, stroke, and polycystic ovary syndrome; and 1–2 for cancer mortality, obstetric complications, and asthma.[1] The relationship between fat mass and health in older age is inconclusive; some studies have reported inconsistent associations between BMI and health outcomes in old age, although this may be partly driven by low lean mass.[40] However, few studies have examined associations between direct measures of fat mass and health outcomes or mortality risk in early or later adulthood. Although direct measures of fat mass are hypothesised as being more closely related to health outcomes than BMI,[41] this requires confirmation as some,[42;43] but not all studies[44] have given evidence to support this.

In addition to whole body fat mass, the distribution of fat mass may be particularly important with fat deposited in the abdomen thought to be worse for health than fat deposited in other regions of the body.[45;46] This may be due to abdominal fat being more active in endocrine systems than peripheral fat.[45;46] High abdominal fat mass is part of the most commonly used criteria for diagnosing metabolic syndrome, a collection of risk factors known to predict the risk of type 2 diabetes and cardiovascular disease.[47-49] Of fat present in the abdomen, visceral fat (present around the viscera and organs) is thought to represent a greater risk to health than subcutaneous fat (present under the skin).[50;51] Indirect measures of abdominal fat mass (such as waist circumference and waist-hip ratio) capture fat mass, but also lean mass and skeletal size; these indirect measures have similar effect sizes as BMI in associations with health outcomes.[52;53] Direct measures of abdominal fat mass have recently become available in epidemiological studies, and there is some evidence that these may be more closely associated with health outcomes than whole body measures of fat mass.[49;54]

While fat distributed in the abdomen may be detrimental to health, there is some evidence (typically from small studies) that higher leg fat mass may be beneficial. Using direct measures of fat mass, higher leg fat mass has been associated with more favourable glucose[55;56] and lipid metabolism.[57-59] The differential associations between abdominal and leg fat mass suggests that a ratio of abdominal: leg fat mass may be particularly related to health. This is suggested in studies which have found associations between higher ratio of android (abdominal): gynoid (upper leg) fat mass and adverse glucose metabolism,[60;61] and increased risk of cardiovascular disease in females.[62]

Population levels of fat mass have substantial public health implications across the world, but vary by nation and period. There have been substantial changes in the recorded population averages of BMI, with countries moving through the epidemiological transition—the transition in the principle causes of mortality (from infectious to chronic and degenerative diseases) that take place in tandem with economic development and demographic change[63-65]—typically experiencing an increase in the prevalence of overweight and obesity.[63]

In England, the prevalence of obesity more than doubled between 1970 and 2005,[17] an increase mirrored in other nations (including USA, Japan, Germany, and Australia).[17] Health Survey for England data show that in 2010, 68% of adult males (and 58% of females) in England were overweight or obese (BMI ≥25), and 26% of

both male and female adults obese (BMI >30).[66] The economic burden of obesity is also substantial, with the direct and indirect costs in England estimated to be around £7 billion per year in 2002,[17] and similarly high estimations for other developed and developing nations.[67] Given its increasing prevalence, future projections of the cost impacts have been estimated to be even higher—£49.9 billion per year in the UK in 2050.[17] There is also growing recognition of an increasing prevalence of obesity in the developing world, leading the WHO to recognise obesity as a global epidemic.[68]

In summary, there is substantial evidence that high fat mass is associated with increased risk of chronic diseases and mortality, and leads to worse physical functioning. There is also some evidence that abdominal fat distribution may be particularly important for subsequent health. As such, there is justification for examining how factors across life affect fat mass levels in adulthood.

### 1.2.1 ***Changes in fat mass across life***

The point in life at which fat is measured is an important consideration when using measures of fat mass in epidemiological studies, as fat mass is known to vary across life. For example, cross-sectional studies of both sexes suggest that gains in fat mass occur in infancy (0–2 years), tend to plateau in early childhood (2–7 years), and then increase again in late childhood (7–11 years), with sex-specific changes in adolescence (11–18; females continue to gain fat mass, while males plateau),[69;70] resulting in female adults tending to have more fat mass than males. Cross-sectional and longitudinal studies suggest that gains in whole body and abdominal fat mass typically occur during adulthood (30–80 years) in both sexes, along with increasing fat deposition in other tissues (such as skeletal muscle, cardiac tissue, and the liver).[36]

The amount of fat mass in adulthood, determined by both the number and size of fat cells,[71] has been shown to track across life, with those with higher fat mass in childhood tending to maintain their higher levels into adulthood.[72-74] Factors that affect fat mass in pre-adulthood may therefore affect the amount of fat mass in adulthood. Further, pre-adulthood factors may also affect the probability of gaining or losing fat mass in adulthood. As such, factors that operate both in early and adult life may influence fat mass levels in adulthood.[75]

## 1.3 **Lean mass: importance for health and physical functioning**

In this thesis, unless otherwise specified, lean mass is used to refer to the mass of the body excluding fat and bone mass.[18] It is an amalgamation of tissue types, including muscle tissue and the organs and is equivalently termed fat-free mass. As direct measures of lean mass are a relatively recent development in population studies, there are fewer studies examining the consequences of higher or lower lean mass for subsequent health outcomes. In addition, as lean mass is comprised of a number of distinct parts, with distinct functions, the health significance of lower or higher amounts of lean mass are not as intuitively clear as with fat mass. However, research has shown that in healthy subjects around 50% of whole body lean mass is skeletal muscle,[76] suggesting that lean mass can be considered a marker of muscle mass. The proportion of lean mass that is skeletal muscle is likely to be higher for appendicular lean mass (lean mass of the arms and legs) than whole body lean mass, as appendicular lean mass excludes the organ mass contained in the trunk of the body.

Muscle is comprised of three main types: skeletal, smooth, and cardiac. Smooth muscle is involved in involuntary processes such as digestion and cardiac muscle forms the heart, enabling the transfer of blood around the body. Skeletal muscle is used for movement (with more than 500 separate muscles) and as a source of metabolic heat for surrounding tissues.[20;77] Given the essential role of skeletal muscle in movement, low muscle mass may be detrimental for physical functioning. As will be described in more detail later in this chapter, lean mass levels are known to decline in adulthood, and this may lead to impaired physical functioning. This has been termed sarcopenia, a term subject to on-going academic debate.

Sarcopenia was originally defined as the age-related decline in lean mass,[78] a term subsequently used to describe the age-related decline in muscle mass and strength and/or physical performance.[79-81] Although there is currently no agreed definition of sarcopenia, all proposed definitions include measures of low muscle mass (eg, appendicular lean mass (kg)/height $(m)^2$ <7.26 in males and <5.45 in females),[82] with others additionally taking into account fat mass[4;83] and strength or physical performance.[79-81;84]

Some authors have suggested that sarcopenia should be used to refer to declines in muscle mass, and dynapenia used to refer to declines in muscle strength.[85;86] A number of studies have found that low muscle strength is a stronger predictor of mortality and worse physical function than low lean mass,[87;88] suggesting that

including both in a definition of sarcopenia adds additional clinical utility. However, although it is widely assumed that declines in muscle mass lead to declines in muscle strength (which then affects subsequent physical functioning), longitudinal studies have found that changes in lean mass are not always followed by expected changes in muscle strength.[85;89] This suggests that muscle mass and strength have different determinants (eg, strength may be more directly related to neuromuscular functioning), and therefore warrant separate investigation of aetiological factors.[85;90] Following this, the focus of this thesis will be on lean mass (or equivalently muscle mass). As described below, low lean mass may be related to worse physical functioning and health.

A number of studies have found low lean mass to be associated with concurrent[4;83;91;92] and future measures[3;93] of worse physical functioning assessed by either self-report (eg, self-reported functioning limitations) or objectively (eg, slow walk speed or chair rise time). In these studies associations in females tend to be only found using a definition of low appendicular lean mass which also takes into account fat mass.[3;4;83] One study used repeat measures of lean mass and found that greater decline in lean mass over 5.5 years was associated with greater risk of self-reported physical disabilities.[94] However, not all findings are consistent, with some studies finding that lean mass was not associated with concurrent[95;96] or future[97] physical functioning. Overall, there is some evidence that lower lean mass is related to worse physical functioning, although inconsistent findings suggest the need for future research.

In addition to use in movement and physical functioning, lean mass is also involved in physiological processes which have health consequences.[98] Since muscle is an important site for glucose uptake in response to insulin,[99;100] low levels of lean mass could lead to deregulated increases in blood glucose levels, insulin resistance, and therefore increase the risk of diabetes.[7;101;102] Since insulin resistance and diabetes are risk factors for cardiovascular disease,[103] lower levels of lean mass could ultimately lead to higher risk of cardiovascular disease. A recent large cross-sectional study (n=14,528) showed that those of low lean mass in later adulthood (>60 years) tended to have worse glucose metabolism, although it was acknowledged that longitudinal data are required to elucidate the direction of association.[7] A pathway between low muscle mass and chronic disease has been hypothesised in studies which report associations between low intrauterine muscle development (indicated by low birth weight) and both low lean mass and later elevated risk of cardiovascular disease in adulthood.[101;104;105]

As well as potentially impacting on glucose metabolism, lean mass may also be related to bone mineral content. According to the mechanistic model of bone development, bone mineral content may be driven by the mechanical load driven by muscle mass.[106-108] Repeat measures of lean and bone mass in adolescence have supported this suggestion, with increases in lean mass preceding increases in bone mass.[108] This relationship is thought to extend to later adulthood, with cross-sectional studies showing lean mass to be positively correlated with bone mineral content[5;6] and density.[109] The decline in lean tissue in later adulthood may lead to a decline in bone mineral content,[110] and a consequent increased risk of fracture.[111]

Other potential roles of lean mass in health include its role in basal metabolic rate, with higher lean mass associated with faster resting metabolic rate.[112;113] In addition, skeletal muscle is thought to act as a source of protein which can be used by other bodily organs during periods of malnutrition or acute ill health.[98] As such, higher muscle mass may be protective for health and in response to acute stressors. For example, greater muscle loss in cancer is associated with increased risk of mortality.[98] However, it should be noted that studies examining associations between lean mass and mortality in non-diseased populations have produced inconsistent findings.[87]

Although the wider public health implications of low lean mass are likely to partly depend on the particular cut-points used, the estimated prevalence of sarcopenia (typically defined solely by low lean mass) suggests that a sizable proportion of the UK population are at risk. Van Kan in 2009[114] synthesised the available epidemiological data in the USA and non-UK European countries and found prevalence estimates to be between 8 to 40% in those aged 60 years or older. The high variability was attributed to differences in cut point and definitions used, but may also be caused by differences in subject characteristics in each study, and dual-energy x-ray absorptiometry (DXA) software and hardware.[115] Although data for the UK were not included (and to the author's knowledge are not available), the prevalence would be expected to be near to the USA and other European cohorts studied. As an increasing proportion of the UK population are surviving into old age,[116] the public health and economic impacts of low lean mass are likely to be substantial as increasing numbers are exposed declines in lean mass and therefore detrimentally low lean mass levels. The economic costs of sarcopenia have been estimated to be $18.5 billion in the USA in 2000, due to increasing need for disability assistance in those with low lean mass.[117]

In summary, while the relationship between lean mass and health outcomes is less well researched than with fat mass, there is some evidence that low lean mass is related to worse physical functioning, adverse glucose metabolism, lower bone mineral content and lower basal metabolic rate. There is therefore justification in examining the factors associated with lean mass levels in adulthood. As with fat mass, the period of life in which lean mass is measured may be important to consider in analyses as lean mass is known to vary across life.

### 1.3.1 *Changes in lean mass across life*

Cross-sectional data have shown that gains in lean mass take place in both sexes from birth to early adulthood (18–20 years), with males tending to gain more lean mass in adolescence (12-18 years) than females, leading to male adults typically having more lean mass than females.[20;70] Lean mass levels are thought to decline in adulthood, particularly in later adulthood; both cross-sectional[118;119] and longitudinal data[120] suggest steep declines from around age 50 onwards—a total of a 25–30% reduction in mass up to age 80.[118;119;121] Although not the focus of this thesis, muscle strength and other muscle parameters (power and endurance) are also known to decline in adulthood—[122] muscle strength has been shown to decline more rapidly than declines in lean mass,[85;89] which may be partly explained by morphological changes in muscle tissue with ageing including fat infiltration.[36;123]

The amount of lean mass in later adulthood—determined by the number, size, and density of muscle fibres—is likely to be influenced by the peak levels attained during earlier periods of life, the rate of subsequent decline, and the time at which the decline begins.[77;124] Pre-adult factors may feasibly influence the peak level of lean mass attained as well as the timing and rate of adulthood decline, while factors in adulthood may affect both the timing and rate of adulthood decline. As such, factors in both early and adult life may be important in influencing the lean mass levels in later adulthood.

While lean mass is typically used as a measure of skeletal muscle mass, it should be noted that lean mass also contains organ mass which, as highlighted in recent studies, has been found to decline in later adulthood.[125;126] However, the consequences of higher or lower organ mass are not well understood and are not the focus of this thesis.

## 1.4 **The relationship between fat and lean mass**

In the previous sections, the roles of fat and lean mass in health and functioning were outlined separately. While they are discrete sections of the human body with distinct functions, the relationship between these masses is important and warrants discussion.

Fat and lean mass in adulthood have been shown to be strongly positively correlated in cross-sectional analyses, and studies have found gains or losses in fat mass tend to be followed by gains or losses in lean mass.[127-131] While the mechanisms underlying these associations are not fully understood, they could result from adaptive mechanisms in which changes in fat mass lead to downstream changes in lean mass; gains in fat mass would lead to greater muscle loading, and therefore the need for higher lean mass to support the resulting additional weight. The relationship between fat and lean mass may be important to consider in the study of aetiological factors as associations with fat mass may drive associations with lean mass. The relationship between these masses may however differ in later adulthood, with losses of lean mass typically occurring alongside gains in fat mass in old age, and those of greater fat mass in old age experiencing greater subsequent losses of lean mass.[132]

Although fat and lean mass have been found to be positively correlated, in some cases individuals have high fat mass and low lean mass. While high fat and low lean mass have in isolation been related to worse physical functioning, the simultaneous presence of both may be particularly detrimental for physical functioning as the presence of low muscle mass is compounded by the need to carry excess fat mass. This has been termed sarcopenic obesity,[133;134] although there is no agreed consensus on the definition. Some[135;136] population studies in later adulthood (using both cross sectional and longitudinal designs) have found that sarcopenic-obese individuals tend to have lower physical functioning than obese-only or sarcopenic-only subjects, although other studies have not found this.[137;138] These studies have tended to find that the effects are additive, and not multiplicative. The differences in findings may be partly explained by the different ways in which sarcopenia and obesity are defined, suggesting that further research is required.[39]

In addition to implications for physical functioning, the relative amounts of fat and lean mass may be important for health outcomes. While adipose tissue is known to secrete pro-inflammatory compounds, recent research in mice has shown that muscle tissue secretes anti-inflammatory compounds (myokines).[139;140] These have

been shown to have protective effects on the vascular system and cardiac tissue, and are hypothesised to counter the detrimental impact of pro-inflammatory compounds secreted by fat tissue.[139] If this is also true in humans, it would suggest that the proportions of muscle and fat mass are important for health.[141]

The ratio of fat: lean mass may be a useful outcome in the study of life course factors that influence fat and lean mass, as this provides a clear means of assessing whether an explanatory variable has a stronger association with fat or lean mass. For example, two hypothetical risk factors may both lead to higher fat and lean mass levels, but lead to either higher or lower fat: lean mass ratio (depending on the strength of the individual associations, and mean levels of fat and lean mass). As such, the factor which lead to a lower fat: lean mass ratio would be considered beneficial.

In this thesis, whole body fat and lean mass will be the main outcomes of interest, and the life course influences of these will be explored in subsequent chapters. Both whole body and appendicular lean mass will be used; while both are measures of skeletal muscle mass, the use of the former enables fairer comparison with studies which have used this outcome (eg, those which cannot distinguish appendicular regions such as bioelectrical impedance analysis, BIA), and the latter is likely to be a more accurate measure of skeletal muscle mass. In addition, the ratio of fat: lean mass will also be used, to show how explanatory variables considered affect the relative amounts of fat and lean mass. Android: gynoid fat mass ratio will also be used as an additional outcome for fat mass, as high abdominal fat distribution may be additionally detrimental to health.

Previous studies have tended to examine how explanatory factors across life relate to BMI, not direct measures of fat and lean mass. In the following section the limitations of BMI will be discussed.

## 1.5 **Limitations of body mass index**

Anthropometric measures of the body have historically dominated the published epidemiological literature in studies investigating fat mass as either the predictor or outcome of interest.[75] Although BMI is reasonably easy to obtain, and therefore feasible for use in large population studies, it has a number of limitations.

As BMI does not distinguish between fat and lean mass, associations between an explanatory factor (or outcome) and BMI may be driven by associations with fat

mass, lean mass, or both. The extent to which associations with BMI are due to fat and/or lean mass is likely to differ by age and sex: as previously described in this chapter, ageing is associated with gains in fat and declines in lean mass,[25] and males typically have less fat and more lean mass than females.[70] Given the importance of both fat and lean mass to health and physical functioning there is a need to understand the aetiological factors which influence both masses; this requires the use of direct measures of fat and lean mass.

The extent to which BMI is an accurate measure of fat mass is also uncertain. Studies have reported substantial variation in associations between BMI and direct measures of fat mass (eg, correlations between 0.68 and 0.89), with differences in correlations reflecting differences in the body composition (amount of fat and lean mass) in each population investigated.[142;143] While high BMI is used to diagnose overweight and obesity, these are defined by excess accumulation of body fat;[26] it is through fat mass, and not weight, that obesity is thought to be associated with health outcomes. The use of direct measures of fat mass may therefore be most relevant for health, suggesting that where possible direct measures of fat mass should be used in aetiological studies.

For the reasons outlined above, the use of direct measures of fat and lean mass may be more informative than BMI. As direct measures of fat and lean mass have increasingly become available for use in population studies, a growing number of studies have examined associations between exposures in adulthood with these masses. A smaller number of studies have investigated associations with exposures at earlier points in life. These studies have theoretical support as exposures in both early and adult life may affect the amount of fat and lean mass in adulthood. The influence of exposures acting across life on subsequent outcomes in adulthood is considered within life course epidemiology.

## 1.6 **Life course epidemiology**

From World War II until the 1970s, epidemiological research tended to focus on associations between adult risk factors—such as life style factors—and chronic disease.[10] These included the now well-established risk factors for lung cancer (tobacco smoking) and cardiovascular disease (eg, hypertension, raised blood cholesterol).[10] However, later findings in the 1980s and 90s began to highlight the importance of early life factors in the development of later adult chronic disease; these findings, particularly those published by Barker and Forsdahl, re-catalysed the pre-World War II interest in the role of early life factors on later health.[10]

Barker, in landmark work in the 1990s, reported associations between low birth weight and increased risk of type 2 diabetes and cardiovascular disease.[144;145] It was hypothesised that impaired foetal development—indicated by low birth weight—had lasting adverse effects on adult health. Forsdahl also published work outlining the association between adverse socioeconomic position (SEP) in childhood and adult mortality, suggesting other post-natal life stages were also important in the development of later health outcomes.[146]

The two hypotheses of adult chronic disease—early life factors and adult risk factors—were initially interpreted as competing models of disease aetiology.[10] To counteract this, and reflect the greater explanatory power of both models in combination, Kuh and Ben-Shlomo coined the term life course epidemiology and defined it as: "…the study of long-term biological, behavioural, and psychosocial processes that link adult health and disease risk to physical or social exposures acting during gestation, childhood, adolescence, earlier in adult life, or across generations."[147] (p.3)

A number of main pathways have been proposed to explain how factors operate across life to influence outcomes in adulthood, each of which may operate simultaneously.[147-149] Risk factors may have a particularly strong effect in one particular period of life, and can be described as either a critical period (where the change is unlikely to be to subsequently reversed) or a sensitive period. For example, maternal exposure to thalidomide during pregnancy permanently impairs offspring limb development,[150] whereas exposure later in life has no effect. This could be described as a critical period effect. Both critical and sensitive period effects may be modified by a later exposure, which could either attenuate or strengthen their effects. Risk factors may also have cumulate effects on the outcome—for example, physical inactivity across adulthood may have cumulate effects in leading to higher fat mass (due to the tracking of gains in fat mass caused by low activity levels at each age). Risk factors may also form chains of risk, with the final exposure in the chain ultimately affecting the outcome—for example, low educational attainment may lead to low occupational class and low income which, by impacting on the capacity to purchase leisure and dietary resources, leads to higher fat mass.

By its definition, life course epidemiology requires data from multiple time points across life. Consequently, various prospective and retrospective studies have dominated the published literature in this field, including prospective cohort studies

based in Britain. These include the NSHD, the oldest British birth cohort study which will be used in this thesis.

In the following section, a life course approach will be used to briefly outline the factors that influence adult fat and lean mass in adulthood. The limitations of previous studies will be described followed by the benefits of using the NSHD to conduct further work. The NSHD is described in detail in Chapter 2.

## 1.7 **Life course influences on fat mass**

From a metabolic perspective, the amount of fat mass an individual has is the product of a relatively simple process—the balance between energy input and expenditure over a period of time.[17;41;151] An imbalance in this system over time is likely to alter the levels within an individual, with greater energy input leading to an accumulation of fat mass, and greater expenditure leading to lower fat mass.[17] However, research has suggested that the factors that influence this process are varied and numerous, and operate across life.

An obvious starting point when trying to identify the factors that influence fat mass is research investigating the relatively recent trends of increasing obesity prevalence. In a substantial inter-disciplinary body of work commissioned by the UK government, the Foresight team reviewed the causes of obesity in the UK.[17] The authors concluded that there are a number of factors that may act to increase obesity risk, at the biological, behavioural, societal, and economic levels. Although the evidence for each contributory factor was not always fully established, the authors concluded that the secular trends of increased obesity (in both childhood and adulthood) can be explained by changes at the societal and economic levels that have taken place primarily in the 20$^{th}$ century. These changes have led to reductions in physical activity and increased availability of high-energy foods. The report also briefly outlined other factors which may influence the amount of fat mass in adulthood. These included genetic factors and factors acting in early life. For example, the authors highlighted research suggesting greater weight gain in infancy is associated with increased risk of obesity in adulthood, while breast feeding during this period is associated with reduced obesity risk.[17]

While higher physical activity levels are hypothesised as leading to lower fat mass, few studies have examined associations between physical activity and direct measures of fat mass.[152] Of these studies, few have used objective measures of

physical activity or examined whether activity levels across adulthood are cumulatively beneficial in leading to lower fat mass.

Although not discussed in more detail in this thesis, researchers have examined a number of factors other than physical activity and energy intake that may influence fat mass. These include genetic factors, with evidence from twin and familial relation studies suggesting heritability of fat mass are approximately 70%,[153-157] and with specific genes identified which are associated with increased risk of obesity.[158-160] Other factors investigated include tobacco smoking, endocrine disruption from exogenous agents (such as pesticides and heavy metals), pharmaceutical agents, ambient temperature levels, sleep debt, maternal factors (such as age at childbirth), and intergenerational effects;[161;162] others have included the effects of pathogens and environmental–epigenetic processes.[161]

Although many of the factors described above could act earlier in life and have lasting effects on adult fat mass, in most cases this has not been tested. Using available data, a growing body of research has examined the influence of factors that act across life on adult fat mass.[75;163-165] In 1999 Parsons et al conducted a systematic review of studies examining the early life predictors of obesity in adulthood[166] and concluded there was evidence for "parental fatness, low SES (socioeconomic status), higher birth weight, earlier maturation and inactivity" (p.31) being associated with greater risk of adult obesity.[166] Since this publication, this area of research has received more attention, with further summary reviews also concluding that factors in early life independently influence fat mass in adulthood.[75;164;165] Many of the specific findings stated by Parsons et al have since been reproduced, with associations reported between low SEP in childhood,[167-169] high birth weight,[170] early pubertal development[171] and increased risk of obesity in adulthood. There has also been active interest in other factors that act in early life, including growth during infancy; a number of systematic reviews have now shown higher rates of growth in infancy to be associated with increased risk of obesity in adulthood.[172-174] There have also been studies investigating the potentially protective influence of breastfeeding on adult obesity,[175;176] while other studies have investigated dietary patterns across life.[177]

As will be detailed in later chapters, the studies that have examined associations between factors across life with adult fat mass have a number of limitations which necessitate the need for further research. Most of the published studies have used BMI as a surrogate measure of fat mass. As outlined previously, BMI is only a crude indicator of fat mass that does not distinguish between fat and lean mass. To make

inferences about factors that may influence fat mass (as distinct from lean mass), direct measures of fat mass are required. In many of the population studies that have measured fat mass directly, relatively inaccurate and imprecise measures have been used (such as SFT and BIA),[178-180] presumably due to the higher cost of more accurate measures. There is a need to build on previous studies using direct and accurate measures of fat mass. In addition to whole body measures of fat mass, abdominal fat distribution may be additionally important for health, but few studies have direct measures of this.

The study of life course influences on adult body composition requires data from multiple points across life. At a minimum, two time points are required (eg, one in adulthood and another at a previous life stage). Many of the published studies have been limited by only having a small number of measures from across life; although these have highlighted the importance of factors at specific points (for example, weight gain in infancy), they do not enable the relative contribution of factors at different periods of life to be determined (for example weight gain in infancy, childhood, and adolescence). Further research is therefore required with a study which has repeat data of relevant factors across life. In addition, most previous studies tend to have limited available data for potential confounders. For example, while studies have found greater weight gain in infancy to be associated with higher BMI in adulthood, this could feasibly be confounded by SEP in early life.

Previous studies that examined how early life factors influence fat mass in adulthood have typically focused on single explanatory factors. While the identification of individual risk factors is likely to be useful in providing risk factors for intervention or preventative strategies, the study of how these factors operate together may be informative in order to provide information about aetiology. For example, associations between low SEP in childhood and high adult fat mass could be mediated by patterns of growth in childhood and physical activity levels in adulthood.

## 1.8 **Life course influences on lean mass**

The factors across life that influence adult lean mass have received comparatively less attention than factors that influence fat mass, presumably due to the relatively recent development of lean mass measurement in population studies, and the less well appreciated public health implications of low lean mass.[98] Both the lack of studies and limitations of previous research—discussed in more detail in subsequent chapters—suggest the need for future research.

Given the high protein content of muscle, the amount of muscle mass (and therefore lean mass) an individual has is partly the product of a balance between protein synthesis and degradation.[181-183] As with fat mass, factors influencing this process may also operate across life.

In adulthood, a large number of experimental studies have shown that resistance training interventions lead to gains in lean mass.[184-186] While there is evidence that specifically designed resistance exercise is beneficial in leading to higher lean mass, few population studies have examined whether more commonly undertaken types of physical activity are associated with lean mass.[187-190] Of the studies that have been conducted, most use a single measure of physical activity in relation to concurrent or future lean mass; to the author's knowledge no studies have examined whether there are cumulative benefits of activity across adulthood in leading to higher lean mass.

In addition to physical activity, genetic factors have been investigated, with heritability estimates for whole body lean mass of 60-70%.[109;153;154;191;192] Studies have also examined dietary factors, with some experimental trials and observation studies suggest that greater amino acid or protein intake is associated with higher lean mass.[186;193;194]

While a large number of studies have examined how SEP relates to BMI, few studies have used lean mass as an outcome.[195-199] These have tended to use only single indicators of SEP at one point in life, and not examined the factors which mediate these associations.

Using data from across life, the growth that takes place in utero (as indicated by birth weight)[200;201] and weight gain in infancy[202-204] have been investigated in relation to adult lean mass, with positive correlations found. However, few of the published studies have repeat measures across the growth trajectory—from birth, infancy, childhood, adolescence and adulthood—leaving the relative contribution of growth during each of these periods to adult lean mass unclear.

Population studies examining the factors across life that are associated with lean mass have typically not considered how fat mass may impact on associations. As discussed previously, those with more fat mass may also, as a result of adaptive mechanisms, develop more lean mass. In addition, most previous studies have

used whole body measures of lean mass such as those obtained by BIA or SFT measures which do not distinguish between bone, organ, and muscle mass.

In the following section the NSHD will be proposed as a useful study to investigate the factors across life that influence fat and lean mass.

## 1.9 Benefits of using the MRC National Survey of Health and Development

The NSHD is a British birth cohort study comprised of births that took place during one week of March 1946 in England, Wales, and Scotland (described in more detail in Chapter 2). The sample has been followed-up in full 23 times, giving a number of repeat measures across life including measures of growth, SEP, and physical activity. In most cases, these data were prospectively ascertained by trained health professionals using standardised protocols rather than self-reported, helping to ensure their accuracy.[205]

The rich data collected in the NSHD provides a number of benefits for conducting research. Firstly, it enables the investigation of multiple factors across life that may influence body composition in adulthood, such as measures of growth, SEP, and physical activity. The repeat data available within the NSHD enable a number of specific hypotheses to be tested. For example, both intrauterine[206] and infant growth[207;208] have been hypothesised to be critical periods in influencing obesity risk in later life. However, few studies have data for both periods of growth, leaving their relative contributions unclear. The repeat measures of physical activity in the NSHD are also a strength as they enable the cumulative effects of activity levels across adulthood to be examined.[209]

Further, the NSHD enables analyses to be performed which investigate the extent to which associations are confounded or mediated by other factors. The investigation of both confounding and mediating factors provides additional support for the hypothesised direction of association, and enables pathways of associations to be better understood. For example, while some studies have examined the associations of SEP with fat and lean mass, few have examined whether these associations are mediated by measures of pre-adulthood growth and/or physical activity.

In addition to rich data for explanatory factors, the NSHD has direct measures of body composition obtained using DXA at the most recent data collection at 60–64

years. This method provides both whole body and regional measures of fat and lean mass, and is thought to be relatively highly accurate and precise. DXA and the outcomes of this thesis are described in detail in Chapter 2.

Finally, the NSHD has a relatively large sample size, and so sufficient statistical power for a range of analyses. The NSHD contains both sexes, enabling sex-specific associations to be tested, and contains study members of varied social background living across mainland Britain. Findings may therefore be more generalizable to the British population than other studies using more selective samples. The representativeness of the NSHD is discussed in Chapter 2.

## 1.10 Public health significance of this research

As highlighted previously, a substantial proportion of the British population are estimated to be affected by the adverse health and functional outcomes related to high fat and low lean mass. This suggests that the research questions addressed in this thesis have important public health implications, since factors that affect fat and lean mass, even if their overall effect is relatively small, can be identified and potentially modified therefore benefiting a large number of people. For fat mass, intervention studies that aim to reverse obesity in adulthood tend to have only limited success: as has been previously argued elsewhere, it may be more effective to focus finite public health resources towards prevention and intervention in prior life stages rather than treatment in adulthood.[75;210;211]

The body composition measures taken in the NSHD are at 60–64 years. The identification of factors that affect fat and lean mass at this older age are particularly important since age is a risk factor for most major chronic diseases.[212] Since substantial evidence indicates associations between higher fat mass and increased risk of chronic diseases (as outlined earlier), elucidating contributory factors of fat mass in later adulthood may help to guide public health policy in reducing obesity, and thereby risk of chronic disease. In addition, in later adulthood the consequences of low lean mass for physical functioning may become clinically manifest, suggesting that the identification of factors that influence lean mass in later adulthood could ultimately be used to help reduce the number of individuals who suffer the adverse consequences of low lean mass.

## 1.11 Literature review summary and overall aim of the thesis

In summary, there is evidence that high fat mass leads to increased risk of chronic diseases, mortality, and worse physical functioning. There is also evidence that low lean mass is associated with worse physical functioning, low bone mineral content and density, and adverse glucose metabolism. Plausible biological mechanisms have been proposed to explain these associations, and there is evidence suggesting that factors across life affect the levels of fat and lean mass in adulthood. However, the published studies examining these tend to use surrogate and/or inaccurate measures of fat and lean mass, and have limited data for explanatory factors, limiting the hypotheses that can be tested. The NSHD has been proposed as a study which could be used to overcome these limitations and add to this important field of scientific research.

The overall aim of this thesis is to examine the associations between a number of explanatory factors across life and body composition outcomes in later adulthood using the NSHD. The explanatory variables are chosen on the basis of both scientific and practical rationale: each can be hypothesised to influence body composition—though further research is required (more detailed scientific justification is presented in subsequent chapters)—and each was measured in the NSHD. The explanatory variables chosen are: measures of indicators of SEP across life, birth weight (an indicator of prenatal growth) and growth after birth (in infancy, childhood and adolescence), and measures of physical activity across adulthood.

Some explanatory variables, also measured in the NSHD, were excluded in order to restrict the scope of the thesis—exclusion was also judged appropriate on the basis of scientific rationale. The most notable example of this is the exclusion of direct measures of dietary intake, collected in the form of parental recall or self-report in the NSHD.[213] Research has pointed towards inaccuracy and systematic bias in self-reported diet intake data (such that individuals of higher fat mass are more likely to report eating less),[214;215] suggesting that study of dietary intake in relation to body composition may be complicated, and beyond the scope of the work conducted in this thesis. In addition, relatively few participants have provided dietary intake in the NSHD, leading to lower statistical power. However, as will be outlined and discussed in subsequent chapters, dietary intake may be indicated by other factors collected in the NSHD that will be examined in this thesis. For example, measures of growth in infancy, childhood and adolescence are likely to be partly driven by dietary factors.

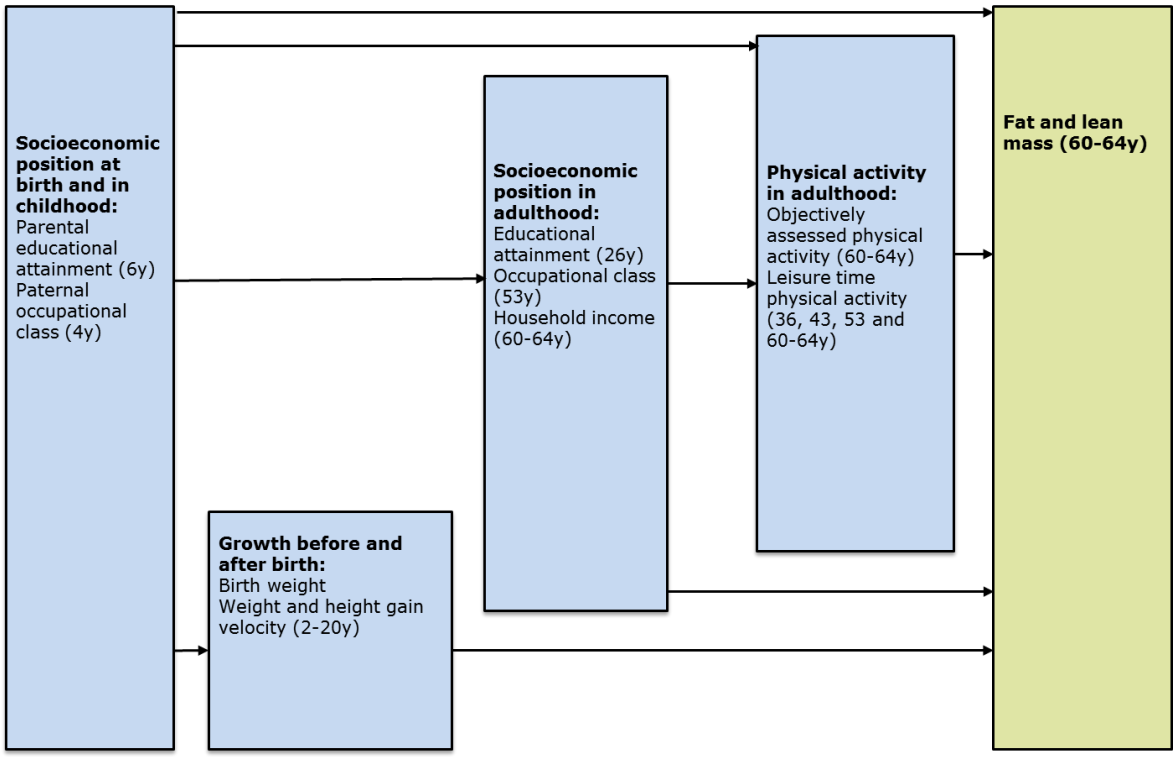
## 1.12 Structure of the thesis

The source of data used in this thesis, the NSHD, is described in Chapter 2 and particular detail is given to the body composition outcomes used. Also outlined in this chapter are the analytical strategies and statistical methods used in subsequent chapters.

The conceptual framework used in this thesis is shown in Figure 1, with arrows indicating the hypothesised relationships between the different explanatory variables considered in this thesis and outcomes. Chapters 3-6 each focus on the independent associations between specific explanatory factors and body composition outcomes, and follow the same structure: a literature review is presented followed by justification for future research—the specific hypotheses of each chapter are then outlined followed by the methods, results and discussion sections.

Chapter 3 examines associations between birth weight (an indicator of prenatal growth) and body composition outcomes, Chapter 4 extends this work by examining associations with measures of growth after birth (in infancy, childhood and adolescence), while Chapter 5 examines associations between physical activity levels in adulthood and body composition outcomes. In Chapters 3, 4 and 5 SEP is considered a potential confounder. Chapter 6 then examines the separate associations between indicators of SEP and outcomes, and investigates whether the associations found are mediated by the explanatory factors investigated in previous chapters (birth weight, measures of growth after birth, and physical activity levels in adulthood), as suggested in Figure 1. Finally, Chapter 7 summarises the main findings of the thesis and discusses the implications, the strengths and weaknesses of the work conducted, and recommendations for future work.

Figure 1. Conceptual framework of the factors examined in this thesis




Note: explanatory variables are shown in the blue boxes, and outcomes in the yellow box; arrows represent the main directions of influence, with explanatory variables influencing both other explanatory variables and outcomes; the framework is limited to the associations analysed in this thesis

# 2. Chapter 2: An introduction to the data and analytical strategy

This chapter introduces the cohort and dataset used in this thesis—the MRC NSHD, also known as the 1946 British Birth Cohort Study—and the specific outcomes used to address the objectives of this thesis; the explanatory variables used are described in subsequent chapters. Height-adjusted outcomes are derived and, to aid the interpretation of results in subsequent chapters, correlations between the different outcomes are examined. The representativeness of the NSHD is discussed and the characteristics of study members with complete outcome data are compared with those that do not. Finally, the analytical strategy and statistical methods used across subsequent chapters are briefly described.

## 2.1 Introduction to the MRC National Survey of Health and Development

The history of the NSHD has been extensively described in a series of publications,[213;216-219] and is therefore outlined only briefly below.

The NSHD is the oldest British birth cohort study and began as a national maternity survey carried out in 1946 to investigate the efficacy of maternal care services following concerns regarding falling fertility rates.[213] Of 16695 births in the maternity survey that occurred between the 3rd and 9th of March 1946 in mainland Britain, 5362 births were selected for follow-up: those born in a local authority that agreed to take part (92.6%), those born from mothers who were married, and a stratified selection based on parental employment status: all births from females with husbands in non-manual and agricultural employment, and a random selection of one in four births to females with husbands in manual employment.[218;220]

The entire cohort has been followed-up 23 times at birth, infancy, childhood, adolescence and adulthood, most recently at 60–64 years when measures of body composition were obtained. As the study has continued, it has been used to address a number of areas of research relating to public policy: maternal care, educational attainment, socio-economic differences in employment prospects and health and—most recently—the ageing process. Although the principal research interests have changed, a number of variables have been measured repeatedly throughout life (such as measures of height and weight), and these data will be used as explanatory variables in this thesis.

Like all birth cohort studies, the NSHD has experienced attrition—this differed in each of the different follow-ups and was highest in early adulthood (likely due to the more frequent address and name changes that occurred in this period). Table 1 presents a summary of the overall response rates of the study, and shows that in each wave the proportion of the target sample that provided at least some data was high.

Body composition data (derived using DXA) from the most recent wave of data collection, at 60-64 years, will be used as the main outcomes in this thesis. The collection of these data is described in the following section.

Table 1. Response rates in the MRC National Survey of Health and Development

| Year | Age | Respondent | Number that provided some valid data | % Target |
|---|---|---|---|---|
| 1946-50 | 0-4 | Mother | 4695 | 95 |
| 1951-61 | 5-15 | Mother and study Member | 4307 | 89 |
| 1962-81 | 16-35 | Study Member | 3538 | 78 |
| 1982 | 36 | Study Member | 3322 | 86 |
| 1989 | 43 | Study Member | 3262 | 87 |
| 1999 | 53 | Study Member | 3035 | 83 |
| 2006-10 | 60-64 | Study Member | 2661 | 84 |

Modified from Wadsworth et al, 2003[220]

## 2.2 **The derivation of body composition outcomes**

Between 2006 and 2010 (at 60–64 years), 3163 study members still alive and living in England, Scotland or Wales were sent a postal questionnaire that assessed, among other factors, their health and socioeconomic circumstances. No contact was attempted for those who had died (n=718), who were living abroad (n=567), had previously withdrawn from the study (n=594), or had been lost to follow-up for more than 10 years (n=320). Following this postal questionnaire, 2856 participants (who were still alive, traceable, and living within the catchment area) were invited for an assessment at a regional clinical research facility (CRFs; in Cardiff, Manchester, Birmingham, Edinburgh, and two in London) or, if not able to attend a CRF, were asked if they were willing to be visited by a research nurse at home.[219] Of those invited, 1690 (59.2%) attended a CRF and 541 were visited at home; as

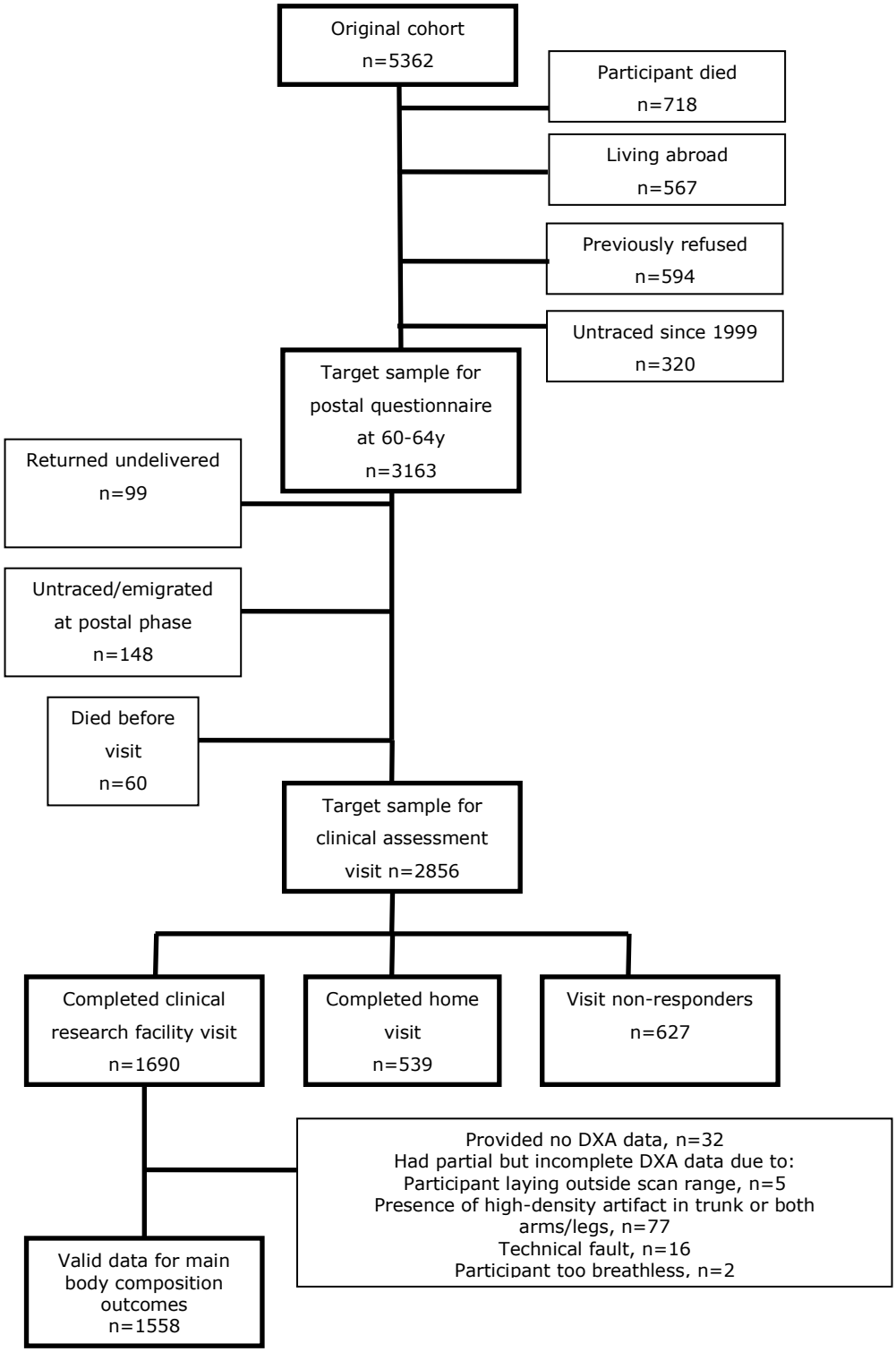
such, the majority of study members that had an assessment did so at a CRF (75.8%). Clinic visits took place between 2006 (60 years) and 2010 (64 years). Relevant ethical approval was obtained for all aspects of data collection.

During the visits to the CRF, measures of body composition were obtained in the supine position using a QDR 4500 Discovery DXA scanner (Hologic Inc, Bedford, MA, USA)—these scans were then reviewed by a single operator (Professor Judith Adams at Manchester University) using APEX 3.1 software to confirm that the different regions of the body had been correctly defined and high-density artefacts detected. Local quality assurance procedures were monitored centrally and cross-calibration between scanners was performed by scanning the European Spine Phantom at the start and end of the study.[221;222] From these scans, measures of fat and lean mass were obtained for the whole body and for the arms, legs, trunk, android (abdomen) and gynoid (upper legs/hips) regions. Lean mass was defined as mass excluding fat and bone mass, and in all measures data from the head were excluded due to the high proportion of bone mass in this region known to affect the accuracy of soft-tissue measures.[115] Where one limb was missing or contained a high-density artefact (eg, a knee replacement in the left leg) the data were replaced with the other limb (eg, the right leg).

From the DXA scans, the following measures were chosen for use as the main outcomes in this thesis: whole body fat and lean mass, and appendicular lean mass (in kilograms). Two ratios were derived—android: gynoid fat mass (higher values indicating greater fat distribution in the abdomen (android region) than upper legs/hips (gynoid region)) and whole body fat: lean mass; these were multiplied by 100 to increase the number of significant digits. Routine anthropometric measures were taken during the clinic visit using standardised protocols by trained nurses.[219] Of the 1690 participants that attended the clinic, 1558 participants had complete data available for all main body composition outcomes (all of which had valid height and weight data), 32 participants had no DXA measures taken, and 100 had partial but incomplete DXA measures due to the following reasons: both of the participant's arms or legs lay outside the scan range (n=5), high-density artefacts were detected in either the trunk or both arms or legs (n=77), technical faults occurred (n=16), or the participant was too breathless to be scanned (n=2). In addition, in five of the six clinics 1262 participants had measures of forearm cross-sectional muscle area ($cm^2$) obtained using peripheral quantitative computed tomography (XCT 2000 Stratec Medizintechnik GmbH, Pforzheim, Germany) at the 50% site of the non-dominant forearm. This was used as an additional outcome in Chapter 3, but was unavailable in one London clinic due to funding limitations.

A flow diagram is presented in Figure 2 and shows the number of study members with valid outcome data and those lost to follow-up. 1558 participants had complete body composition outcome data. Of these, 326 attended a CRF in Manchester, 209 in Edinburgh, 191 in Birmingham, 185 in Cardiff, and 647 in London. Visits to the Manchester CRF took place first, when participants were 60 to 63 years, while study members were aged between 62 to 64 years in all other CRF visits. In total, 2661 participants provided at least some data at 60–64 years (either a clinic or home visit or via postal questionnaire).

Figure 2. A flow chart summarising response rates for those who provided valid body composition outcome data at 60-64 years




Note: modified from Stafford et al, 2012;[223] valid body composition measures were whole body fat and lean mass, appendicular lean mass, android fat mass, and gynoid fat mass

### 2.2.1 *Summary of main outcomes used in this thesis*

The list below summarises the main outcomes used in this thesis:

1) Whole body fat mass (kg), excluding the head
2) Whole body lean mass (kg), excluding the head
3) Appendicular lean mass (kg)
4) Fat: lean mass ratio (whole body fat mass/whole body lean mass)
5) Android: gynoid fat mass ratio (android/gynoid fat mass)

In addition to whole body fat and lean mass (and their ratio), two regional measures were included—appendicular lean mass and android: gynoid ratio. Appendicular lean mass is likely to be a better indicator of skeletal muscle mass than whole body lean mass as it excludes organ mass and the bone-dense trunk of the body where DXA is likely to be less accurate in assessing lean mass. Whole body lean mass was also included as its use enables fairer comparison with previous studies that have used this outcome. While there is no consensus on the most appropriate measure of fat distribution derived from DXA, there is some evidence (described in Chapter 1) that greater abdominal fat mass is detrimental to health, while greater leg fat mass may be protective, suggesting that the ratio of these masses may be important (as indicated in the android: gynoid fat mass ratio). As such, android: gynoid ratio was used as an additional outcome. As associations between explanatory variables and android: gynoid ratio are driven by the separate associations with android and gynoid fat mass, associations between explanatory variables and these two masses will also be discussed in the subsequent chapters.

In some instances outcomes 1-3 will be adjusted for adult height in analyses. This is discussed in more detail in the following section.

### 2.2.2 *Creation of outcomes adjusted for body size*

The measures of body composition used in epidemiological analyses have been the subject of recent academic debate.[224-226] While fat mass has often been expressed as a percent of total mass, this has been criticised as it does not provide a discrete measure of fat mass: high percent fat mass can be driven by high fat mass, low lean mass, or both.[224-226] Adjustment for contemporaneous height has been suggested for both fat and lean mass, by the creation of discrete height-adjusted indices of fat and lean mass.[225;226] This takes into account that, on average, taller

individuals have more fat and lean mass—they have longer bones, and therefore longer muscles of greater mass, and also presumably require more fat mass to sustain normal metabolic functioning. The amount of fat and lean mass that individuals have may be more closely related to health and physical functioning outcomes where adjustment is made for their height. VanItallie et al (1990)[225] provided an example of this, highlighting two individuals of approximately identical lean mass: one was short, the other taller (and experiencing malnutrition). This is also likely to apply to fat mass—for example, if a short individual has the same amount of fat mass as a much taller individual, then the impact of fat mass on health may be greater for the shorter individual.

A number of previous studies have made adjustment for height by the creation of height-adjusted indices which are comparable to BMI: fat mass (kg) / height $(m)^2$, and lean mass (kg) / height $(m)^2$. These indices assume that both fat and lean mass scale to height to the power of 2. However, this may not necessarily be the case: the relationship between height and fat may differ to that with lean mass, and both may differ by sex and at different ages. As such, in this chapter, the associations between height and fat and lean mass were examined using log-log regression. As previously described,[226] fat or lean masses (kg) and height (m) were logged (using the natural logarithm), and separate regression models constructed with logheight as the explanatory variable and logfat or loglean mass as the outcome. The coefficients of the regression models give the power that height should be raised to in the index in order to remove the association with height (eg, a coefficient of 4 for lean mass would suggest that lean mass should be divided by $height^4$ to produce an index uncorrelated with height).

Results of log-log regressions are presented in Table 2. Results show that the appropriate power height should be raised to was approximately 1.2 for fat mass, and 95% confidence intervals did not overlap with 2 in either sex. However, the values obtained for both appendicular and whole body lean mass were closer to 2, and 95% confidence intervals did overlap with 2 in both sexes. Therefore, in order to minimise the association with height fat mass should be divided by $height^{1.2}$, and lean mass by $height^2$.

Table 3 shows the correlations between height and i) fat or lean mass, and ii) fat or lean mass indices (using $height^2$ for both fat and lean mass and $height^{1.2}$ for fat mass). Fat mass was relatively weakly positively correlated with height, and adjustment for $height^2$ did not substantively attenuate the association with height; however using $height^{1.2}$ (as suggested in log-log regression) almost entirely

attenuated this association. Both whole body and appendicular lean mass were more strongly positively correlated with height; as expected, after adjustment for height$^2$ this association was almost entirely attenuated.

In this thesis, adjustment for height will be made using two methods. First, height-adjusted outcomes will be derived and used: whole body or appendicular lean mass/height$^2$, as its correlation with adult height was judged to be sufficiently low (and previous studies have used this outcome, enabling closer comparison with previous studies than using height$^{1.8}$); and fat mass/height$^{1.2}$, since it achieved the stated aim of producing an outcome adjusted for height (while adjustment for height$^2$ did not). Second, where it is preferred that regression coefficients are presented on the same scale both before and after adjustment for height (eg, change in kg), height will be included as a covariate in analyses (as a linear term) and sensitivity analyses performed using height-adjusted indices as outcomes to check that similar results are obtained.

The following section describes DXA in more detail and discusses its strengths and limitations.

Table 2. Regression of log fat mass or log lean mass (outcome variables) on log height (m; explanatory variable)

| | Coefficient (95% CI) | P-value |
|---|---|---|
| Log fat mass (kg) | | |
| Both sexes (n=1558), adjusted for sex | 1.21 (0.78, 1.64) | <0.001 |
| Males (n=746) | 1.32 (0.72, 1.92) | <0.001 |
| Females (n=812) | 1.10 (0.50, 1.71) | <0.001 |
| Log lean mass (kg) | | |
| Both sexes (n=1558), adjusted for sex | 1.82 (1.65, 1.99) | <0.001 |
| Males (n=746) | 1.86 (1.64, 2.08) | <0.001 |
| Females (n=812) | 1.78 (1.53, 2.03) | <0.001 |
| Log appendicular lean mass (kg) | | |
| Both sexes (n=1558), adjusted for sex | 1.99 (1.81, 2.16) | <0.001 |
| Males (n=746) | 2.01 (1.77, 2.24) | <0.001 |
| Females (n=812) | 1.97 (1.70, 2.23) | <0.001 |

Note: variables were logged using the natural logarithm; analyses were restricted to those with valid data for body composition outcomes

Table 3. Correlations between height (m) and i) fat or lean mass, and ii) fat or lean mass indices

| | i) | ii) | |
|---|---|---|---|
| | Fat mass (kg) | Fat mass (kg) /height (m)$^2$ | Fat mass (kg) /height (m)$^{1.2}$ |
| Males (n=746) | 0.16 | -0.08 | 0.01 |
| Females (n=812) | 0.12 | -0.10 | -0.01 |
| | Lean mass (kg) | Lean mass (kg)/height (m)$^2$ | |
| Males (n=746) | 0.51 | -0.05 | |
| Females (n=812) | 0.43 | -0.06 | |
| | Appendicular lean mass (kg) | Appendicular lean mass (kg)/height (m)$^2$ | |
| Males (n=746) | 0.53 | -0.00 | |
| Females (n=812) | 0.44 | -0.02 | |

Note: analyses were restricted to those with valid data for body composition outcomes

## 2.3 **An introduction to dual-energy X-ray absorptiometry**

DXA projects a series of X-ray beams of two different energies across the body. As the X-rays pass through the body they are attenuated (ie, they lose energy) according to the mass of the substance they pass through. Based on the differential attenuation of X-rays by each of the tissues in the body, algorithms are used to estimate the amount of fat, lean, and bone mass in the body (where the density of each is assumed to be homogeneous).[18;115;227;228;228] The mass of each tissue is represented in 2-dimensional computerised form by a series of pixels; each pixel contains information on the amount of fat, lean, and bone mass, with the total number of pixels representing the total mass of the body. Where bone tissue is present, the bone and non-bone soft tissue components are measured, and the amount of fat and lean mass is subsequently assumed to be the same as adjacent non-bone sites. The two-dimensional nature of DXA means that it does not provide true volumetric measures of fat, lean, or bone tissue. Although this may be problematic when deriving density measures such as bone mineral density, it does not affect the measures of mass.

DXA has previously been extensively used for its measures of bone; the bone mineral content and density measures obtained in the hip and spine by DXA are used to diagnose osteoporosis,[18;111] and the use of DXA in epidemiological studies has enabled risk factors of osteoporosis to be identified.[229] More recent studies have used DXA measures of fat and lean mass as either explanatory or outcome variables.

DXA is thought to be a comparatively accurate and precise means of assessing fat and lean mass,[18;115;228] with studies typically reporting relatively minor differences in fat and lean mass measures compared with more accurate methods such as 5-compartment models of body composition.[230] However, there is some evidence from both human and animal studies that DXA tends to overestimate fat mass in those with low fat, and underestimate fat mass in those with high fat mass.[115;231] Despite this potential limitation, DXA has increasingly been used in large epidemiological studies. For example, DXA has been used to provide reference fat and lean mass data for the US population using the National Health and Nutrition Examination Survey.[232]

Differences in DXA hardware and software version may impact on reported accuracy and precision, as different DXA machines and software version have been shown to lead to different estimates of fat and lean mass.[115] Although these

discrepancies are poorly understood in terms of their cause and their significance, they are thought to be minimised in multicentre studies by cross-calibration, and by standardising hardware and software across centres.[115;233]

Other methods of body composition assessment used in large epidemiological studies include BIA, SFT measures, and air-displacement plethysmography. While comparisons of the accuracy and precision of these measures partly depends on the hardware and software used, BIA and SFT measures are likely to be less accurate and precise than DXA; both depend on the suitability of predictive equations used, and the former depends on recent food/beverage consumption, recent exercise and medical conditions,[178] while the latter may vary by measurement technique.[179;234] BIA, SFT measures, and air-displacement plethysmography all measure the body in two components (fat and lean mass), and as such lean mass includes muscle, organ, and bone mass.

A major strength of DXA is that it enables regional measures of fat and lean mass to be obtained, such as appendicular (limb) lean mass and abdominal fat mass. As discussed in Chapter 1, these may be more closely related to health outcomes than whole body measures. Computerized tomography and magnetic resonance imagery are thought to be reference technologies for these measures (eg, enabling visceral and subcutaneous fat to be distinguished),[115] but are typically more expensive than DXA and, in the case of computerized tomography, involve relatively high radiation exposure.[18] In 2010, The European Working Group on Sarcopenia in Older People recommended DXA for its assessment of low appendicular lean mass (as part of their proposed definition of sarcopenia); this was suggested above BIA and SFT measures, but behind computed tomography and magnetic resonance imaging.[79] Measures of abdominal fat mass and fat distribution obtained using DXA have also been derived and used in studies—initial software was able to differentiate trunk fat mass, with more recent updates able to differentiate android (abdominal/lower part of the trunk which excludes the rib cage) and gynoid (upper leg/hip) fat mass.

The following sections describe the DXA outcomes used in this thesis and the analytical strategy used in subsequent chapters.

## 2.4 **Descriptive analyses of the outcomes used in this thesis**

Descriptive statistics for anthropometric and body composition measures at 60–64 years are shown in Table 4. As expected, there was notable sexual dimorphism, with males being taller and heavier; although BMIs were similar in both sexes, females had more fat mass and less (whole body and appendicular) lean mass than males, differences were also found when height-adjusted indices were used. Males had more android fat mass, less gynoid fat mass, and a resulting higher android: gynoid fat mass ratio.

Table 5 shows the proportion of participants within the standard BMI cut-points. According to BMI, the majority of participants were classified as either overweight (46.92% of males, and 37.68% of females) or obese (26.81% of males and 27.59% of females). Although there are no accepted obesity cut-points for direct measures of fat mass, over 81.23% of males and 87.93% of females were classified as obese when using commonly used (albeit arbitrarily defined) cut-points for percent fat mass of >25% in males and >35% in females.[29;30] Those who were obese according to BMI also tended to be obese according to high percent fat mass: only one male was obese according to BMI but not according to percent fat mass. Approximately 20% of both males and females were classified as sarcopenic using a definition based solely on low appendicular lean mass.[79;82] The prevalence of sarcopenia at 60-64 years in the NSHD (and the overlap between different definitions) has been described in detail elsewhere (Cooper et al, submitted).

Table 6 shows correlations between anthropometric and body composition measures. Overall, correlations were similar in both sexes. Weight and BMI were both positively correlated with fat and lean mass. Regional measures of body composition were strongly positively correlated with whole body measures (appendicular lean mass with whole body lean mass, and both android and gynoid fat mass with whole body fat mass). In addition, all measures of fat mass were positively correlated with all measures of lean mass, both before and after adjustment for height.

As discussed in Chapter 1, positive associations between fat and lean mass may be important to consider in analyses of the life course determinants of lean mass as associations with fat mass may drive associations with lean mass (eg, if high fat mass increases muscle loading and leads to increased muscle mass). Adjustment for fat mass when examining associations with lean mass may therefore enable associations between an exposure and lean mass to be examined, for a given

amount of fat mass. As such, where it was hypothesised that associations between an exposure and fat mass could drive associations with lean mass, associations with lean mass were adjusted for fat mass. Fat mass was included as a linear term in these models as further analyses suggested that fat and lean mass were positively associated in a linear manner in males, with only minor deviation from linearity in females (Appendix 1 and 2).

Table 4. Mean age, anthropometric and body composition measures

| | Males Mean (SD) (N=746) | Females Mean (SD) (N=812) | P# |
|---|---|---|---|
| Age (years) | 63.23 (1.15) | 63.31 (1.08) | 0.15 |
| Height (cm) | 175.29 (6.45) | 162.17 (5.76) | <0.001 |
| Weight (kg) | 85.27 (13.05) | 72.34 (13.63) | <0.001 |
| Body mass index (kg/m$^2$) | 27.74 (3.94) | 27.51 (5.02) | 0.31 |
| Whole body fat mass (kg) | 23.79 (7.19) | 29.00 (9.22) | <0.001 |
| Whole body fat mass index (kg/m$^{1.20}$) | 12.13 (3.62) | 16.23 (5.11) | <0.001 |
| Android fat mass (kg) | 2.51 (0.96) | 2.33 (1.01) | <0.001 |
| Gynoid fat mass (kg) | 3.76 (1.01) | 5.11 (1.46) | <0.001 |
| Android/gynoid fat mass ratio | 65.69 (15.35) | 44.74 (12.36) | <0.001 |
| Whole body lean mass (kg) | 53.69 (7.06) | 37.26 (5.35) | <0.001 |
| Whole body lean mass index (kg/m$^2$) | 17.46 (1.99) | 14.16 (1.84) | <0.001 |
| Appendicular lean mass (kg) | 24.62 (3.40) | 16.21 (2.54) | <0.001 |
| Appendicular lean mass index (kg/m$^2$) | 8.00 (0.94) | 6.16 (0.87) | <0.001 |
| Arm lean mass (kg) | 6.73 (1.06) | 3.78 (0.63) | <0.001 |
| Leg lean mass (kg) | 17.89 (2.53) | 12.43 (2.03) | <0.001 |
| Fat: lean ratio (whole body fat/lean mass) | 44.09 (10.99) | 77.21 (18.91) | <0.001 |
| Percent fat (whole body fat/total weight) | 29.39 (5.19) | 41.97 (5.96) | <0.001 |
| Forearm muscle area (cm$^2$)* | 36.48 (6.13) | 21.65 (3.43) | <0.001 |

Note: #P-value from test of sex difference using t-test; *smaller sample size for this measure (males=658; females=697); analyses were restricted to those with valid data for body composition outcomes

Table 5. Distribution of participants according to body mass index categories, and prevalence of overweight and sarcopenia

| | Males Number (%) (N=746) | Females Number (%) (N=812) |
|---|---|---|
| Body mass index (kg/m$^2$) category: | | |
| Underweight (<18.5) | 2 (0.27) | 7 (0.86) |
| Normal (18.5-24.9) | 194 (26.01) | 275 (33.87) |
| Overweight (≥25-30) | 350 (46.92) | 306 (37.68) |
| Obese (>30) | 200 (26.81) | 224 (27.59) |
| Obese according to percent fat mass (males >25%, females >35%)[29] | 606 (81.23) | 714 (87.93) |
| Obese according to both high body mass index and percent fat mass | 199 (26.64) | 224 (27.59) |
| Sarcopenia, defined as low appendicular lean mass (kg/m$^2$) (males <7.26; females <5.5)[79;82] | 159 (21.31) | 174 (21.43) |

Note: analyses were restricted to those with valid data for body composition outcomes

Table 6. Correlations between anthropometric and body composition measures

a) Males (n=746)

| | Height (cm) | Weight (kg) | BMI (kg/m$^2$) | Fat mass (kg) | Fat mass index | Lean mass (kg) | Lean mass index | Fat: lean mass ratio | App.lean mass (kg) | App.lean mass index | Android fat mass (kg) | Gynoid fat mass (kg) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Weight (kg) | 0.39 | | | | | | | | | | | |
| BMI (kg/m$^2$) | -0.09 | 0.88 | | | | | | | | | | |
| Fat mass (kg) | 0.16 | 0.89 | 0.87 | | | | | | | | | |
| Fat mass index | 0.01 | 0.84 | 0.90 | 0.99 | | | | | | | | |
| Lean mass (kg) | 0.51 | 0.88 | 0.68 | 0.57 | 0.50 | | | | | | | |
| Lean mass index | -0.05 | 0.76 | 0.86 | 0.56 | 0.58 | 0.83 | | | | | | |
| App.lean mass (kg) | 0.53 | 0.82 | 0.61 | 0.50 | 0.43 | 0.95 | 0.76 | | | | | |
| App.lean mass index | -0.01 | 0.71 | 0.78 | 0.49 | 0.50 | 0.80 | 0.94 | 0.85 | | | | |
| Android fat mass (kg) | 0.07 | 0.84 | 0.87 | 0.93 | 0.93 | 0.56 | 0.60 | 0.47 | 0.51 | | | |
| Gynoid fat mass (kg) | 0.21 | 0.85 | 0.80 | 0.92 | 0.90 | 0.59 | 0.54 | 0.52 | 0.48 | 0.82 | | |
| Fat: lean mass ratio | -0.08 | 0.60 | 0.68 | 0.89 | 0.92 | 0.16 | 0.23 | 0.10 | 0.16 | 0.82 | 0.78 | |
| Android: gynoid ratio | -0.12 | 0.44 | 0.54 | 0.51 | 0.53 | 0.27 | 0.39 | 0.19 | 0.30 | 0.72 | 0.23 | 0.49 |

b) Females (n=812)

| | Height (cm) | Weight (kg) | BMI (kg/m$^2$) | Fat mass (kg) | Fat mass index | Lean mass (kg) | Lean mass index | Fat: lean mass ratio | App.lean mass (kg) | App.lean mass index | Android fat mass (kg) | Gynoid fat mass (kg) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Weight (kg) | 0.27 | | | | | | | | | | | |
| BMI (kg/m$^2$) | -0.11 | 0.93 | | | | | | | | | | |
| Fat mass (kg) | 0.12 | 0.95 | 0.93 | | | | | | | | | |
| Fat mass index | -0.01 | 0.92 | 0.96 | 0.99 | | | | | | | | |
| Lean mass (kg) | 0.43 | 0.85 | 0.71 | 0.65 | 0.60 | | | | | | | |
| Lean mass index | -0.06 | 0.79 | 0.84 | 0.66 | 0.67 | 0.87 | | | | | | |
| App.lean mass (kg) | 0.44 | 0.82 | 0.68 | 0.64 | 0.59 | 0.96 | 0.82 | | | | | |
| App.lean mass index | -0.01 | 0.78 | 0.82 | 0.65 | 0.66 | 0.85 | 0.95 | 0.89 | | | | |
| Android fat mass (kg) | 0.05 | 0.89 | 0.90 | 0.93 | 0.93 | 0.62 | 0.66 | 0.59 | 0.64 | | | |
| Gynoid fat mass (kg) | 0.17 | 0.88 | 0.84 | 0.92 | 0.91 | 0.61 | 0.59 | 0.61 | 0.59 | 0.82 | | |
| Fat: lean mass ratio | -0.09 | 0.70 | 0.76 | 0.88 | 0.90 | 0.23 | 0.31 | 0.24 | 0.31 | 0.81 | 0.80 | |
| Android: gynoid ratio | -0.09 | 0.50 | 0.55 | 0.51 | 0.53 | 0.35 | 0.44 | 0.30 | 0.38 | 0.74 | 0.24 | 0.47 |

Note: App=appendicular; fat mass index=kg/(m$^{1.2}$); lean mass indices=kg/m$^2$; BMI=body mass index; analyses were restricted to those with valid data for body composition outcomes

## 2.5 **Representativeness of the study and characteristics of those with body composition outcome data**

Like all birth cohort studies, the NSHD has experienced attrition which may affect the representativeness of the study and could introduce bias (ie, weakening or strengthening of association estimates). Both the representativeness of the NSHD and the nature of attrition up to 60–64 years have been examined in a recent study by Stafford et al (2012), described below. Previous studies have reported on these issues at prior ages.[213;220;235]

Stafford et al (2012)[223] compared demographic, socioeconomic and health characteristics of participant who provided at least some information at 60-64 years with two other British cohorts of similar age ranges (the 2001 English Census and the Integrated Household Survey). Compared to these cohorts, the NSHD had a similar sex ratio (of slightly more females than males) and similar occupational class distributions to the other cohorts, although NSHD participants were more likely to be employed, to own their home, and less likely to have a limiting long-term illness. However, as discussed in the study by Stafford et al, all longitudinal studies (including the reference populations) suffer from non-response, and the NSHD may only be considered nationally representative with respect to its original sample of those singletons born in mainland Britain to married mothers (which reflected the majority of the population at the time). As such there may be no 'gold standard' with which to compare representativeness.

As previously described, while the NSHD has had high rates of follow-up across life, not all of the original NSHD participants attended a CRF visit at 60–64 years and provided full body composition data. The characteristics of those that provided data are important to consider as differences between these and those with missing data may result in bias of the estimate of association between explanatory variable and outcomes. A strength of the NSHD is the availability of prospectively ascertained data which can be used to determine the characteristics of those who took part in data collection at 60-64 years, thereby providing information about the likelihood of bias.

The characteristics of study members who provided data at 60–64 years in the NSHD has been previously comprehensively examined by Stafford et al (2012).[223] Among the variables investigated in this study, the following predicted greater likelihood of providing at least some data at 60–64 years: female sex; higher SEP

(non-manual paternal occupational class at 4 years, higher own educational attainment, and being in non-manual occupational classes at 53 years); being a homeowner and married at 53 years; high childhood and adulthood cognition (53 years); no reported difficulties in walking or health problems at 53 years; and being a non-smoker and physically active at 53 years.

In this chapter, the predictors of providing full body composition outcome data at 60-64 years were analysed using logistic regression. The outcome was a binary variable which indicated whether participants did or did not provide full body composition outcome data at 60–64 years, and analyses were restricted to the 2856 participants that were the target sample for clinical assessment visit. Predictor variables were main explanatory variables in subsequent chapters (indicators of SEP in childhood and adulthood, weight and height in pre-adult life, and physical activity measures) and other factors which may predict body composition outcomes (sex, weight and height at 53 years). As taller individuals tend to be heavier, models examining weight as a predictor were adjusted for height at the same age.

Results from logistic regression analyses are shown in Table 7. The following characteristics were associated with greater likelihood of providing complete body composition outcome data at 60–64 years: female sex; being of higher SEP in childhood and adulthood; more frequent self-reported reported participation in leisure time physical activity at 53 years; lower weight at 53 years (after adjustment for height); and greater height at 2, 7, 15 and 53 years.

Results from the above analyses will be used in subsequent chapters to infer the extent to which missing body composition data may bias associations found.

Table 7. Predictors of providing full body composition outcome data at 60–64 years

| Predictor | N (did not/did provide data) | % Did not provide data | % Provided data | P* |
|---|---|---|---|---|
| Sex | | | | |
| Male | 650/746 | 50.08 | 47.88 | |
| Female | 648/812 | 49.92 | 52.12 | <0.001 |
| | | | | |
| Paternal occupational class (4y) | | | | |
| I Professional | 61/113 | 4.95 | 7.65 | |
| II Intermediate | 193/282 | 15.67 | 19.09 | |
| III Skilled (Non-Manual) | 194/334 | 15.75 | 22.61 | |
| III Skilled (Manual) | 406/406 | 32.95 | 27.49 | |
| IV Partly skilled | 280/267 | 22.73 | 18.08 | |
| V Unskilled | 98/75 | 7.95 | 5.08 | <0.001 |
| | | | | |
| Own educational attainment (26y) | | | | |
| Degree or higher | 78/193 | 6.43 | 13.08 | |
| GCE A level or Burnam B | 233/472 | 19.19 | 32.00 | |
| GCE 'O' level or Burnam C | 215/326 | 17.71 | 22.10 | |
| Sub GCE or sub Burnham C | 96/110 | 7.91 | 7.46 | |
| None attempted | 592/374 | 48.76 | 25.36 | <0.001 |
| | | | | |
| Highest household occupational class (53y) | | | | |
| I Professional | 120/200 | 9.88 | 13.09 | |
| II Intermediate | 471/800 | 38.77 | 52.36 | |
| III Skilled (Non-Manual) | 278/325 | 22.88 | 21.27 | |
| III Skilled (Manual) | 223/136 | 18.35 | 8.90 | |
| IV Partly skilled | 100/56 | 8.23 | 3.66 | |
| V Unskilled | 23/11 | 1.89 | 0.72 | <0.001 |
| | | | | |
| Participation in leisure time physical activity in last 4 weeks (53y) | | | | |
| None | 606/606 | 56.11 | 40.70 | |
| 1-4 times | 155/317 | 14.35 | 21.29 | |
| 5 or more | 319/566 | 29.54 | 38.01 | <0.001 |
| | | Mean (SD) | Mean (SD) | |
| Weight at birth (kg) | 1295/1553 | 3.40 (0.53) | 3.40 (0.49) | 0.84 |
| Weight at 2 (kg) | 1071/1307 | 12.89 (1.51) | 12.93 (1.46) | 0.56 |
| Weight at 7 (kg) | 1063/1309 | 22.75 (3.24) | 22.94 (2.97) | 0.12 |
| Weight at 15 (kg) | 978/1223 | 51.62 (9.26) | 52.12 (8.64) | 0.34 |
| Weight at 53 (kg) | 1065/1484 | 78.26 (15.94) | 76.55 (14.03) | <0.001 |
| | | | | |
| Height at 2 (cm) | 1071/1307 | 85.21 (5.06) | 85.54 (4.68) | 0.07 |
| Height at 7 (cm) | 1063/1309 | 119.68 (5.81) | 120.51 (5.30) | <0.001 |
| Height at 15 (cm) | 978/1223 | 159.94 (7.95) | 160.91 (7.71) | 0.001 |
| Height at 53 (cm) | 1065/1484 | 167.40 (9.17) | 168.38 (8.78) | <0.001 |

Note: *P-values derived using logistic regression adjusted for sex; weight at 2, 7, 15 and 53 were also adjusted for height at the same age; analyses were restricted to the target sample for clinical assessment at 60-64y (n=2856), 1558 participants provided complete body composition outcome data

## 2.6 **Analytical strategy and statistical methods used**

The specific methodologies employed in future chapters vary depending on the variables used and research questions addressed. To avoid repetition, the methodologies that are shared across the chapters are outlined below. Unless otherwise stated statistical analyses were conducted using Stata 12 (Statacorp, College Station, TX, USA). The main statistical method used to examine associations between explanatory and outcome variables in this thesis was linear regression. Modelling fat and lean mass as continuous outcomes was preferred to categorising them as there are no accepted cut-points for the different outcomes used, and categorisation leads to reduced information and statistical power.[236;237] Non-linearity was assessed by inclusion of a quadratic term in regression models, or by using likelihood ratio tests (to compare models with the exposure modelled as a linear versus a categorical term) and where evidence was found this was reported along with a description of the cause of the deviation from linearity.

### 2.6.1 ***Data checking***

Prior to conducting analyses, the distribution of all variables was checked for outliers by using summary statistics and plotting each variable as histograms. The results of this for explanatory variables are described in the relevant subsequent chapters. As expected given prior data checking by Professor Judith Adams no body composition measures were too low or too high to suggest that they were implausible. In addition, the distribution of values for whole body fat and lean mass were compared with data from different cohorts of similar ages, and data from the NSHD was judged to be similar, with relatively minor differences between the cohorts which could be attributable to a number of factors (such as differences in age, ethnicity and sample representativeness; Table 8).

### 2.6.2 ***Exploration of potential confounding, mediating, and moderating variables***

In this thesis a number of variables will be considered as potential confounders, mediators, and/or moderating variables. These variables will be chosen a-priori on the basis of previous research, and justification provided in each of the relevant chapters.

A confounder is a variable that biases the association between the exposure and outcome;[64] it is not on the causal pathway between exposure and outcome, but is independently associated with both.[238] For example, considering SEP at birth as a hypothetical confounding factor (of the association between low birth weight and high adult fat mass), it may be that those of low SEP at birth tend to have mothers who were malnourished during pregnancy (leading to low birth weight); as adults, these individuals may themselves have a low SEP which may be associated with physical inactivity (leading to high fat mass). Depending on the difference between unadjusted and confounder-adjusted effect estimates, confounding can either be described as positive (when estimates are attenuated after adjustment) or negative (when estimates are greater after adjustment).[239]

A mediator is defined as a variable which explains, at least partially, how or why another explanatory variable affects the outcome.[240] For example, considering adult height as a hypothetical mediating variable (of the association between low birth weight and low lean mass), it may be that those of lower birth weight tend to become shorter adults who, as previously described, tend to have lower lean mass. Distinction between mediating and confounding factors will be based on a-priori hypotheses of the causal pathways operating. To help in understanding the likelihood of a variable being a confounder or mediator, the relationships between potential confounding/mediating variables and both the exposure and outcome of interest will be assessed in each chapter. Potential confounders and mediators will then be included in adjusted regression models: the change in regression coefficient (of the main explanatory variable) will indicate the extent to which the chosen variable is mediating or confounding the relationship of interest.

Moderating variables are defined as those which modify the effect of the exposure on the outcome of interest (synonymous with interaction or effect modification).[240] For example, considering sex as a modifying variable/effect modifier (in the relationship between low SEP and high fat mass), it may be that the effects of lower SEP on higher fat mass are greater in females. In this thesis, moderation will be tested by the inclusion of an interaction term in regression models.

Table 8. Comparison of whole body fat and lean mass (and other relevant characteristics) between the MRC NSHD and other adult cohorts

| | MRC NSHD | | Li et al, 2009[232] | | Skidmore et al, 2009[241] | Demerath et al, 2009[203] | | Kensara et al, 2005[242] | Gale et al, 2001[243] | |
|---|---|---|---|---|---|---|---|---|---|---|
| Sex | Males | Females | Males | Females | Females | Males | Females | Males | Males | Females |
| N | 746 | 812 | 6559 | 6507 | 3170 | 114 | 119 | 32 | 102 | 41 |
| Age | 60–64 | 60–64 | >20 | >20 | 46.9 (12.8) | 46.0 (15.3 | 47.0 (14.1) | 67.7 (0.47) | 70–75 | 70–75 |
| | Mean (SD) | | Mean (SE) | | Mean (SD) | Mean (SD) | | Mean (SE) | Mean (SD) | |
| Adult height (cm) | 175.29 (6.45) | 162.17 (5.76) | 176.2 (0.1) | 162.1 (0.1) | 162 (6.14) | 179.7 (6.8) | 165.3 (6.4) | 174 (0.01) | 168 (0.07) | 156 (0.06) |
| Adult weight (kg) | 85.27 (13.05) | 72.34 (13.63) | 86.9 (0.3) | 74.2 (0.4) | - | - | - | 83.61 (1.9) | 75.4 (11.7) | 66.9 (11.9) |
| Fat mass (kg) | 23.79 (7.19) | 29.00 (9.22) | 25.4 (0.2) | 30.8 (0.3) | 23.1 (8.44) | 20.2 (8.0) | 26.1 (9.8) | 23.10 (1.1) | 19.62 (6.5) | 28.16 (7.9) |
| Lean mass (kg) | 53.69 (7.06) | 37.26 (5.35) | 62.3 (0.2) | 44.0 (0.2) | 39.8 (5.51) | 67.0 (8.0) | 47.6 (7.0) | 57.77 (1.3) | 50.15 (5.2) | 35.36 (4.3) |
| Sample location /majority ethnicity /other information | UK /Caucasian | | USA /Mixed | | UK /Caucasian /twins | USA /Caucasian | | UK /Caucasian /low and high birth weight groups | UK /Caucasian | |

Note: -=not applicable (data not presented); NSHD=the MRC National Survey of Health and Development

# 3. Chapter 3: Prenatal growth and body composition

Main objective: to examine whether birth weight is associated with body composition outcomes at 60–64 years.

There is substantial interest in the possibility that exposures acting in the womb have lifelong effects on the composition of our bodies. Associations between birth weight and a number of health-related outcomes have been a frequent area of research in life course epidemiology—this is because birth weight is considered an important and meaningful marker of intrauterine development,[244] and is often the only measure available in population studies. While studies have found that high birth weight is associated with increased obesity risk in adulthood, fewer studies have used direct measures of fat and lean mass. The aim of this chapter is to add to this area of research by examining associations between birth weight and body composition outcomes at 60–64 years.

## 3.1 Introduction

Birth weight is a crude but readily measured indicator of the growth and development that takes place in the intrauterine period.[244] During this period, many of the critical and potentially non-reversible developmental processes such as organogenesis take place.[20] As such, impaired growth (indicated by low birth weight) may have lasting effects on subsequent health. This has been suggested in systematic reviews which have found low birth weight to be associated with increased risk of diabetes[245;246] and cardiovascular and all-cause mortality.[247] Body composition may feasibly be on the pathway linking birth weight with these later outcomes.[101;248]

There are a number of potential mechanisms that may underlie associations between birth weight and adult body composition. Environmental factors may affect the acquisition of fat and/or lean mass before birth which then track into adulthood. This mechanism may especially be the case for muscle mass, as while both muscle and fat cells are known to undergo hyperplasia (increase in size) in adulthood, only fat cells are thought to readily undergo hypertrophy (increase in number) in adulthood.[20] As such, the number of muscle cells in adulthood may depend on the number attained in the intrauterine and neonatal periods. This is supported by experimental research in rats and mice showing that impaired foetal development

tends to lead to lower subsequent muscle mass in mature animals,[249;250] and research in farmed animals such as pigs (where the amount of muscle tissue is paramount) showing that low birth weight is closely related to low muscle fibre number at birth, and this tends to track to adulthood.[251;252]

Both under[161;202] and over nutrition[253;254] in the foetal period may trigger epigenetic and/or hormonal changes that result in the greater accrual of fat mass across life. Although this potential mechanism remains speculative, there is some evidence that impaired growth before birth may lead to higher fat mass. During the Dutch 'hunger winter' of 1944-1945—a famine that took place during the Second World War—a number of pregnant women were exposed to famine during different stages of pregnancy.[255] Follow-up of the offspring subsequently born showed that those exposed to famine in the first and second trimesters of pregnancy were at higher risk of obesity (defined by BMI) in young adulthood (at 19 years); those exposed to famine in late pregnancy had reduced risk.[255] Later follow-up at 50 years showed similar obesity risk—assessed by waist circumference and BMI—in females, but not males.[256] The importance of intrauterine growth and adult body composition is also suggested in studies showing higher adult BMI in those born to diabetic mothers.[75;248;250]

Alternatively, associations between birth weight and body composition may be explained by confounders such as SEP before birth, by differences in rates of growth after birth which go on to influence body composition, or by genetic factors which influence both birth weight and body composition. For example, genes that are involved in foetal muscle development have been associated with muscle mass in adulthood.[257]

A number of epidemiological studies have examined associations between birth weight and body composition measures in adulthood. The sections below summarise and discuss these studies: first where anthropometric measures of fat mass were used, and second where direct measures of whole body fat and/or lean mass were used in adolescence or adulthood. The focus of the second section was on studies using accurate measures of body composition which were not included in prior systematic reviews. As such, studies using DXA were included regardless of publication date, while studies using SFT measures or BIA were only included if they were published after 2003 (the date of a systematic review by Rogers et al[170]). Findings from these studies in adulthood are summarised in Table 9.

Table 9. Summary of studies that examined associations between birth weight and whole body fat and/or lean mass in adulthood

| Study | N | Location /majority ethnicity | Age at outcome measure | Birth weight ascertainment | Measure of body composition | Main adjustments | Fat mass association<br>+<br>— | Lean mass association<br>+(positive)<br>—(negative) |
|---|---|---|---|---|---|---|---|---|
| Victora et al, 2007[258] | 2250 | Brazil /Mixed | 18 | Measured | BIA | Height, ASEP maternal height | Males: +<br>Females: N/A | Males: +<br>Females: N/A |
| Euser et al, 2005[259] | 403 | Netherlands /Caucasian | 19 | Measured | SFT | Height, ASEP | None | + |
| Leunissen et al, 2009[260] | 312 | Netherlands /Caucasian | 20 (SD=1.7) | Measured | DXA | Height | — | + |
| Kuzawa et al, 2012[261] | 1612 | Philippines /Filipino | 21 (SD=0.3) | Measured | SFT | Height, parity | + | + |
| Weyer et al, 2000[262] | 272 | USA /Pima Indians | 25 (18-49) | Measured | DXA/UWW | None | None | + |
| Rillamas-Sun et al, 2012[263] | 587 | USA /Caucasian | 24–50 | Self-reported | BIA | None | Males: N/A<br>Females: + | Males: N/A<br>Females: + |
| Sachdev et al, 2005[264] | 1526 | India /Indian | 29 (SD=1) | Measured | SFT | Height, ASEP | Males: no assoc.<br>Females: + | + |
| te Velde et al, 2004[265] | 282 | Netherlands /Caucasian | 36 | Participant recall | DXA | Weight | N/A | + |
| Rolfe et al, 2010[266] | 1092 | UK /Caucasian | 43 (30–55) | Participant recall | DXA | ASEP, BMI | None | N/A |
| Skidmore et al, 2009[241] | 3170 | UK /Caucasian | 46 (18–80) | Participant recall | DXA | BMI | Males: N/A<br>Females: + | Males: N/A<br>Females: + |
| Demerath, et al, 2009[203] | 233 | USA /Caucasian | 46 (18-76) | Measured | DXA | Height, ASEP, Gage | None | + |
| Gunnarsdottir et al, 2004[267] | 3707 | Iceland /Caucasian | 50 (SD=7) | Measured | SFT | BMI | Males: no assoc.<br>Females:— | N/A |
| Yliharsila et al, 2007[268] | 2003 | Finland /Caucasian | 61 (56–70) | Measured | BIA | Height, Gage, CSEP, ASEP, maternal BMI | Males:+<br>Females: no assoc. | + |

| Study | N | Location /majority ethnicity | Age at outcome measure | Birth weight ascertainment | Measure of body composition | Main adjustments | Fat mass association<br>+<br>— | Lean mass association<br>+(positive)<br>—(negative) |
|---|---|---|---|---|---|---|---|---|
| Aihie Sayer et al, 2004[269] | 737 | UK /Caucasian | 64 (SD=2.6) | Measured | SFT | CSEP, ASEP | Males: +<br>Females: N/A | Males: +<br>Females: N/A |
| Kensara et al, 2005[242] | 32 | UK /Caucasian | 67 (SD=0.47) | Measured | DXA | Height and weight, Gage, CSEP, ASEP | Males: —<br>Females: N/A | Males: +<br>Females: N/A |
| Gale et al, 2001[243] | 143 | UK /Caucasian | 70-75 | Measured | DXA | Height | None | + |

Note: ASEP=adult socioeconomic position; BIA=bioelectrical impedance analysis; BMI=body mass index; CSEP=childhood socioeconomic position; DXA=dual energy X-ray absorptiometry; Gage=gestational age; SFT=skinfold thickness; UWW=under-water weighing; N/A=not applicable

### 3.1.1 *Literature review: birth weight and fat and lean mass*

#### 3.1.1.1 *Birth weight and fat mass*

A large number of studies have examined associations between birth weight and anthropometric measures of fat mass in adolescents and adults, and most have been included in the systematic reviews outlined below.

Yu et al conducted a systematic review and meta-analysis in 2011[270] of studies examining associations between birth weight and risk of obesity (BMI >30). In 33 studies identified in the systematic review, high birth weight (>4kg) was associated with increased risk of obesity (odds ratio=2.07 in 20 studies) compared with those of lower birth weight (≤4kg); however, only two studies were in adults. While low birth weight was also associated with increased obesity risk, heterogeneity was reported, with studies with larger sample sizes and of higher quality tending to report no association. Rogers[170] et al conducted a systematic review in 2003 of studies that examined associations between birth weight and later fat mass (typically measured using BMI). Though there were substantial differences among the 52 studies identified, most reported positive associations between birth weight and later BMI/overweight. As in the review by Yu et al, most studies were conducted in adolescence or young-adulthood (<30 years). This relationship was either linear or in some cases 'J' or 'U' shaped—implicating both low and high birth weight as risk factors for higher BMI in adulthood. In the few studies that had adjusted for maternal BMI, associations were typically largely attenuated, suggesting that genetic factors may have confounded these associations. An association between higher birth weight and higher adult BMI was also evident in the systematic review by Parsons et al published in 1999,[166] and in other more recent narrative reviews.[206;248;250]

However, at the time of the most recent systematic review by Rogers et al,[170] relatively few studies had used direct or accurate measures of whole body fat and lean mass. For example, only one study reported by Rogers used DXA,[243] less than 10 used SFT and/or BIA, and the remainder used BMI. The interpretation of these studies is therefore ambiguous: where BMI was used, it is unclear whether birth weight was associated with fat and/or lean mass, and (as discussed in Chapter 2) SFT and BIA are thought to be comparatively inaccurate and imprecise.

Since the publication of Rogers' systematic review a number of other studies have been published and an increasing number have used direct measures of fat and

lean mass such as those obtained using DXA or computer tomography. The following section outlines the main findings of these studies where measures of whole body fat and/or lean mass were taken in adolescence or adulthood.

Eight studies have examined associations between birth weight and fat mass in adolescence, with conflicting findings reported. One study in a developing nation (the Philippines) reported positive associations (using SFT).[261] Using DXA, two studies reported no association in either sex;[271;272] using BIA, one study found positive associations in males but not females,[204] and two others found no association in either sex.[101;273] Using SFT measures, two studies found positive associations in both sexes; in a Latin American[274] and European cohort.[275] Inconsistent findings may be explained by the substantial sex-dependent changes in body composition that occur during adolescence.[171] These changes may lead to greater variability of body composition, thereby affecting subsequent associations.

In studies of cohorts in young to early adulthood (18–29) associations between birth weight and fat mass have been mixed: positive (using SFT or BIA),[258;261;263;264;276] negative (using DXA, after adjustment for adult weight),[260] and null associations between birth weight and fat mass (using DXA[262] or SFT[259]) have all been reported. As with the findings in other age groups, associations typically remained after adjustment for potential confounders. However, these studies have used participants from various ethnic groups: Caucasians,[258-260] Pima Indians,[262] and Filipinos.[261;276] Since fat mass is known to vary by ethnicity,[36;277] it may be that the factors that influence body composition also differ, thereby affecting associations with birth weight.

Inconsistent findings of associations between birth weight and fat mass have also been reported in studies that examined participants in mid–later adulthood (means from 40 to 75 years): positive associations (using DXA in a female-only sample[241] or SFT in both sexes,[269] or in males but not females using BIA[268]), negative associations (using DXA in a male-only sample[242] or SFT in females but not males[267]) or no association in either sex (using either DXA[203;243;266] or SFT[269]) have been reported. The negative associations found were dependent on adjustment for adult weight or BMI; this is methodologically controversial since the birth weight coefficient after this adjustment can be interpreted as reflecting the rate of growth after birth.[266;278]

Of the three studies that reported positive associations between birth weight and fat mass in later adulthood, two used comparatively inaccurate and imprecise

techniques to measure body composition (SFT[269] and BIA[268]); results obtained may therefore be more affected by measurement error than results from DXA studies. Only one study using DXA reported positive associations between birth weight and fat mass.[241] This study had the largest sample size (n=3170) in this age group, and was comprised of Caucasian participants of a wide age range (mean=46.9, range=18–79). However, no associations were found in other DXA studies using Caucasian participants: in a cohort of similar age (n=232, mean age=46.8, range=18-76),[203] or in an older (n=143, age range=70–75 years).[243] It may be that these two studies, due to their smaller sample sizes, had insufficient statistical power. In support of this, Skidmore et al reported substantially smaller effect sizes for fat mass measures compared with lean mass (1 kg increase in birth weight leading to a 1.72 kg increase in lean mass, and 0.25 kg increase in fat mass), suggesting that these associations require greater statistical power to be detected.

However, differences may also be due to differences in the cohorts used. Skidmore et al's study,[241] unlike the others, used a female-only sample and was comprised exclusively of twins. Although the use of twins enabled the relative contribution of environmental and genetic factors to be explored, findings reported in twins may not necessarily translate to those in singletons.[279] Although the authors gave evidence suggesting that their sample was representative of the UK population in terms of adult phenotype, it is thought that twins experience a potentially important different intrauterine environment to singletons.[279;280] For example, a large observational study showed that twins had substantially higher (8-fold) risk of being of low birth weight than singletons,[280] a finding also reported by Skidmore et al. In addition, Skidmore et al's study used unverified recalled birth weight data that may have led to reporting error. This error may have been systematic and may introduce bias, for example if individuals of low birth weight were less accurate at self-report (as has been previously found[281]). Finally, Skidmore et al did not adjust for potential confounders such as socio-economic circumstances at birth or maternal BMI and did not adjust for adult height. Positive associations between birth weight and fat mass could be explained by adult height, as heavier babies tend to become taller adults[282] who, as shown in Chapter 2, tend to have higher fat mass. The findings therefore need to be replicated in a large, mixed-sex cohort of singletons, with objective measures of birth weight and adjustment for potential confounders.

Of the studies included in this section, a number have used DXA or computed tomography measures of abdominal fat mass as outcomes in adulthood, while other studies have examined central and not whole body measures of fat mass. Mixed

findings have been reported in these studies: negative,[242;266] positive,[203] and no association.[241;283;284] As with whole body measures of fat mass, negative associations were only found where adjustment was made for adult weight,[242;266] suggesting that the associations found may reflect rates of growth after birth, and not during the pre-natal period.[278] When examining unadjusted associations between birth weight and central fat mass in adulthood, most studies have found no association. The only study to report a positive association found an association with subcutaneous but not visceral fat mass, a distinction not possible using DXA.

#### 3.1.1.2 ***Birth weight and lean mass***

Studies examining associations between birth weight and lean mass in adolescents (11–17 years) have tended to show that higher birth weight is associated with higher lean mass, although findings have been shown to differ by sex: using DXA, one study found positive associations in males (but not females),[271] and another study reported the opposite finding.[272] Using SFT[101;261] and BIA[204;273] positive associations were reported in both sexes, and in females but not males in another study (using SFT).[275] One recent study in an obese cohort of adolescents reported no association in either sex (using DXA[285]). However, as with conflicting findings reported between birth weight and fat mass in adolescence, associations with lean mass may also be affected by the substantial sex-specific changes in body composition that occur during adolescence.

More consistent results have been reported in younger adults (18–36 years): positive associations between birth weight and lean mass derived from DXA in both sexes,[260;262;265;286] from BIA in male-only[258] and female only samples,[263] and from SFT measures in both sexes.[259;264]

In five studies that measured lean mass in mid–later adulthood (mean ages from 40 to 75 years), all reported positive associations between birth weight and lean mass—measured using DXA, in both sexes[203;243] and in male-only[242] and female-only[241] samples; using BIA in both sexes;[268] or in a male-only sample using SFT measures.[269] One study reported positive associations between birth weight and cross-sectional muscle area using computed tomography.[124]

In all age groups, the positive associations between birth weight and lean mass typically remained after adjustment for adult height and potential confounders (including indicators of socio-economic circumstances at birth, maternal height or BMI). Except one small study in males (n=32),[242] studies in adulthood have all used

whole body lean mass; appendicular lean mass is likely to provide a more accurate measure of skeletal muscle mass.

#### 3.1.1.3 *Literature discussion: birth weight and body composition*

Studies in adulthood have found birth weight is positively associated with lean mass, but relatively few have been conducted in later adulthood. Associations between birth weight and fat mass in adulthood are not consistent, suggesting the need for future research.

The studies examining associations between birth weight and adult body composition have often made statistical adjustment for other factors in their analyses; some of these could be considered as either confounders or mediators. Justification for the variables included in adjusted analyses has seldom been provided, leading to confusion in interpretation. There is also substantial inconsistency across studies, with different studies adjusting for different factors.

A number of studies have adjusted for contemporaneous height,[124;203;242;268] a factor which may mediate associations between higher birth weight and higher fat and lean mass. However, other studies have adjusted for contemporaneous weight[265] or BMI,[241] and provided no justification. Some studies have adjusted for measures of socio-economic circumstances at birth[203;268;269] and other maternal factors which may be socially stratified. These have included parity/birth order,[204;268;274] age at birth,[268] and smoking status.[204] Others have adjusted for factors which could be considered under hereditary influence, including maternal BMI,[268;271;274] maternal SFT measures and height,[276] or maternal height alone.[258] Some studies have adjusted for lifestyle factors of the study sample—typically smoking status[243;264;267;269] and alcohol intake.[242;243;264;269] Finally, other studies have adjusted for gestational age.[268;271;272;275;276;287]

There is a need for a study with sufficient data to enable adjustment for a number of potential confounders and mediators. The NSHD is suited to this since it has data available for many of the factors which could be considered potential confounders (eg, measures of socioeconomic circumstances in early life, birth order, maternal height and BMI, and maternal age). Although the reported associations between birth weight and fat/lean mass are typically unchanged after adjustment for these, this may not necessarily be the case in different cohorts.

#### 3.1.1.4 *Prior findings from the MRC National Survey of Health and Development*

Kuh et al (2002)[288] previously examined associations between birth weight and anthropometric outcomes at 43 years (BMI, waist circumference and waist-hip ratio). A number of sex-specific findings were reported: in males, birth weight was positively associated with waist circumference (before and after adjustment for adult BMI), but not waist-hip ratio; in females, birth weight was negatively associated with waist-hip ratio (after adjustment for adult BMI) due to those of lower birth weight tending to have a reduced hip size in adulthood, but not with waist circumference.[288] In males, birth weight was positively associated with BMI (associations in females were not reported).

The NSHD has no prior measures of lean mass, though studies have examined associations between birth weight and both muscle strength and physical functioning. As described in Chapter 1, this thesis has focused on studies using lean mass as an outcome (given the potentially different determinants of muscle strength, function, and mass). However, studies using these outcomes in the NSHD are described below in order to give an indication of the types of analyses that have been conducted using the same explanatory variable.

Kuh et al (2002)[289] found that birth weight was positively associated with grip strength at 53 years, independently of adult height and weight, and SEP in both childhood and adulthood. Birth weight was positively associated with standing balance time in females but not males, but not associated with chair rise time in males or females.[290] The association between birth weight and standing balance in females was largely attenuated after adjustment for weight and height gain velocities from 0–53 years.

This chapter will build on the earlier work conducted in the NSHD by examining associations between birth weight and direct measures of both fat and lean mass.

#### 3.1.1.5 *Literature summary*

While studies have found high birth weight to be associated with high adult BMI, fewer studies have used direct measures of fat and lean mass, and most of these used cohorts in young-mid adulthood. Conflicting results across age groups have been given for associations between birth weight and fat mass, suggesting the need for further research. Previous studies have found birth weight is positively

associated with whole body lean mass, and there is also a need to replicate findings using appendicular measures which more accurately assesses skeletal muscle mass. In addition, most previous studies have made only limited adjustment for potential confounders.

### 3.1.2 *Chapter objectives and hypotheses*

The objective of this chapter is to test the hypothesis that birth weight is not associated with fat mass, but is positively associated with lean mass.

## 3.2 **Methods**

### 3.2.1 *Explanatory variable*

The explanatory variable used in this chapter is birth weight. This was extracted from birth records a few days after birth (recorded to the nearest quarter of a pound), converted to metric grams[288] and then kilograms.

### 3.2.2 *Outcomes*

The outcomes used in this chapter are the main outcomes of this thesis, outlined in Chapter 2 (whole body measures of fat and lean mass, appendicular lean mass, fat: lean mass ratio, and android: gynoid fat mass ratio). Since this chapter has only one explanatory variable, it was considered feasible to include additional outcomes which might help to strengthen the analyses conducted (BMI and forearm muscle area). These were measured at the same time as the main outcomes (60–64 years). BMI was included to test whether similar associations were found with BMI as with whole body measures of fat and lean mass, and forearm muscle area ($cm^2$) was included to help elucidate whether associations between birth weight and lean mass were explained by associations between birth weight and skeletal muscle size and mass. This was measured in the non-dominant arm using pQCT (Stratec XCT 2000) at the 50% cross-sectional site (see Chapter 2).

### 3.2.3 *Potential confounding and mediating variables*

In this chapter a number of variables will be considered as potential confounders, mediators, or moderating variables. These have been chosen a-priori on the basis of previous research and are listed below along with justification.

- Sex. This was considered as a potential confounder, since males tend to be heavier at birth (Chapter 2) and have more lean mass and less fat mass as adults. It was also considered a potential moderator, since associations between birth weight and body composition have been shown to differ by sex—eg, positive associations between birth weight and lean mass in males but not females,[271] or vice versa.[275]
- Paternal occupational class at 4 years (or at 11 (n=24) and 15 (n=13) years if missing at 4), using the Registrar General's social classification. This was used as an indicator of socioeconomic circumstances at birth, considered a potential confounder since babies born in worse socioeconomic circumstances tend to be lighter at birth;[291;292] these circumstances tend to track into adulthood, and worse socioeconomic circumstances in adulthood were hypothesised as being associated with higher fat and lower lean mass—these associations will be examined in Chapter 6.
- Maternal age at birth of survey child. This was considered a potential confounder since younger and older maternal ages are associated with increased likelihood of low birth weight,[293] and older maternal age at birth has been associated with lower central fat mass[203] and higher lean mass[268] in adulthood.
- Birth order, reported by the mother. This was considered a potential confounder since those born later tend to be heavier at birth[293] and have less fat mass as adults.[294]
- Maternal height (cm) and BMI (kg/m$^2$), measured or self-reported when the study members were 6 years old. These variables were chosen as indicators of the genetic factors which may influence both birth weight and adult body composition. These have been previously shown to confound associations between birth weight and body composition,[170] with higher maternal BMI and height associated with heavier birth weight and higher fat mass in adulthood.
- Adult height at the time of DXA measurement was considered a potential mediator, since those of heavier birth weight tend to be taller as adults,[282] and those taller as adults tend to have more fat and lean mass (Chapter 2).

### 3.2.4 ***Analytical strategy***

A series of linear regression models were constructed to examine associations between birth weight and outcome variables, with adjustment then made for potential confounders and mediators. Potential confounders were added to models as continuous variables (where associations between confounder and both exposure

and outcome are linear) or as categorical variables (where there is no evidence of linear association). Evidence of departure from linearity in the association between birth weight and outcomes was assessed by inclusion of a quadratic term and reported where evidence was found. Tests of interaction were conducted to formally test for evidence of sex interaction—where evidence was found ($P<0.05$) results were stratified by sex.

Adjustment was made for potential confounders in a sequential manner using three models. First, adjustment was made for paternal occupational class at 4 years, considered an indicator of socioeconomic circumstances at birth. Adjustment was then made for factors which are also likely to be socially stratified, but may confound associations between birth weight and body composition via additional biological (birth order and maternal age) and genetic (maternal BMI and height) pathways. To examine the influence of missing data on potential confounders on findings, the associations between birth weight and outcomes were compared using the restricted and maximum available samples.

While associations with birth weight may reflect the influence of prenatal growth, associations may also be due to birth weight-related differences in growth after birth—for example, positive associations between birth weight and adult lean mass could be explained by heavier babies undergoing greater weight gain (and accrual of lean mass) in infancy and childhood which then tracks into adulthood. To test whether this explanation was possible, associations between birth weight and weight and height (and their velocities) from infancy to adolescence were examined using linear regression. Chapter 4 will then examine associations between measures of growth after birth (weight and height gain) and body composition outcomes and discuss the extent to which associations between birth weight and body composition can be explained by subsequent periods of growth.

Adjustment of birth weight and body composition associations for measures of growth after birth was not conducted in this thesis as it was thought that this would not be able to distinguish whether associations between birth weight and outcomes were due to prenatal or post-natal growth.[278] In addition, the high correlation between measures of weight could lead to multicollinearity.

### 3.2.5 ***Sample used in analyses***

In total, 1264 participants had valid data for both birth weight, all potential confounders, and main outcomes (fat and lean mass, appendicular lean mass, fat:

lean and android: gynoid ratios); 289 participants with valid birth weight and outcome data were excluded from analyses due to missing data for one or more potential confounder. As tests of sex interaction tend to have only limited statistical power these were conducted using the maximum available sample size.

## 3.3 **Results**

### 3.3.1 ***Investigation of potential confounders and mediators***

Appendix 3 shows the associations between potential confounding/mediating variables and a) birth weight and b) fat and lean mass at 60-64 years. The following variables met part of the formal definition of a confounder since they were associated with both birth weight and fat or lean mass index:

- Sex: males were heavier at birth, and had more lean mass and less fat mass than females (shown in Chapter 2).
- Maternal BMI: study members with heavier mothers (higher BMI) were heavier at birth, and had more fat and lean mass.
- Birth order: study members born later were heavier at birth; in males, but not females, those born later had higher lean mass, while females, but not males, had higher fat mass.

Paternal occupational class was not associated with birth weight—associations between this and other indicators of SEP will be examined in Chapter 6. Maternal height and maternal age were positively associated with birth weight but not associated with fat or lean mass. Adult height, a potential mediator, was positively associated with birth weight and, as shown in Chapter 2, positively associated with fat and lean mass.

### 3.3.2 ***Birth weight and body composition outcomes***

Table 10 presents results from unadjusted regression models examining associations between birth weight and body composition outcomes. Birth weight was weakly positively associated with whole body fat mass, but this association was entirely attenuated after adjustment for adult height. Birth weight was positively associated with both whole body and appendicular lean mass in both sexes with evidence for sex interaction reflecting a larger effect size in males. Positive associations between birth weight and height-adjusted whole body and appendicular lean mass indices were also found. When height was included as a covariate in regression models it was found to partly attenuate the associations

(Appendix 4). Higher birth weight was associated with lower fat: lean and android: gynoid ratios in both sexes.

Tests of linearity showed little evidence for deviation from linearity except for associations between birth weight and whole body and appendicular lean mass index. Further analyses showed that the coefficient of the quadratic term was small and negative for both outcomes (-2.84E-07 and -1.32E-07, respectively). Upon plotting these data, this appeared to be driven by a levelling off of the positive association at the higher values of birth weight; when those with a birth weight of >4.5 kg (n=26) were excluded, no evidence for deviation from linearity was found, while the positive association remained ($P<0.001$ in both cases).

Associations between birth weight and additional outcomes (BMI and forearm muscle area) are shown in Appendix 5. Birth weight was not associated with BMI, but was positively associated with forearm muscle area.

Table 11 shows associations between birth weight and body composition outcomes before and after adjustment for i) paternal occupational class at 4 years, ii) birth order and maternal age, and iii) maternal height and BMI. The associations described above remained, in most cases with minor attenuation of effect, in fully adjusted models. Of these groups of potential confounders, adjustment for maternal height and BMI had the most substantial impact on associations—attenuating but not removing most associations. However, associations between birth weight and lean mass index were largely entirely attenuated after adjustment for maternal BMI and height. Further analyses showed that this was driven by maternal BMI.

Appendix 6 and Appendix 7 show associations between birth weight and weight and height (and their velocities) from 2–20 years. As expected (due to tracking of weight and height), in both sexes birth weight was positively correlated with weight and height from 2–20 years. In both sexes, birth weight was positively correlated with weight gain velocities from 2–15 years but generally not with height gain velocity, except positive associations between birth weight and height gain from 7–11 years in males and 2-4 years in females.

Table 10. Mean difference in body composition outcomes per 1 kg increase in birth weight

| Outcome | β (95% CI) | P | P(quad) | P(sex interaction)# |
|---|---|---|---|---|
| Fat mass (kg) | 0.54(-0.41, 1.49) | 0.27 | 0.88 | 0.87 |
| Fat mass index (kg/m$^{1.2}$) | -0.01(-0.53, 0.50) | 0.96 | 0.85 | 0.92 |
| Lean mass (kg) – males | 2.82(1.76, 3.87) | <0.001 | 0.22 | 0.04 |
| Lean mass (kg) – females | 1.81(0.92, 2.69) | <0.001 | 0.67 | – |
| Lean mass index (kg/m$^2$) | 0.25(0.03, 0.46) | 0.03 | 0.06 | 0.48 |
| Appendicular lean mass (kg) – males | 1.47(0.97, 1.98) | <0.001 | 0.15 | 0.03 |
| Appendicular lean mass (kg) – females | 0.91(0.49, 1.33) | <0.001 | 0.91 | – |
| Appendicular lean mass index (kg/m$^2$) | 0.16(0.06, 0.27) | <0.01 | 0.06 | 0.38 |
| Fat: lean mass ratio | -1.99(-3.78, -0.20) | 0.03 | 0.23 | 0.71 |
| Android: gynoid fat mass ratio | -2.65(-4.21, -1.08) | <0.01 | 0.10 | 0.39 |

Note: Models were adjusted for sex unless sex-stratified; analyses restricted to those with valid data for birth weight, paternal occupational class, maternal age, height, and BMI, birth order, and body composition outcomes; N=1264 in all models (males=610; females=654); P(quad)=test for deviation from linearity—likelihood ratio test comparing models including and excluding birth weight$^2$; #formal test of sex interaction using the maximum available sample size (with all outcome measures, n=1553)

Table 11. Mean difference in body composition outcomes per 1 kg increase in birth weight: a) adjusted for paternal occupational class at 4 years; b) identical to model a with additional adjustment for birth order and maternal age; c) identical to model b with additional adjustment for maternal height and body mass index ($kg/m^2$)

| | a) | | b) | | c) | |
|---|---|---|---|---|---|---|
| Outcome | β (95% CI) | P | β (95% CI) | P | β (95% CI) | P |
| Fat mass (kg) | 0.61(-0.34, 1.56) | 0.21 | 0.80(-0.17, 1.78) | 0.11 | -0.26(-1.25, 0.74) | 0.61 |
| Fat mass index ($kg/m^{1.2}$) | 0.03(-0.48, 0.54) | 0.91 | 0.13(-0.39, 0.65) | 0.63 | -0.36(-0.90, 0.17) | 0.19 |
| Lean mass (kg) - males | 2.82(1.77, 3.88) | <0.001 | 2.91(1.83, 3.99) | <0.001 | 1.95(0.83, 3.07) | <0.01 |
| Lean mass (kg) - females | 1.80(0.91, 2.68) | <0.001 | 2.02(1.12, 2.93) | <0.001 | 1.18(0.28, 2.09) | 0.01 |
| Lean mass index ($kg/m^2$) | 0.26(0.04, 0.48) | 0.02 | 0.28(0.06, 0.51) | 0.01 | 0.13(-0.10, 0.36) | 0.28 |
| Appendicular lean mass (kg), males | 1.47(0.96, 1.97) | <0.001 | 1.52(1.00, 2.04) | <0.001 | 1.09(0.56, 1.63) | <0.001 |
| Appendicular lean mass (kg), females | 0.90(0.48, 1.32) | <0.001 | 1.03(0.60, 1.46) | <0.001 | 0.65(0.22, 1.08) | <0.01 |
| Appendicular lean mass index ($kg/m^2$) | 0.17(0.07, 0.27) | <0.01 | 0.18(0.08, 0.29) | <0.01 | 0.12(0.01, 0.22) | 0.04 |
| Fat: lean mass ratio | -1.81(-3.59, -0.03) | 0.05 | -1.51(-3.33, 0.32) | 0.11 | -2.61(-4.50, -0.73) | <0.01 |
| Android: gynoid fat mass ratio | -2.48(-4.04, -0.93) | <0.01 | -2.59(-4.19, -1.00) | <0.01 | -2.79(-4.45, -1.12) | <0.01 |

Note: Models were adjusted for sex unless sex-stratified; analyses restricted to those with valid data for birth weight, paternal occupational class, maternal age, height, and BMI, birth order, and body composition outcomes; N=1264 in all models (males=610; females=654)

## 3.4 **Discussion**

### 3.4.1 ***Main findings***

The main findings of this chapter are weak positive associations between birth weight and fat mass at 60–64 years which were entirely explained by adult height. Birth weight was more strongly positively associated with lean mass, and this association remained after adjustment for adult height. Those of higher birth weight also tended to have lower fat: lean and android: gynoid ratios.

The above associations remained with only minor attenuation of effect after adjustment for a number of potential confounders (socioeconomic circumstances in childhood, birth order, maternal age, BMI and height), while associations between birth weight and whole body lean mass index were largely attenuated after adjustment for maternal BMI.

### 3.4.2 ***Comparison with previous findings***

The findings of no association between birth weight and whole body fat mass (after adjustment for adult height) are consistent with some previous studies, described in the literature review of this chapter, although overall previous studies have yielded inconsistent results. Some studies have reported negative associations, although these tend to depend on statistical adjustment for weight or BMI in adulthood.[242;266;267] Few studies have reported positive associations; of those that have, small effect sizes are typically found compared with lean mass associations.[241;269] In this chapter higher birth weight was associated with lower android: gynoid ratio; to the author's knowledge, these associations have not been previously examined.

Previous studies have also reported positive associations between birth weight and whole body lean mass in adulthood, with most previous studies conducted at younger ages. Only one previous study has used appendicular lean mass, and also reported positive associations in a sample of 32 males in later adulthood.[242] Findings from this chapter build on these results by showing that higher birth weight was associated with higher whole body and appendicular lean mass, and forearm muscle area, in much larger sample containing both sexes. In addition, findings were independent of potential confounders which were typically not available in previous studies.

Findings from this chapter build on previous work in the NSHD at earlier ages which found birth weight to be positively associated with BMI at 43 years;[288] findings from this chapter suggest that this association may reflect associations with lean but not fat mass. Higher birth weight was associated with higher waist circumference in males and lower waist-hip ratio in females at 43 years (after adjustment for contemporaneous BMI).[288] The analyses conducted in this chapter extend these findings by using a longer period of follow-up and by using direct measures of fat and lean mass.

### 3.4.3 *Birth weight and fat mass: explanation of findings*

Weak positive associations between birth weight and fat mass were explained by adult height, as those of higher birth weight tended to become taller adults who, as shown in Chapter 2, have more fat mass.

The weak evidence for association between birth weight and fat mass (with no evidence after adjustment for height) could reflect a genuine lack of association between prenatal growth and subsequent fat mass. Associations between birth weight and lean but not fat mass may reflect the different properties of the different cell types across life, with only fat cells thought to readily undergo hyperplasia in adulthood.[20] Alternatively, the findings may be due to insufficient statistical power; the only study using DXA in later adulthood that reported positive associations had a larger sample size than this and other studies, and therefore had superior power to detect the reported small effect size for fat mass. However, this other study was conducted in female twins and the results do not necessarily generalise to mixed-sex singletons; further, no adjustment was made for adult height or socioeconomic circumstances.

The lack of association between birth weight and fat mass may be a result of the inability, when using birth weight, to distinguish between the potentially differential effects of different periods of foetal growth. Examination of in-utero ultrasound measures have suggested that impaired growth only goes on to influence birth weight if it occurs in the third trimester of pregnancy,[295] and the Dutch 'hunger winter' study suggested that impaired growth in the first two trimesters of pregnancy, but not the third, is associated with higher subsequent fat mass.[255;256]

A higher birth weight was consistently associated with a lower android: gynoid ratio, and further analyses showed that these were driven by associations between higher birth weight and higher gynoid fat mass (Appendix 5). Further analyses

(data not shown) showed that these associations remained after adjustment for adult height. These findings suggest that prenatal growth may have lasting effects on fat distribution, but not necessarily whole body fat mass. While it has been suggested that prenatal under-nutrition may lead, via epigenetic or hormonal pathways, to the preferential accrual of abdominal fat after birth,[202] findings from this chapter do not support this: associations may either reflect the greater accrual of gynoid fat mass before birth, which tracks to adulthood, or the preferential accrual of gynoid fat mass after birth among those of higher birth weight.

### 3.4.4 *Birth weight and lean mass: explanation of findings*

Positive associations between birth weight and lean mass may be explained by the tracking of muscle fibres attained at birth. While previous studies have reported this finding using whole body lean mass. The positive associations found between birth weight and both appendicular lean mass and forearm muscle area found in this chapter provide further evidence that prenatal growth may have a lasting effect on lean mass in adulthood. While the effect sizes were larger in males than females, this was explained by males being taller as adults. The difference in association between birth weight and fat and lean mass led, as expected, to those of higher birth weight having a lower fat: lean mass ratio.

After adjustment for height, associations between higher birth weight and higher lean mass were attenuated but were not abolished in both sexes, suggesting that body size explains in part the associations found—such that heavier babies went on to become taller adults who in turn developed higher lean mass, potentially due to taller adults having longer bones and therefore longer muscles of higher mass. The fact that birth weight and lean mass associations remained after adjustment for height suggests that factors other than muscle length explain the associations found. Given the positive association between birth weight and forearm muscle area these may include differences in muscle width, ie, the number of adjacent muscle fibres or their thickness (driven by the number of myofibrils/muscle filaments they contain). Those with higher birth weight may also have developed higher muscle density (the number of muscle fibres and/or fibre mass per unit area of muscle). The suggestion that foetal growth influences muscle density and composition is supported by studies in animal models showing that under-nutrition during gestation is associated with lower muscle density in neonates.[296;297] A recent study demonstrated similar findings in humans, where lower birth weight was associated with lower muscle density.[298] However, the study was conducted in

males only and had a limited sample size (the association was reported only as a non-significant trend) suggesting the need for future research.

Prenatal growth could feasibly impact on physical activity levels, which then impact on lean mass. However, studies that have examined associations between birth weight and physical activity do not support this. For example, in a study of four cohorts, birth weight was not associated with objectively assessed physical activity in adolescence.[299] In a large study of 13 Nordic cohorts, associations between birth weight and self-reported physical activity (in adolescents and adults) were described as negligible (across the normal birth weight range).[300]

Associations between birth weight and lean mass could reflect genetic factors which affect both birth weight and lean mass.[170] Although the present study was not designed to explore the relative importance of genetic and environmental exposures, maternal height and BMI have been previously used as crude indicators of genetic influence[170] and were considered as potential confounders in this chapter. Adjustment for these variables did not fully explain associations between birth weight and appendicular lean mass, suggesting that these associations were independent of genetic influence; similar findings after adjustment for maternal height and BMI have been reported in other studies reporting positive associations between birth weight and lean mass.[204;258;268;271;274;276] Only one association (between birth weight and whole body lean mass index) was substantially attenuated upon adjustment for maternal BMI. Since associations between birth weight and appendicular lean mass measures were not substantially attenuated this may suggest that central lean mass (both muscle and organ mass) is more strongly influenced by genetic factors than appendicular regions.

Maternal height or BMI may not be accurate measures of genetic influence since they are associated with offspring body composition by both genetic and social pathways.[301] Further evidence for non-genetic influence comes from twin studies which have shown positive associations between intra-pair differences in birth weight and lean mass, for both mono and di-zygotic twins,[241;302-304] and experimental studies in adulthood (described in the literature review of this chapter).

### 3.4.5 ***Methodological considerations and limitations***

Although commonly used in epidemiological studies, birth weight is only a crude indicator of prenatal growth and has a number of limitations.[244] As a measure of

weight, it does not distinguish fat and lean mass; separate measures of these masses at birth may be more closely related to subsequent fat and lean mass in adulthood. Birth length was not collected in the NSHD, and it may be that length at birth, or height-adjusted weight, is also more closely related to body composition outcomes than birth weight.[282] As previously discussed, birth weight does not distinguish between impaired growth in different periods (eg, in the 1st, 2nd, or 3rd trimesters), and these may be differentially important for subsequent body composition outcomes.

More refined measures of prenatal growth such as ultrasound measures are able to isolate and quantify distinct periods of growth, and may be used to show which periods are important for subsequent body composition. However, ultrasound measures are a relatively recent development—they are not available for use in older cohorts (given their development in the 1950s[305]) and are not easily implemented in large population studies. Despite its limitations, evidence of associations between birth weight and a substantial number of health outcomes in adulthood—independent of potential confounders—suggests that birth weight may be a useful if crude marker of foetal growth for use in epidemiological studies.[245-247]

Another limitation of this chapter is the lack of data on gestational age (not collected in the NSHD), a variable which may confound associations between birth weight and body composition. However, studies have tended to find associations between higher birth weight and higher lean mass are similar after this adjustment,[268;271;272;275;276;287] suggesting that it may not substantively influence the overall findings. In addition, there was less variation in gestational age in the NSHD than younger cohorts—the survival of babies of young gestational age was less likely in the 1940s when the NSHD participants were born, before the National Health Service was established (1948) and before subsequent improvements in obstetrics and neonatal care.

Although the analyses in this chapter utilised a relatively large sample size (compared with previous studies), 289 participants were excluded from analyses due to missing data for potential confounders. While missing data could introduce bias, further analyses showed that the unadjusted associations between birth weight and outcomes were similar in the maximum available sample (data not shown) and restricted sample (presented above), suggesting that this source of potential bias was unlikely to substantially impact on the main associations reported.

Another potential source of bias is the attrition that occurred in the NSHD; not all of the original NSHD sample providing full body composition data at 60-64 years. However, this is unlikely to have impacted on findings as there was no evidence for differences in birth weight between participants with and without full body composition outcome data at 60-64 years (Chapter 2).

### 3.4.6 ***Strengths***

Chapter 1 presents the overall strengths of the NSHD, while the strengths specific to this chapter are outlined below.

The rich data previously collected in the NSHD enabled the influence of a number of potential confounders to be investigated, unavailable in most other studies. These, and the main explanatory variable, were prospectively ascertained limiting retrospective recall error and associated biases. The fact that most associations remained after adjustment for potential confounders provides further evidence for an association between foetal growth and adult body composition.

Detailed outcome data were available in this study, including regional measures of body composition unavailable in other studies (such as appendicular lean mass and forearm muscle are). The use of these measures gave further support to the hypothesis that prenatal growth may influence adult skeletal muscle mass and fat distribution.

In this chapter, potential confounders, mediators, and moderators were selected a-priori with explicit rationale for inclusion, while previous studies have tended not to provide justification for adjustment in analyses. Formal tests of interaction were performed to test interactions by sex, and outcomes were stratified by sex only where sufficient evidence was found. Previous studies have often stratified by sex without justification—this reduces the statistical power (by 50% in samples of equal sex ratio). Adjustment for body size was conducted by using adult height; results showed that birth weight and lean mass associations were partly mediated by body size. Such conclusions are not possible in studies which have made adjustment for other anthropometric variables in adulthood such as weight or BMI.

### 3.4.7 ***Conclusions and links to other chapters***

This chapter has shown evidence for a positive association between birth weight and lean mass and of no association between birth weight and fat mass. Positive

associations were also found between birth weight and appendicular lean mass and forearm muscle area, suggesting that prenatal growth may influence skeletal muscle mass in adulthood. These associations were independent of a number of potential confounders and only partly mediated by adult height. In addition, higher birth weight associated with lower fat: lean and android: gynoid ratio.

The prenatal period is part of a wider continuum of growth that continues into infancy, childhood, and adolescence. Chapter 4 builds on the work done in this chapter by examining associations between periods of growth in these periods and adult body composition.

# 4. Chapter 4: Growth after birth and body composition

Main objective: to examine whether periods of growth in infancy, childhood and adolescence are associated with body composition outcomes at 60-64 years.

In Chapter 3 associations between birth weight (an indicator of prenatal growth) and measures of body composition in adulthood were examined, with positive associations found between birth weight and lean mass. Prenatal growth is a relatively short period of the entire growth trajectory which extends into infancy, childhood, and adolescence. This chapter extends the work done in Chapter 3 by examining associations between periods of growth (in weight and height) after birth (in infancy, childhood, and adolescence) and body composition in later adulthood.

## 4.1 Introduction

In Chapter 3, studies finding associations between impaired prenatal growth, indicated by low birth weight, and increased risk of ill-health in adulthood were described. In some cases, associations between birth weight and later health outcomes were only found after statistical adjustment for adult BMI, where the birth weight coefficient can also be interpreted as reflecting rates of growth after birth.[278] Patterns of growth after birth have also been associated with health outcomes in adulthood, with growth typically quantified as change in weight, height or BMI in periods of infancy, childhood, and/or adolescence. For example, greater weight gain in infancy has been shown to be associated with increased risk of adult insulin resistance and cardiovascular disease.[306;307] Body composition may in part mediate these associations, such that patterns of growth impact on body composition, which then affects subsequent health.

Although seldom explicitly stated, there are at least two mechanisms which may explain associations between growth after birth and body composition in adulthood. First, associations may reflect the tracking of fat or lean masses attained during periods of weight gain, as both are thought to track across life (discussed in Chapter 1). Second, associations may reflect tracking of the factors which influence subsequent changes in fat and lean mass.[308] For example, patterns of physical activity and diet in adult life are thought to be associated with those already present in adolescence;[77] obesogenic tendencies (low physical activity and high energy intake) would lead to greater weight gain in adolescence and, assuming these traits track across life, would also lead to greater gains in fat mass in

adulthood. Patterns of growth may also reflect changes in metabolic mechanisms which have effects on subsequent changes in body composition. For example, rapid growth in infancy has been suggested to prime (or programme) the metabolic system towards a propensity to accumulate fat mass across life.[176;309] Though unconfirmed, this may be mediated through behavioural and/or biological mechanisms eg, through changes in leptin secretion,[310;311] a hormone known to be involved in satiety regulation.[21;23] Greater weight gain in infancy and early childhood has been associated with earlier pubertal maturation[312;313] which may have consequent metabolic consequences that impact on body composition. For example, earlier puberty may lead to an extension of exposure to the higher levels of sex hormones triggered by puberty—for example oestrogen in females (which may lead to higher fat mass[314;315]), and testosterone in males (which may lead to higher lean mass[69;316]).

Different periods of growth may be differentially important for subsequent fat or lean mass, and this can be examined by comparing associations across periods investigated; stronger associations would be expected for periods which are more important. If associations only reflect the tracking of attained masses during periods of weight gain, then the strength of association would be greater for periods where these masses are attained. As described in Chapter 1, available data from cross-sectional studies of both sexes suggest that fat mass is attained in infancy (0–2 years), tends to plateau in early childhood (2–7 years), and then increases again in late childhood (7–11 years), while lean mass is continuously accrued across these periods (with males accruing more in late adolescence; 15–18 years).[69;70] The effects of increased growth in one period may differ depending on the extent of preceding growth. For example, restrictions to in-utero growth (as indicated by low birth weight for a given gestational age) tend to be followed by more rapid growth in early infancy (termed 'catch-up' growth), and this type of growth may be differentially associated with body composition outcomes than non-catch-up growth.[317;318]

A number of epidemiological studies have examined associations between periods of growth and subsequent body composition in adolescence or adulthood; the following section summarises and discusses these studies. Studies using BMI as an outcome are first described, followed by studies that have used direct measures of whole body fat and/or lean mass in adolescence or adulthood. As in Chapter 3, the focus of the literature review was on studies using accurate measures of body composition which were not included in prior systematic reviews. As such, studies using DXA were included regardless of publication date, while studies using SFT or

BIA were only included if they were published after 2005 (the date of a systematic review by Monteiro and Victoria (2005)).[173] The studies are separated according to the period of growth investigated: infancy (0-2 years), childhood (2-11 years) and adolescence (12-17 years). Findings from studies with measures of body composition in adulthood are summarised in Table 12.

Table 12. Summary of studies that examined associations between growth after birth and whole body fat and/or lean mass in adulthood

| Study | N | Location /majority ethnicity | Age at outcome measure (years) | Type and period of growth investigated | Body composition measure | Main adjustments | Fat mass association +(positive) –(negative) | Lean mass association +(positive) –(negative) |
|---|---|---|---|---|---|---|---|---|
| Victora et al, 2007[258] | 2250 # | Brazil /Mixed | 18 | Weight: 0–1, 1–2, 2–4 and 4–15y | BIA | Height, ASEP maternal height | Males: + all Females: N/A | Males: + all Females: N/A |
| Kindblom et al, 2009[319] | 612 | Sweden /Caucasian | 18 (SD=0.5) | BMI: 1-4 4-10 10–18y | DXA | None | Males: + all Females: N/A | + Males: + all Females: N/A |
| Euser et al, 2005[259] | 403 | Netherlands /Caucasian | 19 | Weight: 0–3 mo 3 mo – 1y | SFT | Height, ASEP | + all | + all |
| Kuzawa et al, 2012[261] | 1612 | Philippines /Filipino | 21 (SD=0.3) | Weight: 0–12 mo 12–24 mo 2–8 y | SFT | Height, parity | + all | + all |
| Sachdev et al, 2005[264] | 1526 | India /Indian | 29 (26–32) | BMI: 0-6, 6-12 mo 1–2, 2–5, 5–8, 8–11, 11–14y | SFT | Height, ASEP | + all | + all |
| Demerath et al, 2009[203] | 232 | USA /Caucasian | 46 (18-76) | Weight: 0–2y | DXA | Sex, height, education, Gage | + all | + all |
| Yliharsila et al, 2008[197] | 1917 | Finland /Caucasian | 61.5 (56–70) | BMI: 0–2, 2–7, 7–11y | BIA | Height | No assoc. 0–2 yr + 2 to 11 yr | + all |

Note: ASEP=adult socioeconomic position; BIA=bioelectrical impedance analysis; BMI=body mass index; DXA=dual energy X-ray absorptiometry; SFT=skinfold thickness; UWW=under-water weighing; N/A=not applicable; mo=month; y=year; #n=110 with all data available

### 4.1.1 *Literature review: growth and body composition*

#### 4.1.1.1 *Growth and anthropometric measures of fat mass*

Most of the numerous studies that have examined associations between growth after birth and anthropometric measures of fat mass in adolescence/adulthood have been included in the systematic reviews outlined below.

Monteiro and Victoria (2005)[173] examined associations between infant and childhood growth (0–15 years) and later risk of obesity (from 3-70 years). Of 16 studies identified, most used BMI as an outcome; five used SFT measures, with one study using DXA measures (at 9 years). In the majority of studies (13 of 15), measures of greater growth (in weight, height, or height-adjusted weight) were associated with increased risk of subsequent obesity.

Ong and Loos[174] conducted a systematic review (2006) of the associations between weight gain in infancy and subsequent obesity, and conducted additional analyses of the collated results—calculating the odds of obesity given a standardised exposure (rapid weight gain in infancy: >+0.67 change in weight standard deviation score between 0 and 2 years). Of 21 studies identified, 15 studies uniformly reported positive associations between weight gain in infancy and increased risk of obesity (defined by high BMI or SFT measures). Those who grew rapidly in infancy had 2–3-fold higher odds of subsequent obesity. None of the studies included in this review found evidence for interaction between infant growth and birth weight—the effect of infant weight gain was equivalent in all levels of birth weight,[311] suggesting that catch-up growth does not differentially impact on subsequent obesity risk. Associations between greater weight gain in infancy and higher obesity risk was also found in a systematic review in 2005[172] and in a meta-analysis of 10 cohorts (including the NSHD with BMI measures at 43 years) in 2011.[320]

No systematic reviews have examined the specific associations between adolescent growth and subsequent anthropometric measures of fat mass. At least one original research article has examined these associations and reported positive associations between BMI gain in adolescence (11-16 years) and subsequent BMI at 25–33 years.[309]

In summary, evidence from anthropometric studies suggests that growth during infancy, childhood and adolescence is positively associated with subsequent fat

mass. However, BMI has a number of limitations (outlined in full in Chapter 1), primarily that it does not distinguish fat and lean mass. A number of studies have since examined associations between periods of growth and direct measures of fat mass in adolescence (11-17 years), young adulthood (18-36 years), and mid-later adulthood (mean age between 45 and 65 years). These studies are outlined below. Also included are relevant experimental trials conducted in humans.

#### 4.1.1.2 *Infant growth (0–2 years) and direct measures of fat mass*

Fourteen studies have reported positive associations between weight or BMI gain in infancy and fat mass in adolescence (using DXA,[311;319;321-323] BIA[204] or SFT[261;324]), young adulthood (using BIA[258] or SFT [259;261;264]) and mid-later adulthood (using DXA[203]), while one study in later adulthood found no association (using BIA[197]). Two of these were included in the same paper by Kuzawa et al (2012).[261]

Six of these studies obtained repeat measures of infant growth: two found that earlier, (0–3 and 0–6 months) and not later (3–9 and 6–12 months),[311;322] periods of BMI gain were positively associated with subsequent fat mass in adolescence, while four others found that both earlier (0–12 months) and later (12 months – 2 years) periods of weight, ponderal index or BMI gain were positively associated with subsequent fat mass (in adolescence[261;321;324] or young adulthood[261]).

One study examined the associations with height gain and reported positive associations between periods of height gain in infancy (0-6 months, 6 months-1 year, 1-2 years) and subsequent fat mass (using SFT) in adolescence.[324] The first and last of these associations became negative when adjusted by weight gain in the same period; in contrast, weight gain in infancy was positively associated both before and after adjustment for height gain. Negative associations between height gain and fat mass were interpreted as suggesting that greater height gain without excessive weight gain was beneficial in leading to lower fat mass, although the mechanisms underlying these associations were not discussed.

Singhal et al (2010)[208] gave experimental evidence for the positive association between rapid infant growth and subsequent fat mass: they conducted two randomised controlled trials in which small for gestational age infants were fed either control or nutrient-enriched formulas (for 6–9 months from birth). Those fed nutrient-enriched formulas tended to gain more weight and height in infancy and had higher fat mass at follow-up (either BIA or deuterium dilution measures at age

5–8 years). However, the extent to which findings are generalisable to those not born small for gestational age is uncertain, given differences in subsequent of growth in those born small for gestational age.

#### 4.1.1.3 *Childhood growth (2-11 years) and direct measures of fat mass*

Eight studies have reported positive associations between weight or BMI gain in childhood and fat mass in adolescence (using DXA[322;323] or SFT[261]), young adulthood (using DXA,[319] BIA[258] or SFT[261;264]) or mid-later adulthood (using BIA[197]).

Howe et al (2010) obtained a large number of repeat measures of childhood BMI from the Avon Longitudinal Study of Parents and Children, and found that all periods of BMI change (2–5, 5–5.5, 5.5–6.5, 6.5–7, 7–8.5, and 8.5–10 years) were associated with subsequent DXA-measured fat mass in adolescence.[321] The patterns of associations found were complex—associations were both positive and negative across the periods, and the interpretation of these associations were further complicated by the mean BMI across the periods investigated which both increased and decreased. Positive associations indicated either greater BMI gain where BMI increased, or a slower decline where BMI declined; negative associations indicated a slower BMI increase where BMI increased, or a faster decline where BMI declined.

#### 4.1.1.4 *Adolescent growth (12–17 years) and direct measures of fat mass*

Only two studies have examined associations between adolescent growth and fat mass: both reported positive associations between BMI gain in adolescence and subsequent fat mass in young adulthood (measured using SFT[264] or DXA[319]).

#### 4.1.1.5 *Literature summary: growth and fat mass*

In summary, studies have tended to report positive associations between weight and BMI gain in infancy, childhood, and adolescence and subsequent fat mass. The studies differ in the measures (eg, weight, BMI, and height) and timing of periods of growth, as well as in the age at outcome and body composition measure, making comparison between results difficult. Of the studies that used repeat measures of weight or BMI gain in infancy and childhood, most suggested that gain in childhood is more strongly positively associated with fat mass than gain in

infancy,[197;258;264;319] with later periods in childhood more strongly associated than earlier periods. These studies were all conducted in adolescents or young adults. Only one study used a sample in mid-later adulthood (Yliharsila et al (2008),[197] mean age=61.5) and found that BMI gain in childhood was positively associated with subsequent fat mass while BMI gain in infancy was not.

Few studies have utilised measures of growth across infancy, childhood and adolescence—the two studies that did suggest all periods of BMI gain are positively associated with subsequent fat mass (with later periods being more strongly associated). However, these studies (by Sachdev et al (2005)[264] and Kindblom et al (2009)[319]) have a number of limitations which suggest the need for future research, and are both conducted in samples of limited generalisability. The first used SFT measures of fat mass (at 29 years) which, as discussed in Chapter 2, are likely to be comparatively inaccurate and imprecise. This study was conducted in an Indian cohort which may have different patterns of growth to cohorts in more developed nations. The second assessed adolescent growth as change in BMI between 10 and 18 years, with fat mass measured using DXA at 18 years; this study is therefore unable to determine the long term effect of adolescent growth on subsequent fat mass. In addition, this study was comprised exclusively of males and no adjustment was made for potential confounders such as SEP in childhood.

Although studies have seldom discussed the reasons for different strengths of associations between different periods of growth and fat mass, stronger positive associations between weight gain in later periods (eg, later childhood and adolescence) than earlier periods (eg, early childhood and infancy) may be explained by the greater accrual of fat mass in these periods, which then tracks into later life. However, given evidence from cross-sectional studies that suggest accrual of fat mass occurs in both infancy and later childhood, associations in later childhood may be stronger if they reflect additional phenomena—for example, if greater weight gain in these periods is also associated with greater subsequent gains in fat mass (eg, through the tracking of behavioural factors such as physical activity).

#### 4.1.1.6 *Infant growth (0–2 years) and direct measures of lean mass*

Twelve studies have reported positive associations between weight or BMI gain in infancy and lean mass in adolescence (using DXA,[322;323] BIA,[204] or SFT[261;324]), young adulthood (using DXA,[319] BIA[258] or SFT[259;261;264]) or mid-later adulthood (using

DXA[203] or BIA[197]). Two of these studies were included in the same publication by Kuzawa et al (2012).[261]

Four studies used repeat measures of growth in infancy—these showed that both early (0–1 years) and later (1–2 years) periods of weight or BMI gain are positively associated with lean mass in young adulthood, with later periods being more strongly associated.[258;259;264] However, one study found that weight gain from 0–3 months was positively associated with lean mass in adolescence, whereas weight gain from 3–12 months was not.[322] Two studies conducted in developing nations found that weight gain in early (0–12 months) and later infancy (12 months–2 years) were both positively associated with lean mass (of similar strength) in adolescence and young adulthood (although associations found in one study were largely attenuated in males after adjustment for adult height).[261]

#### 4.1.1.7 *Childhood growth (2–11 years) and direct measures of lean mass*

Seven studies reported positive associations between greater weight or BMI gain in childhood and lean mass in adolescence (using DXA[323] or SFT[261]), young adulthood (using DXA,[319] BIA[258] or SFT[261]), or mid-later adulthood (using SFT[264] or BIA[197]).

#### 4.1.1.8 *Adolescent growth (12–17 years) and direct measures of lean mass*

Two studies examined associations between adolescent growth and subsequent lean mass: both reported positive associations between BMI gain in adolescence and lean mass in young adulthood (measured using SFT[264] or DXA[319]).

#### 4.1.1.9 *Literature summary: growth and lean mass*

Studies have tended to find that periods of weight and BMI gain in infancy, childhood, and adolescence are positively associated with lean mass in adulthood. As with studies using fat mass as an outcome, comparison between different periods of growth is problematic due to differences between the studies. Of the studies with repeat measures of weight or BMI gain in infancy and childhood, some suggested that periods in later childhood[258;264] are more strongly positively associated with lean mass than earlier periods, while other studies found inconsistent patterns of strength of association[197;261;319] or no substantial difference

across periods.[323] As with studies examining fat mass as an outcome, only one study used a sample in later adulthood and reported positive associations between BMI gain in infancy and childhood and subsequent lean mass.[197] The use of BIA in this study meant that lean mass comprised bone, organ, and skeletal muscle mass.

Only two studies have used measures of growth across infancy, childhood and adolescence, and both found that BMI gain in all periods was positively associated with subsequent lean mass, with no clear pattern in the strength of associations.[264;319] The limitations of these studies were outlined previously in section 4.1.1.5.

The finding of consistent positive associations between weight or BMI gain and lean mass is consistent with evidence from cross-sectional studies suggesting that gains in lean mass occur consistently from infancy into adolescence. However, no studies have examined associations with weight or BMI gain in later adolescence (eg, 15-18 years); positive associations between weight or BMI gain in this period and lean mass may be stronger in males, as evidence suggests that the accrual of lean mass is greater in these periods in males.

#### 4.1.1.10 *Literature discussion: growth and body composition*

Of the studies examining associations between periods of growth after birth and subsequent body composition, most have assessed growth as conditional change in weight or BMI, while only one study (by Menezes et al, 2011[324]) used change in height. This study attempted to distinguish the associations of height and weight gain in infancy on subsequent fat mass in adolescence by using models mutually adjusted for both weight and height gain. Before adjustment, both height and weight gain were positively associated with fat mass; after mutual adjustment, weight gain was positively, and height gain negatively associated. Although the mechanisms underlying the associations were not discussed, associations with height gain were interpreted as suggesting that greater height gain (without excessive weight gain) was beneficial in leading to lower subsequent fat mass. However, this study used inaccurate and imprecise measures of fat mass, did not include lean mass as an outcome, or analyse periods of growth beyond infancy. Positive associations in unadjusted analyses between height gain and subsequent fat and lean mass may be expected, if gains in height gain track across life and leads to greater adult height and greater body size, since taller individuals tend to have more fat and lean mass (Chapter 2).

Aside from conducting mutually adjusted models to distinguish the influence of weight and height gain, assessing growth in terms of BMI change may show the influence of weight gain independent of height gain. BMI is designed to be a measure of height-adjusted weight, such that division of weight (kg) by height $(m)^2$ removes the association between weight and height. However, BMI may still be correlated with height, and this correlation is likely to differ at different ages and in different cohorts.[325] BMI may therefore potentially be an inappropriate measure of height-adjusted weight if its association with height is strong, or differs substantially in the different periods of growth investigated. However, of the studies that have assessed growth as change in BMI, few have explicitly outlined associations between BMI and height, while one used ponderal index $(m/kg^3)$ in infancy and BMI in childhood.[321]

While some studies have measured body composition using DXA,[203;311;319;321;322] other studies have used techniques such as air-displacement plethysmography,[323] or those considered inaccurate and imprecise such as BIA[197;204;258] or SFT.[259;264;324] In addition, no studies used appendicular lean mass as an outcome, a more accurate indicator of skeletal muscle mass, and few have used objective measures of fat distribution.

The published studies examining associations between periods of growth and body composition have made statistical adjustment for a number of variables in their analyses, some of which can be considered potential confounders. These differ across studies and have included contemporaneous height, indicators of SEP in childhood or adulthood, pubertal timing, maternal factors (including smoking status, height and BMI, and age), parity, and behavioural factors such as smoking status and physical activity. Although justification for the inclusion of these covariates in analyses has seldom been given, SEP in childhood may be a confounder since it may (indirectly) be causally related to subsequent growth in pre-adult life[326;327] and adult body composition. Contemporaneous height could be a potential mediator, as it may be on the causal pathway between greater weight or height gain and higher adult fat and lean mass.

#### 4.1.1.11 *Prior findings from the MRC National Survey of Health and Development*

Braddon et al (1986)[328] investigated the predictive potential of childhood obesity (at 7 years) in relation to obesity at 36 years. The predictive power was concluded to be poor, with only 21% of obese 36 year-olds obese at 11 years. This work was

updated using subsequent follow-ups, where the mean BMI of the cohort increased. Hardy et al (2000)[168] found that higher relative weight at age 14 years was associated with higher mean BMI across adulthood (20, 26, 36, and 43 years). These associations were independent of educational achievement and adult occupational class. Kuh et al (2002)[288] examined associations between childhood (age 7) weight on anthropometric measures of fat mass at age 43. Weight at age 7 was positively associated with waist-to-hip ratio and waist circumference (in both sexes); after adjustment for BMI at 43 years, these associations became negative.

As in Chapter 3, while the NSHD has no previous measures of lean mass, studies using grip strength and physical functioning outcomes are described below in order to give an indication of the types of analyses that have been conducted using measures of growth.

Kuh et al (2006) examined associations between periods of growth (in weight and height) and grip strength at 53 years. Height at 2 years was positively associated with grip strength in both sexes, as was height gain between 2-7 and 15–53 years. There was evidence for sex interaction at 7–15 years: greater weight (males only) or height gain (females only) from 7–15 years was positively associated with grip strength. Weight gain between 0–7 was weakly positively associated with grip strength in both sexes, while weight gain from 15–53 years was weakly positively associated with grip strength in males, but negatively associated in females. These findings were independent of paternal occupational class, pubertal timing, and physical activity and health status in adulthood. Similar analyses were conducted in relation to standing balance time and chair rise time. Weight gain from 0-7 years was positively associated with standing balance time and chair rise time in males only (with no association in females), and negative associations from 7-15 and 15-26 years in both sexes (but stronger in females).[290] Height gain from 2-4 years was negatively associated with standing balance in males, but positively associated in females, with no associations in later periods. Height at 2 years and height gain from 2-7 years were negatively associated with chair rise time in both sexes. These associations were independent of indicators of SEP in childhood and adulthood.

Another NSHD study, by Silverwood et al (2009),[329] is described here since it may have implications for the generalisability of findings from this chapter. Silverwood et al compared BMI from 4–15 years in the NSHD with two younger reference populations (based on cross-sectional measures taken in the UK in ~1990 and in the USA ~2000). In both sexes, median BMI z-scores were higher in the NSHD in early childhood (4, 6 and 7 years) than both reference populations. At 11 and 15

years, male z-scores were similar (UK 1990 sample) or slightly lower (USA 2000 sample) than reference populations, while in females z-scores were lower at 11 years, then higher at 15 years compared with both populations. However, BMI is driven by both weight and height, and these two components may differ in the NSHD compared with younger cohorts; further analyses eluded to in this study suggested that despite higher BMI, z-scores for weight in childhood were typically negative in the NSHD, with z-scores for height being more negative.

This chapter will build on previous studies in this cohort by, for the first time, examining associations between measures of weight and height gain after birth and subsequent direct measures of fat and lean mass.

#### 4.1.1.12 *Literature review summary*

In summary, a large number of studies have reported associations between greater weight or BMI gain in infancy and higher BMI in adulthood. Fewer studies have used direct measures of body composition; these have tended to find that greater weight and BMI gain in infancy, childhood and adolescence are associated with higher fat and lean mass in adolescence and adulthood. However, these studies have a number of limitations which necessitate the need for further research: most have used limited measures of growth (typically spanning only infancy and childhood) and have focused exclusively on weight or BMI gain—none have examined associations between height gain and body composition in adulthood; few studies have been conducted using cohorts in later adulthood; and most have used inaccurate and imprecise measures of body composition and have not considered appendicular lean mass or fat distribution.

### 4.1.2 *Chapter objectives and hypotheses*

The objectives of this chapter are to test the following hypotheses:

1. That all periods of weight gain from birth to 20 years are positively associated with subsequent fat and lean mass, due to the tracking of attained fat and lean mass that comprise weight gain or due to being associated with subsequent gains in fat and lean mass. It was further hypothesised that:
    a. As found in previous studies of both sexes, positive associations between weight gain and fat mass would be stronger in later

childhood and adolescence (7-20 years) than in early childhood and infancy (0-7 years).

b. In males but not females positive associations between weight gain and lean mass would be stronger in later adolescence (15-20 years) than in earlier periods, as evidence suggests lean mass accrual is greater in this period

2. That all periods of height gain from 2–20 years are positively associated with subsequent fat and lean mass, due to the tracking of increased height and body size (and the greater fat and lean mass incurred due to greater body size) or due to being associated with subsequent gains in fat and lean mass. As such, associations would be strongest in the periods which were most strongly positively associated with adult height.

## 4.2 **Methods**

### 4.2.1 ***Explanatory variables***

The main explanatory variables used in this chapter are periods of weight and height gain, derived from birth weight and measures of height and weight prospectively measured between 2 and 15 years by trained professionals, and self-reported at 20 years. The ages selected were chosen to maximise the number of discrete periods of weight and height gain in infancy, childhood, and adolescence. The following ages were selected: birth (weight only), 2, 4, 7, 11, 15, and 20 years; measures available at 6 years were not included, since it was hypothesised that measurement error would have a disproportionately greater effect on the observed change in weight or height between ages 6 and 7 years. Instead, age 7 was selected following a previous study demonstrating strong positive associations between BMI gain from 7–11 years and BMI in adulthood.[309]

Gains in weight (kg) and height (cm) were calculated by subtracting a later measure by the equivalent earlier measure (eg, weight at 11 minus weight at 7). To enable more equal comparison between periods of growth these were converted into velocities by dividing by the exact number of months between measures. These variables were then plotted to check for outliers and in 4 instances distributions were right-skewed (males: weight gain from 0–2 and 7–11 years; females: weight gain from 4–7 and 7–11 years); these were then log-transformed. All velocities were then converted into sex-specific standard deviation scores (where the mean value equals approximately 0 and standard deviation approximately 1). In summary, the following variables were created for use in this chapter:

- Weight gain velocity during infancy: 0-2 years
- Weight and height gain velocity during childhood: 2-4, 4-7, and 7-11 years
- Weight and height gain velocity during adolescence: 11-15, and 15–20 years

Change in BMI was not used as an explanatory variable in this chapter for the following reasons: it was strongly correlated with height at different periods; the strength and sign of the correlation was highly variable: strongly negatively correlated in infancy, positively at 11 years, and negatively correlated at 20 years (Appendix 8); and mean BMI both increased and decreased across these periods (Appendix 9), leading to potential complications in the interpretation of resulting coefficients. Pubertal timing was not used as a main explanatory variable in this chapter since it was hypothesised as being partly the result of weight and height gain in infancy and childhood. Associations between pubertal timing and body composition outcomes in the NSHD have been previously published for males (using voice-breaking status),[330] are presented for reference purposes for both sexes in Appendix 10.

### 4.2.2 ***Outcomes***

The outcomes used in this chapter are the main outcomes of this thesis, described in more detail in Chapter 2: whole body fat and lean mass, the ratio of these masses, appendicular lean mass and android: gynoid fat mass ratio.

### 4.2.3 ***Potential confounding and mediating variables***

Potential confounders and mediators were chosen a-priori on the basis of previous research or, where research was lacking, on hypothesised relationships between variables. Paternal occupational class at 4 years (or 11 (n=24) or 15 years (n=13) if missing at 4 years) was used as an indicator of early life SEP and considered a potential confounding factor since it was hypothesised that socioeconomic circumstances may influence patterns of weight and height gain; these circumstances tend to track into adulthood, and low SEP was hypothesised as being associated with higher fat and lower lean mass (Chapter 6 will examine these associations). Adult height at the time of body composition measurement was considered as a potential mediator, since it was hypothesised that greater weight and height gain would lead to greater adult height, with taller individuals tending to have more fat and lean mass (Chapter 2).

### 4.2.4 ***Analytical strategy***

The mean weight (kg/year) and height (cm/year) gain velocities in each period examined were plotted by sex. Associations between periods of growth and potential confounders/mediators were then examined using linear regression.

Linear regression models were used to analyse associations of weight and height (converted to sex-specific standard deviation scores) at 2–20 years with body composition outcomes. Since weight and height at each age were positively correlated (Appendix 8), they were both entered into the same regression model to attempt to elucidate their independent associations with outcomes. These models provide a crude indication of the periods of growth likely to be associated with outcomes—for example, positive associations between weight at 2 years and lean mass suggests that weight gain in infancy is positively associated with lean mass, but this association may be solely explained by the positive association between weight at birth and lean mass. Further models, described below, were therefore constructed to examine associations with discrete periods of weight and height gain.

To examine associations of weight and height gain with body composition outcomes, weight and height gain velocity were included in models alongside weight and height at the beginning of each period (as sex-specific standard deviation scores). For example, to examine associations between weight gain from 7-11 years and subsequent fat mass, weight gain velocity between 7-11 years was included, with adjustment for weight and height at 7 years, and height gain velocity between 7-11 years. Since height was not available at birth, models examining associations with weight gain from 0-2 years were only adjusted for weight at birth and height at 2 years. Periods of weight and height gain in the same period were adjusted for each other as they were all positively correlated (Appendix 11), and such models enable the independent associations of both weight and height gain on outcomes to be examined. Weight and height at the beginning of each period was also adjusted for to take into account preceding weight and height gain. These models can therefore be interpreted as showing, with respect to a period of weight gain, the mean difference in outcome per standard deviation increase in weight gain velocity, for a given weight and height at the beginning of the period investigated, and concurrent height gain velocity. Interpretations of results for height gain velocity are equivalent.

The above models were conducted separately in males and females given hypothesised sex differences in association, and tests of interaction were conducted to formally test for evidence of sex interaction. Non-linearity was assessed in all models by the inclusion of a quadratic term, and outlined where evidence was found.

The coefficients (and 95% confidence intervals) of the above models were then plotted by outcome to enable informal comparison of the strength of associations across periods. To examine whether associations were confounded by SEP, the above models were repeated with additional adjustment for paternal occupational class (as a categorical term). To examine whether associations were mediated by adult height, these models were repeated with additional adjustment for adult height (included as a continuous term). Adjustment for adult height by inclusion as a covariate in analyses was preferred to using height adjusted indices to enable coefficients from unadjusted and adjusted models to be compared on the same scale.

### 4.2.5 *Sample used in analyses*

Unless otherwise specified all analyses were restricted to those with valid body composition outcome data. Analyses were restricted to those with valid data for at least one period of growth and paternal occupational class. As such, the available sample in each period differed slightly: (male/female N): 0–2 (574/603); 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549). In each period, small numbers of participants with valid growth and outcome data were excluded due to missing data for paternal occupational class (male/female N): 0–2 (18/22); 2–4 (7/10); 4–7 (7/8); 7–11 (7/8); 11–15 (7/6); 15–20 (7/6).

## 4.3 **Results**

### 4.3.1 *Descriptive statistics*

Figure 3 shows the mean weight and height gain velocities in each period examined in this chapter. In summary, both males and females gained height and weight across the periods analysed; weight gain velocity was highest in infancy and early adolescence (11-15 years); height gain velocity was highest in early childhood (2-4 years) and declined thereafter. Velocities in weight and height were similar in males and females, although females tended to gain less weight and height from 15-20 years. Appendix 11 shows the mean weight (birth to 20 years) and height (2-20

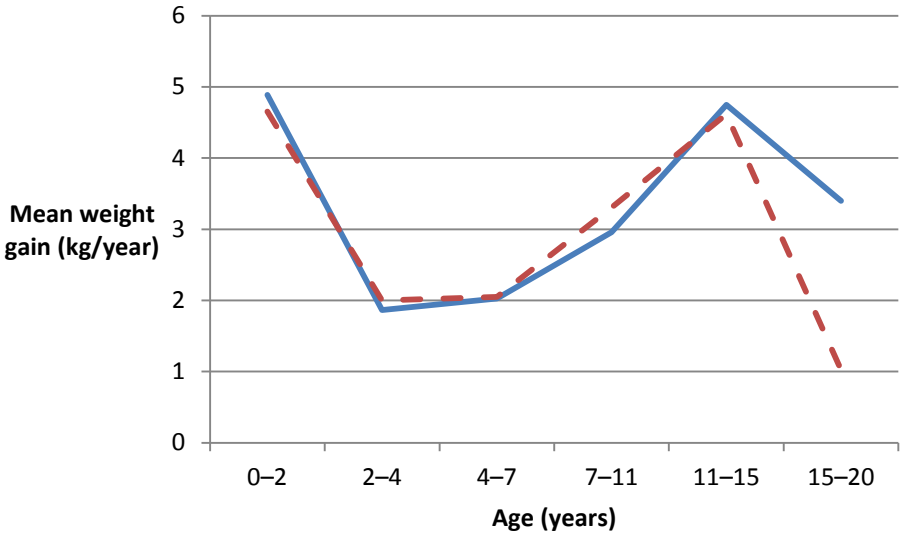
years) in tabular form. The variation in weight increased with age in both sexes; similar, but less pronounced patterns of increased variance with age were observed for height.

### 4.3.2 *Investigation of potential confounders and mediators*

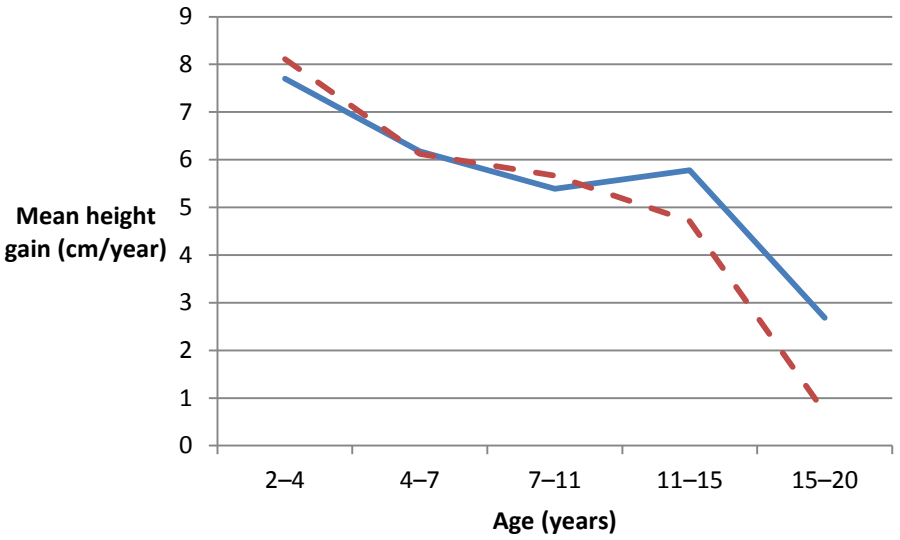
Participants with fathers of lower occupational class tended to gain less weight in infancy, but gain more weight from 7–20 years, and gain less height in most periods (2–20 years; Appendix 12). Weight gain from 0–4 years (both sexes) and 15-20 years (females only) were positively associated with adult height, while weight gain from 7–15 years was negatively associated with adult height in both sexes (Appendix 13). Height gain from 2–20 years was positively associated with adult height in both sexes (Appendix 13).

Figure 3. Mean a) weight and b) height gain per year in infancy to adolescence

a)




b)



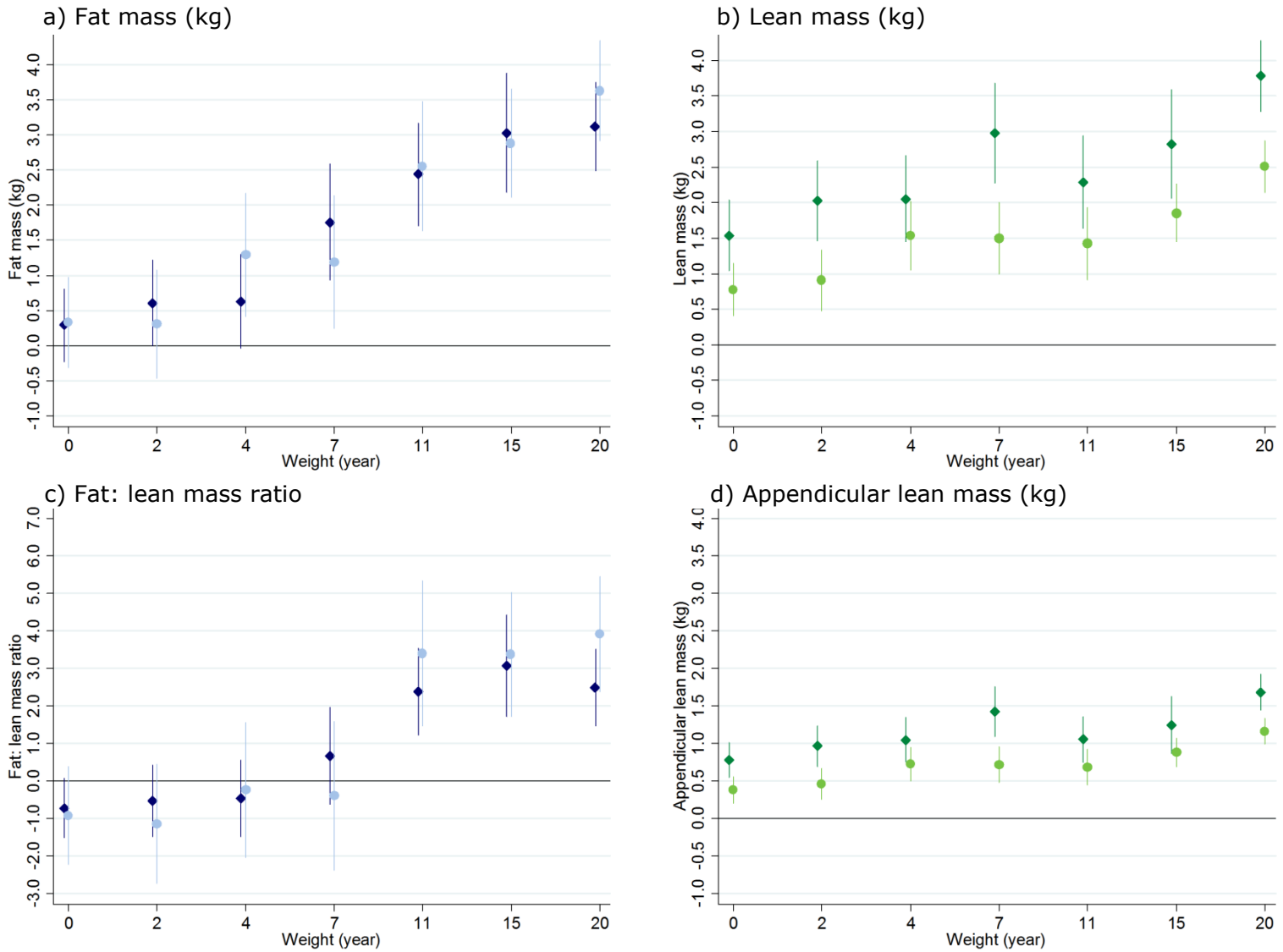

Note: males=connected line; females=dashed line; sample sizes in the different periods were (male/female): 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549); depicted are those with valid data for weight and height at each age and body composition outcomes

### 4.3.3 *Weight and height from 2–20 years and body composition outcomes*

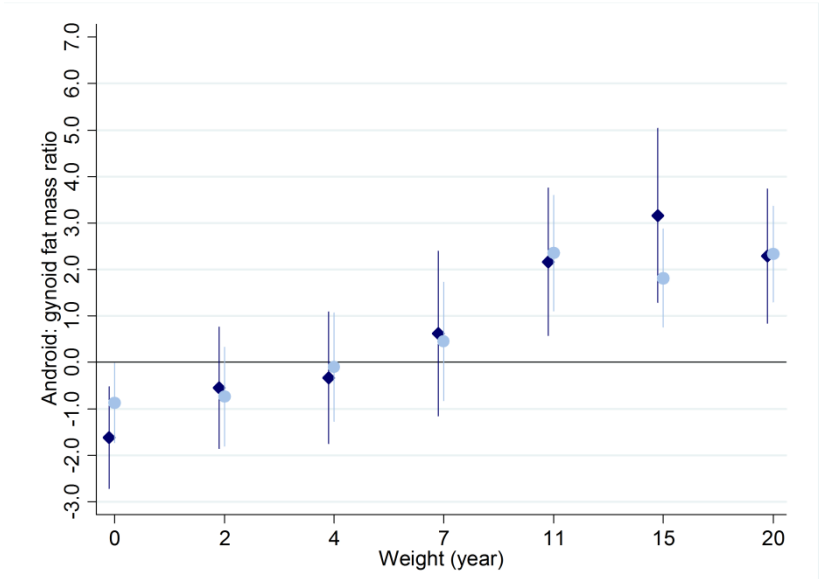
Figure 4 a-e shows associations between weight at each age (2, 4, 7, 11, 15 and 20 years) and body composition outcomes. Birth weight is also included for reference purposes. Weight at ages between 4 and 20 years was positively associated with fat mass (Figure 4 a) and weight from birth to 20 years was positively associated with whole body and appendicular lean mass (Figure 4 b and d). Greater weight from 7-20 years was associated with higher fat: lean (Figure 4 c) and android: gynoid (Figure 4 e) ratios.

Figure 5 a-e shows associations between height from 2 to 20 years and body composition outcomes. Heights at each age were generally not associated with fat mass (Figure 5 a), except for a negative associations in men at 15 years. Height was positively associated in all periods with whole body (Figure 5 b) and appendicular (Figure 5 d) lean mass (except at 15 years in males). Greater height from 11-20 years was associated with a lower fat: lean mass ratio (Figure 5 c), and a lower android: gynoid ratio (Figure 5 e) from 2-20 years in males and from 11-20 years in females.

Figure 4. Mean differences in fat and lean mass (with 95% confidence intervals) per 1 standard deviation increase in weight (standard deviation score), adjusted for height at the same age

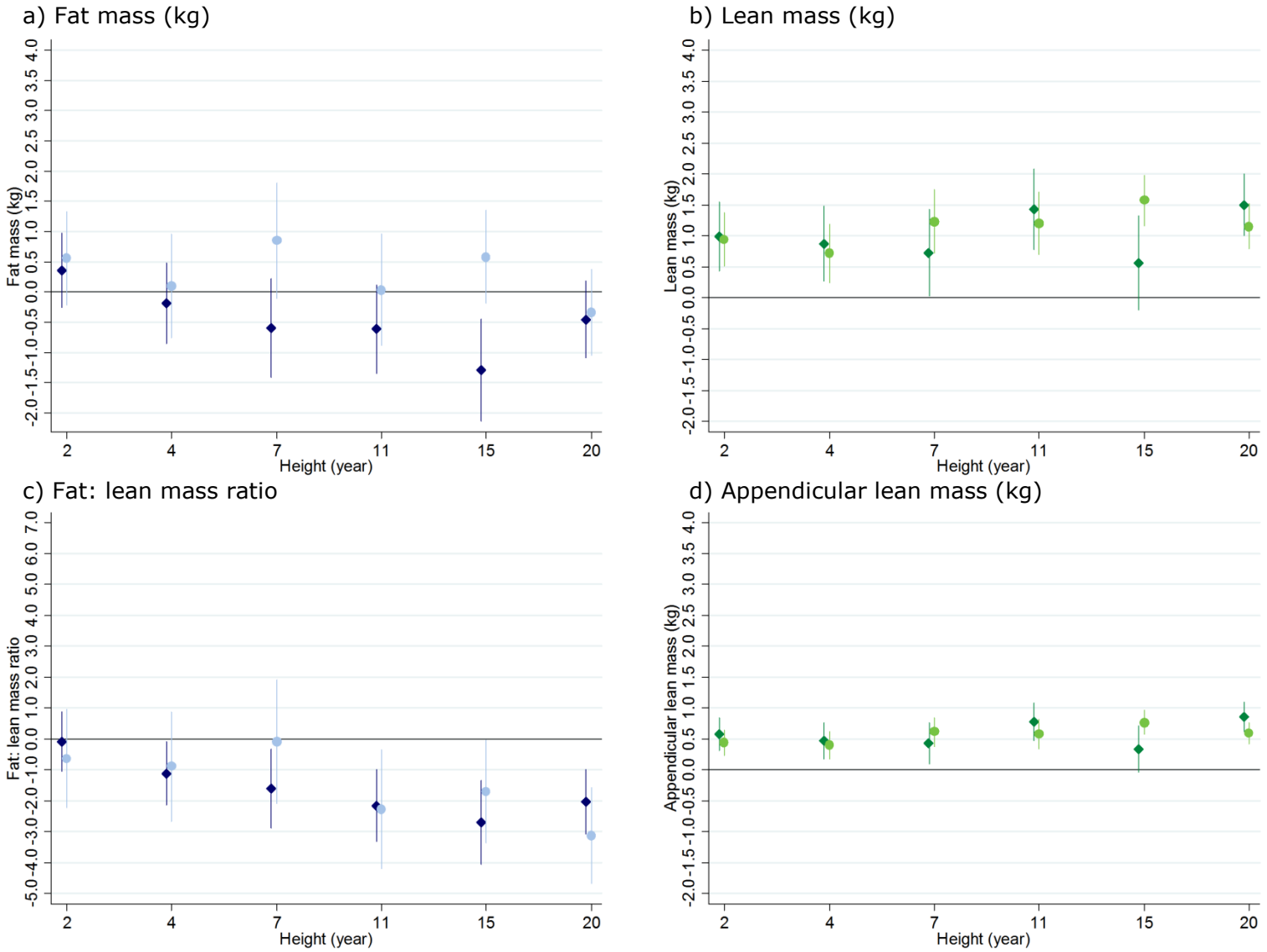


e) Android: gynoid fat mass ratio

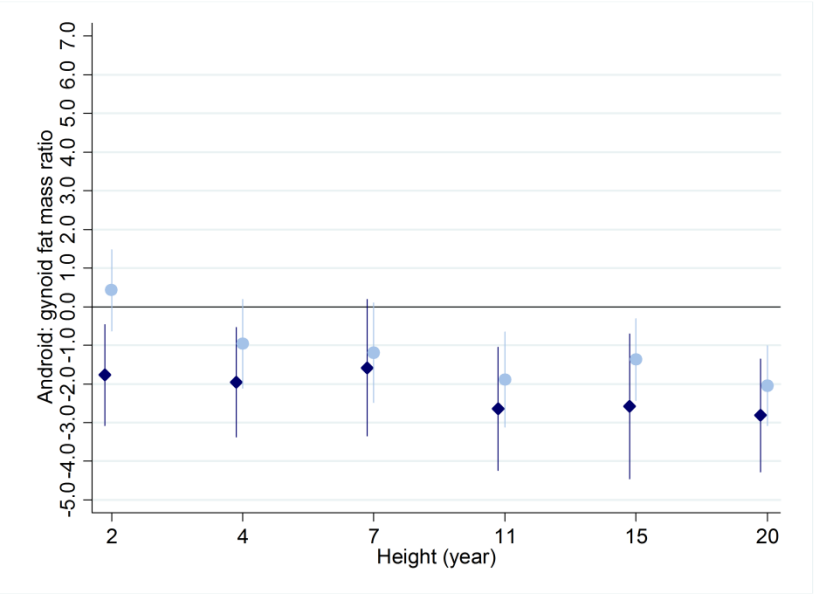



Note: males=dark-coloured diamonds; females=light-coloured circles; sample sizes in the different periods were (male/female): 0 (745/808); 2 (593/627), 4 (653/700), 7 (624/679), 11(628/679), 15 (582/623), 20 (601/682); associations with birth weight were not adjusted for any measure of height

Figure 5. Mean differences in fat and lean mass (with 95% confidence intervals) per 1 standard deviation increase in height (standard deviation score), adjusted for weight at the same age



e) Android: gynoid fat mass ratio




Note: males=dark-coloured diamonds; females=light-coloured circles. Sample sizes in the different periods were (male/female): 2 (593/627), 4 (653/700), 7 (624/679), 11(628/679), 15 (582/623), 20 (601/682)

### 4.3.4 *Pre-adulthood weight gain and body composition outcomes*

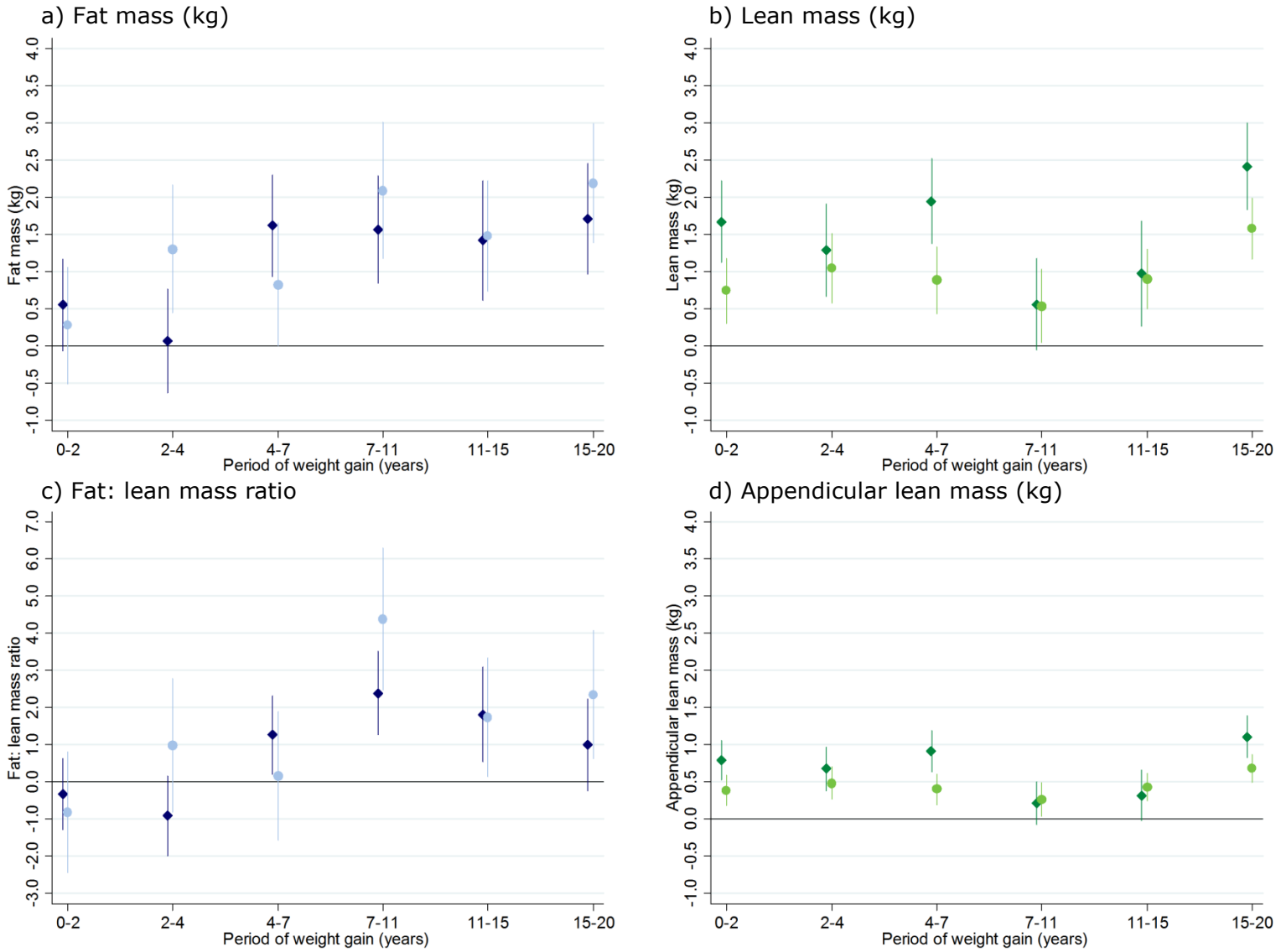
Figure 6 a-e shows the results from a series of linear regression models examining associations between weight gain velocities and body composition outcomes, adjusted for weight and height at the beginning of each period and concurrent height gain; these results are presented in tabular form in Table 13 a, and P-values for sex interaction terms are shown in Appendix 14.

Weight gain from 4-20 years in males and 2-20 years in females was positively associated with fat mass (Figure 6 a). All periods of weight gain from birth to 20 years were positively associated with whole body and appendicular lean mass (Figure 6 b and d)—these associations were stronger in males at 0–2, 4–7, and 15–20 years, and weaker in both sexes at 7-11 years. Greater weight gain from 7-20 years was associated with higher fat: lean mass ratio (Figure 6 c), with stronger positive associations from 7–11 years in females. Greater weight gain was associated with higher android: gynoid ratio from 4–15 years in males, and 7-11 and 15-20 years in females (Figure 6 e). However, there was little evidence for differences by sex with android: gynoid ratio when formally tested (P(sex interaction) >0.1 in all cases).

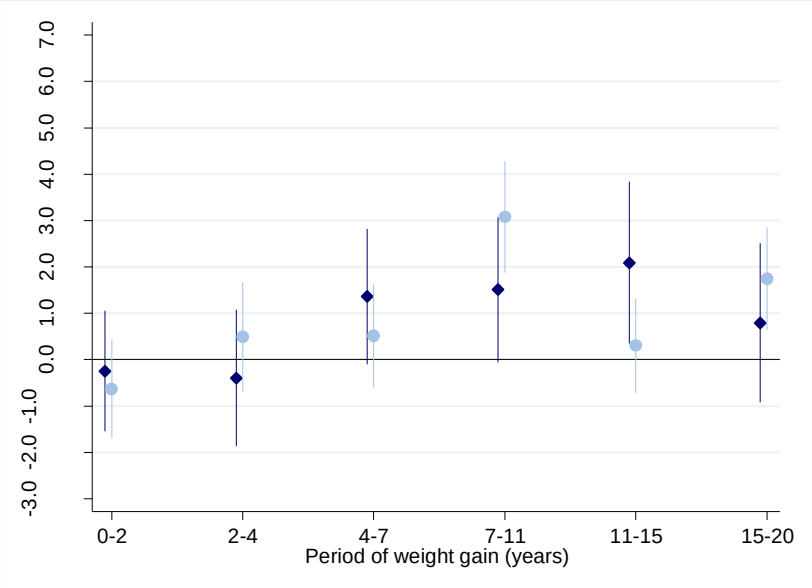
There was evidence for departure from linearity in the positive associations of weight gain from 2–4 years (females only) and 4–7 years (males only) with both whole body and appendicular lean mass (P(quadratic term) <0.05 in all cases; quadratic coefficients were negative in all cases). Further graphical analyses suggested that non-linear effects were small, and reflected a levelling off of the positive association between weight gain and lean mass among those who gained the most weight. In all other associations, there was little evidence for departure from linearity (P-values for quadratic terms >0.1 in all cases).

Overall patterns of associations between weight gain and body composition outcomes were similar when adjustment was made for paternal occupational class and then adult height—in some instances estimates were attenuated, while in other instances they were strengthened (Table 13 b and c). Associations of weight gain in infancy with fat and lean mass were partly attenuated in males and largely attenuated in females after adjustment for adult height, while positive associations between weight gain from 7–15 years in males and 7–11 years in females were strengthened after this adjustment. Further analyses showed similar patterns of association when height-adjusted indices were used as outcomes (data not shown).

Figure 6. Mean differences in fat and lean mass (with 95% confidence intervals) per 1 standard deviation increase in weight gain velocity, adjusted for weight and height at the beginning of each period and concurrent height gain



e) Android: gynoid fat mass ratio




Note: males=dark-coloured diamonds; females=light-coloured circles; sample sizes in the different periods were (male/female): 0–2 (574/603); 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549); weight gain from 0-2 years was adjusted for birth weight and height at 2 years only; analyses were restricted those with valid data for height and weight at each age, paternal occupational class, and body composition outcomes

Table 13. Mean differences in fat and lean mass (95% confidence intervals, P-value) per 1 standard deviation increase in weight gain velocity: a) adjusted for weight and height at the beginning of each period and height gain velocity in the same period, b) identical to model a with additional adjustment for paternal occupational class; c) identical to model b with additional adjustment for adult height

| Period (years) | Males | | | Females | | |
|---|---|---|---|---|---|---|
| | a) | b) | c) | a) | b) | c) |
| Fat mass (kg) | | | | | | |
| 0-2 | 0.56(-0.06, 1.17), 0.08 | 0.68(0.06, 1.30), 0.03 | 0.49(-0.15, 1.12), 0.13 | 0.28(-0.50, 1.06), 0.49 | 0.41(-0.37, 1.20), 0.31 | 0.10(-0.70, 0.90), 0.81 |
| 2–4 | 0.07(-0.63, 0.77), 0.84 | 0.13(-0.57, 0.83), 0.71 | -0.03(-0.73, 0.67), 0.94 | 1.30(0.44, 2.16), <0.01 | 1.20(0.34, 2.06), 0.01 | 1.13(0.27, 1.99), 0.01 |
| 4–7 | 1.62(0.94, 2.30), <0.01 | 1.63(0.95, 2.31), <0.01 | 1.66(0.99, 2.34), <0.01 | 0.83(0.00, 1.66), 0.05 | 0.77(-0.04, 1.59), 0.06 | 0.86(0.05, 1.68), 0.04 |
| 7–11 | 1.57(0.85, 2.29), <0.01 | 1.53(0.81, 2.25), <0.01 | 1.72(0.99, 2.44), <0.01 | 2.09(1.18, 3.01), <0.01 | 1.97(1.07, 2.88), <0.01 | 2.52(1.56, 3.48), <0.01 |
| 11–15 | 1.42(0.62, 2.22), <0.01 | 1.44(0.63, 2.25), <0.01 | 1.87(1.03, 2.70), <0.01 | 1.47(0.73, 2.22), <0.01 | 1.37(0.63, 2.11), <0.01 | 1.40(0.65, 2.14), <0.01 |
| 15-20 | 1.71(0.96, 2.46), <0.01 | 1.63(0.87, 2.38), <0.01 | 1.62(0.87, 2.38), <0.01 | 2.19(1.39, 2.98), <0.01 | 1.99(1.18, 2.79), <0.01 | 2.02(1.22, 2.83), <0.01 |
| Lean mass (kg) | | | | | | |
| 0-2 | 1.67(1.12, 2.22), <0.01 | 1.72(1.16, 2.27), <0.01 | 1.07(0.54, 1.59), <0.01 | 0.74(0.31, 1.18), <0.01 | 0.74(0.30, 1.18), <0.01 | 0.24(-0.18, 0.66), 0.26 |
| 2–4 | 1.29(0.67, 1.91), <0.01 | 1.34(0.71, 1.96), <0.01 | 0.96(0.38, 1.54), <0.01 | 1.05(0.58, 1.52), <0.01 | 0.96(0.48, 1.43), <0.01 | 0.83(0.38, 1.27), <0.01 |
| 4–7 | 1.95(1.37, 2.52), <0.01 | 1.96(1.39, 2.54), <0.01 | 2.02(1.48, 2.56), <0.01 | 0.88(0.44, 1.33), <0.01 | 0.87(0.43, 1.32), <0.01 | 1.04(0.61, 1.47), <0.01 |
| 7–11 | 0.56(-0.05, 1.18), 0.07 | 0.55(-0.06, 1.17), 0.08 | 0.95(0.36, 1.54), <0.01 | 0.54(0.05, 1.03), 0.03 | 0.52(0.02, 1.01), 0.04 | 1.26(0.76, 1.76), <0.01 |
| 11–15 | 0.97(0.27, 1.68), 0.01 | 0.87(0.16, 1.58), 0.02 | 1.89(1.21, 2.57), <0.01 | 0.90(0.50, 1.30), <0.01 | 0.86(0.46, 1.26), <0.01 | 0.98(0.59, 1.37), <0.01 |
| 15-20 | 2.42(1.83, 3.00), <0.01 | 2.37(1.77, 2.96), <0.01 | 2.29(1.70, 2.87), <0.01 | 1.58(1.17, 1.99), <0.01 | 1.29(0.88, 1.70), <0.01 | 1.20(0.79, 1.61), <0.01 |
| Appendicular lean mass (kg) | | | | | | |
| 0-2 | 0.79(0.52, 1.05), <0.01 | 0.79(0.53, 1.06), <0.01 | 0.48(0.23, 0.73), <0.01 | 0.38(0.17, 0.59), <0.01 | 0.38(0.17, 0.58), <0.01 | 0.14(-0.05, 0.34), 0.15 |
| 2–4 | 0.68(0.38, 0.97), <0.01 | 0.69(0.39, 0.98), <0.01 | 0.51(0.23, 0.78), <0.01 | 0.48(0.27, 0.70), <0.01 | 0.45(0.23, 0.67), <0.01 | 0.39(0.18, 0.61), <0.01 |
| 4–7 | 0.91(0.64, 1.19), <0.01 | 0.92(0.65, 1.20), <0.01 | 0.95(0.69, 1.21), <0.01 | 0.40(0.19, 0.61), <0.01 | 0.40(0.19, 0.60), <0.01 | 0.47(0.27, 0.67), <0.01 |
| 7–11 | 0.22(-0.07, 0.50), 0.15 | 0.21(-0.08, 0.50), 0.16 | 0.41(0.13, 0.68), <0.01 | 0.26(0.03, 0.49), 0.03 | 0.26(0.02, 0.49), 0.03 | 0.60(0.37, 0.84), <0.01 |
| 11–15 | 0.32(-0.02, 0.66), 0.07 | 0.26(-0.08, 0.60), 0.14 | 0.77(0.45, 1.09), <0.01 | 0.43(0.24, 0.61), <0.01 | 0.42(0.23, 0.61), <0.01 | 0.47(0.29, 0.65), <0.01 |
| 15-20 | 1.11(0.82, 1.39), <0.01 | 1.09(0.81, 1.38), <0.01 | 1.05(0.77, 1.33), <0.01 | 0.68(0.49, 0.87), <0.01 | 0.56(0.37, 0.76), <0.01 | 0.53(0.34, 0.72), <0.01 |

| Period (years) | Males | | | Females | | |
|---|---|---|---|---|---|---|
| | a) | b) | c) | a) | b) | c) |
| Fat: lean ratio | | | | | | |
| 0-2 | -0.33(-1.29, 0.63), 0.50 | -0.14(-1.10, 0.83), 0.78 | 0.05(-0.94, 1.03), 0.92 | -0.81(-2.43, 0.81), 0.33 | -0.46(-2.07, 1.16), 0.58 | -0.29(-1.95, 1.37), 0.73 |
| 2–4 | -0.92(-1.99, 0.16), 0.10 | -0.83(-1.91, 0.25), 0.13 | -0.81(-1.90, 0.28), 0.15 | 0.98(-0.82, 2.78), 0.29 | 0.90(-0.90, 2.70), 0.33 | 0.98(-0.83, 2.78), 0.29 |
| 4–7 | 1.26(0.20, 2.32), 0.02 | 1.28(0.22, 2.34), 0.02 | 1.28(0.22, 2.35), 0.02 | 0.16(-1.58, 1.90), 0.86 | 0.05(-1.66, 1.76), 0.95 | -0.04(-1.76, 1.69), 0.97 |
| 7–11 | 2.39(1.27, 3.51), <0.01 | 2.32(1.20, 3.45), <0.01 | 2.32(1.18, 3.46), <0.01 | 4.38(2.46, 6.29), <0.01 | 4.11(2.22, 6.00), <0.01 | 4.08(2.05, 6.11), <0.01 |
| 11–15 | 1.82(0.53, 3.10), 0.01 | 1.95(0.65, 3.24), <0.01 | 1.85(0.50, 3.20), 0.01 | 1.74(0.14, 3.33), 0.03 | 1.54(-0.05, 3.12), 0.06 | 1.38(-0.20, 2.97), 0.09 |
| 15-20 | 1.00(-0.24, 2.24), 0.12 | 0.88(-0.37, 2.12), 0.17 | 0.94(-0.31, 2.19), 0.14 | 2.35(0.63, 4.07), 0.01 | 2.35(0.63, 4.08), 0.01 | 2.58(0.85, 4.31), <0.01 |
| Android: gynoid ratio | | | | | | |
| 0-2 | -0.25(-1.54, 1.05), 0.71 | 0.12(-1.18, 1.41), 0.86 | 0.36(-0.96, 1.69), 0.59 | -0.63(-1.69, 0.43), 0.25 | -0.39(-1.46, 0.67), 0.47 | -0.33(-1.43, 0.77), 0.56 |
| 2–4 | -0.39(-1.87, 1.08), 0.60 | -0.18(-1.65, 1.28), 0.81 | -0.08(-1.56, 1.40), 0.92 | 0.50(-0.68, 1.67), 0.41 | 0.55(-0.64, 1.73), 0.37 | 0.55(-0.64, 1.73), 0.37 |
| 4–7 | 1.36(-0.10, 2.82), 0.07 | 1.40(-0.05, 2.86), 0.06 | 1.37(-0.09, 2.82), 0.07 | 0.51(-0.60, 1.63), 0.37 | 0.44(-0.67, 1.55), 0.44 | 0.46(-0.65, 1.58), 0.42 |
| 7–11 | 1.51(-0.06, 3.08), 0.06 | 1.37(-0.20, 2.94), 0.09 | 1.06(-0.52, 2.64), 0.19 | 3.08(1.87, 4.28), <0.01 | 2.97(1.77, 4.18), <0.01 | 3.28(1.99, 4.56), <0.01 |
| 11–15 | 2.09(0.34, 3.84), 0.02 | 1.92(0.17, 3.68), 0.03 | 1.41(-0.42, 3.24), 0.13 | 0.30(-0.71, 1.32), 0.56 | 0.27(-0.74, 1.28), 0.60 | 0.35(-0.67, 1.37), 0.50 |
| 15-20 | 0.79(-0.92, 2.51), 0.37 | 0.46(-1.27, 2.18), 0.60 | 0.52(-1.20, 2.25), 0.55 | 1.74(0.64, 2.85), <0.01 | 1.59(0.48, 2.70), 0.01 | 1.50(0.38, 2.62), 0.01 |

Note: sample sizes in the different periods were (male/female): 0–2 (574/603); 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549); weight gain from 0-2 years was adjusted for birth weight and height at 2 years only; analyses were restricted those with valid data for height and weight at each age, paternal occupational class, and body composition outcomes

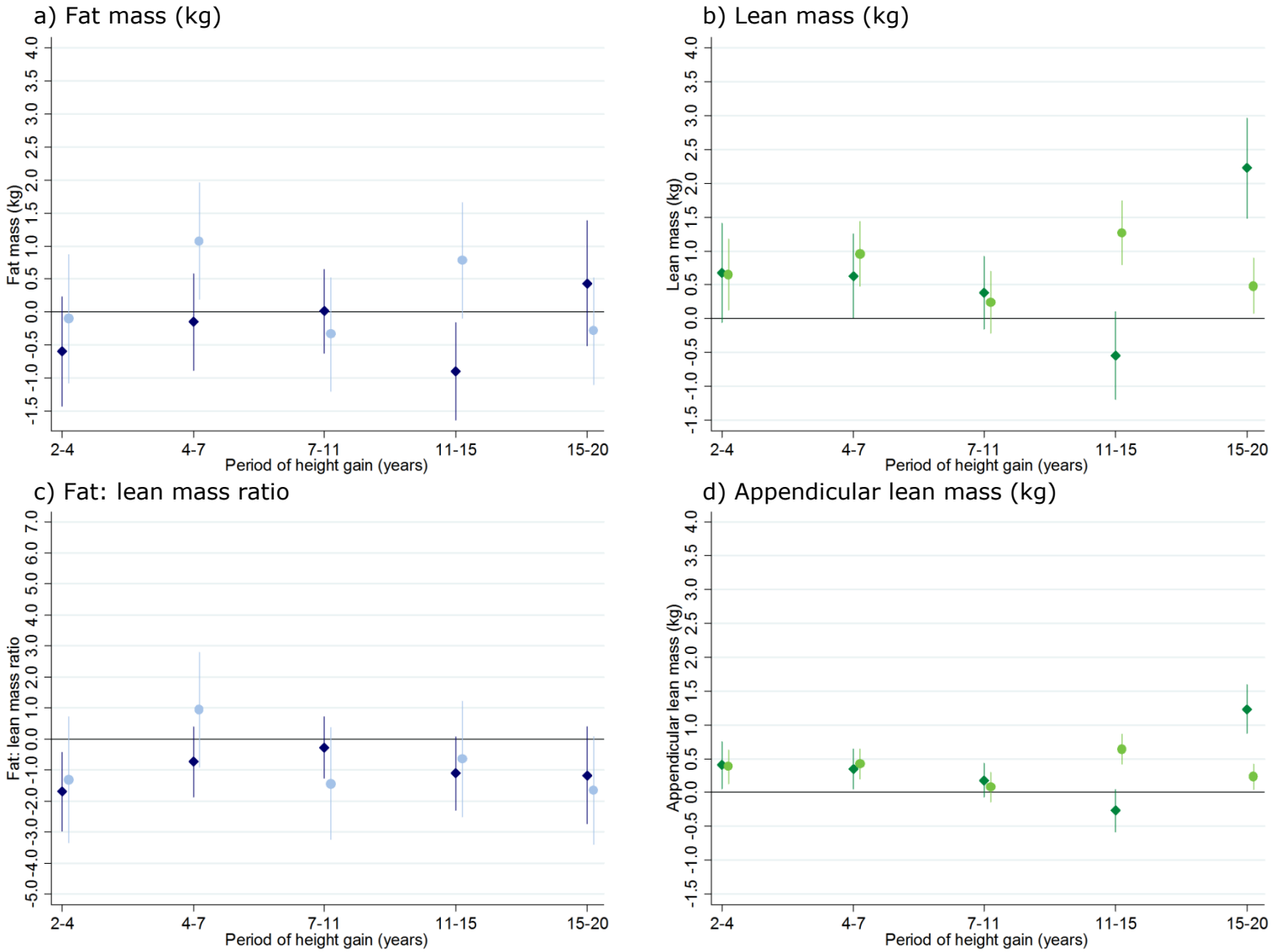
### 4.3.5 ***Pre-adulthood height gain and body composition outcomes***

Figure 7 a-e and Table 14 a show results from a series of linear regression models examining associations between height gain velocities and body composition outcomes, adjusted for height and weight at the beginning of each period and concurrent weight gain. Appendix 14 shows the P-values for sex interaction terms.

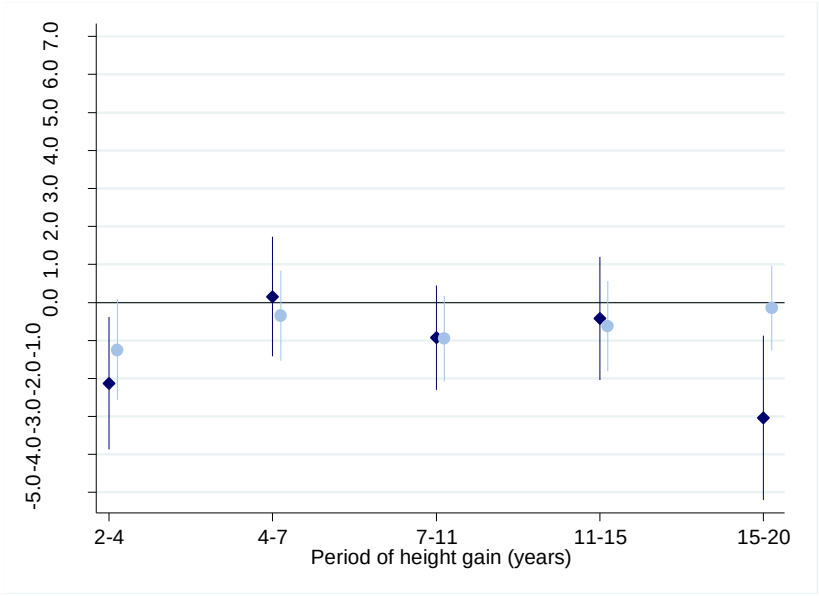
Across the periods investigated, height gain was generally not associated with fat mass, except for positive associations from 4-7 years and 11-15 years in females, and a negative association from 11-15 years in males (Figure 7 a). Height gain was more consistently associated with lean mass (Figure 7 b), with positive associations from 2-7 years (both sexes), and differing associations by sex thereafter: negative associations from 11-15 years in males, and positive association in females in this period, and positive associations in both sexes from 15-20 years (but stronger in males). Associations with appendicular lean mass were similar to those with whole body lean mass (Figure 7 d). Across the periods investigated, greater height gain was weakly associated with a lower fat: lean ratio across (Figure 7c). Greater height gain from 2–4 years (both sexes) and 15-20 years (males only) was associated with a lower android: gynoid ratio (Figure 7e).

There was little evidence for departure from linearity in the above associations (P-values for quadratic terms >0.1 in all cases). The same patterns of association were found when adjustment was made for paternal occupational class (Table 14 b). However, associations differed after adjustment for adult height (Table 14 c); all positive associations found between height gain and lean mass (whole body and appendicular) were largely attenuated. Associations were similarly attenuated when height-adjusted indices were used as outcomes (data not shown). Associations between height gain and lower fat: lean and android: gynoid ratios were typically largely attenuated after this adjustment, although associations between greater height gain and lower fat: lean mass ratio remained in males from 2–4 years.

Figure 7. Mean differences in fat and lean mass (with 95% confidence intervals) per 1 standard deviation increase in height gain velocity, adjusted for height and weight at the beginning of each period and concurrent weight gain



e) Android: gynoid fat mass ratio




Note: males=dark-coloured diamonds; females=light-coloured circles. Sample sizes in the different periods were (male/female): 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549); analyses were restricted those with valid data for height and weight at each age, paternal occupational class, and body composition outcomes

Table 14. Mean differences in fat and lean mass (95% confidence intervals, P-value) per 1 standard deviation increase in height gain velocity: a) adjusted for weight and height at the beginning of each period and concurrent weight gain; b) identical to model a with additional adjustment for paternal occupational class; c) identical to model b with additional adjustment for adult height

| Period (years) | Males a) | b) | c) | Females a) | b) | c) |
|---|---|---|---|---|---|---|
| Fat mass (kg) | | | | | | |
| 2–4 | -0.59(-1.42, 0.24), 0.16 | -0.51(-1.34, 0.32), 0.23 | -1.13(-2.03, -0.24), 0.01 | -0.10(-1.07, 0.87), 0.84 | 0.17(-0.81, 1.16), 0.73 | -0.35(-1.44, 0.74), 0.53 |
| 4–7 | -0.15(-0.88, 0.58), 0.69 | -0.08(-0.82, 0.65), 0.82 | -0.62(-1.40, 0.16), 0.12 | 1.08(0.19, 1.96), 0.02 | 1.27(0.40, 2.14), <0.01 | 0.86(-0.10, 1.82), 0.08 |
| 7–11 | 0.01(-0.62, 0.64), 0.97 | -0.01(-0.64, 0.62), 0.98 | -0.43(-1.11, 0.26), 0.22 | -0.34(-1.19, 0.52), 0.44 | -0.26(-1.11, 0.59), 0.54 | -0.67(-1.56, 0.21), 0.14 |
| 11–15 | -0.89(-1.64, -0.15), 0.02 | -0.99(-1.74, -0.24), 0.01 | -1.29(-2.05, -0.53), <0.01 | 0.78(-0.09, 1.65), 0.08 | 0.98(0.11, 1.85), 0.03 | 0.68(-0.51, 1.88), 0.26 |
| 15-20 | 0.43(-0.51, 1.38), 0.37 | 0.65(-0.31, 1.61), 0.19 | 0.46(-1.12, 2.04), 0.57 | -0.29(-1.09, 0.52), 0.48 | -0.13(-0.94, 0.67), 0.75 | 0.16(-0.92, 1.24), 0.77 |
| Lean mass (kg) | | | | | | |
| 2–4 | 0.68(-0.05, 1.41), 0.07 | 0.74(0.00, 1.48), 0.05 | -0.75(-1.49, -0.01), 0.05 | 0.65(0.12, 1.18), 0.02 | 0.81(0.27, 1.35), <0.01 | -0.19(-0.76, 0.38), 0.51 |
| 4–7 | 0.63(0.02, 1.25), 0.04 | 0.65(0.03, 1.27), 0.04 | -0.42(-1.04, 0.21), 0.19 | 0.96(0.49, 1.44), <0.01 | 1.00(0.52, 1.48), <0.01 | 0.23(-0.27, 0.74), 0.36 |
| 7–11 | 0.38(-0.15, 0.92), 0.16 | 0.39(-0.15, 0.93), 0.15 | -0.51(-1.06, 0.04), 0.07 | 0.24(-0.22, 0.70), 0.31 | 0.24(-0.22, 0.71), 0.31 | -0.30(-0.76, 0.17), 0.21 |
| 11–15 | -0.54(-1.19, 0.11), 0.10 | -0.49(-1.15, 0.17), 0.14 | -1.19(-1.81, -0.57), <0.01 | 1.27(0.80, 1.74), <0.01 | 1.33(0.86, 1.80), <0.01 | -0.05(-0.67, 0.58), 0.88 |
| 15-20 | 2.23(1.49, 2.96), <0.01 | 2.31(1.56, 3.07), <0.01 | 0.16(-1.06, 1.37), 0.80 | 0.49(0.08, 0.89), 0.02 | 0.50(0.09, 0.91), 0.02 | -0.20(-0.74, 0.34), 0.47 |
| Appendicular lean mass (kg) | | | | | | |
| 2–4 | 0.41(0.05, 0.76), 0.02 | 0.43(0.08, 0.78), 0.02 | -0.29(-0.64, 0.07), 0.12 | 0.38(0.13, 0.63), <0.01 | 0.44(0.19, 0.69), <0.01 | 0.01(-0.26, 0.28), 0.95 |
| 4–7 | 0.35(0.05, 0.64), 0.02 | 0.36(0.06, 0.65), 0.02 | -0.17(-0.47, 0.13), 0.28 | 0.42(0.20, 0.65), <0.01 | 0.43(0.21, 0.65), <0.01 | 0.09(-0.15, 0.32), 0.48 |
| 7–11 | 0.18(-0.07, 0.43), 0.16 | 0.19(-0.07, 0.44), 0.15 | -0.26(-0.52, 0.00), 0.05 | 0.08(-0.14, 0.30), 0.46 | 0.08(-0.14, 0.30), 0.47 | -0.16(-0.38, 0.05), 0.14 |
| 11–15 | -0.27(-0.58, 0.05), 0.10 | -0.23(-0.55, 0.09), 0.16 | -0.58(-0.87, -0.28), <0.01 | 0.64(0.42, 0.86), <0.01 | 0.66(0.44, 0.88), <0.01 | 0.06(-0.23, 0.36), 0.68 |
| 15-20 | 1.23(0.87, 1.59), <0.01 | 1.25(0.88, 1.61), <0.01 | 0.04(-0.55, 0.63), 0.89 | 0.24(0.05, 0.43), 0.02 | 0.23(0.04, 0.43), 0.02 | -0.05(-0.30, 0.21), 0.72 |

| Period (years) | Males a) | b) | c) | Females a) | b) | c) |
|---|---|---|---|---|---|---|
| Fat: lean ratio | | | | | | |
| 2–4 | -1.70(-2.97, -0.43), 0.01 | -1.60(-2.87, -0.32), 0.01 | -1.51(-2.90, -0.12), 0.03 | -1.32(-3.34, 0.71), 0.20 | -0.91(-2.97, 1.14), 0.38 | -0.36(-2.64, 1.92), 0.76 |
| 4–7 | -0.74(-1.88, 0.41), 0.21 | -0.63(-1.78, 0.51), 0.28 | -0.70(-1.94, 0.53), 0.27 | 0.95(-0.91, 2.80), 0.32 | 1.38(-0.45, 3.22), 0.14 | 1.79(-0.23, 3.81), 0.08 |
| 7–11 | -0.27(-1.26, 0.71), 0.59 | -0.32(-1.30, 0.67), 0.53 | -0.31(-1.38, 0.76), 0.57 | -1.44(-3.23, 0.35), 0.12 | -1.24(-3.02, 0.54), 0.17 | -1.27(-3.14, 0.60), 0.18 |
| 11–15 | -1.11(-2.30, 0.08), 0.07 | -1.34(-2.54, -0.14), 0.03 | -1.30(-2.53, -0.07), 0.04 | -0.64(-2.51, 1.23), 0.50 | -0.22(-2.09, 1.64), 0.81 | 1.58(-0.97, 4.12), 0.22 |
| 15-20 | -1.17(-2.73, 0.39), 0.14 | -0.85(-2.44, 0.74), 0.29 | 0.64(-1.97, 3.24), 0.63 | -1.67(-3.41, 0.07), 0.06 | -1.28(-3.01, 0.45), 0.15 | 0.51(-1.80, 2.83), 0.66 |
| Android: gynoid ratio | | | | | | |
| 2–4 | -2.12(-3.87, -0.38), 0.02 | -1.91(-3.65, -0.18), 0.03 | -1.54(-3.43, 0.35), 0.11 | -1.24(-2.57, 0.08), 0.07 | -1.17(-2.52, 0.18), 0.09 | -1.17(-2.67, 0.34), 0.13 |
| 4–7 | 0.15(-1.42, 1.73), 0.85 | 0.34(-1.24, 1.91), 0.68 | 0.92(-0.77, 2.62), 0.29 | -0.35(-1.54, 0.84), 0.57 | -0.13(-1.31, 1.06), 0.83 | -0.22(-1.53, 1.08), 0.74 |
| 7–11 | -0.93(-2.30, 0.44), 0.19 | -0.95(-2.33, 0.42), 0.17 | -0.24(-1.73, 1.24), 0.75 | -0.95(-2.08, 0.18), 0.10 | -0.85(-1.98, 0.28), 0.14 | -1.16(-2.34, 0.02), 0.06 |
| 11–15 | -0.42(-2.04, 1.20), 0.61 | -0.45(-2.08, 1.18), 0.59 | -0.11(-1.78, 1.56), 0.89 | -0.62(-1.81, 0.57), 0.31 | -0.52(-1.71, 0.67), 0.39 | -1.46(-3.10, 0.17), 0.08 |
| 15-20 | -3.04(-5.20, -0.87), 0.01 | -2.45(-4.65, -0.26), 0.03 | -0.83(-4.44, 2.77), 0.65 | -0.15(-1.26, 0.97), 0.80 | 0.07(-1.04, 1.19), 0.90 | -0.62(-2.12, 0.87), 0.41 |

Note: sample sizes in the different periods were (male/female): 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549); analyses were restricted those with valid data for height and weight at each age, paternal occupational class, and body composition outcomes

## 4.4 **Discussion**

### 4.4.1 ***Main findings***

The main findings of this chapter are positive associations between periods of pre-adulthood weight gain and fat and lean mass at 60–64 years. These associations began earlier for lean mass (birth to 20 years) than fat mass (2–20 years in females and 4–20 years in males), and were similar after adjustment for paternal occupational class and adult height.

Across the periods investigated (2-20 years), height gain was generally not associated with fat mass, but was more consistently positively associated with lean mass. However, these associations were largely attenuated after adjustment for adult height.

Results from these growth analyses were consistent with results from simpler models, where associations between weight (and height) at each age were examined in relation to body composition outcomes.

### 4.4.2 ***Comparison with previous studies***

Findings from this study extend previous studies, described in the literature review of this chapter, that have generally been in younger cohorts and only examine limited sections of the growth trajectory (eg, infancy or childhood only).

In contrast with findings from this chapter, previous studies in younger cohorts (<30 years) have found weight or BMI gain in infancy to be positively associated with fat mass. Consistent with this chapter, the only study examining these associations in later life (~61 years) reported no association with fat mass index ($kg/m^2$).[268] In this study, as found in this chapter, weight gain in childhood was positively associated with fat mass, and weight gain in infancy and childhood were also positively associated with lean mass.

To the author's knowledge, no previous studies have examined associations between weight or BMI gain and appendicular lean mass or android: gynoid ratio. In addition, no previous studies have examined associations between height gain and subsequent fat or lean mass in adulthood.

Findings from this chapter build on previous findings in the NSHD which have found greater weight gain in infancy to be associated with increased obesity risk (high BMI) at 43 years;[320] findings from this chapter suggest that this association may primarily reflect lean and not fat mass. The analyses conducted in this chapter extend these findings by using a longer period of follow-up, by considering weight and height gain in childhood and adolescence, and by using direct measures of fat and lean mass.

### 4.4.3 *Explanation of findings*

#### 4.4.3.1 *Weight gain and fat mass*

In partial support of the hypothesis (see section 4.1.2), periods of weight gain in childhood and adolescence were positively associated with fat mass while weight gain in infancy was only weakly associated. Positive associations between weight gain and fat mass may be explained by the tracking of fat attained during weight gain and/or the tracking of behavioural and/or biological factors which lead to greater subsequent weight gain (in later periods of pre-adult life or in adulthood). Similar findings after adjustment for paternal occupational class suggest that associations were unlikely to have been confounded by SEP in early life. This is supported by further analyses (data not shown) showing similar patterns of association with additional adjustment for paternal and maternal educational attainment.

In both sexes, the weak positive associations between weight gain in infancy and fat mass were attenuated by adult height, suggesting that height partly mediated these associations—such that those who gained more weight in infancy went on to become taller adults who tend to have more fat mass. Studies in younger cohorts have tended to find positive associations between weight gain in infancy and fat mass before and after adjustment for height. Given the higher prevalence of childhood obesity in these cohorts, infancy weight gain may primarily reflect gains in fat mass, while in older cohorts such as the NSHD infancy weight gain may predominantly reflect gains in lean mass.

Positive associations between weight gain and fat mass began earlier for females (2 years) than males (4 years). If results reflect the tracking of fat mass, it may be that weight gain from 2–4 years was predominantly driven by the acquisition of lean mass in males, and fat mass in females. In both sexes positive associations between childhood and adolescent weight gains and fat mass were either partly

attenuated, unchanged, or strengthened after adjustment for adult height suggesting that this may only partially explain the associations found.

As hypothesised, there was some evidence that associations between weight gain and fat mass were stronger in later periods (eg, from 7-20 years compared with 0-2 years in both sexes). These may be periods where accrual of fat mass is greater, and/or may reflect the fact that those who gained more weight in these periods tended to gain more fat mass in later periods. For example, late childhood and adolescence may be periods in which lifelong patterns of physical activity and diet are partially determined. There is some evidence that physical activity in childhood and adolescence tend to track into adulthood,[331;332] and patterns of low physical activity in these periods may result in gains in weight, and future gains in fat mass across adult life.

Greater weight in later childhood and adolescence (7-20 years) was also associated with a higher android: gynoid ratio. These associations were driven by the separate associations with android and gynoid fat mass, shown in Appendix 15. While greater weight gain in this period was associated with higher android and gynoid fat mass, associations with the former were either stronger or similar in size, leading to a higher android: gynoid ratio (as on average both males and females had more gynoid than android fat mass; shown in Chapter 2). If these findings are explained by tracking of fat mass into adulthood, it suggests that weight gain from 7-20 years is a period when android fat mass is preferentially accrued.

A series of further analyses were conducted to examine whether associations found in the main analyses were explained in part by the choice of methodology used or further confounders or mediators. First, similar results were obtained when no adjustment was made for measures of height or height gain, suggesting that this adjustment had minimal influence on results (Appendix 16 a). Second, while it could be suggested that these associations were either confounded or mediated by differences in pubertal timing, further analyses showed that adjustment for this made little difference to the associations (Appendix 16 b). Third, further adjustment for maternal BMI and height made little difference to associations found (Appendix 16 b)—this adjustment is discussed in more detail below.

Both environmental and genetic factors may explain the associations found between weight gain and fat mass, and analyses conducted in this chapter cannot distinguish between these. In Chapter 3, associations between birth weight and outcomes were adjusted for maternal BMI and height, crude indicators of genetic

factors that may affect both birth weight and body composition. This adjustment was not conducted in the main analyses of this chapter in order to preserve the available sample size. However, further analyses on a sub-sample showed similar patterns of association with additional adjustment for maternal BMI and height (Appendix 16 b), as has been found in previous studies that have made this adjustment.[258;322;323] As discussed in Chapter 3, this adjustment is unlikely to provide a definite estimate of genetic influence as it captures both genetic and environmental pathways, and the proportion of variance attributable to each may differ depending on the period of growth investigated and outcome used. The likely importance of environmental factors is suggested in the socioeconomic patterning of weight and height gain found in this chapter, and in experimental studies which have shown that nutritional enrichment leads to greater weight and height gain in infancy and increased subsequent fat mass in childhood.[208]

#### 4.4.3.2 ***Weight gain and lean mass***

Supporting the hypothesis (see section 4.1.2), all periods of weight gain were positively associated with lean mass. As with associations with fat mass, positive associations may reflect the tracking of lean mass and/or the tracking of factors which influence subsequent gains in lean mass. Associations were also similar after adjustment for paternal occupational class and additional adjustment for paternal and maternal educational attainment (data not shown), suggesting that associations were not confounded by childhood SEP.

Associations between weight gain in infancy and early childhood (0–4 years) and lean mass were partly attenuated by adult height, suggesting that this mediated part of the associations found—such that those who gained more weight went on to become taller adults (with longer bones and longer muscles therefore of greater mass). However, associations thereafter typically remained after adjustment; weight gain may therefore have impacted on lean mass through other mechanisms such as the development of greater muscle width (the number of adjacent muscle fibres and/or their thickness) and/or greater muscle density (number of muscle fibres per unit area of muscle).

As hypothesised, positive associations between weight gain and lean mass in males were stronger from 15-20 years than in earlier periods, where evidence suggests lean mass accrual is greater. For both sexes, the mechanisms explaining associations with later periods may differ to those in earlier periods. Since the number of muscle fibres in adulthood is thought to be largely determined in early

life,[298] associations in infancy and early childhood may reflect both increased hyperplasia (cell division) and hypertrophy (increase in cell size), with positive associations in later periods primarily reflecting hypertrophy.

Given the strong positive associations between fat and lean mass (shown in Chapter 2), associations between weight gain and lean mass may have been driven by associations between weight gain and fat mass—such that gains in weight in pre-adult life led to greater fat mass which in turn led to increased lean mass (due to increased fat loading driving increased muscle mass). This is more likely to have been the case for associations from early childhood onwards (4 years in males and 2 years in females), where weight gain was positively associated with both fat and lean mass. Further analyses showed that this hypothesis is likely to explain positive associations between weight gain from 7–11 years and lean mass in males only—these associations were largely attenuated after additional adjustment for whole body fat mass: β (mean kg change per one standard deviation increase in weight gain velocity (95% CIs), P-value): 0.17(-0.33, 0.66), 0.51 (whole body lean mass); 0.08(-0.16, 0.33), 0.51 (appendicular lean mass), after adjustment for weight and height at 7 years, concurrent height gain, and adult height. In all other periods, positive associations remained (albeit partly attenuated), suggesting that weight gain may have impacted on lean mass through other mechanisms. As with associations between weight gain and fat mass, those with lean mass were not explained by pubertal timing or maternal BMI and height (Appendix 16 b).

The differing associations of weight gain with fat and lean mass resulted in associations with fat: lean mass ratio, suggesting that greater weight gain in later childhood and adolescence (7-20 years) led to a higher fat: lean mass ratio. In most cases, a greater fat: lean mass ratio was the product of stronger positive associations with fat than lean mass. However, this was not always the case for males who, as shown in Chapter 2, have on average substantially less fat mass (mean=23.79kg) than lean mass (mean=53.69kg). As such, a 1kg increase in fat mass had a greater impact on the fat: lean mass ratio than a 1kg increase in lean mass.

#### 4.4.3.3 ***Height gain and fat mass***

Patterns of association with height gain and fat mass were less consistent than those with weight gain. Most periods of height gain were not associated, with some evidence for both negative (11–15 years in males) and positive (4–7 and 11–15 years in females) associations. The positive associations found in females from 4–7

to 11–15 years were only partly mediated by adult height, suggesting that females who gained greater height in these periods went on to have more fat mass than is solely attributable to a resulting increase in adult height (and body size).

Although it was hypothesised that all periods of height gain would be positively associated with fat mass (due to the tracking of height and body size, with taller adults tending to have more absolute fat mass), lack of association may reflect the fact that although adult fat mass is positively associated with height, this association is weaker than the positive association between lean mass and height (Chapter 2). As such, the increase in height in each period may have had a stronger more demonstrable impact on lean than fat mass.

In a number of instances (eg, height gain from 4–11 and 15–20 years in males), height gain was positively associated with fat mass before adjustment for weight gain in the same period (Appendix 17), but these associations were attenuated when this adjustment was made. Weight gain is likely to be on the pathway between height gain and fat mass, such that greater height gain leads to an increase in body size and resulting fat mass which then tracks into adulthood. Adjustment for concurrent weight gain could therefore be considered an over-adjustment, and the negative association between height gain from 11–15 years and fat mass (in males) could be a statistical artefact, since there was no association before adjustment (Appendix 17). Alternatively, as suggested in a previous study which made the same adjustment,[324] this association may suggest that greater height gain in this period, without excessive weight gain, is associated with lower fat mass. Although the interpretation of these results is somewhat uncertain, such adjustment was considered necessary to enable the independent associations of weight and height gain to be investigated (as weight and height gain were positively correlated).

Associations between greater height gain from 2-4 years (both sexes) and 15-20 years (males only) with lower android: gynoid ratio were driven by the separate associations with android and gynoid fat mass, shown in Appendix 15. The explanation for these findings differed in each period and by sex: height gain from 2-4 years was associated with lower android fat mass but not with gynoid fat mass in males, and weakly with lower android fat and higher gynoid fat mass in females; greater height gain from 15-20 years was not associated with android fat mass, but was associated with higher gynoid fat mass in males. Associations between height gain and android: gynoid ratio were partly (2–4 years) or largely (15–20 years) attenuated by adult height, suggesting that adult height may have mediated these

associations. However, adjustment for adult height could be considered an over-adjustment, since the statistical models used were already adjusted for height at the beginning of each period (from 2–15 years), and height in childhood is a strong predictor of adult height.[333]

#### 4.4.3.4 *Height gain and lean mass*

In partial support of the hypothesis (see section 4.1.2), most periods of height gain were positively associated with lean mass, and these tended to be strongest in the periods which were most strongly associated with adult height (15–20 years in males, and 11–15 years in females; Appendix 13). Associations with lean mass were more frequently found than with fat mass and may reflect the stronger positive association between adult height and lean mass than fat mass. As associations were found with both whole body and appendicular lean mass, positive associations found likely reflect gains in lean mass in both the appendicular and trunk regions. The different periods may however be differentially associated with lean mass of the legs and the trunk—previous studies have shown that gains in leg length tend to be greater in infancy and early childhood than gains in trunk length.[334-336]

All the reported positive associations found between height gain and lean mass were largely attenuated by adult height, suggesting that attained adult height and body size mediated these associations. However, as discussed previously, this may be an over-adjustment.

Due to the positive associations between height gain and lean mass, and either no association or weaker positive associations between height gain and fat mass, in most periods examined greater height gain led to lower fat: lean mass ratio. Greater height gain from 2–4 and 15–20 years (in both sexes) were weakly associated with lower fat: lean mass ratio both before and after adjustment for concurrent weight gain (Appendix 17), suggesting that over-adjustment is unlikely to explain these findings.

As with associations between weight gain and outcomes, associations with height gain may reflect both environmental and genetic pathways, and analyses cannot distinguish between these two explanations.

### 4.4.4 *Methodological considerations and limitations*

The periods of growth investigated in this chapter were chosen to maximise the number of discrete periods investigated, but were contingent on the measures available in the NSHD. Other periods of growth unavailable in the NSHD may be particularly important for subsequent body composition: for example, some previous studies have suggested that weight gain in the first weeks or months of the postnatal period may be particularly important for subsequent fat mass,[311;337] however only weight gain from 0–2 years was only available in the NSHD. However, the periods of growth used in this chapter—spanning infancy, childhood and adolescence—were greater than all previous studies in later adulthood, and overall can be considered a strength. In addition, the consequences of faster growth in one period may differ depending on the rate of growth in prior periods. For example, catch-up growth (indicated by increased weight gain in early infancy following low birth weight) may be differentially associated with outcomes compared with non-catch-up growth. However, this was not considered appropriate for analysis in the NSHD as catch-up growth occurs in early infancy, and is unlikely to be captured from 0–2 years.

The periods of growth analysed in this chapter were converted into velocities and, where available, the exact number of months was used as a denominator. However, the exact date of measurement was not available at 2 and 20 years—this is likely to have increased the measurement error of weight and height at these ages, and may have impacted on associations found. However, further analyses showed almost identical patterns of association in the other periods when not converted into velocities (data not shown), suggesting that this source of measurement error was likely to be small. A further source of measurement error was the self-reporting of weight and height at 20 years. Young adults (unlike older adults) have been found to recall their height and weight with a relatively high degree of accuracy, suggesting that measurement error may have been minor.[205] However, misreporting may have been differential with respect to weight or height, potentially introducing some bias in the associations found with weight or height gain from 15-20 years. For example, shorter individuals may have overestimated their height, and heavier individuals may have underestimated their weight.

In this chapter complete case analyses were conducted with some participants with valid body composition outcome excluded due to missing weight and/or height gain data. Some statistical methods, such as multilevel models, do not require complete

cases and may therefore have greater statistical power. However, the NSHD has a large sample size compared with many other previous studies, and evidence was found for associations suggesting that analyses were not under-powered.

In addition to leading to loss of power, the use of complete case analyses in this chapter may have resulted in bias. However, only small numbers of participants were excluded from analyses due to missing data for paternal occupational class, and similar results (data not shown) were found when analyses were repeated on the maximum available sample size. Further analyses showed that the estimates obtained were also similar when only those with valid data for all periods of growth were included in analyses (Appendix 16 and Appendix 17), suggesting that the use of different sample sizes in the periods examined was unlikely to substantially impact on the results found.

Another potential source of bias is loss to follow-up, with not all of the original NSHD sample providing full body composition data at 60-64 years. However, this source of bias may be unlikely to have substantially impacted on findings, as analyses in Chapter 2 showed that participants with valid body composition outcome data had only minor differences in height (slightly taller) in infancy and childhood compared with those who did not.

### 4.4.5 ***Strengths***

Chapter 1 presents the overall strengths of the NSHD, while the strengths specific to this chapter are outlined below.

A main strength of this chapter is the large number of prospectively assessed measures of weight and height used across pre-adult life—greater than most previously published studies. These data enabled the periods of importance for subsequent fat and lean mass to be investigated. In addition, associations between periods of pre-adulthood height gain and adult body composition were assessed for the first time in this chapter, providing some evidence that greater height gain may lead, in some periods, to a lower fat: lean mass ratio.

The analytical strategy and statistical methods used had a number of strengths. First, models were constructed to examine associations with discrete periods of weight and height gain, and this would not be possible by only examining associations between weight or height at each age and outcomes. Second, efforts were made to ensure that associations across different periods were comparable:

periods of weight and height gain were converted into velocities and then sex-specific standard deviation scores were used. This enabled the strengths of associations across periods to be more easily compared. Third, the independent influences of weight and height gain were estimated by their mutual adjustment. Such adjustment showed that associations with weight gain were unlikely to have been confounded by height gain, conclusions not possible in previous studies which have made no adjustment for height gain. Some other previously published studies have used change in BMI in pre-adult life; however, as found in this chapter BMI may not appropriately adjust for height, and may further complicate the interpretation of results given the fact that mean BMI increases in some periods and decreases in other periods. Fourth, in this chapter, unlike most previous studies, associations with body composition outcomes were presented both unadjusted and adjusted for adult height. This enabled the pathways of associations to be better understood, although it is acknowledged that this adjustment could be considered over-adjustment in models containing a measure of height in pre-adult life.

### 4.4.6 *Conclusions and links to other chapters*

This chapter has shown evidence for positive associations between periods of pre-adulthood weight gain and both fat and lean mass. These associations began earlier for lean mass, such that greater weight gain in infancy was associated with higher lean but not fat mass. Greater weight gain in later childhood and adolescence (7-20 years) was associated with higher fat and lean mass, and a higher fat: lean mass ratio. Across the periods investigated, greater height gain was associated with higher lean mass but not fat mass, associations largely explained by adult height.

Findings from this chapter may in part explain the positive associations found between birth weight and lean mass found in Chapter 3. As discussed in Chapter 3, those of higher birth weight tended to gain more weight in childhood which, as shown in this chapter, was associated with higher lean mass.

The following chapter, Chapter 5, will continue the work of this thesis and examine associations between physical activity in adulthood and body composition outcomes.

# 5. Chapter 5: Physical activity and body composition

Main objective: to examine whether physical activity across adulthood is associated with body composition outcomes at 60–64 years.

It is widely believed that higher physical activity levels lead to lower fat and higher lean mass. However, relatively few epidemiological studies have examined how physical activity relates to direct measures of fat and lean mass, and fewer still have used objective measures of physical activity. This chapter adds to the literature by examining the cross-sectional associations between physical activity, measured objectively using Actiheart monitors at 60–64 years, and body composition outcomes. In addition, associations between leisure time physical activity levels across adulthood and body composition outcomes are examined.

## 5.1 Introduction

A widely cited definition of physical activity is "any bodily movement produced by skeletal muscle that results in energy expenditure".p126[338] This definition, adopted for use in this thesis, includes all types of bodily movement including exercise, a sub-type of purposeful physical activity.

Physical activity is often quantified using the following three dimensions: the duration of time spent physically active and the intensity and frequency of the activity.[339] These can be used to calculate the total energy expenditure attributable to physical activity, which is often used in studies relating physical activity to health outcomes and body composition. Intensities of physical activity are typically categorised in multiples of the resting metabolic rate—being inactive or sedentary is 1–1.5 metabolic equivalents (METs),[340] low intensity or light physical activity (eg, walking) >1.5–3 METs, and moderate-vigorous physical activity (eg, running) >3.0 METs.[339;341;342] While the mechanisms linking specific intensities of activity with body composition are not understood, it has been suggested that spending less time inactive[343;344] and greater time in moderate-vigorous intensity physical activity[188] may be especially important in achieving and maintaining lower fat mass, independently of total physical activity energy expenditure. In addition to the duration, frequency and intensity of activity, different types of physical activity may also be differentially important for either fat or lean mass. For example, evidence

from intervention studies suggests that resistance exercise is important in maintaining and increasing lean mass levels.[185;186]

Both total physical activity and its dimensions can be measured in a number of different ways, either by self-report (in questionnaires or interviews) or objectively (eg, using accelerometers, pedometers, or heart rate monitors).[345-347] Objective measures are a relatively recent development and may derive measures of greater precision and accuracy,[152;341;348] while self-reported measures typically provide information about physical activity across a longer time span and provide information about the types of activities undertaken. Most population studies have used self-reported measures.

A small number of prospective studies have shown that leisure-time physical activity declines from childhood to early adulthood,[349-351] and this decline may continue into later adulthood. Most adults in the UK do not meet the physical activity guidelines set in 2004 of moderate or vigorous intensity physical activity for 30 minutes per day for at least five days per week.[352;353] Recent guidelines published in 2011 recommend that older adults (>65 years) participate in physical activity twice a week to improve muscle strength (activities which use the muscles against resistance or body weight).[354] The patterns of physical activity also differ by sex, with recent evidence from the Health Survey for England showing that in adulthood males tend to spend more time sedentary and in moderate-vigorous physical activity than females (who spend more time in lower intensity physical activity).[353] Although population averages of physical activity are low, there is sufficient variation to enable the associations between physical activity and outcomes to be investigated.

Physical activity has been shown to be related to a number of health outcomes; a report by the Department of Health in 2004 summarised the existing scientific literature and concluded that participation in regular physical activity (typically defined by self-report) was protective against coronary heart disease and type 2 diabetes, stroke, musculoskeletal disorders (such as osteoporosis, osteoarthritis, back pain), and cancer.[352] Similar conclusions were drawn in a report by the US Department of Health and Human Services in 2008.[355] For some of the health outcomes, body composition may be on the causal pathway, such that reduced physical activity leads to changes in body composition (such as increased fat and reduced lean mass), which in turn lead to increased risk of ill-health (such as type 2 diabetes).

Physical activity is an essential component of energy balance (along with energy intake) that (as discussed in Chapter 1) is widely thought to govern the amount of fat mass that individuals have. There are plausible hormonal pathways which may underlie associations between higher physical activity levels and lower fat mass.[356] For example, experimental studies have shown that aerobic exercise stimulates secretion of the growth hormone, a hormone with lipolytic (fat metabolising) properties, in a dose-response manner with higher exercise intensities.[357-359] The effect of physical activity on fat mass may be greater if it is of high compared with low intensity (even if total physical activity energy expenditure is identical). For example, moderate-vigorous intensity activity may lead to reduced appetite[360] and increased basal metabolic rate (the energetic costs of normal bodily functioning such as respiration),[361] leading to reductions in fat mass. Moderate-vigorous physical activity may increase basal metabolic rate both directly and through increased lean mass—as higher lean mass has been shown to be associated with greater resting metabolic rate.[112;113]

There are also plausible biological mechanisms which may link physical activity with higher lean mass. For example, there is evidence that hypertrophy following resistance exercise is mediated by exercise-induced secretion of hormones such as testosterone, insulin-like growth factor 1, and mTOR (mammalian target of rapamycin).[362-364] In population studies, high intensity physical activity may be particularly strongly associated with higher lean mass, as these types of activities are likely to include those which lead to higher loading of the muscle. These activities may include resistance exercises and other types of leisure time activities. For example, activities such as tennis could be described as being high weight-bearing as they require muscle strength and power to lift the weight of the body and to support the weight of the body when falling, potentially stimulating gains in muscle mass.

Spending more time sedentary may lead to higher fat and lower lean mass as more sedentary individuals are likely to have lower physical activity energy expenditure (and undertake less moderate-vigorous intensity activity).[365] For some outcomes such as cardiovascular disease, it has been suggested that sedentary time may affect disease risk independently of physical activity energy expenditure, as there may be particular physiological mechanisms which are activated when the body is sedentary for prolonged periods.[366;367] While this may be true for fat and lean mass, to the author's knowledge this has not been demonstrated, nor have potential mechanisms been described.

Although it is widely assumed that physical activity is causally related to subsequent body composition,[368] associations could feasibly operate in the reverse direction, or be bi-directional. For example, there are a number of barriers which may make obese adults less likely to undertake physical activity, including psychological barriers (eg, unwillingness to undertake public physical activity when obese)[369] and physiological barriers (eg, due to phenomena associated with obesity that impair physical activity such as breathlessness[370] and reduced physical functioning, described in Chapter 1). Although less researched, it is also feasible that having lower lean mass may lead to psychological barriers to physical activity, and lower lean mass has been associated with worse physical functioning (outlined in Chapter 1) which may in turn lead to lower physical activity levels.

While physical activity levels in adulthood are likely to affect adult body composition, activity levels earlier in life may also play a role. For example, lower physical activity levels in childhood may lead to gains in fat mass which then track into adulthood. As there is some evidence that physical activity levels track across life,[331;332;371] lower physical activity in childhood may track to adulthood, leading to further fat mass gains in adulthood. As lean mass levels are also thought to track across life, activity levels in both early and adult life may both lead to gains in lean mass in adulthood. As such, there may be cumulative benefits of conducting greater activity across life in leading to lower fat and higher lean mass. The same patterns of associations may also be found if the relationship between physical activity and body composition is bi-directional. For example, lower physical activity in childhood may lead to gains in fat mass which then lead to lower subsequent physical activity levels and in turn higher fat mass, resulting in a positive feedback loop.

Given the increases in population levels of fat mass (described in Chapter 1), ecological observations may provide some clues as to the association between physical activity and fat mass. These have highlighted that increased obesity prevalence has occurred alongside technological and societal changes which likely led to reduced physical activity levels (such as increased car ownership, increased average television viewing times, and a reduction in labour-intensive occupations), suggesting that physical activity influences fat mass.[17;152;372] However, other societal changes have also occurred alongside the increase in obesity prevalence (such as increased fat intake as a proportion of overall diet[151]), leaving the independent influence of physical activity unclear; individual-level data provide a stronger source of evidence of association, enable different intensities of physical

activity to be investigated, and are likely to provide a more accurate estimate of the effect sizes of interest.[373]

A number of epidemiological studies have examined associations between physical activity and whole body fat and/or lean mass in adolescents and adults, including cross-sectional and prospective studies. The sections below summarise and discuss these studies: first, those where anthropometric measures of fat mass have been used (such as BMI), and second where measures of physical activity or sedentary time have been used with direct measures of fat and/or lean mass in adolescence and adulthood. Studies using both self-reported and objectively assessed measures of activity are included, and those using the latter are summarised in Table 1. Direct measures of fat and lean mass included DXA, BIA, and air displacement plethysmography. In addition to epidemiological studies, findings from intervention studies are also summarised.

Table 15. Summary of studies that examined associations between objective measures of physical activity (or sedentary time) and whole body fat and/or lean mass in adulthood

| Study | N | Location/ majority ethnicity | Age at outcome measure | Physical activity measure | Body composition measure | Main adjustments | Fat mass association +(positive) —(negative) | Lean mass association +(positive) —(negative) |
|---|---|---|---|---|---|---|---|---|
| den Hoed and Westerterp, 2008[374] | 134 | The Netherlands /Not stated | 21 (SD~2) | Accelerometer: total, moderate, high intensities | Helium/ deuterium dilution: Cross-sectional | Height, weight | — all | N/A |
| Mestek et al, 2008[375] | 88 | USA /Caucasian | ~22 (19-25) | Accelerometer: average steps/day | BIA: cross-sectional | None | Males: no assoc<br>Females: — | N/A |
| Bailey et al, 2007[376] | 228 | USA /Caucasian | ~40 (35–45) | Accelerometer: light, moderate, vigorous activity groups | Air displacement: cross-sectional and after ~2y | None | Males: N/A<br>Females: — | N/A |
| Paul et al, 2004[377] | 91 | USA /Not stated | ~47 (SD~10) | Calorimetry | DXA: Cross-sectional | None | Males: —<br>Females: no assoc. | N/A |
| Ekelund et al, 2005[190] | 739 | UK /Caucasian | ~53 (SD~10) | HR: total PA | DXA: cross-sectional and change after ~5y | Smoking, dietary fat intake | Cross-sectional — all.<br>Change (modified by age):<br>-younger ages (<53y)<br>+ older ages (>53y) | Cross-sectional + all.<br>Change (modified by age):<br>No assoc. younger ages (<53y)<br>+ older ages (>53y) |
| Ekelund et al, 2008[378] | 396 | UK /Caucasian | ~55 (SD~8) | HR: % time sedentary | DXA: cross-sectional and change after ~5y | ASEP | + cross-sectional<br><br>no assoc. change after ~5y | N/A |
| Barbat-Artigas et al, 2011[379] | 57 | Canada /Caucasian | ~62 (50–70) | Accelerometer: total steps/day | BIA: cross-sectional | N/A | Males: N/A<br>Females:— | Males: N/A<br>Females: no assoc. |

| Study | N | Location/ majority ethnicity | Age at outcome measure | Physical activity measure | Body composition measure | Main adjustments | Fat mass association +(positive) —(negative) | Lean mass association +(positive) —(negative) |
|---|---|---|---|---|---|---|---|---|
| Park et al, 2010[380] | 175 | Japan /Japanese | ~72 (65–84) | Accelerometer: total steps/day (1y) MVPA (>3 METs) | DXA: after 1y | Height | N/A | +all Stronger MVPA |
| Manini et al, 2009[381] | 302 | USA /Mixed | ~75 (70-82) | Doubly-labelled Water: total PA | DXA: cross-sectional and change after 5y | Age, smoking, and race | No assoc. all | + cross sectional (no assoc. change after 5y) |
| Chastin et al, 2011[382] | 32 | Finland /Caucasian | ~79 (SD~3) | Accelerometer: total sedentary time | DXA: cross-sectional | None | Males: + Females: no assoc. | N/A |

Note: ASEP=adult socioeconomic position; BIA=bioelectrical impedance analysis; DXA=dual energy X-ray absorptiometry; MVPA=Moderate-vigorous physical activity; PA=physical activity; N/A=not applicable; y=year; HR=heart rate monitors

## 5.1.1 *Literature review: physical activity and body composition*

### 5.1.1.1 *Physical activity and fat mass*

A large number of studies have examined associations between physical activity and anthropometric measures of fat mass in adolescents and adults, and most have been included in the systematic and narrative reviews outlined below.

A systematic review included in a report commissioned by the US Department of Health and Human Services in 2008 examined the cross-sectional associations between measures of physical activity (typically assessed by self-report) and body weight or BMI.[355] Twenty-four studies were identified, 23 of which found that higher physical activity was associated with lower body weight or BMI. Wilks et al (2010)[383] conducted a systematic review of prospective studies examining the relationship between objective measures of physical activity and subsequent change in fat mass in adulthood. In four of the six studies identified, fat mass was assessed by change in BMI or body weight, and in two studies direct measures of fat mass were used. Three studies found that higher physical activity was weakly associated with reductions in fat mass (or less gain in fat mass), while the remaining three studies found no association. The authors concluded that physical activity may not be a key determinant of excessive weight gain. Similar findings, of weak and/or inconsistent associations between physical activity and future weight or fat gain, have also been reported in previous systematic reviews that have included studies using both self-reported and objective measures of physical activity—in 2000,[384] 2005,[152] and 2009.[385] The studies included in these reviews typically used one measure of physical activity at baseline; to the author's knowledge, none have examined whether there are cumulative benefits of physical activity levels across adulthood in leading to lower fat mass.

Most of the studies included in the above reviews examined associations with total physical activity energy expenditure, and few examined associations with different intensities of physical activity which may be differentially important for fat mass. Further, body weight and BMI are unable to distinguish fat and lean mass, and these may be differentially related to physical activity.[25] For example, higher physical activity may lead to lower fat and higher lean mass, but have little or no association with body weight or BMI.

Five studies examined associations between objective measures of physical activity and fat mass in adolescents (12–17 years). Four found some evidence that higher

physical activity was associated with lower fat mass—in both sexes,[188;386;387] or in females but not males[388]—while one study found no association.[389] Three of these studies used the Avon Longitudinal Study of Parents and Children (with DXA measures at different ages): in one study, lower physical activity was associated with less gain in fat mass over 2-years (at ~14 years),[188] while in subsequent cross-sectional analyses only greater vigorous physical activity (and not light or moderate physical activity) was associated with lower fat mass (at ~15 years).[387] In a cross-sectional study by Deere et al (2012)[388] conducted at ~17 years, accelerometers were used to measure the 'impact' of physical activities, based on the gravitational force that different activities produce. High impact activities (such as jumping) lead to high gravitational forces, and low impact activities (such as walking) lead to low gravitational forces. Results showed no associations in males, while in females greater moderate impact physical activity (but not light or high impact) was associated with lower fat mass. However, the justification for such categorisation was based on previous findings relating such activities to bone outcomes, and there were no specific hypotheses outlined in relation to fat mass. The inconsistent findings may suggest that fat mass is more closely related to physical activity measures which are more closely related to energy balance (such as total physical energy expenditure). Two other cross-sectional studies were conducted using different adolescent cohorts—one found higher physical activity was associated with lower fat mass (using DXA),[386] while another study in a developing nation (Brazil) reported no association (using SFT[389]).

Two cross-sectional studies examined associations between objective measures of physical activity and fat mass in young adulthood (19–25 years). Higher physical activity was associated with lower fat mass in one study (in both sexes using deuterium dilution),[374] while in the other study this association was found in females but not males (using BIA[375]), although the small sample size (44 males and 44 females) may have resulted in this study being under-powered (as although associations in males were not statistically significant at the $P<0.05$ level, the direction of association was in the same direction as in females).

Seven studies examined associations between objective measures of physical activity or time spent sedentary and fat mass in mid-later adulthood (mean ages ≥40 years). Five found evidence that higher physical activity or less time spent sedentary was associated with lower fat mass: in both sexes,[378] in exclusively female cohorts,[376;379] in males but not females,[377;382] or in younger (<53 years) but not older (>53 years) adults (with no age range provided).[190] One study found no association.[381] Two of these studies that used exclusively female cohorts found that

higher physical activity was associated with lower fat mass: in cross-sectional analyses (using BIA[379]), or with lower gain in fat mass over two years (using air-displacement[376]). In a larger study by Ekelund et al (2005)[190] lower physical activity was associated with higher fat mass in cross-sectional analyses (using DXA), but associations with change in fat mass (after ~5 years) were modified by age (those older or younger than 53 years (standard deviation=~10 years; no age range was provided)): higher physical activity was associated with declines in fat mass in younger participants, but gains in fat mass in older participants. Although the mechanism underlying the association in older adults was not explained, the findings were discussed as having potentially important public health implications as results suggested that higher physical activity in old age may prevent weight loss which is associated with increased risk of mortality in old age.

Using the same cohort as described above, Ekelund et al (2008)[378] examined the associations of time spent sedentary and cross-sectional measures of fat mass, and change in fat mass after ~5 years (using DXA). Greater sedentary time was associated with higher fat mass in cross-sectional analyses, but not with subsequent change in fat mass. This study also examined the reverse associations (between change in fat mass (over 5 years) and subsequent time spent sedentary) and results showed that greater gain in fat mass was associated with greater time spent being sedentary at follow-up (after adjustment for baseline sedentary time). In this study, unlike the previously described study using the same cohort, there was no evidence for effect modification by age. While associations found suggest that fat mass influences sedentary time (and not vice versa), it was acknowledged that associations may be bi-directional in nature. Another study reported no association between physical activity and cross-sectional measures of fat mass, or change in fat mass over 5 years in later adulthood (using DXA[381]). Finally, a small cross-sectional study found that greater time spent sedentary was associated with higher fat mass in males but not females,[382] although this study used a very small sample size (16 males and 14 females) and was therefore likely to have been underpowered (associations in females were in the same direction as those found in males).

In three adolescent studies associations between different intensities of objectively assessed physical activity and fat mass were compared. Two studies found that associations between lower physical activity and higher fat mass were only found when moderate-vigorous intensity activity was used, compared with light intensity activity.[386;387] In the remaining study, associations between lower physical activity and higher fat mass were stronger when using moderate-vigorous physical activity

compared with total physical activity energy expenditure, and when both measures were mutually adjusted for one another, only associations with moderate-vigorous intensity remained.[188]

A number of intervention studies have examined whether physical activity-based interventions impact on fat mass. A systematic review by Wareham et al (2005)[152] found six studies in adulthood that used physical activity interventions to try and prevent weight gain: four studies found that weight either declined, did not increase, or increased less than the control group, while the remaining two studies found no difference. In these studies, interventions were typically employed over a long period of time (12 weeks to 5 years), with follow-up in most cases immediately after intervention. However, all of these studies also included dietary change in the interventions, leaving the independent influence of physical activity on fat mass unclear. A systematic review and meta-analysis in 2009 examined weight loss intervention studies and compared those that included both dietary change and physical activity with those that only included dietary change.[390] Of the 18 included studies, those that included physical activity led to greater weight loss than those only using dietary interventions. Interventions were between 3 months to 6 years in length, with follow-up from 0 to 2.5 years after intervention. The reported effect sizes were small, with interventions leading to an average 1.64kg reduction in body weight after follow-up, which may be partly attributable to poor compliance and/or gains in lean mass. Findings were similar in six studies that used direct measures of fat mass.

Intervention studies have also examined the impact of resistance exercise on fat mass reduction. These have tended to find that the resulting loss of fat mass in aerobic-only interventions is similar to those that additionally include resistance training,[391;392] suggesting that this type of activity is not especially important in leading to lower fat mass.

In summary, a number of experimental studies have suggested that aerobic exercise interventions tend to lead to lower fat mass. Epidemiological studies, using broader summary measures of physical activity (including non-exercise activities) have also tended to show that higher physical activity is associated with lower fat mass, although few studies have been conducted using direct measures of fat mass and associations have been found to vary by sex and age.

#### 5.1.1.2 *Physical activity and lean mass*

Three observational studies have examined associations between objective measures of physical activity and lean mass in adolescents (all used DXA)—two found evidence that higher physical activity was associated with higher lean mass,[387;388] while one study found no association.[189] Two of these studies used the Avon Longitudinal Study of Parents and Children. In one cross-sectional study (at 15 years), greater light and vigorous (but not moderate) intensities of physical activity were associated with higher lean mass.[387] In subsequent cross-sectional analyses (at 17 years), the study previously outlined by Deere et al (2012)[388] examined associations of activities of low, moderate and high impact physical activity with lean mass. In both sexes, greater high impact physical activity was associated with higher lean mass, but light and moderate impact activities were not.[388] These findings suggest that types of activities that are classified as high impact (such as jumping) may lead to higher lean mass. This may be due to the fact that such activities produce high gravitational forces that require muscle strength and power to overcome. Finally, a study using a different cohort in adolescence reported no cross-sectional association between objective measures of physical activity and lean mass.[189]

Four studies examined associations between objective measures of physical activity and lean mass in mid-later adulthood (mean ages ≥40 years). Three found evidence that higher physical activity was associated with higher lean mass: this was found in all ages in one study,[380] in older (>53 years) but not younger (<53 years) participants in another study,[190] and in cross-sectional but not longitudinal analyses in another study.[381] In one small (and likely underpowered) cross-sectional study of 57 females, no association was found (using BIA[379]). To the author's knowledge, no studies have examined associations between objective measures of sedentary time and lean mass.

The study by Ekelund et al (2005) (outlined previously) found that higher physical activity was associated with higher lean mass in cross-sectional analyses, but associations with change in lean mass over 5 years were modified by age (those older or younger than 53 years (standard deviation=~10 years; no age range provided): higher physical activity was not associated with change in lean mass in younger adults, but was associated with gains in lean mass in older participants (using DXA[190]). In the older group, higher physical activity was associated with gains in both fat and lean mass, suggesting that associations with lean mass could have been driven by fat mass—eg, if gains in fat mass led to increased muscle

loading and resulting gains in lean mass. However, no adjustment was made for fat mass in this study. One study found that higher physical activity (assessed using pedometers for 1 year) was associated with higher lean mass (using DXA[380]), while another study found that higher physical activity was associated with higher lean mass in cross-sectional analyses, but was not associated with change in lean mass over 5 years (using DXA[381]). Lack of association in this study with subsequent change in lean mass (in contrast with findings from Ekelund et al (2005)) may be due to the physical activity measure used (doubly-labelled water) not capturing the types of activities which led to gains or preservations in lean mass (such as weight-bearing physical activity).

Three of the above studies compared associations between different intensities of physical activity and lean mass. Two studies were conducted using adolescent cohorts: one found that greater moderate-vigorous intensity activity (but not lower intensities) was associated with higher lean mass,[387] while another study reported no associations with either total or moderate-vigorous intensity physical activity.[189] One study compared associations in later adulthood and found that greater moderate-vigorous intensity physical activity was more strongly associated with higher lean mass than a measure of total physical activity.[380]

In addition to the above studies using objective measures of physical activity, three studies were identified which examined associations between self-reported measures of physical activity and direct measures of lean mass in adulthood. As in studies using objective measures of physical activity, findings were not consistent. Two studies reported no association between self-reported activity and lean mass, in cross sectional analyses (using BIA at 15-64 years),[393] or with change in lean mass after 9-years (using under-water weighing at ~61 years).[394] In contrast, the remaining study found that in males but not females higher physical activity was associated with reduced declines in lean mass over 9 years (using BIA at ≥65 years).[395]

To the author's knowledge, no studies have examined whether there are cumulative effects of physical activity levels across adulthood in leading to higher lean mass.

A large number of intervention studies have been conducted to examine the influence of resistance exercise on lean mass. Most have shown that interventions lead to an increase in lean mass. For example, a systematic review and meta-analysis of 49 studies (in adults >50 years) reported a pooled estimate of a 1.1kg increase in whole body lean mass after intervention.[184] In the included studies, lean

mass was always measured directly (eg, using DXA or air-displacement techniques) and interventions typically consisted of 2-3 sessions of resistance exercise per week for 10–50 weeks. The intensity of the activities ranged from 50–80% of the maximum that could be lifted once (one rep maximum), and the volume of activities varied from 7–39 sets performed in one session. The post-intervention increase in lean mass was found across all ages but was weaker in older adults, and was not associated with the intensity of exercise, but was greater in studies that used a higher volume. In contrast with the numerous studies examining resistance exercise interventions, few have examined whether aerobic exercise impacts on lean mass.[396] In one study, a 4-week aerobic cycling intervention had no impact on whole body lean mass (n=78; aged 19-87 years).[397]

In summary, there is consistent evidence that specific resistance exercise interventions lead to short term gains in lean mass. However, epidemiological studies examining associations between summary measures of physical activity and lean mass in adults have yielded mixed findings. Lack of association between measures such as total physical activity energy expenditure and lean mass suggests that the types of activities that lead to gains in lean mass are not being sufficiently undertaken in free-living environments. Alternatively, assuming that these activities are being undertaken, the measures of physical activity used in epidemiological studies may not adequately capture these types of activities.

#### 5.1.1.3 *Literature discussion: physical activity and body composition*

This section discusses findings from the studies described above which examined associations between objective measures of physical activity and direct measures of fat and/or lean mass.

Of the studies identified, relatively few used cohorts in adulthood, and those that did had comparatively small sample sizes (N<400 in 9 of 10 studies). While larger sample sizes have been used in studies of adolescents, findings from younger cohorts do not necessarily generalise to those in later life. The evidence for effect modification by age (for associations with both fat and lean mass) given in the study by Ekelund et al (2005)[190] suggests that associations may differ in younger and older middle-aged adults, although the reasons for these differences are not understood.

While ten studies have examined associations between physical activity and fat or lean mass in adolescence or adulthood, only three have examined associations with both outcomes. As further discussed in Chapter 1, examining the influence of exposures on both outcomes may be useful to better understand aetiology—since fat and lean mass are positively correlated (Chapter 2), associations with lean mass may be driven by fat mass (due to greater loading of fat mass driving increased muscle mass). However, no studies using adults have made adjustment for fat mass when examining associations with lean mass. Further, most studies have used only whole body measures of fat and lean mass—as outlined in Chapter 1, appendicular lean mass is likely to be a more accurate measure of skeletal muscle mass.

All of the included studies used single objective methods of physical activity measurement. While potentially more accurate and precise than self-reported measures of physical activity, each objective method has corresponding strengths and weaknesses. For example, accelerometers (used in six adult studies) may not measure types of physical activity where participants remain seated (such as cycling and resistance training), while heart rate monitors (used in two adult studies) measure physical activity, but may also include phenomena aside from physical activity which increase heart rate (such as acute stress).[398] The use of combined methods to assess physical activity may therefore overcome the limitations of each single method,[341] and the consequent decrease in measurement error may increase the likelihood of finding a genuine association and would enable a more accurate estimation of the associations of interest.

Most of the included studies only examined total or average physical activity—only three adult studies examined different intensities. There was some evidence in these studies that associations of higher moderate-vigorous intensity physical activity with lower fat and higher lean mass were typically larger than associations with lower intensities (or total physical activity), suggesting that moderate-vigorous intensity activity may be particularly important. In addition, only two studies examined sedentary behaviour. While spending greater time sedentary may lead to higher fat mass as greater sedentary time likely predicts lower total physical activity energy expenditure, few studies have available data to examine this.

Studies using both objectively assessed and self-reported measures of physical activity have typically used only a single measure of physical activity captured at one point in time in their analyses. As described in the introduction of this chapter, there may be cumulative benefits of physical activity across adulthood which lead

to lower fat and higher lean mass. However, to the author's knowledge, no studies have tested this.

Studies examining associations between physical activity and body composition have made adjustment for different sets of covariates in their analyses (with little explicit justification), some of which could be considered potential confounders. Of these, aspects of diet that impact on fat mass (eg, total energy intake) and lean mass (eg, protein intake) may be potential confounders since those who undertake less physical activity may also have diets that lead them to have higher fat and lower lean mass. Concurrent SEP may be a distal indicator of these dietary factors. However, only one adult study made adjustment for an indicator of SEP, and one made adjustment for dietary fat intake (in associations between physical activity and fat mass. In addition, it is feasible that health status in adulthood may confound associations, as limiting illnesses may impair activity levels and lead to gains in fat and reductions in lean mass.

#### 5.1.1.4 *Prior findings from the MRC National Survey of Health and Development*

Only one study has examined associations between physical activity and an indicator of higher fat mass in the NSHD. Braddon et al (1985)[399] examined the cross-sectional associations between self-reported leisure time physical activity and obesity (BMI >30) at 36 years. Higher leisure time physical activity participation was associated with lower risk of obesity in females, but not males.

As discussed in Chapter 3, while the NSHD has no previous measures of lean mass, studies using grip strength and physical functioning outcomes are described below in order to give an indication of the types of analyses that have been conducted using physical activity measures in the NSHD.

Kuh et al (2005)[400] examined the cross-sectional associations of leisure time physical activity with grip strength, standing balance and chair rise time at 53 years. Higher physical activity was associated with greater grip strength in males, but not in females, and was associated with greater balance time and chair rise time in both sexes. These associations were independent of measures of ill health and occupational class at 53 years.

Cooper et al (2011)[209] examined associations between leisure time physical activity (at 36, 43, and 53 years) and grip strength, standing balance and chair rise time at

53 years. There was evidence of cumulative benefits of physical activity across adulthood in leading to better performance in tests of chair rise and standing balance. Physical activity was not associated with grip strength in females, but was associated with greater grips strength at 53 years in males (but not at other ages).

Two studies using the NSHD have examined the predictors and patterns of physical activity and are described below as their findings may be relevant for this chapter.

Kuh and Cooper (1992)[401] examined the predictors and patterns of physical activity at 36 years, measured by self-report over the previous month of interview date. The types of activities differed by sex, with males undertaking more heavy gardening, and females walking and cycling more. Higher own and maternal education were both independently associated with a higher levels of leisure time physical activity. Silverwood et al (2011)[402] used latent class analysis to characterise participants according to their levels of physical activity at 31, 36, 43 and 53 years (in walking, cycling, and leisure time physical activity). The following classes were used to describe physical activity classes across these periods: two for walking (low and high), two for cycling (low and high), and three for leisure-time physical activity (low activity, sports and leisure activity, and gardening and do-it-yourself activities). Silverwood et al (2012)[403] examined associations between indicators of SEP (paternal occupational class at 4 years, own educational attainment at 26 years, and highest household's occupational class at 36 years) and physical activity measures (leisure-time activity at 36, 43, and 53 years, and sedentary time at 36 years, and walking during the working day at 36 and 43 years). Higher SEP was associated with greater participation in leisure-time physical activity but also greater time spent sedentary and less walking time.

This chapter builds on previous work in the NSHD by using, for the first time, objective measures of physical activity and direct measures of fat and lean mass. Further, it will examine whether there are cumulative benefits of activity across adulthood in leading to higher fat and lower lean mass.

#### 5.1.1.5 *Literature review summary*

A number of studies have reported inconsistent associations between physical activity (typically measured using self-report) and anthropometric measures of fat mass. Fewer studies have examined associations of objective measures of physical activity with direct measures of fat and lean mass. These studies have tended to show that higher physical activity is associated with lower fat mass and higher lean

mass, although few have been conducted in later adulthood and those that have produced inconsistent findings (eg, differences in association by age and sex). In addition, previous studies in adulthood have a number of limitations that suggest the need for further research: few have examined associations with both fat and lean mass, or considered associations with regional measures; most have only used measures of total physical activity energy expenditure (and have not considered different intensities of activity or sedentary time); few have made adjustment for potential confounders; none have used combined measures of physical activity which are likely to have less measurement error than single measures; and none have examined whether there are cumulative benefits of physical activity across adulthood in leading to lower fat and higher lean mass.

### 5.1.2 *Chapter objectives and hypotheses*

The objective of this chapter is to test the hypothesis that higher total physical activity energy expenditure is associated with lower fat and higher lean mass, and that there are cumulative benefits of activity across adulthood in leading to lower fat and higher lean mass. It was also hypothesised that greater time spent sedentary was associated with higher fat and lower lean mass.

## 5.2 **Methods**

### 5.2.1 *Explanatory variables*

The main explanatory variables used in this chapter are measures of physical activity obtained both objectively (at 60–64 years) and by self-report at (36, 43, 53 and 60–64 years).

Objective measures of physical activity were obtained using Actiheart monitors (CamNtech, UK) which were worn for up to five days by participants that attended a clinical research facility visit (where body composition outcome data were obtained) or were visited at home by a research nurse. The Actiheart is a small waterproof two-part device (connected by a wire) that is worn by attachment to the skin of the chest using two standard electrocardiogram electrodes (weight=8g).[404] Using two component parts, it measures both movement on the vertical axis (using an accelerometer) and heart-rate (using an electro cardio-gram); both of these are used to measure physical activity parameters in 60 second periods (epochs). A previous experimental study has shown that measures obtained using Actiheart are both precise and accurate with respect to movement (compared with calorimetry)

and heart-rate (compared with detailed electro cardio-gram readings) during rest, walking, and running on a treadmill.[405] All Actiheart data were centrally managed in Cambridge, UK. As previously described,[404] these data were calibrated to take into account individual differences in the relationship between physical activity intensity and heart rate. Calibration was conducted in two ways: first, for participants who completed a step test (8 minutes of increasing speed), these data were used for calibration; second, for participants who did not complete a step test (due to health complications such as angina and high blood pressure), sleeping heart rate, sex and body weight were used (the formulae is shown in Appendix 18). The most accurate form of calibration was used where available—using step test data (n=954) or, if not available, using sleeping heart rate, sex and body weight (n=356). In all cases analyses were restricted to those with valid data for both heart-rate and accelerometery measures. To ensure that physical activity estimates were reasonably accurate reflections of normal behaviour, only those with valid Actiheart data for a period of 48 hours or more were included in analyses, with 30 participants excluded due to low wear-time.

The following Actiheart-derived measures were chosen for use as explanatory variables in this chapter:

1. Total physical activity energy expenditure (kJ/kg/day)
2. Hours per day spent sedentary (≤1.5 METs)
3. Hours per day spent in light intensity physical activity (>1.5-3 METs)
4. Hours per day spent in moderate-vigorous physical activity (>3 METs)

In addition to objective measures, self-reported measures of leisure time physical activity were obtained at 36, 43 and 53 years by interview with nurses during home visits and at 60–64 years by a self-completion questionnaire (completed in advance of a clinic or nurse visit). At 36 years, participants were asked how often in the previous month they had participated in 27 different leisure time activities such as badminton, football and jogging using a modified Minnesota leisure time physical activity questionnaire.[406] At 43, 53 and 60–64 years, participants were asked how often they participated in any sports, vigorous leisure activities, or exercises. Participation was reported per month at 43 years, and in the previous 4 weeks at 53 and 60–64 years. Activity at each age was categorised into three groups: inactive (no participation), moderately active (participated one to four times) and most active (participated five or more times).

### 5.2.2 *Outcomes*

The outcomes used in this chapter are the main outcomes of this thesis, described in more detail in Chapter 2 (whole body measures of fat and lean mass, the ratio of these masses, appendicular lean mass, and android: gynoid fat mass ratio).

### 5.2.3 *Potential confounding variables*

Indicators of low SEP were considered potential confounders of associations with fat and lean mass as they were hypothesised as being related to lower physical activity levels[407] and higher fat and lower lean mass, by being distal measures of relevant lifestyle factors (such as greater total energy intake and lower protein intake). The indicators chosen for use were paternal occupational class (4 years) and own educational attainment (26 years); low SEP according to these indicators was previously found in the NSHD to be associated with lower participation in leisure time physical activities at 36, 43 and 53 years.[403]

In addition, physical health was considered a potential cofounder as it was hypothesised that participants with a limiting illness would be less physically active and have higher fat and lower lean mass. During clinic visits at 60–64 years, participants were asked whether they have any long-term illness, health problem or disability that limits their activities or work (no/yes).

As in other chapters, adjustment for adult height was made when using fat and lean mass as outcomes by the use of height-adjusted indices. The justification for adjusting for height when using body composition outcomes is presented in Chapter 2. In addition, shorter adult height has been associated with lower SEP,[408;409] and this could, as described above, confound main associations. As a sensitivity analyses, main analyses were repeated with no adjustment for adult height and results compared.

### 5.2.4 *Analytical strategy*

Physical activity measures at each age were presented and the associations between them assessed in each sex (using Pearson's correlations, chi-squared tests, and linear regression as appropriate). Associations of potential confounders

with physical activity measures and outcomes were then examined using linear regression.

Linear regression models were used to examine associations between objective measures of physical activity and outcomes. To ensure that coefficients were presented consistently all Actiheart-derived measures were converted into sex-specific standard deviation scores. As time spent in moderate-vigorous activity was highly right-skewed in both sexes it was transformed using the natural logarithm (+1 as values of 0 were recorded)[410] before being standardised, leading to a more normal distribution. Associations between self-reported physical activity at 36, 43, 53 and 60–64 years with outcomes were also examined using linear regression.

All models were conducted separately by sex as sex differences in associations have been found in previous studies and, given the large number of explanatory variables used, it was thought that stratification would enable a clearer comparison of effect sizes in each sex. Tests of interaction were conducted to formally test for evidence of sex interaction, and deviation from linearity assessed and outlined where evidence found ($P<0.05$).

As associations with fat mass may drive associations with lean mass, models using appendicular lean mass as an outcome were additionally adjusted for whole body fat mass index by its inclusion as a linear term. All models were conducted with additional adjustment for potential confounders (paternal occupational class at 4 years, own educational attainment at 26 years, and limiting illness at 60–64 years), each entered into models as categorical terms.

A series of different analyses were conducted to examine whether physical activity levels across adulthood have cumulative effects across life on fat and lean mass. First, associations between activity measures earlier in adulthood (at 36, 43 and 53) were adjusted for current activity levels (self-reported activity at 60–64 years), to test whether activity earlier in adulthood had additional benefits in leading to lower fat and higher lean mass than current activity levels. Next, a lifetime physical activity score was derived by adding together self-reported activity measures at 36, 43, 53 and 60-64 years (each age coded as 0 (inactive), 1 (moderately active) and 2 (most active)). This score—from 0 (inactive at all ages) to 8 (most active at all ages)—was then categorised into four groups of similar size (0–1, 2–3, 4–5, and 6–8), and associations with outcomes examined in each sex using linear regression. A graded association between this score and outcomes would be expected if there are

cumulative benefits of physical activity (assuming that activity at each age has the same size of effect).

To provide an additional source of evidence to test whether physical activity levels across adulthood have cumulative effects on fat and lean mass, the structured modelling approach described by Mishra et al (2009)[411] was used to determine whether accumulation models (either specifying equal or varying effect sizes at each age) fitted the data as well as a more complex saturated model (which contained parameters specifying accumulation, sensitive periods of activity at each age, and interactions between activity at each age). These models were compared using partial F-tests, with the resulting P-values from this comparison indicating how well each individual nested model fits the data: low P-values indicate that the nested model provides a different fit to the saturated model (and therefore does not fit the data as well), and large P-values indicate that the nested model provides a similar fit to the saturated model (and therefore does fit the data as well). Appendix 19 provides the formulae for the models used in these analyses. These models have been previously used in the NSHD by Cooper et al (2011)[209] to examine whether there are cumulative benefits of physical activity across adulthood (36, 43, and 53 years) for physical function at 53 years.

### 5.2.5 ***Sample used in analyses***

Unless otherwise specified, all analyses were restricted to those with valid body composition outcomes. When using objective measures of physical activity, analyses were restricted to 564 males and 598 females with valid data for all four main objectively assessed explanatory variables (total physical activity energy expenditure, time spent sedentary, in light and moderate-intensive activity) and potential confounders (paternal occupational class, own educational attainment, and limiting illness): 54 males and 63 females with valid physical activity and outcome data were excluded due to missing data for one or more potential confounder. When using self-reported measures of physical activity, analyses were restricted to 569 males and 642 females with valid data for activity measures at all ages (at 36, 43, 53 and 60–64 years) and potential confounders: 45 males and 60 females with valid physical activity and outcome data were excluded due to missing data for one or more potential confounder.

## 5.3 **Results**

### 5.3.1 ***Descriptive statistics***

Descriptive statistics for measures of physical activity are shown in Table 16. Males had higher total physical activity energy expenditure and spent more time in moderate-vigorous physical activity than females. In both sexes the majority of time was spent sedentary, with less time spent in light physical activity and even less time spent in moderate-vigorous intensity physical activity. More males than females self-reported participating in activities at 36 and 43 years, and levels of participation at 60–64 years were lower than at all previous ages in both sexes.

Correlations between objective measures of physical activity are shown in Appendix 20. Total energy expenditure was strongly correlated with intensity measures in the expected directions: strongly negatively correlated with time spent sedentary (–0.88 in males and –0.89 in females), and strongly positively correlated with time spent in light (0.61 in males and 0.67 in females) and moderate-vigorous intensity activity (0.90 in males and 0.86 in females).

Cross-tabulations of self-reported physical activity measures at 36, 43, 53 and 60–64 years are shown in Appendix 21. All measures were associated, with those active at one age more likely to be active at other ages than those inactive at that age. However few participants remained in the same category at all ages; only 71 males and 95 females were inactive at all ages and 45 males and 41 females most active at all ages.

Associations between objectively assessed and self-reported physical activity measures at 60–64 years are shown in Appendix 22. Those who reported participation in leisure time activity tended to have higher total physical activity energy expenditure and spend more time in moderate-vigorous activity, although these associations were weak.

Table 16. Physical activity descriptive statistics measured both objectively and by self-report

| | Males Mean (SD) (N=564) | Females Mean (SD) (N=598) | P# |
|---|---|---|---|
| Objective measures at 60-64y | | | |
| Total activity energy expenditure (kJ/kg/day) | 40.63 (15.89) | 36.84 (13.86) | <0.001 |
| Sedentary (≤1.5 METs) hours/day | 16.49 (2.26) | 16.51 (2.14) | 0.84 |
| Light intensity activity (>1.5–3 METs) hours/day | 5.98 (1.70) | 6.10 (1.66) | 0.21 |
| Moderate-vigorous intensity activity (>3 METs) hours/day* | 1.29 (1.23) | 1.18 (1.16) | <0.01 |
| Self-reported measures | | | |
| 36 years | N (%) | N (%) | |
| Inactive | 166 (29.17) | 227 (35.36) | |
| Moderately active | 161 (28.30) | 180 (28.04) | |
| Most active | 242 (42.53) | 235 (36.60) | 0.04 |
| | | | |
| 43 years | | | |
| Inactive | 241 (42.36) | 313 (48.75) | |
| Moderately active | 143 (25.13) | 168 (26.17) | |
| Most active | 185 (32.51) | 161 (25.08) | 0.01 |
| | | | |
| 53 years | | | |
| Inactive | 226 (39.72) | 274 (42.68) | |
| Moderately active | 138 (24.25) | 132 (20.56) | |
| Most active | 205 (36.03) | 236 (36.76) | 0.28 |
| | | | |
| 60-64 years | | | |
| Inactive | 345 (60.63) | 365 (56.85) | |
| Moderately active | 86 (15.11) | 114 (17.76) | |
| Most active | 138 (24.25) | 163 (25.39) | 0.34 |

Notes: #comparison of sexes, using t-tests or chi-squared test. METs=metabolic equivalent; analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes;*median(interquartile range) presented due to right-skew (p-value derived using the Mann-Whitney U test)

### 5.3.2 *Investigation of potential confounders*

Neither paternal occupational class nor own education attainment were associated with objectively measured total physical activity expenditure (Appendix 23). However, both low paternal occupational class and low educational attainment were associated with lower self-reported leisure time physical activity levels at all ages (36, 43, 53 and 60–64 years; Appendix 24). Low SEP was hypothesised as being associated with higher fat mass and lower lean mass; this will be tested in Chapter 6.

Those who reported a limiting illness at 60–64 years had lower total objectively measured total physical activity expenditure than those who did not, but associations with self-reported leisure time physical activity were weaker and inconsistent; there was little difference in physical activity levels at 36 and 60–64 years, but those who reported a limiting illness tended to undertake less leisure time physical activity at 53 years in males and 43 years in females. Those who reported a limiting illness had higher fat and lean mass indices ($P<0.001$ in all cases for both sexes, data not shown).

### 5.3.3 *Objectively measured physical activity and body composition outcomes*

Associations between objectively measured total physical activity energy expenditure at 60–64 years and body composition outcomes are shown in Table 17. Higher total physical activity energy expenditure was associated with lower fat mass, lower fat: lean and android: gynoid ratios, and lower whole body and appendicular lean mass (females only). Associations were stronger in females for all outcomes except android: gynoid ratio. After adjustment for fat mass, higher physical activity was associated with higher appendicular lean mass in both sexes.

Associations between objectively measured time spent sedentary, in light and moderate-vigorous intensity activity at 60–64 years and outcomes are shown in Table 18. Greater time spent sedentary was associated with higher fat mass, higher fat: lean ratio, and (weakly) with higher android: gynoid ratios. Associations were stronger in females for fat mass and fat: lean mass ratio. Greater time spent sedentary was associated with higher whole body and appendicular lean mass in females (but not males), but after adjustment for fat mass was associated with lower appendicular lean mass in both sexes.

Greater time spent in light intensity activity was associated with lower fat mass, lower fat: lean ratio, and (weakly) with lower android: gynoid ratios. Associations were stronger in females for fat mass and fat: lean mass ratio. Greater time spent in light intensity activity was associated with lower whole body and appendicular lean mass (females only), but after adjustment for fat mass was only weakly associated with higher appendicular lean mass in both sexes. When additional analyses were conducted with adjustment for sex (leading to higher power), greater time spent in light intensity activity was weakly associated with higher appendicular lean mass, after adjustment for fat mass (β(mean difference in appendicular lean mass index ($kg/m^2$))=0.03, 95% CI: 0.00 to 0.05).

Greater time spent in moderate-vigorous intensity activity was weakly associated with lower fat mass in both sexes, lower fat: lean mass ratio, but not with android: gynoid ratio. In contrast, greater time spent in moderate-vigorous activity was associated with higher whole body and appendicular lean mass—both before and after adjustment for fat mass. When additional analyses were conducted with adjustment for sex, greater time spent in moderate-vigorous activity weakly and not significantly associated with fat mass index (β(-0.17) 95% CI: -0.42 to 0.08).

The coefficients of the above associations were similar when adjustment was made for paternal occupational class, own educational attainment and limiting illness (Appendix 25 and Appendix 26). In light of the strong correlations between objectively assessed measures of physical activity they were not mutually adjusted for each other.

### 5.3.4 *Self-reported physical activity across adulthood and body composition outcomes*

Associations between self-reported physical activity at 36, 43, 53 and 60–64 years with outcomes are shown in Figure 8, and tabulated in Appendix 27. Those who were active tended to have lower fat mass and lower fat: lean and android: gynoid ratios; these associations were found at 36 and 43 years in females only, and at 53 and 60–64 years in both sexes. Males who were active at each age tended to have higher appendicular lean mass, while females who were active at each age tended to have lower appendicular lean mass. After adjustment for fat mass, both males and females who were active at each age tended to have higher appendicular lean mass; these associations were stronger in males at each age, and weak at 36 years in both sexes.

Associations with all outcomes were similar after additional adjustment for potential confounders (paternal occupational class, own educational attainment and limiting illness; Appendix 28). Associations of physical activity at 36, 43 and 53 years with outcomes were similar after adjustment for activity levels at 60–64 years (Appendix 29).

Associations between the lifetime physical activity summary score and body composition outcomes are shown in Table 19. In males, there was little evidence for graded association between this measure and fat mass, fat: lean or android: gynoid ratios, while those who were more active across adulthood tended to have higher whole body and appendicular lean mass. After adjustment for fat mass, the activity score was associated in a graded manner with higher appendicular lean mass, suggesting that there were cumulative benefits of activity across adulthood. Results of life course model comparisons supported this, as models specifying cumulative benefits of activity across adulthood in leading to higher appendicular lean mass (after adjustment for fat mass) fitted the data as well as the saturated model (P-value of comparison assuming equal and varying effect sizes=0.16 and 0.08, respectively; Appendix 30).

In females, there was evidence for graded association between the lifetime physical activity score and lower fat mass, and lower fat: lean and android: gynoid ratios (Table 19). Results of life course model comparisons supported this, with models specifying cumulative benefits of activity across adulthood in leading to lower fat mass, lower fat: lean and android: gynoid ratios all fitting the data as well as the saturated model (P-value of comparison assuming equal and varying effect sizes >0.4 in all cases; Appendix 30). As in males, there was evidence for cumulative benefits of activity across adulthood in leading to higher appendicular lean mass (after adjustment for fat mass), as shown by the association between a higher lifetime physical activity score and higher appendicular lean mass (Table 19). Comparison of life course models also supported this, with a model specifying cumulative benefits of activity across adulthood fitting the data as well as the saturated model (P-value of comparison assuming equal and varying effect sizes=0.06 and 0.1, respectively; Appendix 30).

In all the main analyses findings were similar when fat and lean mass were not adjusted for adult height (data not shown).

Table 17. Mean differences in body composition outcomes per 1 standard deviation increase in total physical activity energy expenditure (kJ/kg/day) at 60-64 years

| | Physical activity energy expenditure | | | | |
|---|---|---|---|---|---|
| | Males (n=564) | | Females (n=598) | | |
| Outcome models | β (95% CI) | P | β (95% CI) | P | P (sex interaction) |
| Fat mass index (kg/m$^2$) | -0.79(-1.08, -0.50) | <0.001 | -1.81(-2.17, -1.44) | <0.001 | <0.001 |
| Lean mass index (kg/m$^2$) | -0.17(-0.34, -0.01) | 0.04 | -0.36(-0.50, -0.21) | <0.001 | 0.10 |
| Fat: lean mass ratio | -2.44(-3.33, -1.54) | <0.001 | -6.46(-7.80, -5.12) | <0.001 | <0.001 |
| Android: gynoid fat mass ratio | -1.98(-3.24, -0.72) | <0.01 | -2.25(-3.18, -1.32) | <0.001 | 0.73 |
| Appendicular lean mass index (kg/m$^2$) | -0.03(-0.11, 0.05) | 0.45 | -0.14(-0.21, -0.07) | <0.001 | 0.04 |
| Appendicular lean mass index (kg/m$^2$), adjusted for fat mass index | 0.08(0.01, 0.14) | 0.03 | 0.08(0.03, 0.14) | <0.01 | 0.66 |

Note: analyses restricted to those with valid data for paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Table 18. Mean differences in body composition outcomes per standard deviation increase in hours spent sedentary, in light and moderate-vigorous physical activity at 60-64 years

a) Males (n=564)

| | Sedentary | | | Light | | | Moderate-vigorous | | |
|---|---|---|---|---|---|---|---|---|---|
| Outcome models | β (95% CI) | P | P# | β (95% CI) | P | P# | β (95% CI) | P | P# |
| Fat mass index (kg/m$^2$) | 0.35(0.05, 0.65) | 0.02 | <0.001 | -0.34(-0.64, -0.04) | 0.03 | <0.001 | -0.27(-0.57, 0.02) | 0.07 | 0.44 |
| Lean mass index (kg/m$^2$) | -0.02(-0.18, 0.15) | 0.86 | 0.07 | -0.06(-0.23, 0.11) | 0.49 | 0.03 | 0.13(-0.04, 0.29) | 0.13 | 0.92 |
| Fat: lean mass ratio | 1.30(0.39, 2.22) | <0.01 | <0.001 | -1.12(-2.04, -0.20) | 0.02 | <0.001 | -1.28(-2.19, -0.38) | <0.01 | 0.85 |
| Android: gynoid ratio | 0.53(-0.76, 1.81) | 0.42 | 0.44 | -0.49(-1.78, 0.80) | 0.46 | 0.21 | -0.54(-1.81, 0.73) | 0.40 | 0.34 |
| Appen. lean mass index (kg/m$^2$) | -0.04(-0.12, 0.04) | 0.34 | 0.04 | -0.01(-0.09, 0.06) | 0.73 | 0.02 | 0.11(0.04, 0.19) | <0.01 | 0.65 |
| Appen. lean mass index (kg/m$^2$), adjusted for fat mass index | -0.08(-0.15, -0.02) | 0.02 | 0.84 | 0.03(-0.04, 0.10) | 0.39 | 0.44 | 0.15(0.08, 0.22) | <0.001 | 0.26 |

b) Females (n=598)

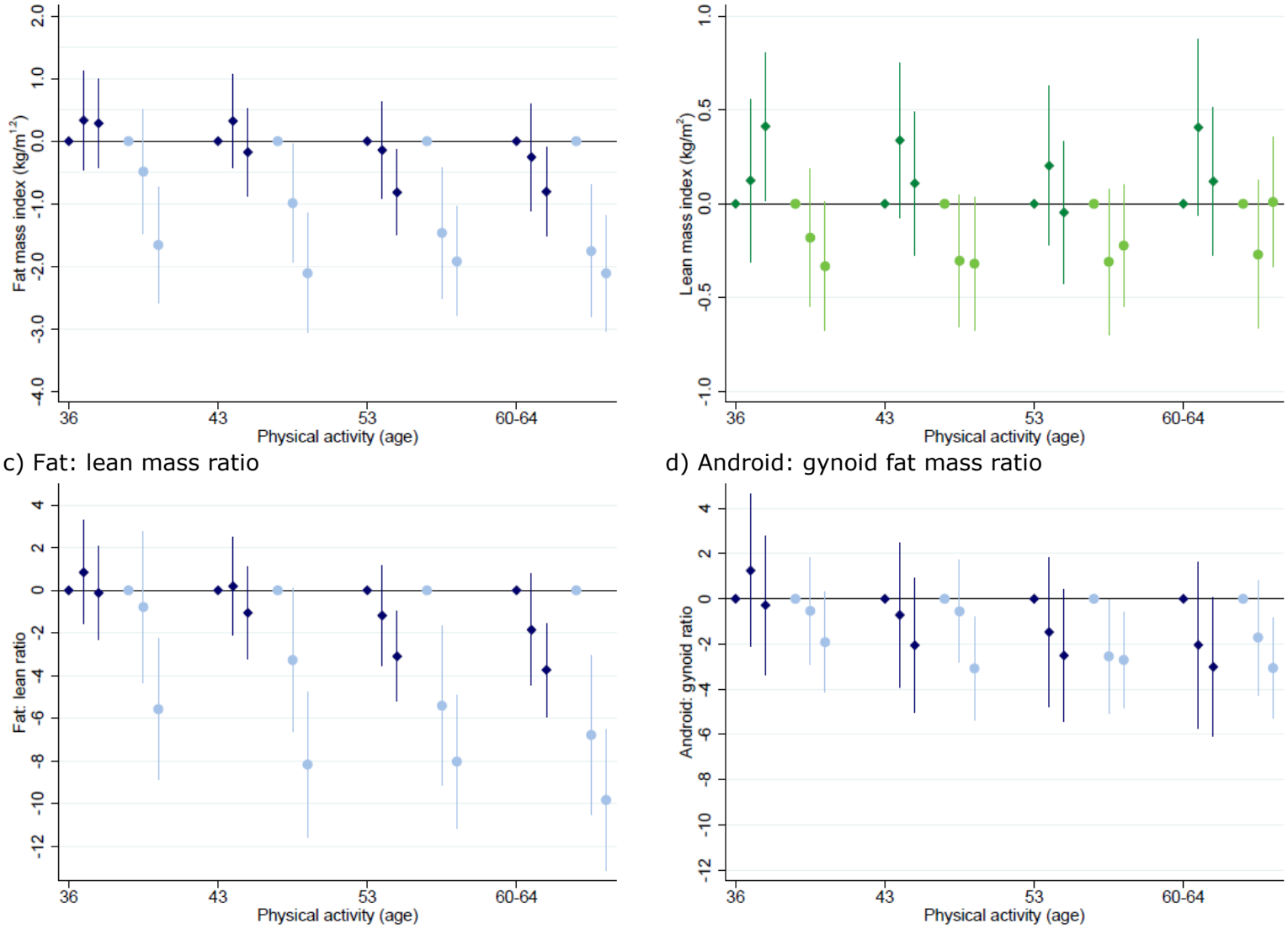
| | Sedentary | | Light | | Moderate-vigorous | |
|---|---|---|---|---|---|---|
| Outcome models | β (95% CI) | P | β (95% CI) | P | β (95% CI) | P |
| Fat mass index (kg/m$^2$) | 1.32(0.94, 1.69) | <0.001 | -1.62(-1.99, -1.25) | <0.001 | -0.08(-0.47, 0.32) | 0.71 |
| Lean mass index (kg/m$^2$) | 0.19(0.04, 0.34) | 0.01 | -0.31(-0.46, -0.17) | <0.001 | 0.14(-0.01, 0.29) | 0.06 |
| Fat: lean mass ratio | 4.90(3.51, 6.29) | <0.001 | -5.60(-6.97, -4.23) | <0.001 | -1.11(-2.55, 0.33) | 0.13 |
| Android: gynoid ratio | 1.16(0.21, 2.10) | 0.02 | -1.52(-2.46, -0.57) | <0.01 | 0.22(-0.73, 1.17) | 0.65 |
| Appen. lean mass index (kg/m$^2$) | 0.07(0.00, 0.14) | 0.04 | -0.14(-0.20, -0.07) | <0.001 | 0.09(0.02, 0.16) | 0.01 |
| Appen. lean mass index (kg/m$^2$), adjusted for fat mass index | -0.09(-0.14, -0.03) | <0.01 | 0.06(0.00, 0.11) | 0.05 | 0.10(0.05, 0.15) | <0.001 |

Notes: #P-value for sex interaction term; Appen=appendicular; sedentary=≤1.5 metabolic equivalent (METs); Light=>1.5–3 METs; Moderate-vigorous=>3 METs; analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Figure 8. Mean difference in body composition outcomes (95% confidence intervals) in those who were moderately and most active (compared with inactive) at 36, 43, 53 and 60-64 years

a) Fat mass index (kg/m$^{1.2}$)

b) Lean mass index (kg/m$^2$)

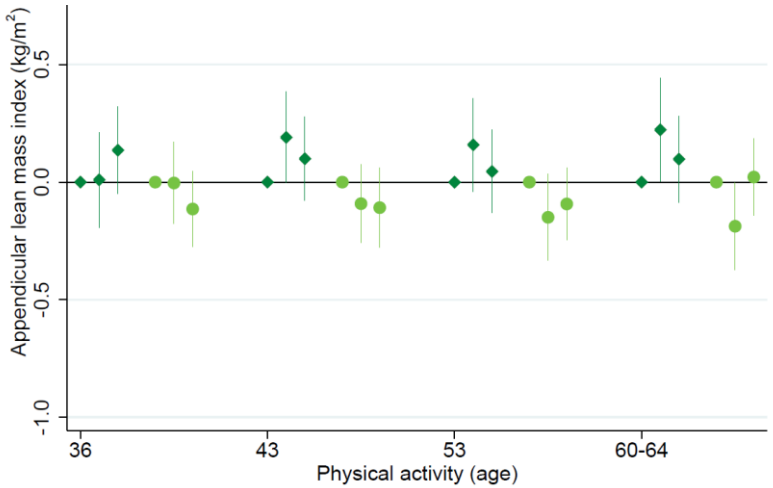



Note:
The point estimates show, from left to right, those who were inactive, moderately, and most active at each age;
males=dark-coloured diamonds;
females=light-coloured circles

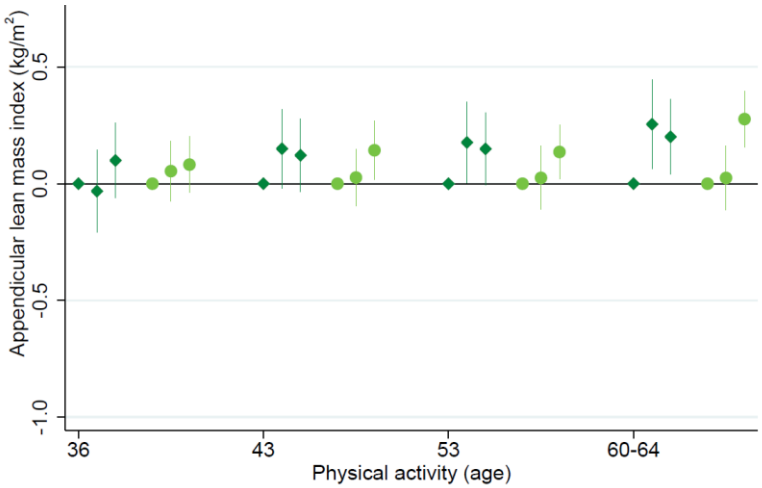
c) Fat: lean mass ratio

d) Android: gynoid fat mass ratio

e) Appendicular lean mass (kg/m$^2$)




f) Appendicular lean mass index (kg/m$^2$), adjusted for fat mass index (kg/m$^{1.2}$)




Note: activity at each age was coded as inactive (no participation), moderately active (participated one to four times) and most active (participated five or more times), in the previous month (36 years), per month (43 years) and in the previous 4 weeks (53 and 60-64 years); sample sizes in the different periods were (male/female): 569/642; analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Table 19. Mean difference in body composition outcomes (95% confidence intervals) by lifetime physical activity score

| Lifetime activity score | N (%) | Fat mass index (kg/m$^2$) | Lean mass index (kg/m$^2$) | Fat: lean ratio | Android: gynoid ratio | Appen. lean mass index (kg/m$^2$) | Appen. lean mass index (kg/m$^2$) + FM |
|---|---|---|---|---|---|---|---|
| Males | | | | | | | |
| 0-1 | 126 (22.14) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | |
| 2-3 | 150 (26.36) | 0.57(-0.28, 1.43) | 0.12(-0.36, 0.59) | 1.51(-1.10, 4.13) | -1.39(-5.07, 2.28) | 0.04(-0.19, 0.26) | -0.04(-0.23, 0.15) |
| 4-5 | 153 (26.89) | 0.80(-0.05, 1.65) | 0.42(-0.05, 0.89) | 1.50(-1.10, 4.11) | -0.59(-4.24, 3.07) | 0.18(-0.04, 0.40) | 0.07(-0.12, 0.27) |
| 6-8 | 140 (24.6) | -0.64(-1.50, 0.23) | 0.19(-0.29, 0.67) | -3.27(-5.93, -0.61) | -4.68(-8.41, -0.95) | 0.14(-0.09, 0.36) | 0.22(0.02, 0.42) |
| P(trend) | | 0.20* | 0.25 | 0.02* | 0.03 | 0.12 | 0.01 |
| P# | | <0.001 | 0.12 | <0.001 | 0.93 | 0.20 | 0.70 |
| | | | | | | | |
| Females | | | | | | | |
| 0-1 | 153 (23.83) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 2-3 | 197 (30.69) | -0.75(-1.80, 0.30) | -0.39(-0.79, 0.00) | -1.37(-5.13, 2.40) | -2.05(-4.60, 0.50) | -0.15(-0.34, 0.04) | -0.06(-0.20, 0.08) |
| 4-5 | 151 (23.52) | -2.18(-3.30, -1.06) | -0.24(-0.66, 0.18) | -8.51(-12.51, -4.50) | -1.90(-4.62, 0.81) | -0.09(-0.29, 0.11) | 0.17(0.03, 0.32) |
| 6-8 | 141 (21.96) | -2.94(-4.08, -1.80) | -0.48(-0.91, -0.06) | -11.20(-15.27, -7.12) | -4.72(-7.48, -1.95) | -0.16(-0.37, 0.04) | 0.19(0.04, 0.34) |
| P(trend) | | <0.001 | 0.07 | <0.001 | <0.01 | 0.20 | <0.01* |

Notes: *evidence for departure from linearity (P<0.05); #P-value for sex interaction term; lifetime physical activity score derived by adding the physical activity measures at 36, 43, 53 and 60-64 years, from none-lowest (0-1) to highest (6-8) activity; activity at each age was coded as 0 inactive (no participation), 1 moderately active (participated one to four times) and 2 most active (participated five or more times), in the previous month (36 years), per month (43 years) and in the previous 4 weeks (53 and 60-64 years); analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes; FM=fat mass index (kg/m$^{1.2}$)

## 5.4 **Discussion**

### 5.4.1 ***Main findings***

The main findings of this chapter are cross-sectional associations between objectively assessed higher total physical activity energy expenditure and lower fat mass and, after adjustment for fat mass, higher appendicular lean mass at 60–64 years. Analyses of different activity intensities suggested that greater time spent in light intensity activity was associated with lower fat mass, while greater time spent in moderate-vigorous was associated with higher appendicular lean mass (both before and after adjustment for fat mass). Greater time spent sedentary was associated with higher fat mass and, after adjustment for fat mass, lower appendicular lean mass. Sex differences were found, with associations between activity measures and fat mass typically stronger in females.

Participation in leisure time physical activity at 60–64 years, assessed by self-report, was also associated with lower fat and higher appendicular lean mass (after adjustment for fat mass). Using comparable measures earlier in adulthood (53, 43, and 36 years), there was evidence for cumulative benefits of activity in leading to lower fat mass in females, and higher appendicular lean mass in both sexes (after adjustment for fat mass).

The above associations were similar after adjustment for indicators of SEP (paternal occupational class and own educational attainment) and limiting illness at 60-64 years.

### 5.4.2 ***Comparison with previous studies***

Findings from this chapter build on the small number of previous studies, described in the literature review of this chapter, that have used objective measures of physical activity in relation to direct measures of fat and lean mass. These have tended to show that measures of higher physical activity are associated with lower fat and higher lean mass, although findings are not always consistent and differ by sex and age. Of these studies, most have been conducted in adolescence or early adulthood, few have examined associations with different intensities of activity, few have examined associations with both fat and lean mass, or made adjustment for potential confounders, and none have used combined measures of objectively assessed physical activity (measures obtained by both heart rate and accelerometer). In addition, to the author's knowledge, no previous studies have

examined whether physical activity levels across adulthood have cumulative benefits for fat and lean mass.

Findings from this chapter build on the previous NSHD study which found participation in leisure time physical activity at 36 years was associated with lower risk of obesity in females, but not males, at 36 years.[399] The analyses conducted in this chapter extend these findings by using a longer period of follow-up, using multiple measures of activity measured both objectively and by self-report, and by using direct measures of fat and lean mass.

### 5.4.3 *Explanation of findings: physical activity and fat mass*

Associations between higher total physical activity energy expenditure and lower fat mass were driven primarily by variations in light intensity activity. Both light and moderate-vigorous intensities of activity would be expected to contribute to greater total energy expenditure and hence lower energy balance, ultimately leading to lower fat mass over time. Light intensity activity may have had a particularly pronounced association with fat mass as more time was spent in this intensity of activity, therefore making a greater impact on total energy expenditure. The benefits of light intensity activity are likely to be particularly relevant for those in older ages—the public health implications of these findings are discussed in Chapter 7.

While moderate-vigorous activity may be particularly beneficial in leading to lower fat mass (over and above its contribution to total energy expenditure), analyses presented in this chapter cannot confirm or refute this, as all objective measures of activity were strongly correlated, and their mutual adjustment was judged to be inappropriate. Similarly, associations between greater time spent sedentary and higher fat mass may be explained by lower energy expenditure among those who were more sedentary; there could also be particular mechanisms (albeit not currently discovered) which link sedentary time with fat mass, over and above this relationship, although these have been suggested for cardiovascular outcomes but not fat mass.[366;367] While these measures were very strongly correlated in this cohort, this may not be the case in other cohorts where activity patterns differ.

The weaker cross-sectional associations between greater objectively assessed higher total physical activity energy expenditure and lower fat mass in males could be explained by sex differences among other behaviours that impact on fat mass. For example, for a given level of physical activity, males may tend to have greater

energy intake than females. Alternatively, the Actiheart may be less capable of capturing activities that males more commonly undertake, such as those which involve less movement across the vertical axis (eg, activities using solely the arms).

Cross-sectional associations between greater participation in leisure time activities and lower fat mass were also weaker in males, and associations between greater leisure time activity at earlier ages and lower fat mass began earlier for females (36 years) than males (53 years). This may be explained by sex differences in energy intake and total physical activity energy expenditure at earlier ages. During younger ages (36 and 43 years) males who undertook greater leisure time activity may have been more inactive in other domains (such as occupational-based physical activity), leading to no difference in total physical activity energy expenditure (and therefore not affecting energy balance). In support of this, at 36 years in the NSHD participation in leisure time activity was not associated with obesity at 36 years in males (but was in females),[399] and greater participation at 36 years was associated with more sedentary (sitting) time in the working day, particularly strongly in males.[403] Previous studies examining associations between physical activity and fat mass have either found no sex difference or reported mixed findings (with associations either being stronger or only present in males or females). Experimental studies in which physical activity interventions are given alongside controlled diets have suggested, contrary to findings from this chapter, that a given amount of physical activity may have stronger effects in leading to lower fat mass in males than females.[355;412] This has been suggested as being due to sex differences in types of fat, with males tending to have more lipolytically-responsive fat mass stores than females.[355]

Higher physical activity levels were also associated with lower android: gynoid ratio. Further analyses showed that these associations were driven by the separate associations with lower android and gynoid fat mass, with stronger relative associations for the former (data not shown). This suggests that physical activity may have stronger effects on abdominal than peripheral fat mass. The responsiveness of abdominal fat mass to physical activity is supported in experimental studies which have found intensive aerobic exercise interventions typically lead to losses in visceral abdominal fat,[413] although studies to the author's knowledge have not examined effects on gynoid fat mass.

While it was hypothesised that higher physical activity leads to lower fat mass, analyses conducted in this chapter cannot distinguish the temporal direction of the

associations found. For example, as previously outlined, those with higher fat mass may, through psychological and physiological barriers, tend to be less physically activity. As such, associations could be explained by reverse causality, or be bi-directional in nature. However, findings from experimental studies (outlined in the literature review of this chapter) suggest that physical activity interventions lead to reductions in fat mass, supporting the hypothesised directions of associations.[152;390-392] In addition, associations between higher physical activity and lower fat mass were similar after adjustment for limiting illness at 60-64 years. This may have confounded associations between higher physical activity and lower fat mass if the principle direction of association was from limiting illness to higher fat mass, which then impaired activity levels.

### 5.4.4 *Explanation of findings: physical activity and lean mass*

The association between higher total physical activity energy expenditure and higher appendicular lean mass was driven by variations in moderate-vigorous activity, which was associated with higher appendicular lean mass both before and after adjustment for fat mass. It may be that this intensity of activity captured activities which are particularly beneficial for muscle mass. These activities may include resistance exercise, which have been found in intervention studies to stimulate gains in muscle mass.[184] Resistance exercise would presumably lead to increased heart rate, and could be captured using the Actiheart's heart rate monitor, but would likely involve only limited movement along the vertical axis, and is unlikely to be captured using the accelerometer. However, associations are unlikely to be solely driven by participation in resistance exercise. Of those with valid body composition outcome data, the vast majority of participants (85% of both sexes) reported no participation in exercises with weights in the last 4 weeks at 60–64 years. In addition, further analyses showed similar associations between moderate-vigorous intensity physical activity and lean mass were found when restricted to participants who reported no participation. Leisure time activities such as running require muscle strength and power to lift the weight of the body, and may also lead to higher lean mass.

There was evidence for cumulative benefits of leisure time activities in leading to higher appendicular lean mass after adjustment was made for fat mass, a potential confounder. As with previously reported associations with fat mass, evidence for cumulative benefits of activity across adulthood for lean mass may be explained by activity at each age leading to gains in lean mass which then track into later adulthood. These associations were stronger in males than females; this may

suggest that males were more likely to participate in the types or intensity of activities which stimulated gains in lean mass.

As with associations between physical activity and fat mass, analyses conducted cannot distinguish the directions of associations. There is however consistent evidence that specific exercise interventions lead to gains in muscle mass, supporting the hypothesised directions of associations.[184] In addition, findings were also found after adjustment for potential confounders, providing further support.

### 5.4.5 *Methodological considerations and limitations*

While multiple physical activity measures were used in this chapter, there may be other parameters which are more closely related to body composition outcomes. For example, it has been suggested that continuous unbroken bouts of sedentary time are particularly detrimental and lead to gains in fat mass, independent of the total duration of time spent sedentary.[414] However, the use of objective measures of sedentary behaviour and physical activity is a relatively new development in epidemiology, and there is no consensus on which parameters are most important for body composition outcomes. The analyses conducted in this chapter are therefore likely to contribute to this on-going field of research.

In this chapter associations were independent of indicators of SEP (paternal occupational class, own educational attainment), considered to be distal measures of relevant lifestyle factors (such as greater total energy intake and lower protein intake), which may confound associations. While further analyses showed similar results were found when repeated with additional adjustment for other indicators of SEP (occupational class at 53 years and household income at 60–64 years; results not shown), there may be residual confounding by these more proximate factors. For example, energy intake may confound associations with fat mass, and protein intake may confound associations with lean mass. One study found that associations between physical activity and fat mass were similar before and after adjustment for fat intake,[190] suggesting that associations were not confounded.

As in previous chapters, analyses were restricted to those with valid data for potential confounders (paternal occupational class, own educational attainment and limiting illness). While this could have introduced bias, this is unlikely to have a substantial impact on findings as this restriction resulted in only small numbers of participants being excluded. In support of this, further analyses (data not shown) showed similar results when analyses were repeated on the maximum available

sample size. Loss to follow-up in the NSHD may have also introduced bias. The predictors of providing full body composition outcome data at 60-64 years were analysed in Chapter 2 which showed that less physically active and heavier participants at 53 years were less likely to provide full body composition outcome data at 60-64 years. This source of attrition was therefore likely to lead to reduced power to detect the association between lower physical activity and higher fat mass.

Comparable measures of leisure time physical activity were used in this chapter to examine whether there were cumulative benefits of physical activity across adulthood in leading to lower fat and higher lean mass. As discussed previously, greater participation in leisure time activity may be sufficient to result in higher total physical activity energy expenditure. As such, measures of total physical activity energy expenditure across adulthood may be more closely related to fat mass, providing stronger evidence for cumulative benefits of activity in leading to lower fat mass. However, these measures were not available in the NSHD and objective measures of total physical activity energy expenditure are a relatively recent development. In addition, leisure time physical activity is an important modifiable target, and may therefore be useful to consider in analyses; other domains, such as occupational physical activity, may be less modifiable. There was evidence that leisure time physical activity was cumulatively beneficial for higher lean mass, suggesting that it captured the types of activities which are important in leading to gains or preservations in lean mass.

### 5.4.6 ***Strengths***

Chapter 1 presents the overall strengths of the NSHD, while the strengths specific to this chapter are outlined below.

Strengths of this chapter include the extensive measures of physical activity used, unavailable in previous studies. Objectively assessed measures were used that combined heart rate and accelerometer data. These measures may have resulted in greater accuracy and precision, leading to a more accurate estimate of the effect size of associations with fat and lean mass,[341] and validated findings using self-reported measures. The use of the Actiheart enabled different intensities of activity to be investigated, providing evidence that light intensity of activity was particularly related to lower fat mass, while moderate-high intensity of activity was particularly related to higher lean mass. These are likely to have important public health implications, and will be discussed in Chapter 7.

In addition to objective measures, the repeat measures of physical activity across adulthood used in this chapter are another strength. These were constructed to be comparable at each age and their use enabled a life course perspective to be applied to physical activity in relation to fat and lean mass. In addition to using a lifetime physical activity score, life course model comparisons were used to test whether there was evidence for cumulative effects. The first method provides a simple indicator of the likelihood of cumulative benefits, but assumes that effect sizes are the same at each age, while the latter enables the effect sizes to vary at each age. To the author's knowledge, no previous studies have examined whether there are cumulative benefits of activity across adulthood in leading to lower fat and higher lean mass. These analyses are therefore a major strength of this chapter.

Potential confounders were considered in this chapter (indicators of SEP and limiting illness at 60–64 years), and associations were similar after taking these into account in analyses, supporting the hypotheses.

### 5.4.7 ***Conclusions and links to other chapters***

This chapter found that in both sexes objectively measured higher total physical activity energy expenditure at 60-64 years was associated with lower fat mass and, after adjustment for fat mass, higher appendicular lean mass. Using leisure time activity measures collected across adulthood (36, 43, 53 and 60-64 years) there was evidence in females but not males of cumulative benefits of greater activity in leading to lower fat mass, and in both sexes of cumulative benefits of greater activity in leading to higher appendicular lean mass (after adjustment for fat mass).

In this chapter and in Chapters 3 and 4 associations were independent of indicators of SEP, considered to be potential confounders. The following chapter examines the separate associations between SEP in childhood and adulthood with fat and lean mass, and examines whether explanatory factors considered in this chapter (physical activity measures) and Chapters 3 and 4 (birth weight and measures of growth after birth) mediate these associations. This may be expected given associations found in this chapter between indicators of low SEP and low leisure time physical activity levels.

# 6. Chapter 6: Socioeconomic position across life and body composition

Main objective: to examine whether indicators of SEP across life are associated with body composition outcomes at 60–64 years.

Previous chapters examined associations between explanatory factors across life (birth weight, an indicator of prenatal growth (Chapter 3), measures of growth after birth (Chapter 4), and physical activity in adulthood (Chapter 5)) with body composition outcomes. In each chapter associations were independent of SEP, considered a potential confounder because lower SEP was hypothesised to be associated with higher fat and lower lean mass, and with growth and physical activity. This chapter examines associations between indicators of SEP across life with body composition outcomes, and examines whether the explanatory factors explored in previous chapters mediate these associations.

## 6.1 Introduction

There is a long-standing interest in the relationship between socioeconomic factors and health.[415-418] A series of government-commissioned reports—the Black Report in 1980,[419] the Whitehead report in 1987,[420] the Acheson Report in 1998[421] and most recently the Marmot Review in 2010[291]—have shown that morbidity and mortality risks are typically higher in those more socioeconomically disadvantaged eg, those with lower wealth, income, or of lower occupational class. The effect sizes are typically substantial: the Marmot Review reported a 7-year difference in life expectancy and 17-year difference in disability-free life expectancy among those in the least compared with most deprived socioeconomic areas.[291] In all of these reports, the importance of socioeconomic factors in both early and adult life were suggested to be important in influencing health in adulthood. This justifies a life course approach to the study of socioeconomic differentials in health.[418] This is also supported by analyses in the NSHD which have found lower SEP in both childhood and adulthood to be independently associated with worse physical function and higher BMI.[422;423]

A number of terms have been used to describe socioeconomic exposures that relate to both health and body composition—these include social class, socioeconomic status, and prestige. These are related terms which have historically been used inconsistently.[424] More recently, SEP has been suggested as the appropriate term

for use in epidemiological research,[424] and this has been broadly accepted.[415;418;425] SEP is an umbrella term used to refer to the position "individuals or groups hold within the structure of a society." (p.7)[425] Low SEP indicates relative deprivation and may, in some contexts, indicate absolute deprivation. SEP can be indicated, but not directly measured, by a wide range of individual-level variables including educational attainment, occupational classification, income, wealth, and household conditions.[425;426] The distribution of these indicators in a population varies depending on the historical period and population investigated.[425] For example, secular trends of increased higher-level education have occurred in the second half of the 20th century in the UK,[425] while in some developing countries higher-level education remains relatively rare. The relevance of these indicators to SEP may therefore change where phenomena become, or cease to become, socially stratified.

Indicators of SEP can be used to reflect SEP across life. In childhood, SEP is typically indicated by parental occupational class, parental education and indicators of housing conditions, while in adulthood SEP is typically indicated by occupational class, income, and wealth.[427] Although SEP tends to track across life,[291;428;429] individuals may remain in the same relative position or move upwards and/or downwards, reflecting social mobility.

A number of aetiological pathways have been proposed to explain associations between SEP and health: these have broadly suggested that such exposures operate through differences in behaviours and cultural traditions (eg, diet and physical activity), material assets (eg, quality of housing), and/or psycho-social pathways (eg, levels of chronic stress) that influence health.[415] Selection theories suggest that health is causally related to subsequent socioeconomic exposures (eg, those of worse health are more likely to be consequently exposed to deleterious socioeconomic exposures), while life course explanations emphasise the importance of exposures across life on subsequent health, and consider bi-directionality in the associations of interest.[415;418] Differences in body composition have been suggested as being on the causal pathway linking SEP to health outcomes, such that SEP influences body composition which in turn affects health.[63;430;431] There is therefore substantial interest in examining associations between socioeconomic factors and body composition. Given that those of lower SEP tend to have worse health and physical functioning,[422;432] it may be expected, given the detrimental impacts of higher fat and lower lean mass (described in Chapter 1), that those of lower SEP have higher fat and lower lean mass.

Associations between SEP and fat and lean mass in adulthood are likely to be caused by the socioeconomic patterning of the determinants of these masses (outlined in Chapter 1), particularly physical activity and diet. The patterning of these determinants may in turn be due to a series of more distal factors, acting on both the individual (adult SEP), or parents or guardians (childhood SEP). These include knowledge of the behaviours which influence fat and lean mass, and the capacity and motivation to modify behaviour in response to such knowledge, social norms and stigma associated with fat and lean mass levels (eg, higher fat and lower lean mass), and access to resources such as leisure activities and/or dietary choices (restricted in turn by income, area of residence and behavioural/cultural traditions).[215;433-435]

SEP at different life stages may relate to fat and lean mass through both shared and distinct mechanisms. SEP in childhood may be particularly related to patterns of growth both before and after birth which have lasting effects:[422] in this thesis lower SEP in childhood was associated with lower weight gain in infancy and greater weight gain in later childhood and adolescence (Chapter 4). SEP in childhood may also be related to body composition outcomes through the tracking of SEP from childhood into adulthood.[291] Additionally, SEP in both childhood and adulthood may relate to behavioural factors in adulthood: analyses in Chapter 5 found that low childhood SEP and low own educational attainment were associated with lower leisure time physical activity participation across adulthood (36, 43, 53 and 60-64 years). More detailed analyses at 36 years in the NSHD found that associations between lower SEP in childhood and lower leisure time physical activity were not fully explained by adult SEP measures (in females only).[403] Analysing associations of SEP in both early and adult life with fat and lean mass may therefore be useful in understanding aetiology.

In addition to using indicators of SEP in both early and adult life, the use of multiple indicators at one particular stage in life may also be informative, as each indicator may reflect particular dimensions of SEP that are more or less relevant to the outcome of interest.[425] For example, research has found indicators of SEP in adulthood (educational attainment, occupational class and income) to be differentially associated with different health outcomes.[436] This may also be the case for body composition outcomes. For example, in relation to fat mass, higher educational attainment may be particularly related to the acquisition of related knowledge and cognitive traits (eg, knowledge of the factors which impact on energy balance, and a capacity to act on that knowledge), while a high income may

be particularly related to the capacity to purchase particular foods which help to lower energy balance.

While a wide range of indicators of SEP have been used in epidemiological research In the UK, occupational classifications have been used most frequently. The Registrar General's social classification was used in official UK statistics from 1911–2000 and classifies occupations according to social standing and occupational skill.[426] Other classifications have more explicit theoretical foundations and can be considered to be derived from the sociological theories of Karl Marx or Max Weber.[437] Scales derived from the former focus on ownership and control of capital (eg, the Wright classification);[426;437] those derived from the latter classify occupations on the basis of working relations that capture information about the extent of autonomy and opportunity in the workplace (eg, the Erikson and Goldthorpe class scheme, and The National Statistics Socio-economic Classification (NS-SEC)). As of 2000, NS-SEC became the official classification used in UK statistics, following criticism of the Registrar General's social classification as having a largely subjective theoretical basis—that the class occupations are placed in is based on notions of prestige and skill that are largely subjective and historically evolving,[438] and may have been partly determined by knowledge of health differences, leading to circular reasoning.[439] While the most appropriate occupational classification system is an active area of academic debate—[440;441] including the purported utility of NS-SEC[442-444]—each have been used in epidemiological research focusing on health and, to a lesser extent, body composition.

A number of epidemiological studies have examined associations between indicators of SEP across life and measures of body composition in adolescence and adulthood. The following sections summarise and discuss these: first where BMI was used (systematic and narrative review articles are summarised), and second where direct measures of fat and/or lean mass have been used in adolescence or adulthood (summarised in Table 20). Associations with childhood and adult SEP are described separately; studies using own educational attainment were categorised in the latter group although this could be considered an indicator of SEP in both childhood and adulthood, as it reflects the result of childhood experiences and is related to subsequent employment opportunities in adulthood.[425] Studies which used DXA or any measure of lean mass were included regardless of publication date; adult studies using other measures of fat mass were included if they were published after systematic reviews in 2009 (childhood SEP)[445] or 2007 (adult SEP).[446] These included studies using BIA.

Table 20. Summary of studies that examined associations between socioeconomic position (in early or adult life) and whole body fat and/or lean mass in adolescence or adulthood

| Study | N | Location /majority ethnicity | Age at outcome measure (years) | SEP indicator/s | Body composition measure | Main adjustments | Fat mass association +(positive) —(negative) | Lean mass association +(positive) —(negative) |
|---|---|---|---|---|---|---|---|---|
| Boot et al, 1997[198] | 403 | Netherlands /Caucasian | 4–20 | Parental occ. class, paternal education | DXA | None | Males: no assoc.<br>Females: — | No assoc. |
| Lantz et al, 2008[195] | 203 | Sweden /Caucasian | 15–20 | Paternal education | DXA | Weight, height, Sex | — | + |
| Ekelund et al, 2005[447] | 445 | Sweden /Caucasian | 17 | Maternal education | Air-displ. | Birth weight | Males: no assoc.<br>Females: — | N/A |
| Gigante et al, 2007[199] | 2250 | Brazil /Mixed | 18 | Household income | BIA | Height | Males: +<br>Females: N/A | Males: +<br>Females: N/A |
| Seppanen-Nuijten et al 2009[196] | 5789 | Finland /Caucasian | >30 | Own education | BIA | BMI | N/A | (Weak) + |
| Brennan et al, 2009[448] | 1110 | Australia /Mixed | 49 (20–92) | Area-based deprivation score | DXA | None | Males: N/A<br>Females: — | Males: N/A<br>Females: no assoc |
| Yliharsila et al, 2008 [197] | 1917 | Finland /Caucasian | 56–69 | cSEP: Paternal occ. class at birth<br>aSEP: Own occ. class | BIA | Height, age | CSEP:<br>Males: —<br>Females: no assoc.<br>ASEP:<br>Both sexes: — | CSEP:<br>Both sexes: no assoc.<br>ASEP:<br>Males: no assoc<br>Females: — |
| Al-Qaoud et al, 2011[449] | 5533 | UK /Caucasian | 55–79 | Own occupational grade | BIA | Height | N/A | Males: no assoc.<br>Females: — |
| Visser et al, 1998[95] | 753 | USA /Caucasian | 72–95 | Own education | DXA | None | No assoc. | No assoc. |

Notes: CSEP=childhood socioeconomic position; ASEP=adulthood socioeconomic position; N/A=not applicable (where association not examined); negative association indicates that higher SEP was associated with lower fat or lean mass; BIA=bioelectrical impedance analysis; BMI=body mass index; DXA=dual energy X-ray absorptiometry; Air-displ=air-displacement

### 6.1.1 *Literature review: socioeconomic position and body composition*

#### 6.1.1.1 *Early life socioeconomic position and fat mass*

Two systematic reviews have examined associations between SEP in childhood and adult obesity, typically defined using BMI. Senese et al (2009)[445] reviewed 30 studies, the majority of which indicated childhood SEP using paternal occupational class (26 studies), while others used parental education, household conditions, or measures of familial economic distress. The authors concluded that lower SEP in childhood was associated with higher adult BMI in females (found in 14 of 20 studies), but not males (associations found in 4 of 15 studies). These associations were also found in the single study which used direct measures of fat mass (using BIA in females). Associations were more frequently observed when SEP was ascertained prospectively in childhood rather than retrospectively recalled in adulthood, suggesting that retrospective recall may have introduced measurement error and bias. Associations were typically partly attenuated after adjustment for SEP in adulthood, suggesting that tracking of SEP into adulthood partially explains the associations found. Similar associations were reported in a systematic review of 16 studies in the UK,[450] and in an earlier systematic review in 1999 of 12 studies from multiple countries.[166]

As previously outlined in Chapter 1, BMI is a surrogate indicator of fat mass and does not distinguish between fat and lean mass; associations found between SEP and BMI may therefore be due to associations with fat mass, lean mass, or both. There is therefore a need to examine associations between SEP and direct measures of fat mass. The use of direct measures of fat mass also enables a more accurate estimate of the effect size of the SEP-fat mass association. If SEP differentially influences body composition in opposing directions—with lower SEP associated with higher fat mass and lower lean mass—the use of BMI may result in an underestimation of the SEP-fat mass association.[451;452]

Four studies have examined associations between SEP in childhood/early life and direct measures of fat mass. Two studies using DXA reported associations of low paternal education and occupational class with higher fat mass (in females but not males),[198] or of low paternal education with higher fat mass (in both sexes).[195] In a study of 17 year-olds, low maternal educational attainment was associated with higher fat mass (measured using air-displacement) in females, but not males.[447] Finally, one study reported an association between low paternal occupation at birth

and higher fat mass in males but not females in later life (at ~61 years, measured using BIA).[197]

#### 6.1.1.2 *Adult socioeconomic position and fat mass*

Three systematic reviews have examined associations between SEP in adulthood and BMI or weight gain in adulthood. McLaren (2007)[446] conducted a systematic review examining cross-sectional associations between SEP in adulthood and obesity. Three hundred and thirty-three studies were identified, with participants from both low and high-income countries. Obesity was typically defined as high BMI. The associations found varied depending on the income level of the countries: lower SEP tended to be associated with higher BMI in more developed nations, while the opposite was found in less developed nations, differences which reflect the different characteristics of countries before and after the epidemiological transition.[63] Associations in developed nations—the focus of this thesis—were more consistently observed in females: indicators of lower SEP (such as low educational attainment, occupational class, and income) were commonly associated with higher BMI. Associations in males tended to vary by indicator, with low educational attainment commonly associated with higher BMI, and low income associated with low BMI. This review article built upon a previous published systematic review in 1989 which reported similar findings.[453] A systematic review in 2012 of 27 studies conducted in the UK found that lower SEP (own occupational class) was associated with increased risk of obesity, with six studies finding stronger associations in females than males.[450]

Ball and Crawford (2005)[433] conducted a systematic review to examine associations between SEP and weight gain in adulthood (exclusively in developed nations). Thirty-three studies were identified, and the authors concluded that there was evidence of an association between low occupational class and greater weight gain in both males and females. This association was more consistently found in studies which used objective measures of weight and had longer periods of follow-up (>4 years). Associations were less consistent when other indicators of SEP such as educational attainment or income were used. In explaining these differences in findings it was suggested that occupation may be more strongly related with the activities undertaken that impact on weight gain, while educational attainment was suggested as being less related (as it may reflect experiences that took place a long time ago), as was income (as many activities needed to lower fat mass are free such as exercising outside).

Four studies have examined associations between SEP in adulthood and direct measures of fat mass and mixed findings have been reported. Indicators of lower SEP were associated with higher fat mass using an area-based measure of deprivation (with DXA measures at 20–92 years[448]) and occupational class (using BIA at ~61 years),[197] while one study reported no association with educational attainment (using DXA at 72–95 years).[95] One study reported associations between high family income and higher fat mass (using BIA at age 18).[199]—this was the only study based in a developing nation (Brazil), and the direction of association is consistent with previous reports using BMI in developing nations.[446]

#### 6.1.1.3 *Early life socioeconomic position and lean mass*

Three studies have examined associations between SEP in early life and subsequent lean mass, and mixed findings have been reported. One study found that low paternal educational attainment was associated with lower lean mass (using DXA at 15–20 years),[195] while another study reported no association with paternal education or parental occupational class (using DXA with adjustment for age at 4–20 years).[198] The third study reported no association between paternal occupation at birth and lean mass (using BIA at ~61 years).[197]

#### 6.1.1.4 *Adult socioeconomic position and lean mass*

Six studies have examined associations between SEP in adulthood and measures of lean mass. Mixed findings have been reported, with one study in mid-later adulthood finding high educational attainment was weakly associated with high lean mass (using BIA[196]) and other studies reporting no association with educational attainment (using DXA[95]) or an area-based measure of deprivation (using DXA).[448] One study reported associations between low occupational class and high lean mass in females, but found no association in males (using BIA at ~61 years).[197] In contrast, another study reported an association between lower SEP and lower lean mass in female civil servants, but not males.[449] However, this study only reported P-values of tests of association—neither effect sizes nor results of sex interaction tests were presented, leading to uncertainty in the association in males. The study in Brazil reported associations between higher household income and higher lean mass (using BIA at 18 years).[199]

#### 6.1.1.5 *Literature discussion: socioeconomic position and body composition*

While a large number of studies have reported associations between lower SEP in early and adult life and higher BMI in adulthood (more consistently in females than males), relatively few have used direct measures of fat or lean mass and these have tended to produce less consistent findings. There was some evidence of an association between lower SEP in early and adult life and higher fat mass in adolescence/adulthood, while more conflicting findings were reported with lean mass. Although most of the studies using direct measures of body composition have been conducted in developed nations only one has been conducted in the UK, and this study provided few details of associations between SEP and fat and lean mass. Research conducted in the UK would provide the strongest source of evidence to inform public health policy within the UK.

Of the four studies examining SEP in early life, three examined body composition in adolescence/early adulthood, one of which included relatively few adults (4–20 years). Only one study examined associations between SEP prospectively measured in childhood and body composition in later adult life (at ~61 years).[197] There is a need to further examine these associations in later life since associations may differ by age, cohort, and SEP indicator. Associations of lower SEP and greater weight gain in adulthood[433] suggest that associations with fat mass may increase across life.

Of six studies examining associations between SEP in adulthood and adult body composition a wide range of indicators have been used. One study used an area-based indicator of SEP,[448] a measure of relative deprivation in geographical areas which may also indicate individual-level SEP. Although area-level and individual-level indicators of SEP are correlated,[454] it has been suggested that the imperfect nature of this association leads to area-based measures having less statistical power than individual-level indicators.[455] In support of this, the study reported no association between SEP and lean mass, while other studies did. The remaining studies used various individual-level indicators of SEP: occupational class[197] or grade,[449] educational attainment,[95;196] or household income.[199] The only study to use household income was also the only study conducted in a developing nation (Brazil); since developing and developed nations tend to have different patterns of associations (eg, between SEP and fat mass[63]).

All of the studies examining associations with adult SEP and direct measures of body composition used only one indicator of SEP. As previously discussed, the use of multiple indicators may be informative as each may reflect different dimensions of SEP and may be more or less relevant to body composition outcomes. While different indicators of adult SEP were used across the different studies (educational attainment, occupational class, and income), differences in associations with outcomes cannot be separated from potential age and cohort differences (including country-specific differences). Only one study used indicators of SEP in both early and adult life,[197] and the focus of this study was on patterns of growth—SEP was principally explored as a potential confounder and, as with a study examining associations with adult SEP,[449] effect estimates were not presented. In this study both early and adult SEP were included as explanatory variables in the same statistical model, and unadjusted results were not presented. The interpretation of these findings is therefore unclear—ie, whether null associations between childhood SEP and adult lean mass could reflect either no association or the effects of adjustment for adult SEP (ie, mediation). The extent to which associations between childhood SEP and adult body composition are explained by continuity of SEP into adulthood is therefore unclear, as is the extent to which associations with SEP in adulthood are confounded by SEP in childhood.

In addition to the indicators of SEP, the measures of body composition used varied between studies and have a number of limitations. Four of nine studies measured body composition using BIA, which as discussed in Chapter 2 is likely to be less accurate and precise than DXA. While four used DXA, a method previously argued in Chapter 2 to be both accurate and precise, all used whole body measures of fat and/or lean mass. No studies examined associations between SEP and direct measures of abdominal fat distribution or appendicular lean mass. As discussed in Chapter 1, these outcomes may be particularly relevant for subsequent health and physical functioning outcomes. Further, given the strong positive correlation between lean and fat mass (Chapter 2), associations between lower SEP and lower lean mass could be confounded by fat mass (if lower SEP, as suggested in previous studies, is associated with higher fat mass). However, no studies have taken this into account in their analyses (eg, by making adjustment for fat mass when examining associations with lean mass).

When interpreting associations with body composition, adjustment for contemporaneous height has been suggested as being important (outlined in Chapter 2). Associations between lower SEP and higher fat mass are likely to be confounded by height, since lower SEP (in childhood and adulthood) is associated

with shorter adult height,[408;409] and shorter individuals typically have less fat mass (Chapter 2). Associations between lower SEP and lean mass may either be confounded or mediated by adult height (depending on how SEP is related to lean mass). However, four of eight studies made no adjustment for adult height.

To the author's knowledge, no studies have examined the factors that mediate associations of SEP with direct measures of fat and lean mass. The investigation of mediating factors has important public health implications (eg, by increasing the number of targets for intervention and preventative strategies) and may provide further evidence in support of the hypothesised association between exposure and outcome.[456]

#### 6.1.1.6 *Prior findings from the MRC National Survey of Health and Development*

A number of publications have used the NSHD to examine associations between indicators of SEP with BMI or waist circumference.

Braddon et al (1986)[328] found that lower educational attainment and lower SEP in childhood (paternal occupational class at 4 years) were associated with higher BMI at 36 years, associations also reported by Power et al (2005)[457] who reported that associations were weaker in males compared with females. Hardy et al (2000)[168] found that lower childhood SEP (paternal occupational class at 4 years) and lower own educational attainment were associated with higher BMI and greater BMI gain between 20 and 43 years in both sexes. However, adult SEP (head of household occupational class at 26, 36 and 43) was not associated with BMI in either sex after adjustment for childhood SEP and own educational attainment (unadjusted analyses were not presented). Associations with childhood SEP were party attenuated after adjustment for educational attainment and adult SEP, suggesting that associations between childhood SEP and BMI were not fully explained by the continuity of SEP into adulthood.

Langenberg et al (2003)[167] also found that lower childhood SEP was associated with higher BMI and waist circumference at 53 years in both sexes. In addition, Langenberg et al investigated associations of SEP in adulthood (head of household occupational class at 26 and 43 years) and intergenerational mobility with BMI and waist circumference at 53 years. Lower occupational class at 26 and 43 years was associated with higher BMI and waist circumference at 53 years in females, while lower occupation class at 26 years was associated with higher BMI at 53 in males.

These associations were entirely attenuated in males but not females when adjustment was made for childhood SEP, suggesting that SEP in childhood was a more important determinant in males. Upwards intergenerational social mobility was associated with lower BMI and waist circumference in both sexes. Murray et al (2011)[423] compared three different life course models (sensitive periods, accumulation of risk, and social mobility; as discussed in Chapter 1) in explaining associations between SEP (dichotomised into manual and non-manual occupational class) in childhood (4 years) and adulthood (26 and 43 years) and BMI at 53 years. In cases where multiple models predicted the data as well as the saturated model, the simpler model was selected as best representing the data. In males, a sensitive period model of childhood SEP fitted the data and was selected (although a model specifying accumulation across life also fitted the data), while in females a model specifying accumulation across life was selected. Strand et al (2012)[458] also used BMI as an outcome (up to 53 years), and investigated whether the strength of associations between childhood SEP and adult BMI changed over time. They found that the adverse effects of lower childhood SEP increased over time in females (from 36, 43, and 53 years), and remained stable in males. Across all periods investigated, associations between childhood SEP and higher adult BMI and waist circumference were stronger in females than males.

As discussed in Chapter 3, while the NSHD has no previous measures of lean mass, selected studies using grip strength and physical functioning outcomes are described below in order to give an indication of the types of analyses that have been conducted using indicators of SEP.

Guralnik et al (2006) examined associations between SEP in childhood and measures of physical function at age 53 (the top and bottom 10% of a score including grip strength, standing balance and chair rise time).[459] Higher paternal occupational class and parental educational attainment were associated with lower odds of low function and higher odds of high function. In a mutually adjusted model, higher maternal education predicted higher function and lower paternal occupation predicted lower function.

Strand et al (2011)[422] examined the pathways underlying associations between childhood SEP and physical functioning (standing balance and chair rise time at 53 years). Associations between lower childhood SEP and worse physical functioning were partly mediated by measures of childhood growth (birth weight, weight gain from 0–7 years, and height gain from 4–7 years), and by measures of childhood cognition and motor co-ordination.

In summary, previous studies using the NSHD have shown indicators of lower SEP to be associated with higher fat mass as assessed by BMI and waist circumference, and worse physical functioning. This chapter will build upon this research by examining associations between SEP and direct measures of fat and lean mass, and by using a wider range of indicators of SEP (including parental educational attainment, NS-SEC derived occupational class, and household income). Finally, this chapter will consider whether factors considered in previous chapters—measures of growth before (Chapter 3) and after birth (Chapter 4) and physical activity levels in adulthood (Chapter 5) mediate associations of SEP with fat and lean mass.

#### 6.1.1.7 *Literature review summary*

A large number of studies have reported associations between indicators of lower SEP and higher BMI in adulthood (more consistently found in females than males). In contrast, fewer studies have examined associations between SEP and direct measures of fat and lean mass in adulthood, and findings are not consistent. In some of these studies, associations between SEP and body composition were not the principle research questions of interest, and as such the analyses and subsequent interpretation lack detail. Overall, these studies have a number of limitations that suggest the need for further research: most have only considered single indicators of SEP (in adulthood), and not used indicators of both childhood and adult SEP; none have examined associations with regional measures of body composition; and few have adjusted for adult height. Finally, no studies have examined which factors mediate associations of SEP with fat and lean mass.

### 6.1.2 *Chapter objectives and hypotheses*

The objective of this chapter is to test the hypothesis that lower SEP in childhood and adulthood are associated with higher fat and lower lean mass. It was further hypothesised that these associations would be partly mediated by the factors identified in previous chapters which were associated with body composition (measures of growth before and after birth, and physical activity measures in adulthood), as illustrated in Figure 1 (Chapter 1). Specifically, it was hypothesised that associations between SEP in childhood and outcomes would be partly mediated by measures of pre-adulthood growth, and that associations of SEP childhood and adulthood with outcomes would be partly mediated by physical activity levels in adulthood.

The methods and results to test the above hypotheses are divided into two sections. Section a) describes the explanatory variables used in this chapter and examines associations between SEP and body composition outcomes; section b) investigates whether factors considered in previous chapters mediate associations between SEP and outcomes.

## 6.2 **Section a) Methods**

### 6.2.1 ***Explanatory variables***

The explanatory variables used in this chapter are indicators of SEP in childhood and adulthood, shown in Table 21. Multiple indicators of SEP were chosen as although likely to be related to each other, each may reflect particular dimensions of SEP (as described in the Introduction of this chapter) and may be more or less relevant for fat and lean mass.

Parental educational attainment and paternal occupational class were used as indicators of childhood SEP, with other indicators reflecting SEP in adulthood (home ownership at 26 years, both own and highest household occupational class at 53 years, and household income at 60-64 years). Educational attainment was considered as an indicator of SEP in both childhood and adulthood, as it reflects the result of experiences that took place largely in childhood, and is related to subsequent employment opportunities in adulthood,[425] and may be particularly related to the acquisition of knowledge and cognitive traits which, through their impact on health behaviours, impact on fat and lean mass in adulthood.

Table 21. Indicators of socioeconomic position used in this chapter

| Indicator | Study members' age when ascertained | Derivation and categorisation |
|---|---|---|
| Paternal occupational class | 4 years | Derived using the Registrar General's classification: I professional, II intermediate, III skilled non-manual, III skilled manual, IV semi-skilled, and V unskilled. Values were replaced with those at age 11 (n=24) or 15 (n=13) if missing at 4 years. |
| Maternal and paternal educational attainment | 6 years | Categorised in four groups: 1) primary only, 2) primary and further education (no qualifications obtained), 3) secondary only (or primary and further education), and 4) secondary and further education or higher. |
| Own educational attainment | 26 years | Categorised in five groups using the Burnham scale:[460] 1) no qualifications, 2) sub GCE or sub Burnham C, 3) GCE O level or Burnam C, 4) GCE A level or Burnam B, and 5) Degree or higher. |
| Home ownership | 26 years | Categorised in two groups: i) owned their home, and ii) rented or lived with their parents |
| Own occupational class (RGSC) | 53 years | Derived using the Registrar General's Classification (as above). Values were replaced with those at 43 (n=55), 36 (n=21), or 26 (n=13) if missing at 53 years. |
| Own occupational class (NS-SEC) | 53 years | Derived using the NS-SEC in three categories since this is considered to be ordinal:[461] I Managerial & professional, II Intermediate, III Routine and manual. Values were replaced with those at 43, 36, 26, or 15 if missing at 53 years (n=64). |
| Highest household occupational class | 53 years | The study member or their partner's occupational class (whichever was highest) derived using the Registrar General's Classification as above. The class of the spouse was taken if that of the study member was missing. Values were replaced with those at 43 (n=58), 36 (n=11), or 26 (n=7) if missing at 53 years. |
| Household income | 60-64 years | Post-tax income from all sources including employment, pensions (public/private), dividends, benefits, etc. Study members were given a card with 13 letters referring to 13 income bands from low (less than £6000 per year) to high (£80,000 or more per year), and asked to select the letter corresponding to their income. |

### 6.2.2 ***Outcomes***

The outcomes used in this chapter are the main outcomes of this thesis, described in more detail in Chapter 2 (whole body measures of fat and lean mass, the ratio of these masses, appendicular lean mass, and android: gynoid fat mass ratio).

### 6.2.3 ***Analytical strategy***

Associations between the different indicators of SEP were examined using chi-squared tests.

Associations between indicators of SEP and outcomes were examined using the slope index of inequality. This enables the different indicators to be examined on the same scale and takes into account differences in the distribution of participants across categories of different variables. Indicators were first converted into ridit scores, where each category is assigned a value representing the proportion of participants above its mid-point. For example, if the highest income group contains 20% of the population it would be assigned a value of 0.1 (0.2/2); if the second highest group contains 30% of the population it would be assigned a value of 0.35 (0.2 + 0.3/2). Scores were calculated separately in each sex. These scores—ranging from 0 (hypothetical lowest) to 1 (hypothetical highest SEP)—were then used as explanatory variables in linear regression: the coefficients show the absolute mean difference in outcome between those of lowest versus highest SEP.[462] These models were used for all outcomes using height-adjusted indices. When using appendicular lean mass index as an outcome, models were additionally adjusted for fat mass index to account for the potential confounding by fat mass.

Tests of deviation from linearity were conducted using likelihood ratio tests to compare a model with the indicator included as a categorical term with a model with it included as a linear term; this was conducted before converting indicators into ridit scores. The means and standard deviations of outcomes were presented by SEP category to enable any causes of deviation from linearity to be inspected.

All models were conducted separately by sex as sex differences in associations have been found in previous studies and, given the large number of explanatory variables used, it was thought that stratification would enable a clearer comparison of effect sizes in each sex. Sex differences in associations were examined by testing for interactions.

A series of multivariable regression models were conducted to determine whether the different indicators of SEP were independently associated with body composition outcomes. These were conducted in order to help elucidate which indicators were most relevant for each outcome. Three discrete outcome measures were used in these and subsequent multivariable analyses: a measure of fat mass (whole body fat mass index), abdominal fat distribution (android: gynoid ratio), and lean mass (appendicular lean mass index, after adjustment for fat mass index), and associations were only carried forward into these multivariable analyses where there was evidence for association in univariable analyses. Models were conducted with sequential adjustment for different SEP indicators, with all fully adjusted models containing childhood SEP, educational attainment, occupational class, and household income, each entered as ridit scores. To limit the number of analyses conducted, only one indicator of childhood SEP and one indicator of occupational class were used in these analyses—those which were most strongly and most consistently associated with outcomes; the indicator of childhood SEP used was additionally chosen on the basis of results of further multivariable analyses with all childhood SEP indicators (parental educational attainment and paternal occupational class) included as explanatory variables in linear regression models.

## 6.3 **Section a) Results**

### 6.3.1 ***Associations between indicators of socioeconomic position***

All indicators of SEP except home ownership at 26 years were positively correlated with each other in expected directions, with those of higher SEP as assessed by one indicator tending to have higher SEP in all other indicators (data not shown; P(chi-squared tests) <0.001 in all cases). For example, those with fathers who attained higher education tended to go on to attain higher education themselves by 26 years, and be of higher occupational class at 53 years. Home ownership at 26 years was less consistently associated with other indicators, and associations differed in each sex.

### 6.3.2 ***Univariable analyses: indicators of socioeconomic position and body composition outcomes***

Table 22 shows univariable associations between indicators of SEP modelled using the slope index of inequality and all outcomes (fat and lean mass indices, and fat: lean and android: gynoid ratios). Lower SEP was consistently associated with higher

fat mass and higher fat: lean mass ratio (typically more strongly in females than males). Lower SEP was also consistently associated with higher android: gynoid ratio, with sex differences only evident for own educational attainment (stronger associations in males). The strength of associations differed by sex—for example, own educational attainment (males) and paternal educational attainment (females) had the largest effect sizes for fat mass, reflecting a 1.65 (95% CI: 0.69, 2.60) and 3.67 (95% CI: 2.28, 5.07) difference in fat mass index between lowest and highest SEP, respectively.

Lower SEP was typically weakly associated with higher appendicular lean mass (except for home ownership at 26, which showed the opposite association in males). However, after adjustment for fat mass index the patterns of association differed: in males, most indicators were not associated except lack of home ownership at 26 and low household income which were both associated with lower appendicular lean mass. In females, all indicators of lower SEP were associated with lower appendicular lean mass after adjustment, except for home ownership at 26 years (no association).

There was little evidence for deviation from linearity, except for associations of paternal occupational class with fat mass in males, and of lower household income and higher fat mass in both sexes. In these cases deviation from linearity was driven by those in the lowest SEP group tending to have lower fat mass than expected given a linear trend. Appendix 31 shows the means and standard deviations of body composition outcomes (whole body fat and lean mass, fat: lean mass ratio, appendicular lean mass, and android: gynoid ratio) by SEP category, and Appendix 32 shows these for height-adjusted indices. When height-adjusted indices of fat and lean mass were used, there was stronger evidence for association between lower SEP and higher fat mass, and there was evidence of association between lower SEP and higher lean mass (except home ownership at 26 years in males which showed the opposite association).

### 6.3.3 *Multivariable analyses: indicators of socioeconomic position and body composition outcomes*

Multivariable associations of childhood and adult SEP indicators with whole body fat mass, android: gynoid ratio, and appendicular lean mass (after adjustment for fat mass) are shown in Table 23, with sequential adjustment for different indicators across life. Paternal educational attainment was used as the sole indicator of childhood SEP in these models, as in females this indicator was most strongly

associated with fat mass and android: gynoid ratio, and remained associated when all indicators of childhood SEP were mutually adjusted for one another (Appendix 33). This indicator was also used in males to enable fairer comparison between the sexes. In females, highest household occupational class was used instead of own occupational class as it tended to be more strongly associated with outcomes in univariable analyses. In males, measures of occupational class were more weakly associated with outcomes and were omitted from multivariable analyses.

In males, associations of low own educational attainment and low household income with higher fat mass remained, albeit partly attenuated, after adjustment for all other indicators of SEP; associations with paternal educational attainment were largely attenuated. Associations of low paternal and own educational attainment with higher android: gynoid ratio remained, while associations with household income were largely attenuated after mutual adjustment for other SEP indicators. Associations of lack of home ownership at 26 years and low household income with lower appendicular lean mass (after adjustment for fat mass) both remained after adjustment for other SEP indicators; the former associations were not attenuated, while the latter associations strengthened after these adjustments.

In females, associations of low paternal educational attainment and low household income with higher fat mass remained after adjustment for all other SEP indicators, while associations with own educational attainment and occupational class were largely attenuated. Associations of low paternal educational attainment and low occupational class with higher android: gynoid ratio remained, while associations with own educational attainment and household income were largely attenuated after mutual adjustment. Associations between all indicators of lower SEP with lower appendicular lean mass (after adjustment for fat mass) were attenuated after mutual adjustment.

Table 22. Differences in fat and lean mass (95% CI) between the hypothetical lowest and highest socioeconomic position (slope index of inequality)

| | | Fat mass index ($kg/m^{1.2}$) | | | | | Lean mass index ($kg/m^2$) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | Males | P | Females | P | P# | Males | P | Females | P | P# |
| Paternal occ. class (4y) | 1477 | 1.04(0.09, 1.99)* | 0.03 | 2.61(1.34, 3.89) | <0.01 | 0.06 | 0.88(0.36, 1.40) | <0.01 | 0.40(-0.06, 0.86) | 0.09 | 0.17 |
| Maternal education (6y) | 1389 | 1.27(0.22, 2.33) | 0.02 | 2.72(1.28, 4.16) | <0.01 | 0.11 | 0.95(0.38, 1.53) | <0.01 | 0.53(0.00, 1.05) | 0.05 | 0.28 |
| Paternal education (6y) | 1378 | 1.07(0.03, 2.10) | 0.04 | 3.67(2.28, 5.07) | <0.01 | <0.01 | 0.82(0.26, 1.38) | <0.01 | 0.74(0.22, 1.25) | <0.01 | 0.83 |
| Own education (26y) | 1475 | 1.65(0.69, 2.60) | <0.01 | 2.08(0.81, 3.35) | <0.01 | 0.60 | 1.07(0.55, 1.59) | <0.01 | 0.24(-0.23, 0.70) | 0.32 | 0.02 |
| Home ownership (26y) | 1408 | -0.03(-1.13, 1.08) | 0.96 | 0.70(-0.79, 2.19) | 0.36 | 0.45 | -0.61(-1.21, -0.01) | 0.05 | 0.23(-0.31, 0.77) | 0.40 | 0.04 |
| Own RGSC occ. class (53y) | 1528 | 0.37(-0.59, 1.33) | 0.45 | 2.09(0.77, 3.41) | <0.01 | 0.04 | 0.49(-0.04, 1.02) | 0.07 | 0.27(-0.21, 0.75) | 0.27 | 0.54 |
| Own NS-SEC occ. class (53y) | 1550 | 0.85(-0.15, 1.84) | 0.10 | 2.08(0.77, 3.39) | <0.01 | 0.15 | 0.63(0.09, 1.18) | 0.02 | 0.38(-0.09, 0.85) | 0.11 | 0.49 |
| H of H RGSC occ. class (53y) | 1528 | 0.72(-0.26, 1.69) | 0.15 | 2.14(0.78, 3.49) | <0.01 | 0.10 | 0.49(-0.05, 1.02) | 0.08 | 0.19(-0.30, 0.68) | 0.44# | 0.43 |
| Household income (60-64y) | 1481 | 1.23(0.32, 2.14)* | <0.01 | 2.17(0.91, 3.42)* | <0.01 | 0.24 | -0.04(-0.55, 0.47)* | 0.88 | 0.30(-0.16, 0.75) | 0.21 | 0.34 |

| | | Fat: lean ratio | | | | | Android: gynoid fat mass ratio | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | Males | P | Females | P | P# | Males | P | Females | P | P# |
| Paternal occ. class (4y) | 1477 | 2.58(-0.30, 5.47)* | 0.08 | 11.70(7.01, 16.39) | <0.01 | <0.01 | 8.03(4.06, 12.01)* | <0.01 | 5.91(2.87, 8.95) | <0.01 | 0.40 |
| Maternal education (6y) | 1389 | 2.96(-0.26, 6.18) | 0.07 | 11.57(6.26, 16.88) | <0.01 | <0.01 | 8.22(3.82, 12.63) | <0.01 | 6.12(2.73, 9.52) | <0.01 | 0.46 |
| Paternal education (6y) | 1378 | 2.26(-0.90, 5.43) | 0.16 | 14.52(9.39, 19.66) | <0.01 | <0.01 | 8.40(4.05, 12.74) | <0.01 | 9.64(6.34, 12.94) | <0.01 | 0.65 |
| Own education (26y) | 1475 | 4.37(1.46, 7.29) | <0.01 | 9.89(5.22, 14.57) | <0.01 | 0.06 | 8.42(4.43, 12.41) | <0.01 | 3.41(0.27, 6.54) | 0.03 | 0.05 |
| Home ownership (26y) | 1408 | 1.81(-1.55, 5.16) | 0.29 | 1.66(-3.81, 7.13) | 0.55 | 0.97 | -1.45(-6.15, 3.26) | 0.55 | 1.45(-2.11, 5.01) | 0.42 | 0.33 |
| Own RGSC occ. class (53y) | 1528 | 0.61(-2.30, 3.53)* | 0.68 | 8.97(4.12, 13.82) | <0.01 | <0.01 | 3.93(-0.14, 8.00)* | 0.06 | 4.02(0.81, 7.23) | 0.01 | 0.97 |
| Own NS-SEC occ. class (53y) | 1550 | 1.99(-1.04, 5.01) | 0.20 | 8.20(3.37, 13.04) | <0.01 | 0.04 | 3.49(-0.72, 7.69) | 0.10 | 3.61(0.43, 6.79) | 0.03 | 0.96 |
| H of H RGSC occ. class (53y) | 1528 | 1.76(-1.21, 4.72) | 0.25 | 9.77(4.81, 14.73) | <0.01 | <0.01 | 3.81(-0.33, 7.96)* | 0.07 | 4.97(1.69, 8.25) | <0.01 | 0.67 |
| Household income (60-64y) | 1481 | 4.93(2.16, 7.69)* | <0.01 | 9.11(4.49, 13.73) | <0.01 | 0.14 | 4.09(0.16, 8.01) | 0.04 | 3.26(0.20, 6.32) | 0.04 | 0.74 |

| | | Appendicular lean mass index ($kg/m^2$) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | Males, unadjusted | P | Males, adjusted for fat mass index | P | Females, unadjusted | P | Females, adjusted for fat mass index | P | P# |
| Paternal occ. class (4y) | 1477 | 0.31(0.06, 0.55) | 0.01 | 0.17(-0.04, 0.39) | 0.11 | 0.04(-0.18, 0.26) | 0.70 | -0.26(-0.42, -0.09) | <0.01 | <0.01 |
| Maternal education (6y) | 1389 | 0.26(-0.01, 0.54) | 0.06 | 0.10(-0.14, 0.34) | 0.39 | 0.11(-0.14, 0.35) | 0.40 | -0.21(-0.39, -0.02) | 0.03 | 0.03 |
| Paternal education (6y) | 1378 | 0.26(-0.01, 0.52) | 0.06 | 0.12(-0.11, 0.36) | 0.30 | 0.16(-0.08, 0.40) | 0.20 | -0.26(-0.45, -0.08) | <0.01 | <0.01 |
| Own education (26y) | 1475 | 0.30(0.05, 0.55)* | 0.02 | 0.09(-0.13, 0.31)* | 0.42 | -0.03(-0.25, 0.19)* | 0.82 | -0.27(-0.43, -0.10) | <0.01 | <0.01 |
| Home ownership (26y) | 1408 | -0.35(-0.64, -0.06) | 0.02 | -0.35(-0.60, -0.10) | <0.01 | 0.08(-0.18, 0.33) | 0.55 | 0.00(-0.19, 0.19) | 0.98 | 0.03 |
| Own RGSC occ. class (53y) | 1528 | 0.15(-0.10, 0.40) | 0.25 | 0.10(-0.12, 0.32) | 0.38 | 0.02(-0.20, 0.25) | 0.85 | -0.22(-0.39, -0.05) | 0.01 | 0.02 |
| Own NS-SEC occ. class (53y) | 1550 | 0.26(0.01, 0.52) | 0.05 | 0.16(-0.07, 0.38) | 0.18 | 0.09(-0.13, 0.32) | 0.42 | -0.14(-0.31, 0.03) | 0.10 | 0.03 |
| H of H RGSC occ. class (53y) | 1528 | 0.14(-0.12, 0.39) | 0.30 | 0.04(-0.18, 0.27) | 0.70 | 0.01(-0.22, 0.24) | 0.94 | -0.24(-0.41, -0.06) | <0.01 | 0.04 |
| Household income (60-64y) | 1481 | -0.08(-0.32, 0.16) | 0.52 | -0.24(-0.45, -0.03) | 0.03 | 0.08(-0.14, 0.29)* | 0.47 | -0.17(-0.33, -0.01) | 0.04 | 0.73 |

Note: #P-value for sex interaction term; *evidence for departure from linearity (P<0.05); analyses restricted to those with valid data for body composition outcomes; NS-SEC=The National Statistics Socio-economic Classification; RGSC=Registrar General's Social Classification; H of H= highest household occupational class (derived using RGSC)

Table 23. Differences in fat and lean mass (95% CI) between the hypothetical lowest and highest socioeconomic position (slope index of inequality), with sequential adjustment for different indicators across life

a) Males (n=605)

| | Fat mass index ($kg/m^{1.2}$) | P | Android: gynoid fat mass ratio | P | Appendicular lean mass index ($kg/m^2$), adjusted for fat mass index | P |
|---|---|---|---|---|---|---|
| 1. Paternal education (4y) | 1.07 (0.01, 2.13) | 0.05 | 9.10 (4.63, 13.56) | <0.001 | | |
| 2. Model 1 + own education | 0.42 (-0.74, 1.57) | 0.48 | 6.14 (1.27, 11.01) | 0.01 | | |
| 3. Model 2 + household income | 0.29 (-0.88, 1.45) | 0.63 | 5.85 (0.95, 10.75) | 0.02 | | |
| | | | | | | |
| 1. Own education (26y) | 1.72 (0.69, 2.75) | <0.001 | 9.49 (5.14, 13.84) | <0.001 | | |
| 2. Model 1 + household income | 1.31 (0.21, 2.42) | 0.02 | 8.36 (3.68, 13.04) | <0.001 | | |
| 3. Model 2+ paternal education | 1.21 (0.02, 2.39) | 0.05 | 6.26 (1.27, 11.24) | 0.01 | | |
| | | | | | | |
| 1. Home ownership (26y)* | | | | | -0.29 (-0.57, -0.02) | 0.04 |
| 2. Model 1 + own education | | | | | -0.30 (-0.58, -0.03) | 0.03 |
| 3. Model 3 + household income | | | | | -0.29 (-0.57, -0.02) | 0.04 |
| 4. Model 4 + paternal education | | | | | -0.29 (-0.57, -0.02) | 0.04 |
| | | | | | | |
| 1. Household income (60–64y) | 1.55 (0.54, 2.56) | <0.001 | 6.01 (1.71, 10.32) | 0.01 | -0.22 (-0.45, 0.02) | 0.07 |
| 2. Model 2 + own education | 1.08 (-0.01, 2.16) | 0.05 | 2.99 (-1.59, 7.58) | 0.20 | -0.32 (-0.58, -0.07) | 0.01 |
| 3. Model 3 + paternal education | 1.05 (-0.05, 2.14) | 0.06 | 2.35 (-2.25, 6.96) | 0.32 | -0.34 (-0.59, -0.08) | 0.01 |

b) Females (n=638)

| | Fat mass index ($kg/m^{1.2}$) | P | Android: gynoid fat mass ratio | P | Appendicular lean mass index ($kg/m^2$), adjusted for fat mass index | P |
|---|---|---|---|---|---|---|
| 1. Paternal education (4y) | 3.56 (2.10, 5.03) | <0.001 | 9.95 (6.40, 13.51) | <0.001 | -0.27 (-0.47, -0.08) | 0.01 |
| 2. Model 1 + own education | 2.95 (1.26, 4.63) | <0.001 | 9.92 (5.83, 14.01) | <0.001 | -0.16 (-0.38, 0.06) | 0.16 |
| 3. Model 2 + occ. class | 2.87 (1.19, 4.56) | <0.001 | 9.61 (5.53, 13.69) | <0.001 | -0.15 (-0.37, 0.07) | 0.19 |
| 4. Model 3 + household income | 2.92 (1.23, 4.60) | <0.001 | 9.68 (5.59, 13.76) | <0.001 | -0.15 (-0.38, 0.07) | 0.18 |
| | | | | | | |
| 1. Own education (26y) | 2.58 (1.17, 3.98) | <0.001 | 4.74 (1.29, 8.19) | 0.01 | -0.30 (-0.48, -0.11) | <0.001 |
| 2. Model 1 + occ. class | 2.04 (0.49, 3.59) | 0.01 | 2.62 (-1.16, 6.40) | 0.17 | -0.23 (-0.43, -0.03) | 0.03 |
| 3. Model 2 + household income | 1.75 (0.17, 3.33) | 0.03 | 2.23 (-1.64, 6.09) | 0.26 | -0.21 (-0.42, -0.01) | 0.04 |
| 4. Model 3 + paternal education | 0.43 (-1.31, 2.17) | 0.63 | -2.14 (-6.37, 2.08) | 0.32 | -0.15 (-0.38, 0.08) | 0.21 |
| | | | | | | |
| 1. Occupational class (53y) | 2.25 (0.76, 3.75) | <0.001 | 6.50 (2.86, 10.14) | <0.001 | -0.28 (-0.48, -0.09) | 0.01 |
| 2. Model 1 + income | 1.57 (-0.03, 3.18) | 0.05 | 5.60 (1.69, 9.51) | 0.01 | -0.24 (-0.45, -0.03) | 0.03 |
| 3. Model 2 + education | 0.94 (-0.76, 2.64) | 0.28 | 4.79 (0.63, 8.95) | 0.02 | -0.16 (-0.38, 0.06) | 0.15 |
| 4. Model 3 + paternal education | 0.74 (-0.95, 2.43) | 0.39 | 4.13 (0.03, 8.23) | 0.05 | -0.15 (-0.38, 0.07) | 0.17 |
| | | | | | | |
| 1. Household income (60–64y) | 2.26 (0.87, 3.65) | <0.001 | 4.19 (0.79, 7.59) | 0.02 | -0.19 (-0.37, -0.01) | 0.04 |
| 2. Model 1 + occ. class | 1.72 (0.23, 3.21) | 0.02 | 2.27 (-1.36, 5.91) | 0.22 | -0.11 (-0.31, 0.08) | 0.27 |
| 3. Model 2 + own education | 1.37 (-0.14, 2.89) | 0.08 | 1.83 (-1.89, 5.54) | 0.33 | -0.07 (-0.27, 0.13) | 0.49 |
| 4. Model 3 + paternal education | 1.45 (-0.06, 2.95) | 0.06 | 2.08 (-1.58, 5.73) | 0.27 | -0.07 (-0.27, 0.12) | 0.46 |

Notes: *smaller available sample size for this indicator, n=594; occupational class refers to the highest household occupational class, derived using the Registrar General's Classification system; analyses were restricted to those with valid measures for all indicators of socioeconomic position and body composition outcomes; associations were only included where evidence was found for association in previous univariable analyses

## 6.4 **Section b) Methods (mediation analysis)**

### 6.4.1 ***Analytical strategy***

The analyses conducted in this section were conducted to examine whether the associations found between SEP and body composition outcomes were mediated by important factors identified in previous chapters (birth weight, measures of growth after birth, and physical activity in adulthood). Specifically, these analyses were conducted to test the hypotheses that associations between lower SEP in childhood with higher fat and lower lean mass were partly mediated by measures of growth in early life, and associations of lower childhood and adult SEP with higher fat and lower lean mass were partly mediated by physical activity levels in adulthood.

A mediator was defined as a variable which explains, at least partially, how or why another explanatory variable affects the outcome.[240] As such, in order for a variable to be a mediator, it should be associated with both the explanatory variable and outcome in expected directions. Associations between SEP indicators and potential mediators were examined in previous chapters and where not considered in previous chapters examined in this chapter.

Associations between SEP indicators and body composition outcomes were only adjusted for potential mediators where there was evidence for association in univariable analyses. In addition, to limit the number of analyses conducted, only those SEP indicators judged to be most relevant for each outcome were included in these analyses—ie, where analyses in section a) found an association between the indicator and outcome after adjustment for all other indicators of SEP. Alternatively, where all indicators were no longer associated after this adjustment, multiple indicators were included.

Childhood SEP was judged to reflect socioeconomic circumstances before birth and in childhood. As such, associations between childhood SEP and body composition outcomes were adjusted for birth weight, as analyses in Chapter 3 found higher birth weight was associated with lower android: gynoid ratio and higher appendicular lean mass. Associations between childhood SEP and outcomes were also adjusted for conditional weight gain from 0–7 and 7–20 years. These were calculated using the standardised exported residuals from sex-specific linear regression models using the earlier measure of weight (eg, 7 years) as the explanatory variable and the later measure (eg, weight at 20 years) as the outcome. These variables are therefore designed to not be correlated with each

other, and therefore reduce the likelihood of multicollinearity impacting on results. These age ranges were selected as analyses in Chapter 4 found that greater weight gain from 7–20 years was associated with higher fat mass and higher android: gynoid ratio, while greater weight gain from both 0–7 and 7–20 years was associated with higher lean mass. Associations between own educational attainment and outcomes were also adjusted for conditional weight gain from 0–7 and 7–20 years; as discussed previously, educational attainment was considered as an indicator of SEP which captures socioeconomic circumstances in both childhood and adulthood. Measures of height gain were not included as analyses in Chapter 4 showed that associations of height gain with fat and lean mass were largely explained by adult height, and adjustment for adult height was made by the use of height-adjusted indices.

Associations between all indicators of SEP and outcomes were adjusted for measures of leisure time physical activity at ages which were judged to temporally mediate the association from SEP to body composition. Associations with childhood SEP, educational attainment, and home ownership at 26 years were adjusted for leisure time physical activity at 36, 43, 53 and 60–64 years, included as categorical terms (inactive, moderately active, and most active), as previously described in Chapter 5. Associations with occupational class at 53 years were adjusted for leisure time physical activity at 53 and 60-64 years, while associations with household income at 60-64 years were adjusted for leisure time physical activity at 60-64 years. Objective measures of physical activity were not included as, unlike self-reported measures, they were not consistently associated with indicators of SEP (Chapter 5), and their inclusion would lead to a further reduction in the available sample size.

## 6.5 **Section b) Results (mediation analysis)**

### 6.5.1 ***Indicators of socioeconomic position and potential mediators***

Associations between indicators of SEP and potential mediators are shown in Appendix 12, Appendix 34, and Appendix 35. Lower paternal educational attainment was weakly associated with lower birth weight, while lower paternal and own educational attainment were associated with greater weight gain in periods from 7-20 years. For all included indicators lower SEP was associated with lower participation in leisure time physical activity in adulthood (associations with own educational attainment shown in Chapter 5).

### 6.5.2 *Mediation analyses: socioeconomic position and body composition outcomes*

Table 24 shows the associations of indicators of SEP with fat mass, android: gynoid ratio, and appendicular lean mass (after adjustment for fat mass), both before and after adjustment for potential mediating variables.

In males, the association between lower own educational attainment and higher fat mass was partly explained by weight gain from birth to 20 years and leisure time physical activity. The association between low household income and higher fat mass was partly explained by leisure time physical activity. Associations of low paternal and own educational attainment with higher android: gynoid ratio were also partly explained by weight gain from birth to 20 years and leisure time physical activity measures.

In males, the association between lack of home ownership at 26 years and lower appendicular lean mass (after adjustment for fat mass) was not attenuated by leisure time physical activity. In contrast with associations found in univariable models, low household income was not associated with lower appendicular lean mass (after adjustment for fat mass) in the sub-sample with available data for leisure time physical activity.

In females, the association between low paternal educational attainment and higher fat mass was partly explained by weight gain from birth to 20 years and leisure time physical activity. The association between lower household income and higher fat mass was also partly explained by leisure time physical activity. The association between lower paternal educational attainment and higher android: gynoid ratio was partly explained by birth weight, weight gain from birth to 20 years, and leisure time physical activity levels. Similarly, the association between lower occupational class at 53 years and higher android: gynoid ratio was also partly explained by physical activity levels.

In females, the association between lower paternal educational attainment with lower appendicular lean mass (after adjustment for fat mass) was similar after adjustment for birth weight and weight gain from birth to 20 years; the association between low own educational attainment and lower appendicular lean mass was partly mediated by weight gain from birth to 20 years. Associations between all indicators of lower SEP with lower appendicular lean mass (after adjustment for fat mass) were partly attenuated (albeit weakly) by adjustment for leisure time

physical activity. Associations with paternal educational attainment and household income were weaker in the sub-sample with available data for leisure time physical activity.

In summary, the above analyses provided some evidence that associations between lower SEP and higher fat and lower lean mass were partly mediated by factors considered in previous chapters.

Table 24. Differences in fat and lean mass (95% CI) between the hypothetical lowest and highest socioeconomic position (slope index of inequality), with adjustment for potential mediators
a) Males (n=407)

| | Fat mass index ($kg/m^{1.2}$) | P | Android: gynoid fat mass ratio | P | Appendicular lean mass index ($kg/m^2$), adjusted for fat mass index | P |
|---|---|---|---|---|---|---|
| 1. Paternal education (4y) | | | 7.86 (2.27, 13.45) | 0.01 | | |
| 2. Model 1 + Birth weight | | | 7.83 (2.27, 13.39) | 0.01 | | |
| 3. Model 1 + conditional weight 0–20y | | | 7.29 (1.65, 12.93) | 0.01 | | |
| 4. Model 1 + physical activity | | | 7.47 (1.69, 13.25) | 0.01 | | |
| 5. Fully adjusted | | | 7.01 (1.22, 12.79) | 0.02 | | |
| | | | | | | |
| 1. Own education (26y) | 1.85 (0.59, 3.12) | <0.001 | 9.94 (4.25, 15.62) | <0.001 | | |
| 2. Model 2 + conditional weight 0–20y | 1.65 (0.41, 2.90) | 0.01 | 9.20 (3.25, 15.14) | <0.001 | | |
| 3. Model 1 + physical activity | 1.62 (0.32, 2.92) | 0.02 | 9.33 (3.42, 15.24) | <0.001 | | |
| 4. Fully adjusted | 1.45 (0.18, 2.72) | 0.03 | 8.77 (2.63, 14.91) | 0.01 | | |
| | | | | | | |
| 1. Home ownership (26y)* | | | | | -0.32 (-0.65, 0.00) | 0.05 |
| 2. Model 1 + physical activity | | | | | -0.32 (-0.65, 0.01) | 0.06 |
| | | | | | | |
| 1. Household income (60-64y) | 1.28 (0.08, 2.48) | 0.04 | | | -0.07 (-0.36, 0.22) | 0.64 |
| 2. Model 1 + physical activity | 1.08 (-0.14, 2.29) | 0.08 | | | -0.01 (-0.30, 0.28) | 0.95 |

b) Females (N=460)

| | Fat mass index (kg/m$^{1.2}$) | P | Android: gynoid fat mass ratio | P | Appendicular lean mass index (kg/m$^2$), adjusted for fat mass index | P |
|---|---|---|---|---|---|---|
| 1. Paternal education (4y) | 4.11 (2.37, 5.85) | <0.001 | 9.57 (5.37, 13.78) | <0.001 | -0.19 (-0.43, 0.04) | 0.10 |
| 2. Model 1 + Birth weight | 4.11 (2.36, 5.86) | <0.001 | 9.40 (5.19, 13.60) | <0.001 | -0.18 (-0.41, 0.05) | 0.13 |
| 3. Model 1 + conditional weight 0–20y | 3.43 (1.79, 5.07) | <0.001 | 8.72 (4.52, 12.92) | <0.001 | -0.18 (-0.40, 0.04) | 0.12 |
| 4. Model 1 + physical activity | 3.10 (1.30, 4.90) | <0.001 | 8.58 (4.18, 12.98) | <0.001 | -0.16 (-0.39, 0.08) | 0.19 |
| 5. Fully adjusted | 2.59 (0.89, 4.29) | <0.001 | 7.74 (3.36, 12.13) | <0.001 | -0.13 (-0.36, 0.10) | 0.25 |
| | | | | | | |
| 1. Own education (26y) | | | | | -0.37 (-0.59, -0.15) | <0.001 |
| 3. Model 2 + conditional weight 0–20y | | | | | -0.31 (-0.53, -0.10) | <0.001 |
| 4. Model 1 + physical activity | | | | | -0.36 (-0.58, -0.13) | <0.001 |
| 5. Fully adjusted | | | | | -0.28 (-0.50, -0.06) | 0.01 |
| | | | | | | |
| 1. Occupational class (53y) | | | 9.02 (4.62, 13.42) | <0.001 | -0.36 (-0.60, -0.12) | <0.001 |
| 2. Model 1 + physical activity | | | 8.16 (3.67, 12.65) | <0.001 | -0.31 (-0.55, -0.08) | 0.01 |
| | | | | | | |
| 1. Household income (60-64y) | 2.22 (0.52, 3.92) | 0.01 | | | -0.16 (-0.38, 0.05) | 0.14 |
| 2. Model 1 + physical activity | 1.78 (0.08, 3.49) | 0.04 | | | -0.11 (-0.33, 0.11) | 0.32 |

Note: *smaller sample size for this measure (N=386); conditional weight gain from 0–7 and 7–20 years were used, calculated using the standardised exported residuals from sex-specific linear regression models, eg, 7–20 years was calculated with a model containing weight at 7 years as the explanatory variable and weight at 20 years as the outcome; paternal and own education, and home ownership were adjusted for leisure time activity at 36, 43, 53 and 60-64 years (at each age categorised as inactive, moderately, and most active); occupational class was adjusted for activity at 53 and 60–64 years, household income was adjusted for activity at 60–64 years; analyses were restricted to those with valid measures for all indicators of socioeconomic position, all potential mediators, and body composition outcomes; associations were only included where evidence was found for association in previous univariable and multivariable analyses

## 6.6 **Discussion**

### 6.6.1 ***Main findings***

The main findings of this chapter are associations between multiple indicators of lower SEP (in childhood and adulthood) and higher fat mass at 60–64 years. Associations between lower SEP in childhood and higher fat mass were partly explained by weight gain from birth to 20 years, while associations of lower SEP in childhood and adulthood with higher fat mass were partly attenuated by leisure time physical activity levels in adulthood.

There was some evidence that lower SEP was associated with lower appendicular lean mass after adjustment for fat mass, although findings differed by sex: in males only lack of home ownership at 26 years and low household income at 60–64 years were associated with lower appendicular lean mass; in females, most indicators of lower SEP (in childhood and adulthood) were associated with lower appendicular lean mass. In some cases these associations were partly explained by leisure time physical activity levels in adulthood.

### 6.6.2 ***Comparison with previous studies***

While a large number of previous studies have reported associations between lower SEP (in both childhood and adulthood) and higher BMI in adulthood (particularly in females), few have examined associations with direct measures of fat or lean mass. Previous studies using direct measures have tended to produce inconsistent findings, have only considered single indicators of SEP, and have not examined mediating factors. In addition, no studies have made adjustment for fat mass when examining associations with lean mass.

Findings from this chapter are concordant with previous NSHD studies finding associations between indicators of lower SEP (in childhood and lower educational attainment) and higher BMI and waist circumference in adulthood at earlier ages.[167;168;328;423;457;458]

The analyses conducted in this chapter build on previous NSHD work by considering a greater range of indicators of SEP in childhood (including paternal educational attainment) and adulthood (home ownership at 26 years, NS-SEC derived occupational class at 53 years and household income at 60–64 years), by using direct measures of fat and lean mass, and by examining whether associations

between SEP and body composition outcomes are mediated by weight gain from birth to 20 years and physical activity levels in adulthood.

### 6.6.3 *SEP and fat mass: explanation of findings*

As outlined previously in this chapter, associations between lower SEP and higher fat mass are likely to be explained by the socioeconomic patterning of the determinants of fat mass. These include diet and physical activity, and are described in more detail in Chapter 1.

While associations between lower SEP and higher fat mass were typically partly explained by the potential mediators considered, the extent to which each potential mediator explained each association varied. This variability is likely to be due to differences in the associations of each potential mediator with SEP indicators and outcomes. Lower childhood SEP was weakly associated with lower birth weight in females, which in turn was associated with higher android: gynoid ratio, but not higher fat mass; as would be expected, associations between lower SEP in childhood and higher android: gynoid ratio in females were partly by explained by birth weight, while those with whole body fat mass were not. Lower SEP in childhood was associated with greater weight gain from 7–20 years, which in turn was associated with higher fat and android: gynoid ratio (Chapter 5); as such, associations between lower SEP in childhood and higher fat and android: gynoid ratios were both partly explained by weight gain. Similarly, lower SEP in childhood and adulthood was associated with lower participation in leisure time physical activity across adulthood, which in turn was associated with lower fat mass (more consistently in females than males); as such, associations between lower SEP and higher fat mass was partly explained by leisure time physical activity levels (to a greater extent in females than males).

Associations between lower SEP and higher fat mass were not fully explained by the potential mediators considered. This could be due to limitations in the measurement of potential mediators. For example, leisure time physical activity measures were used in this chapter although, as discussed in Chapter 5, leisure time activity is likely to be an imperfect measure of total energy expenditure. Measures of total physical activity energy expenditure could better explain the associations between lower SEP and higher fat mass. Although SEP was not strongly associated with objectively assessed total physical activity energy expenditure at 60–64 years (Chapter 5), SEP may have been associated with this measure earlier in life when the socioeconomic differences in fat mass developed.

Factors other than pre-adulthood weight gain and physical activity are also likely to explain the associations between lower SEP and higher fat mass. While it is likely that SEP differences in energy intake may partly explain these associations, the extent to which this is demonstrable depends on the accuracy by which energy intake is measured. As discussed in Chapter 1, research has found evidence that there is inaccuracy and systematic bias in self-reported dietary intake data (such that individuals with higher fat mass are more likely to report eating less).[214;215] Following on from this, studies that have examined associations between SEP and energy intake have produced inconsistent findings,[215] and components of diet have been found to not fully explain associations between lower SEP and higher BMI in previous studies.[463-465] Factors that go on to affect energy intake may however be more accurately measured than energy intake itself, and therefore explain associations between SEP and fat mass. For example, one study found that measures of psycho-social stress in adolescence mediate part of the association between lower SEP and higher BMI.[466]

As in previous chapters, associations with android: gynoid ratio were driven by the separate associations with android and gynoid fat mass (shown in Appendix 36). In males, associations between lower SEP and higher android: gynoid ratio were driven solely by associations between lower SEP and higher android fat mass; in females lower SEP was associated with higher android and gynoid fat mass, with similar effect sizes (as females have on average more gynoid than android fat mass this lead to a higher ratio). These findings suggest that in addition to higher whole body fat mass, those of lower SEP had proportionally more abdominal fat mass. While the factors that regulate fat distribution are unknown, high levels of stress have been hypothesised as causing preferential distribution of fat in the abdominal (android) region, due to higher stress levels stimulating the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system.[467] SEP could therefore feasibly affect fat distribution by leading to differences in stress.

Associations between lower SEP (in both childhood and adulthood) and higher fat mass were typically stronger in females. Sex differences are likely to reflect sex differences in the socioeconomic patterning of factors which influence fat mass. For example, there is some evidence to suggest that social pressure against higher fat mass is higher in females from higher SEP groups.[468] Additionally, females of lower SEP tend to undergo puberty earlier[171] and give birth to more children: both of these factors may lead to an increase in accumulation of fat mass through biological mechanisms (eg, changes in hormone secretion) and social mechanisms (eg,

reduction in physical activity levels).[466;469] In contrast, earlier pubertal maturation in males is associated with higher whole body lean mass (but not fat mass).[330] Sex differences in the pathways leading from lower SEP to higher fat mass have also been suggested in studies investigating mediators of associations between lower SEP and higher BMI, although the pathways operating in each sex are not understood.[464;466]

In this chapter, the strengths of associations between the different indicators of lower SEP and higher fat mass differed by sex and outcome (fat mass index compared with android: gynoid ratio). While a comprehensive study of the pathways that link each indicator with outcomes was beyond the scope of this chapter, differences in associations between indicators and fat mass may be informative. For example, the finding that lower educational attainment had persistent associations with higher fat mass in males but not females suggests that in this cohort females may have benefited less from education (with respect to health behaviours). Differential effects of education between the sexes have previously been found in the NSHD, for example higher educational attainment was associated with lower alcohol consumption in males but higher consumption in females at 36 years.[470] In females, lower paternal educational attainment was more strongly associated with higher fat mass than paternal occupational class, and may therefore have been more closely associated with the development of relevant behavioural traits.

Both household income at 60–64 years and occupational class at 53 years were used as indicators of adult SEP. These may feasibly be related by specific pathways to fat mass. For example, associations between low household income and not occupational class may suggest that associations reflect differences in access to material resources, rather than differences in factors specific to occupational class (such as occupational-based physical activity). In addition, a high income may protect against food insecurity which may increase the likelihood of binge eating.[450] However occupational class at 60–64 years was not used in these analyses since most study members (approximately 61%) had retired from their main occupation. As such, household income may instead have been a more accurate measure of SEP at 60-64 years (and preceding ages) than occupational class at 53 years.

Differences in association between indicators of SEP and fat mass could also be partially influenced by selection (ie, aspects of body composition influencing subsequent SEP).[166] Selection may either strengthen or weaken associations found: for example, if acute illness is followed by loss of weight (and fat mass), a reduced

capacity to undertake work and lower household income, associations between lower income and higher fat mass would be weakened. Alternatively, higher fat mass may impair educational attainment,[471] thereby strengthening associations between low educational attainment and higher fat mass. However, the prevalence of childhood obesity was comparatively low in the NSHD compared with contemporary cohorts, suggesting that this is unlikely to be a major explanation of findings. Selection is unlikely to influence associations with SEP in childhood since the indicators represent events formulated predominantly before the birth of the study member (eg, parental educational attainment).

### 6.6.4 *SEP and lean mass: explanation of findings*

Associations between lower SEP and lower lean mass likely reflect socioeconomic differences in the determinants of lean mass (outlined further in Chapter 1), including the development of peak lean mass in pre-adult life, and physical activity levels in adulthood.

The relative strength of associations between SEP and whole body lean mass mirrored those between SEP and fat mass, and associations between SEP and appendicular lean mass differed after adjustment for fat mass: after adjustment, there was evidence for association between lower SEP and lower appendicular lean mass, although fewer indicators were associated in males (lack of home ownership and low household income only). These findings suggest that associations between lower SEP and lower lean mass were confounded by fat mass.

Associations between lower SEP in childhood and lower lean mass in females (after adjustment for fat mass) were only slightly attenuated after adjustment for birth weight. This may be explained by the weak unadjusted associations between SEP and birth weight. Unlike associations found between SEP and fat mass, associations between lower SEP and lower lean mass were typically not explained by weight gain from birth to 20 years. This may be expected, as those of lower SEP in childhood tended to undergo greater weight gain in this period, which in Chapter 4 was associated with higher fat and lean mass.

Associations between lower SEP and lower lean mass tended to be partly but not fully explained by leisure time physical activity levels (which, as shown in Chapter 5, were associated with higher lean mass). As such, other factors may explain these associations. These may include dietary factors such as protein intake, which has been associated with higher lean mass,[186;193;194] although as discussed

previously the extent to which this is demonstrable depends on the accuracy of dietary assessment which may vary by body weight. Conflicting findings have been reported for associations between SEP and protein intake,[472] and to the author's knowledge no studies have examined the mediators of associations between SEP and lean mass.

That lower SEP was associated with lower lean mass (after adjustment for fat mass) more consistently in females than males suggests that there are sex differences in the socioeconomic patterning of the determinants of lean mass. In males, indicators may reflect conflicting exposures which are both beneficial and detrimental in leading to higher lean mass. For example, lower occupational class in adulthood may be characterised by a history of manual occupations, and thereby greater occupational-based weight-bearing physical activity (leading to higher lean mass), but was also associated with lower participation in leisure time physical activity levels (leading to lower lean mass).

The strength of associations between indicators of lower SEP and lower lean mass differed by indicator. In males, unlike females, lack of home ownership at 26 years was associated with lower appendicular lean mass at 26 years. Home ownership at this age was previously found to be a strong predictor of lower mortality risk in both sexes in the NSHD,[473] and is likely to reflect the acquisition of wealth in early adulthood. It is feasible that this indicator could reflect different phenomena in each sex, such as the personal acquisition of wealth in males (with favourable effects on future disposable income), and home ownership due to marriage in females. However, it is unclear why home ownership was related to lean mass but not fat mass in males, suggesting that further research is required.

In both sexes lower household income was associated with lower appendicular lean mass. Lower disposable income could theoretically impair the purchase of a number of resources which lead to the development of higher lean mass—notably a protein-rich diet and access to leisure based physical activity (such as gym membership).

### 6.6.5 ***Methodological considerations***

While this chapter included more indicators of SEP than used in previous studies, in some instances the indicators used were relatively crude. For example home ownership at 26 years was used and is arguably an indicator of wealth acquisition. More comprehensive measures of wealth in adulthood (value of assets minus debt) were not available—these tend to be more strongly related to health related-

outcomes[474] than cruder estimates, and may therefore be more closely related to body composition. However, lack of home ownership at 26 years was previously strongly associated with increased mortality in the NSHD[473] suggesting that it may be an informative indicator of SEP in this population.

In addition, household income is likely to be only a crude measure of disposable income.[426] Given the same household income, households with more residents, greater housing costs and/or debt payments would have lower disposable income. Additional analyses showed similar results were obtained when household income was equivilised by household size (divided by the square root of household number),[475] suggesting this was unlikely to substantially affect associations found (data not shown). Due to inflation, the value of the state pension and earned income increased in each year of the study (from 2006–2010; 60 to 64 years), and this may have affected the categorisation of household income—participants who attended clinic visits towards the end of data collection (64 years) would be more likely to be placed in a higher household income than those who attended earlier. As expected, household income was associated with other indicators of SEP in the expected direction (with lower income associated with lower SEP in other indicators), suggesting that the measure has some value.

In this chapter the slope index of inequality was used to quantify associations between SEP and body composition outcomes. While this methodology assumes a linear relationship between exposure and outcome, in a minority of associations there was evidence for departure from linearity—for example associations between lower paternal occupational class and higher fat mass index in males. In these cases the use of the slope index of inequality may have been inappropriate, and an oversimplification of the genuine nature of association. The tabulation of the mean body composition outcomes by SEP group enabled the cause of deviation from linearity to be examined and in all cases it was judged that the deviation from linearity was modest in absolute terms. In the majority of associations examined there was little evidence for departure from linearity, suggesting that the slope index was appropriate for use.

The use of complete case analyses in this chapter may have resulted in bias. However, in almost all cases associations were similar in analyses conducted using the maximum available sample size and those conducted in samples restricted to those with valid data for multiple indicators of SEP or for potential mediators. In both sexes, associations between lower household income and lower appendicular lean mass (after adjustment for fat mass) were weaker in the sample with available

data for potential mediators. This was due to those with valid data for all potential mediators tending to have higher household income. However, further analyses showed that associations between lower household income and lower appendicular lean mass (after adjustment for fat mass) were found in both sexes when analyses were restricted to those with valid data for body composition measures and leisure time physical activity at 60–64 years (males: (β(slope index term)=-0.22, 95% CI: -0.44, -0.01; females: β=-0.16, 95% CI: -0.33, 0.00). After adjustment for leisure time physical activity at 60–64 years these associations were partly attenuated in both sexes (males: β=-0.15, 95% CI: -0.37, 0.07; females: β=-0.13, 95% CI: -0.29, 0.04). These further analyses are in concordance with results from main analyses.

Attrition in the NSHD, resulting in some participants not providing full body composition data at 60-64 years, may have also introduced bias. Analyses in Chapter 2 showed that those of lower SEP (in childhood and adulthood) and those who were heavier at 53 years were less likely to provide full body composition outcome data. Assuming that a higher weight is capturing higher fat mass, this pattern of missing data would have led to reduced power to detect the association between lower SEP and higher fat mass.

### 6.6.6 ***Strengths***

Chapter 1 presents the overall strengths of the NSHD, while the strengths specific to this chapter are outlined below.

A major strength of this chapter is the use of a wide number of indicators of SEP in both childhood and adulthood, unavailable in previous studies using direct measures of fat and lean mass. The use of multiple indicators in both childhood and adulthood enabled the pathways underlying associations with outcomes to be investigated. By using multiple indicators (which likely reflect different dimensions of SEP), the most relevant indicator for each outcome was investigated and selected for use in multivariable analyses. The use of the slope index of inequality ensured that the effect sizes for associations with outcomes were comparable across indictors of SEP.

Another major strength of this chapter is the use of direct measures of body composition obtained using DXA: most previous studies have used indirect measures and of those that have used direct measures a sizable proportion have used BIA, considered to be inaccurate and imprecise.[178-180] Previous studies have

also tended not to examine associations with both fat and lean mass, or do not consider how SEP relates to both masses. By considering both masses in this chapter it was found that those of lower SEP tended to have a higher fat: lean mass ratio and that, once adjusted for fat mass, there was some evidence that lower SEP was associated with lower lean mass. In addition, this chapter included regional measures of body composition (appendicular lean mass and android: gynoid ratio)—as discussed in Chapter 1, these may be more closely related to health and physical functioning outcomes, and therefore warrant study. Finally, unlike some previous studies, fat and lean mass were adjusted for adult height in this chapter. As lower SEP predicts shorter adult height,[408;409] and shorter adults tend to have lower fat and lean mass (Chapter 2), adult height could confound associations between lower SEP and higher fat mass, or mediate associations between lower SEP and lower lean mass. The presence of associations after this adjustment suggests that associations were not solely explained by adult height. As discussed in Chapter 2, height-adjusted measures of fat and lean mass are likely to be more closely related to health and physical functioning.

To the author's knowledge, no previous studies have examined the mediators of associations between SEP and direct measures of fat and lean mass. These analyses enabled the pathways underlying association to be better understood than in previous studies. In addition, the study of mediation provides stronger evidence for the hypothesised association between the exposure (SEP) and outcome (body composition).[456]

### 6.6.7 ***Conclusion and links to other chapters***

This chapter has shown evidence for association between multiple indicators of lower SEP (in childhood and adulthood) and higher fat mass at 60–64 years. These associations were partly mediated by factors considered in previous chapters—associations between lower SEP in childhood and higher fat mass were partly explained by weight gain from birth to 20 years, and associations of lower SEP in childhood and adulthood with higher fat mass were partly explained by participation in leisure time physical activity across adulthood.

There was some evidence that lower SEP was associated with lower appendicular lean mass after adjustment for fat mass, although findings differed by sex: in males only lack of home ownership and low household income were associated with lower appendicular lean mass; in females, most indicators of lower SEP (in childhood and adulthood) were associated with lower appendicular lean mass. In some cases

these associations were partly explained by leisure time physical activity levels in adulthood.

The following chapter, Chapter 7, summarises the main findings of the thesis and discusses the implications, the strengths and weaknesses of the work conducted, and recommendations for future work.

# 7. Chapter 7: Summary of main findings, implications, strengths and limitations, and future work

## 7.1 Summary of main findings

This thesis used data from a birth cohort study, the NSHD, and found explanatory factors in both early and adult life were associated with direct measures of fat and lean mass at 60–64 years.

Chapter 3 showed that higher birth weight (an indicator of greater prenatal growth) was associated with higher lean mass and a lower android: gynoid ratio. Chapter 4 found that greater weight gains in infancy, early childhood and in late adolescence (birth to 20 years) were associated with higher lean mass, while greater weight gains in later childhood and adolescence (7–20 years) were associated with higher fat mass and a higher android: gynoid ratio. Greater height gains in childhood and adolescence were associated with higher lean mass, associations which were largely explained by adult height.

Chapter 5 found associations between greater total physical activity energy expenditure at 60-64 years and lower fat mass—this association was driven by variations in light intensity activity. In contrast, greater total physical activity energy expenditure was associated with higher appendicular lean mass (after adjustment for fat mass), and this association was driven by variations in moderate-vigorous intensity activity. Building on these cross-sectional analyses, Chapter 5 found evidence for cumulative benefits of leisure time physical activity across adulthood (36, 43, 53 and 60–64 years) in leading to lower fat mass (in females) and higher appendicular lean mass (in both sexes, after adjustment for fat mass).

Chapter 6 found associations between multiple indicators of lower SEP (in childhood and adulthood) and higher fat mass and higher android: gynoid ratio. After adjustment for fat mass, lower SEP in childhood was associated with lower appendicular lean mass (in females but not males), and lower SEP in adulthood was associated with lower appendicular lean mass (more consistently across indicators in females).

Chapter 6 then examined whether associations between SEP and body composition outcomes were mediated by the explanatory factors examined in Chapter 3–5.

Associations between lower SEP in childhood and higher fat mass were partly explained by weight gain from birth to 20 years, while associations of lower SEP in childhood and adulthood with higher fat mass were partly explained by participation in leisure time physical activity in adulthood. Associations between lower SEP and lower appendicular lean mass (after adjustment for fat mass) were in some cases partly attenuated by leisure time physical activity across adulthood, but not by weight gain from birth to 20 years.

In each chapter the analyses conducted extended previous findings using anthropometric measures of fat mass (such as BMI) in the NSHD and in other cohort studies. Few previous studies have used direct measures of fat and lean mass in adulthood, and as such new findings were presented in each chapter. For example, no previous studies have examined whether there are cumulative benefits of physical activity across adulthood for fat and lean mass, and few have used objective measures of physical activity in later adulthood. The implications of these findings are discussed below.

## 7.2 **Implications of findings**

As discussed in more detail in Chapter 1, there is evidence that high fat mass leads to increased risk of chronic diseases, mortality, and worse physical functioning, and that low lean mass is associated with worse physical functioning, low bone mineral content and density, and adverse glucose metabolism. As such, the identification of factors associated with these masses in later adulthood is important and could be used to inform public health interventions which aim to reduce fat mass and increase lean mass in the population.

This thesis used a life course perspective and found factors across life (from birth to adulthood) were associated with fat and lean mass in later adulthood. These findings suggest that efforts to reduce fat mass and increase lean mass in the population should be implemented from early life onwards. While exercise and dietary interventions in later adulthood may lead to reductions in fat and gains in lean mass, these are economically costly to operate on a national scale and typically lead to only modest long term changes in these masses.[184;390] Further, resistance exercise interventions designed to lead to gains in lean mass tend to be less effective at older ages,[184] and participation in exercise interventions tends to be strongly socioeconomically patterned, with those of low SEP least likely to participate.[476] As such, early life interventions may be a useful additional means of

leading to changes in fat and lean mass in adulthood, and could be more effective than intervening in adulthood.[75;210;211]

Findings from Chapters 3 and 4 suggest that growth in early life may have lasting effects on fat and lean mass that persist into later adulthood. Associations found suggest that greater weight gain in early life (before birth and in infancy) may be beneficial by leading to higher lean mass and a lower android: gynoid ratio, while greater weight gain in later childhood and adolescence (7–20 years) may be detrimental by being particularly related to higher fat mass and android: gynoid ratio. These findings add to the evidence base of the complicated long-term implications of growth before and after birth, and are likely to have greater public health implications than previous studies using BMI as an outcome.

While there is some evidence from experimental studies that birth weight[477] and infancy weight gain can be modified by nutritional interventions,[208] the implications of findings from Chapters 3 and 4 should be considered within the broader context of uncertainty regarding the consequences of growth rates (before and after birth) for health outcomes.[478] For example, meta-analyses have found higher birth weight to be associated with lower risk of cardiovascular disease mortality,[247] but increased risk of cancer mortality (in males)[247] and type 1 diabetes.[479] The promotion of early life weight gain across the entire distribution may also have adverse consequences for the mother by increasing the risk of obesity and need for caesarean sections.[480] As has been suggested, rather than increasing growth rates across the entire distribution, it may instead be more effective to focus on preventing adverse early growth among those in the lower end of the distribution (eg, preventing preterm birth).[480]

Results from Chapter 5 suggest that the benefits of physical activity in leading to lower fat mass are not limited to high-intensity aerobic exercises, as light intensity physical activity was related to fat mass. The benefits of light intensity physical activity are particularly relevant for those in older age: such activities may be less likely to lead to falls and are more feasibly undertaken by those with health complications (which increase in prevalence in old age).[212] Results from Chapter 5 also suggest that participating in greater moderate-vigorous activity may lead to higher lean mass. This suggests a need to encourage greater participation in activities of higher intensities which are feasibly and safely undertaken by older adults. While intervention studies have shown that resistance exercises are effective in leading to gains in lean mass, results from Chapter 5 suggest that a broader range of leisure time activities are also beneficial.

Findings from Chapter 5 suggest that there are cumulative benefits of physical activity across adulthood in leading to lower fat mass (in females) and higher lean mass (in both sexes). These results support the need to encourage higher activity levels across adulthood on the basis of the potential lasting beneficial effects. As there is some evidence that activity levels track across life,[331;332;371] the promotion of physical activity in childhood may have lasting effects across life. The weaker evidence for cumulative benefits in males for fat mass suggests that leisure time physical activity levels need to be sufficiently high to lead to lower fat mass, and not offset by lower activity in other domains or higher energy intake. Although these analyses were limited to leisure time physical activity, this may be an important intervention target during working age in the context of the increasingly sedentary nature of occupations.

As suggested in previous research, efforts to increase population physical activity levels can operate at a number of levels. For example, the health benefits of physical activity can be disseminated, intervention programmes can be offered to individuals and groups, and the external environment can made to be more conducive to physical activity.[476;481] Given the importance of physical activity for body composition and health outcomes, and the uncertain long-term effectiveness of single interventions,[482] it may be prudent to recommend multiple interventions at the individual and societal levels to increase population physical activity levels.

Results from Chapter 6 suggest that reducing socioeconomic inequalities in both childhood and adulthood may have beneficial effects by leading to fewer individuals in later adulthood developing higher fat mass and, particularly for females, lower lean mass. This is provided that inequalities are reduced by upwards mobility in those of lower SEP. Findings from this chapter suggest that reducing socioeconomic inequalities could have favourable downstream effects on fat and lean mass by leading to lower population levels of weight gain in childhood and adolescence, and higher adult leisure time physical activity levels.

As suggested in the government-commissioned Marmot review on health inequalities in 2010, multiple policies operating across life could feasibly reduce socioeconomic inequalities.[291] For example, early life interventions could be used to improve educational attainment, and minimum income levels in adulthood can be set to enable healthy living. The most effective means of reducing socioeconomic inequalities are uncertain and the evidence is typically drawn from the evaluation of government policies which are arguably limited in scope and ineffectively

implemented across socioeconomic groups.[483;484] Further, there is some evidence that the effects of early life interventions on socioeconomic inequalities may only be manifest after prolonged periods of time, suggesting that long term evaluations are required.[485]

In Chapter 6 the strengths of associations found between indicators of SEP and body composition varied by each indicator used. This may have implications for studies which attempt to accurately quantify associations between SEP and outcomes, and suggest that, where possible, multiple indicators should be used. For example, while paternal occupational class is often used to estimate the influence of SEP in childhood, paternal educational attainment was more strongly associated with fat mass in females (~30% larger effect sizes).

## 7.3 **Generalisability**

The extent to which findings from this thesis generalise to younger cohorts may be questionable, particularly for Chapters 3 and 4. Associations between weight gain and body composition in adulthood may differ in younger cohorts that have experienced higher prevalence of childhood obesity—[17;486] in these cohorts weight gain in infancy may predominantly reflect gains in fat mass. In older cohorts including the NSHD, as discussed in Chapter 4, weight gain in infancy may predominantly reflect gains in lean mass. However, consistent with results from Chapter 4, studies conducted in younger adults have also found that greater weight gain in later childhood is associated with higher fat mass.[261;319]

In addition to the generalisability of findings to younger cohorts, it should be noted that the NSHD, similar to many other European cohort studies,[487] is comprised of Caucasians, and as such not all findings may be relevant to those of different ethnic groups. Ethnic differences in body composition have been found both in early[277] and adult life,[488] and the determinants of body composition may differ by ethnicity. Findings could also differ across nations which may have different distributions of the determinants of fat and lean mass.

Ultimately, few studies have been conducted using direct measures of fat and lean mass, limiting the comparison of findings by age, ethnicity or country. There is however some evidence that findings from Chapters 5 and 6 are consistent with those in younger cohorts: using the Avon Longitudinal Study of Parents and Children, lower SEP was associated with higher fat mass in childhood,[452] and higher physical activity levels were associated with lower fat mass in adolescence.[188]

## 7.4 Strengths and limitations of the work conducted in this thesis

The specific strengths and limitations of the analyses conducted in Chapters 3–6 are discussed within each chapter. To avoid repetition, only the overarching strengths and limitations of the work conducted in this thesis will be described below.

### 7.4.1 *Strengths*

The use of a life course perspective is a major strength of this thesis. As described in Chapter 1, this perspective is useful to understand the factors which across life impact on fat and lean mass. The use of this perspective led to the identification of potentially modifiable factors in both early and adult life which may affect fat and lean mass.

The rich data collected in the NSHD was a main strength and enabled analyses to be adjusted for multiple relevant potential confounders. For example, associations found in Chapters 3–5 were independent of indicators of SEP. Multiple indicators of SEP were available and in all cases were prospectively ascertained, limiting measurement error, and thereby reducing the likelihood of residual confounding by SEP. In addition, the rich data also enabled the potential mediators of associations between SEP and body composition outcomes to be investigated.

The repeat measures of weight and height, physical activity, and SEP in the NSHD were used in this thesis to address specific research questions which it would not be possible to address using single measures. For example, repeat measures of weight were used to show which periods of weight gain were associated with fat and lean mass. Repeat measures of leisure time physical activity were used to test for evidence of cumulative benefits of physical activity across adulthood in leading to lower fat and higher lean mass.

Another main strength of this thesis is the use of direct measures of fat and lean mass. As discussed in Chapter 2, these were obtained using DXA, a method which is considered to be relatively highly accurate and precise, and unlike many other

methods enable regional measures of fat and lean mass to be assessed. The use of appendicular lean mass in this thesis provided further evidence for associations with skeletal muscle mass, as associations found in previous studies with whole body lean mass could feasibly be driven by organ or bone mass. The use of android: gynoid ratio showed that factors considered in this thesis were in many instances differentially associated with abdominal and leg/hip fat mass. As discussed in Chapter 2, these may be differentially important for subsequent health, and therefore warrant study.

The ways in which fat and lean mass were used in analyses had a number of strengths. Unlike many previous studies, fat and lean mass were adjusted for adult height and the implication of this adjustment was discussed in each chapter (eg, as a mediator or potential confounder). Finally, fat and lean mass were treated as continuous outcomes and not categorised, preserving statistical power. This was also justified given the lack of agreement on cut-points for direct measures of high fat and low lean mass, and given the need to understand variability in these masses across the full range. Previous studies have typically not considered whether associations with lean mass are driven by associations with fat mass. This was considered in this thesis, and in some cases important associations were only found after this adjustment.

### 7.4.2 ***Limitations***

In this thesis, a decision was taken to use complete case analyses with main analyses restricted to those with valid data for explanatory variables, main confounders, and outcomes. This led to a reduction in sample size and a consequent reduction in statistical power. It also may have introduced bias whereby the genuine associations were either weakened or strengthened in the samples analyses. However, exclusion due to missing data for potential confounders was relatively small in each chapter, and sensitivity analyses showed findings were similar when this restriction was removed, suggesting that this was unlikely to have substantially impacted on findings.

Aside from introducing bias, the use of complete case analyses led to a reduction in sample size and consequent reduction in statistical power. However, in comparison with most previous studies with direct measures of fat and lean mass, the NSHD is comparatively large. As such, in most cases the analyses conducted had sufficient power, with p-values for main associations typically below 0.05. In addition to presenting p-values, for all main analyses confidence intervals were presented,

providing additional information about the likely strength of association in the population.[489] Efforts were made in this thesis to preserve the sample size and therefore maximise the available statistical power. For example, explanatory variables were not categorised where possible.

Multiple imputation could have been conducted to impute missing values, leading to a larger sample size available for analyses; this would have led to an increase in statistical power.[490] While complete case analyses were arguably sufficient to address the aims of this thesis, multiple imputation could be useful in future analyses of smaller, more restricted samples (eg, when investigating in more detail the pathways underlying associations between SEP and body composition). However, multiple imputation assumes that the reason for missing data is dependent on variables within the dataset ('missing at random') and not unmeasured variables ('missing not at random'). Where this assumption is not valid, multiple imputation could feasibly introduce bias.

The NSHD, like all longitudinal studies, has experienced losses to follow-up which could also introduce bias. A strength of the NSHD is that substantial prospective data exists in which to examine the predictors of loss to follow-up, and this can be used to infer the effect of attrition on associations found. This was examined in this thesis in Chapter 2, which found that those who provided full body composition outcome data at 60-64 years were more likely to have been of higher SEP (in childhood and adulthood), be more physically active at 53 years, and weigh less at 53 years. Assuming that weight was capturing fat mass, as discussed in Chapters 5 and 6, this pattern of missing data was likely to have led to a reduced power to detect the associations of lower SEP and lower physical activity levels with higher fat mass. Further, there is no obvious reason why the associations observed should differ in the sample with missing data.

## 7.5 **Future work**

Like all observational studies, the findings presented in this thesis cannot in isolation provide definitive proof that associations observed are causal. The replication of findings found in this thesis may therefore provide further strength of evidence to support the conclusions drawn in each chapter. For example, while a relatively large number of studies have examined associations between birth weight and body composition in adulthood, fewer have been conducted in later adulthood and none have used android: gynoid ratio as an outcome. Few studies have examined associations of measures of growth after birth (Chapter 4), physical

activity (Chapter 5), or SEP (Chapter 6) with fat and lean mass in adulthood. The replication of findings in contexts with different confounding structures may be particularly informative. For example, associations of greater weight gains in childhood and adolescence with higher adult fat mass could be replicated in a cohort or country in which weight gain is not associated with SEP, providing further evidence that these associations are not explained by residual confounding by early life SEP. The replication of findings in cohorts with different physical activity patterns may also be informative. For example, in cohorts where objectively assessed total physical activity energy expenditure and time spent in moderate-vigorous intensity activity are less strongly correlated than in the NSHD, their independent associations with body outcomes may be estimated.

As described in each chapter, the explanatory variables used were largely improvements on previous work. However, other explanatory variables not collected in the NSHD may be more closely related to body composition outcomes. These measures may include direct measures of prenatal growth (within trimesters), weight gain in early infancy, measures of bouts of sedentary time, and more refined indicators of adult SEP such as comprehensive measures of wealth and disposable income.

As associations of lower SEP with higher fat and lower lean mass were not fully explained by the potential mediators considered, future work could examine the roles of other potential mediators. As discussed in Chapter 6, these factors are likely to include dietary factors which may be challenging to accurately assess in population studies.

Chapter 6 focused on associations between SEP in childhood and adulthood with body composition outcomes. Future work could examine whether childhood and adult SEP interact (ie, intergenerational social mobility),[411] and investigate which life course model best fits the data. Previous studies comparing life course models of SEP in relation to BMI at 53 years in the NSHD have used paternal and own occupational class. Results from Chapter 6 suggest that additional indicators of SEP (such as paternal and own educational attainment, and household income) may be more relevant for body composition outcomes, and could be considered in future analyses.

There are a number of methodological and analytical recommendations that arise from the use of body composition in this thesis. While some previous studies have focused exclusively on lean mass as an outcome, and excluded fat mass, findings

from this thesis suggest that in some cases associations with lean mass may be confounded by fat mass. This warrants a-priori consideration in future studies, and supports recent studies which suggest that fat mass should be taken into account when examining associations with lean mass.[4] In addition, a number of previous studies have made no adjustment for adult height when using fat or lean mass as outcomes. Findings from this thesis suggest that adult height may be an important factor which should be taken into account in analyses (and may act as either a mediator or confounder).

As direct measures of whole body and regional fat and lean mass have only recently become available for use in epidemiological studies, there is some uncertainty regarding the parameters which are most important for subsequent health and physical functioning. For example, while there is some evidence that abdominal fat distribution is detrimental for health (Chapter 1), further longitudinal studies are required to demonstrate whether measures of fat distribution provide additional information in predicting health outcomes than whole body fat mass. Further work in this area would guide work which aims to examine the lifetime determinants of adult body composition.

While this thesis has examined how explanatory factors across life relate to measures of fat and lean mass at a single point in time, future work could examine how factors relate to changes in these masses across adulthood. This may aid in the understanding of aetiology, as many explanatory factors considered could feasibly influence the peak levels of lean mass and/or the rates of subsequent decline. In addition, the age-related changes in fat and lean mass may be more closely related to health and physical functioning than measures recorded at one point in time.[94]

As described in Chapter 1, fat and lean mass have important implications for health and physical functioning. As such, the associations found in this thesis may explain how factors across life affect health and physical functioning. Future work, utilising the continued follow-up of birth cohorts such as the NSHD, could examine this and help elucidate the lifetime determinants of health and physical functioning in old age.

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## Appendices

Appendix 1. Mean difference in whole body and appendicular lean mass (95% CI, p-value) per unit increase in fat mass

a) Males (n=746)

| | Appendicular lean mass (kg) | Appendicular lean mass index (kg/m$^2$) |
|---|---|---|
| Fat mass (kg) | 0.24 (0.21, 0.27), <0.001 | 0.06 (0.06, 0.07), <0.001 |
| Fat mass index (kg/m$^{1.2}$) | 0.40 (0.34, 0.47), <0.001 | 0.13 (0.11, 0.15), <0.001 |

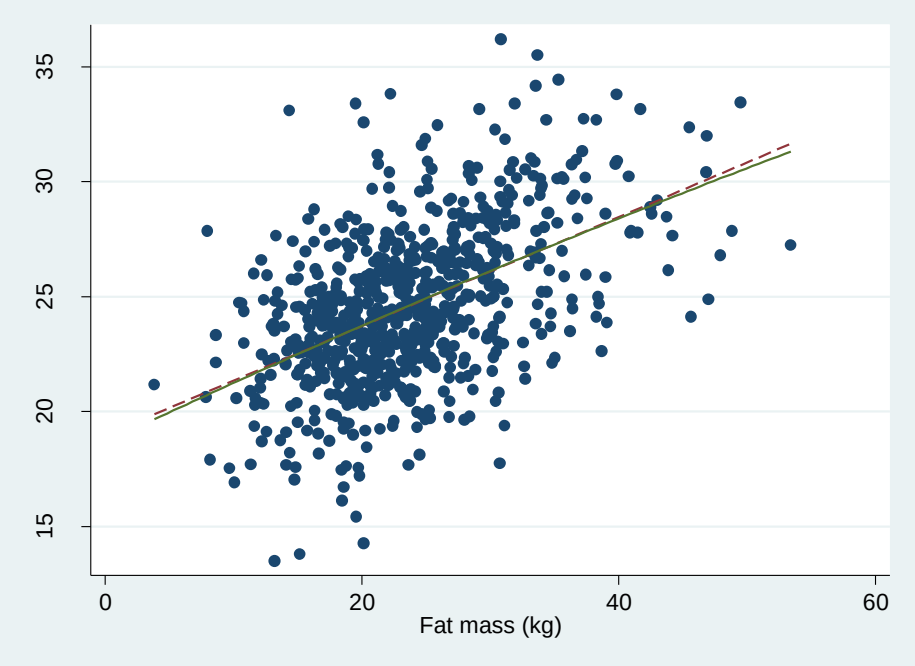
b) Females (n=812)

| | Appendicular lean mass (kg) | Appendicular lean mass index (kg/m$^2$) |
|---|---|---|
| Fat mass (kg) | 0.18 (0.16, 0.19), <0.001* | 0.06 (0.06, 0.07), <0.001* |
| Fat mass index (kg/m$^{1.2}$) | 0.29 (0.26, 0.32), <0.001* | 0.11 (0.10, 0.12), <0.001* |

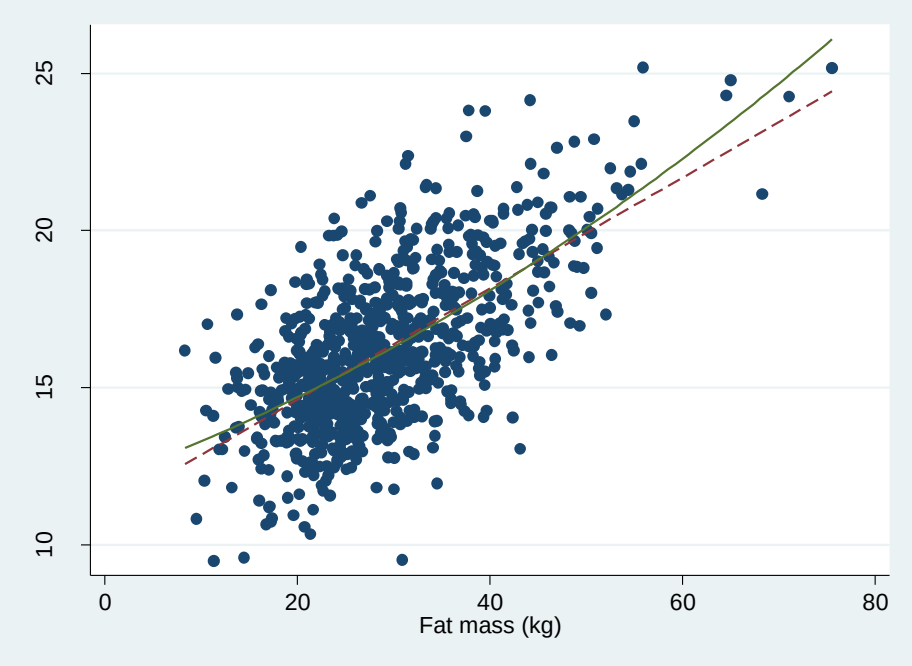
Note: *evidence for deviation from linearity, p(quadratic term)<0.05; analyses were restricted to those with valid data for body composition outcomes

Appendix 2. Scatter plot of appendicular lean mass and fat mass with fitted linear (dashed) and quadratic (solid) lines of best fit

a) Males (n=746)




b) Females (n=812)




Note: depicted are those with valid data for body composition outcomes

Appendix 3. Associations between potential confounders/mediators and (a) birth weight and (b) body composition outcomes
a) birth weight

| Potential confounding/mediating factor (in groups) | N | Mean birth weight (kg), SD | |
|---|---|---|---|
| Sex | | | |
| Male | 709 | 3.44 (0.51) | |
| Female | 763 | 3.36 (0.46) | |
| P-value (t-test) | | | <0.01 |
| | | | |
| Adult height at 60–64 years in cm (60–64y) | | | |
| 1st quartile (≤161.5) | 362 | 3.26 (0.46) | |
| 2nd quartile (>161.5–167.5) | 366 | 3.37 (0.47) | |
| 3rd quartile (>167.5–175) | 372 | 3.41 (0.47) | |
| 4th quartile (>175) | 372 | 3.55 (0.51) | |
| P-value (linear trend) | | | <0.001 |
| P-value (sex interaction) | | | 0.25 |
| | | | |
| Maternal age (years) at birth of study member | | | |
| <20 | 60 | 3.24 (0.48) | |
| 20-25 | 334 | 3.32 (0.46) | |
| >25-30 | 325 | 3.41 (0.50) | |
| >30-35 | 448 | 3.45 (0.49) | |
| >35 | 191 | 3.45 (0.47) | |
| P-value (linear trend) | | | <0.001 |
| P-value (sex interaction) | | | 0.97 |
| | | | |
| Maternal height (cm) when study member 6y | | | |
| 1st quartile (≤155) | 275 | 3.29 (0.48) | |
| 2nd quartile (>155–157) | 190 | 3.32 (0.47) | |
| 3rd quartile (>157–162) | 413 | 3.39 (0.48) | |
| 4th quartile (>162) | 456 | 3.51 (0.49) | |
| P-value (linear trend) | | | <0.001 |
| P-value (sex interaction) | | | 0.33 |
| | | | |
| Maternal body mass index (kg/m$^2$) when study member 6y | | | |
| Underweight (<18.5) | 76 | 3.17 (0.52) | |
| Normal weight (18.5-25) | 894 | 3.37 (0.48) | |
| Overweight (>25-30) | 283 | 3.49 (0.46) | |
| Obese (>30) | 73 | 3.66 (0.52) | |
| P-value (linear trend) | | | <0.001 |
| P-value (sex interaction) | | | 0.77 |
| | | | |
| Paternal occupational class (4y) | | | |
| I professional | 112 | 3.44 (0.48) | |
| II intermediate | 282 | 3.42 (0.46) | |
| III skilled (Non-Manual) | 334 | 3.39 (0.49) | |
| III skilled (Manual) | 404 | 3.39 (0.48) | |
| IV partly skilled | 265 | 3.39 (0.52) | |
| V unskilled | 75 | 3.39 (0.52) | |
| P-value (linear trend) | | | 0.27 |
| P-value (sex interaction) | | | 0.98 |

| Potential confounding/mediating factor (in groups) | N | Mean birth weight (kg), SD |
|---|---|---|
| Birth order | | |
| 1st | 647 | 3.29 (0.45) |
| 2nd | 478 | 3.42 (0.49) |
| 3rd or more | 347 | 3.57 (0.50) |
| P-value (linear trend) | | <0.001 |
| P-value (sex interaction) | | 0.39 |

b) body composition outcomes

| Potential confounder | N | Fat mass index ($kg/m^{1.2}$) | Lean mass index ($kg/m^2$) |
|---|---|---|---|
| | | | |
| Maternal age (years) at birth of study member | | | |
| <20 | 60 | 14.98 (4.75) | 15.85 (2.54) |
| 20-25 | 334 | 14.78 (4.79) | 15.84 (2.63) |
| >25-30 | 325 | 14.00 (5.10) | 15.59 (2.49) |
| >30-35 | 448 | 14.02 (4.79) | 15.78 (2.59) |
| >35 | 191 | 14.47 (5.19) | 15.82 (2.38) |
| P-value (linear trend) | | 0.13 | 0.96 |
| P-value (sex interaction) | | 0.88 | 0.26 |
| | | | |
| Maternal height (cm) when study member 6y | | | |
| 1st quartile (≤155) | 281 | 14.07 (4.49) | 15.90 (2.59) |
| 2nd quartile (>155–157) | 192 | 14.66 (4.59) | 15.73 (2.60) |
| 3rd quartile (>157–162) | 420 | 14.34 (5.15) | 15.83 (2.52) |
| 4th quartile (>162) | 463 | 14.32 (5.21) | 15.70 (2.54) |
| P-value (linear trend) | | 0.71 | 0.39 |
| P-value (sex interaction) | | 0.15 | 0.10 |
| | | | |
| Maternal body mass index ($kg/m^2$) when study member 6y | | | |
| Underweight (<18.5) | 77 | 14.05 (4.99) | 15.13 (2.60) |
| Normal weight (18.5-25) | 906 | 13.86 (4.61) | 15.69 (2.48) |
| Overweight (>25-30) | 289 | 15.42 (5.20) | 15.96 (2.62) |
| Obese (>30) | 76 | 16.05 (6.84) | 16.96 (2.76) |
| P-value (linear trend) | | <0.001 | <0.001 |
| P-value (sex interaction) | | 0.04 | 0.29 |
| | | | |
| Birth order | | | |
| 1st | 681 | 14.45 (5.06) | 15.77 (2.48) |
| 2nd | 506 | 14.18 (4.82) | 15.65 (2.55) |
| 3rd or more | 370 | 14.06 (4.75) | 15.90 (2.62) |
| P-value (linear trend) | | 0.20 | 0.58 |
| P-value (sex interaction) | | 0.02 | 0.02 |

Note: analyses restricted to those with valid data for body composition outcomes; in some instances evidence for sex interaction was also found—for brevity these instances are summarised below:

- Birth order. Being born later was associated with higher lean mass index in males (P(linear trend)=0.05) but not females (P=0.20); being born later was associated with higher fat mass in females (P=0.03) but not males (P=0.20)
- Maternal BMI. The positive association between maternal BMI and fat mass index was stronger in females than males

Appendix 4. Mean difference in lean mass per 1 kg increase in birth weight, (a) unadjusted and (b) adjusted for adult height

| | a) | | b) | |
|---|---|---|---|---|
| Outcome | β (95% CI) | P | β (95% CI) | P |
| Lean mass (kg) – Males | 2.82(1.76, 3.87) | <0.001 | 1.20(0.23, 2.17) | 0.02 |
| Lean mass (kg) – Females | 1.81(0.92, 2.69) | <0.001 | 0.77(-0.06, 1.60) | 0.07 |
| Appendicular lean mass (kg) – Males | 1.47(0.97, 1.98) | <0.001 | 0.66(0.20, 1.12) | <0.01 |
| Appendicular lean mass (kg) – Females | 0.91(0.49, 1.33) | <0.001 | 0.42(0.02, 0.81) | 0.04 |

Note: N=1264 in all models (males=610; females=654); analyses restricted to those with valid data for birth weight, paternal occupational class, maternal age, height, and BMI, birth order, and body composition outcomes

Appendix 5. Mean difference in body mass index and body composition outcomes per 1 kg increase in birth weight

| Outcome | β (95% CI) | P |
|---|---|---|
| Body mass index (kg/m$^2$) | 0.13(-0.39, 0.65) | 0.62 |
| Forearm muscle area (cm$^2$)# | 0.85(0.26, 1.44) | <0.01 |
| Android fat mass (kg) | -0.03(-0.14, 0.09) | 0.64 |
| Gynoid fat mass (kg) | 0.13(-0.01, 0.27) | 0.08 |

Note: All models were adjusted for sex; analyses restricted to those with valid data for birth weight, paternal occupational class, maternal age, height, and BMI, birth order, and body composition outcomes; N=1264 in all models except forearm muscle area, n=1041

Appendix 6. Pearson's correlation coefficients between birth weight and weight and height from 2 to 20 years

| | | a) Weight | | b) Height | |
|---|---|---|---|---|---|
| Age (years) | N (M/F) | Males | Females | Males | Females |
| 2 | 613/651 | 0.34 | 0.32 | 0.21 | 0.11 |
| 4 | 664/717 | 0.30 | 0.28 | 0.23 | 0.23 |
| 7 | 645/703 | 0.34 | 0.26 | 0.25 | 0.19 |
| 11 | 633/686 | 0.29 | 0.17 | 0.28 | 0.13 |
| 15 | 591/631 | 0.26 | 0.19 | 0.21 | 0.16 |
| 20 | 612/691 | 0.27 | 0.16 | 0.24 | 0.20 |

Note: analyses restricted to those with valid data for body composition outcomes

Appendix 7. Mean standard deviation difference in weight and height gain velocity per 1 kg increase in birth weight

| | | a) Weight (kg/year) | | b) Height (cm/year) | |
|---|---|---|---|---|---|
| Age (years) | N (M/F) | Males | Females | Males | Females |
| 0–2 | 593/627 | -0.05(-0.21, 0.10), 0.50 | 0.02(-0.15, 0.19), 0.84 | - | - |
| 2–4 | 664/717 | 0.23(0.07, 0.39), 0.01 | 0.19(0.02, 0.37), 0.03 | 0.07(-0.09, 0.23), 0.37 | 0.32(0.14, 0.50), 0.00 |
| 4–7 | 645/703 | 0.23(0.07, 0.39), <0.001 | 0.24(0.06, 0.41), 0.01 | 0.11(-0.05, 0.27), 0.17 | -0.12(-0.30, 0.05), 0.17 |
| 7–11 | 633/686 | 0.40(0.25, 0.56), <0.001 | 0.20(0.02, 0.37), 0.03 | 0.27(0.11, 0.43), <0.001 | -0.02(-0.19, 0.16), 0.86 |
| 11–15 | 591/631 | 0.23(0.06, 0.39), 0.01 | 0.23(0.06, 0.41), 0.01 | 0.02(-0.15, 0.18), 0.86 | 0.15(-0.03, 0.32), 0.10 |
| 15–20 | 612/691 | -0.04(-0.22, 0.13), 0.61 | -0.03(-0.21, 0.15), 0.72 | -0.14(-0.32, 0.03), 0.11 | 0.12(-0.06, 0.30), 0.18 |

Note: models were constructed using linear regression with birth weight as the exposure and weight or height gain velocity at each age as the outcome; no evidence found for departure from linearity (P(quadratic term)>0.15 in all cases); analyses restricted to those with valid data for body composition outcomes

Appendix 8. Pearson's correlation coefficients between height and a) body mass index (kg/m$^2$) b) weight (kg) in infancy, childhood and adolescence

| | | a) Body mass index (kg/m$^2$) | | b) Weight (kg) | |
|---|---|---|---|---|---|
| Age | N (male/female) | Males | Females | Males | Females |
| 2 | 593/627 | -0.66 | -0.50 | 0.32 | 0.37 |
| 4 | 653/700 | -0.24 | -0.24 | 0.58 | 0.60 |
| 7 | 624/679 | 0.03 | 0.05 | 0.74 | 0.69 |
| 11 | 628/679 | 0.17 | 0.25 | 0.68 | 0.69 |
| 15 | 582/623 | 0.20 | 0.01 | 0.75 | 0.49 |
| 20 | 601/682 | -0.04 | -0.09 | 0.55 | 0.44 |

Appendix 9. Mean body mass index (kg/m$^2$) in infancy, childhood and adolescence

| | | Males | | Females | |
|---|---|---|---|---|---|
| Age (years) | N (male/female) | Mean | SD | Mean | SD |
| 2 | 593/627 | 17.97 | 2.45 | 17.58 | 2.26 |
| 4 | 653/700 | 16.33 | 1.68 | 16.04 | 1.59 |
| 7 | 624/679 | 15.83 | 1.28 | 15.70 | 1.52 |
| 11 | 628/679 | 17.18 | 2.09 | 17.45 | 2.44 |
| 15 | 582/623 | 19.56 | 2.37 | 20.59 | 2.75 |
| 20 | 601/682 | 22.38 | 2.35 | 21.70 | 2.76 |

Note: analyses were restricted those with valid data for body composition outcomes

Appendix 10. Associations between pubertal timing and body composition outcomes

| | | Fat mass index (kg/m$^{1.2}$) | | Lean mass index (kg/m$^2$) | | Appendicular lean mass index (kg/m$^2$) | |
|---|---|---|---|---|---|---|---|
| Pubertal timing | N (M/F) | Males | Females | Males | Females | Males | Females |
| 1 Latest | 63/122 | 12.41 (4.32) | 14.86 (4.75) | 17.65 (2.49) | 13.73 (1.66) | 8.12 (1.17) | 5.96 (0.77) |
| 2 | 207/227 | 11.99 (3.28) | 16.04 (4.55) | 17.21 (1.82) | 14.04 (1.76) | 7.89 (0.89) | 6.08 (0.84) |
| 3 | 190/203 | 12.19 (3.90) | 17.05 (5.25) | 17.43 (1.91) | 14.44 (1.81) | 8.01 (0.87) | 6.28 (0.86) |
| 4 Earliest | 157/109 | 12.63 (3.44) | 17.11 (5.68) | 17.96 (2.00) | 14.57 (2.06) | 8.18 (0.93) | 6.36 (0.97) |
| *P-value (linear trend)* | | 0.27 | <0.001 | 0.01 | <0.001 | 0.08 | <0.001 |

| | | Fat: lean mass ratio | | Android: gynoid ratio | |
|---|---|---|---|---|---|
| Pubertal timing | N (M/F) | Males | Females | Males | Females |
| 1 Latest | 63/122 | 44.40 (11.32) | 72.71 (19.70) | 65.72 (13.09) | 44.69 (12.97) |
| 2 | 207/227 | 44.33 (10.08) | 77.16 (16.92) | 65.92 (14.97) | 44.17 (11.64) |
| 3 | 190/203 | 44.41 (12.30) | 79.42 (18.28) | 65.08 (15.02) | 45.60 (11.23) |
| 4 Earliest | 157/109 | 44.70 (10.76) | 79.66 (20.19) | 67.81 (16.80) | 45.04 (11.61) |
| *P-value (linear trend)* | | 0.79 | <0.001 | 0.33 | 0.47 |

Note: Age at puberty was derived on the basis of medical examination by school doctors at 15 years and divided into quartiles (for males, on the basis of voice breaking status and development of pubic hair and genitalia; and for females into quartiles of similar proportions on the basis of age at menarche), as previously described in detail by Hardy et al, 2006[491]; analyses were restricted those with valid data for body composition outcomes

Appendix 11. Descriptive statistics showing: the mean a) weight and b) height in infancy, childhood and adolescence, and c) Pearson's correlation coefficients between the same periods of weight and height gain (standardised velocities)

a) Weight in kg

| | | Males | | Females | | P (sex difference) |
|---|---|---|---|---|---|---|
| Age (years) | N (M/F) | Mean | SD | Mean | SD | |
| 2 | 630/678 | 13.22 | 1.39 | 12.67 | 1.47 | <0.001 |
| 4 | 682/731 | 17.54 | 2.12 | 17.21 | 2.10 | <0.001 |
| 7 | 629/681 | 23.08 | 2.78 | 22.81 | 3.12 | 0.06 |
| 11 | 633/682 | 34.36 | 5.74 | 35.36 | 6.83 | 0.01 |
| 15 | 593/631 | 51.88 | 9.20 | 52.34 | 8.08 | 0.16 |
| 20 | 616/686 | 70.40 | 8.74 | 57.79 | 8.22 | <0.001 |

b) Height in cm

| | | Males | | Females | | P (sex difference) |
|---|---|---|---|---|---|---|
| Age (years) | N (M/F) | Mean | SD | Mean | SD | |
| 2 | 613/651 | 86.08 | 5.00 | 85.04 | 4.31 | <0.001 |
| 4 | 664/717 | 103.62 | 4.84 | 103.55 | 4.88 | 0.77 |
| 7 | 645/703 | 120.63 | 5.21 | 120.40 | 5.39 | 0.40 |
| 11 | 633/686 | 141.18 | 6.59 | 141.98 | 6.81 | 0.03 |
| 15 | 591/631 | 162.55 | 8.95 | 159.37 | 5.94 | <0.001 |
| 20 | 612/691 | 177.31 | 6.54 | 163.14 | 6.05 | <0.001 |

c)

| | | Males | Females |
|---|---|---|---|
| Age (years) | N (M/F) | | |
| 2–4 | 554/570 | 0.09 | 0.29 |
| 4–7 | 567/608 | 0.28 | 0.32 |
| 7–11 | 566/614 | 0.39 | 0.49 |
| 11–15 | 536/582 | 0.63 | 0.30 |
| 15–20 | 493/549 | 0.57 | 0.36 |

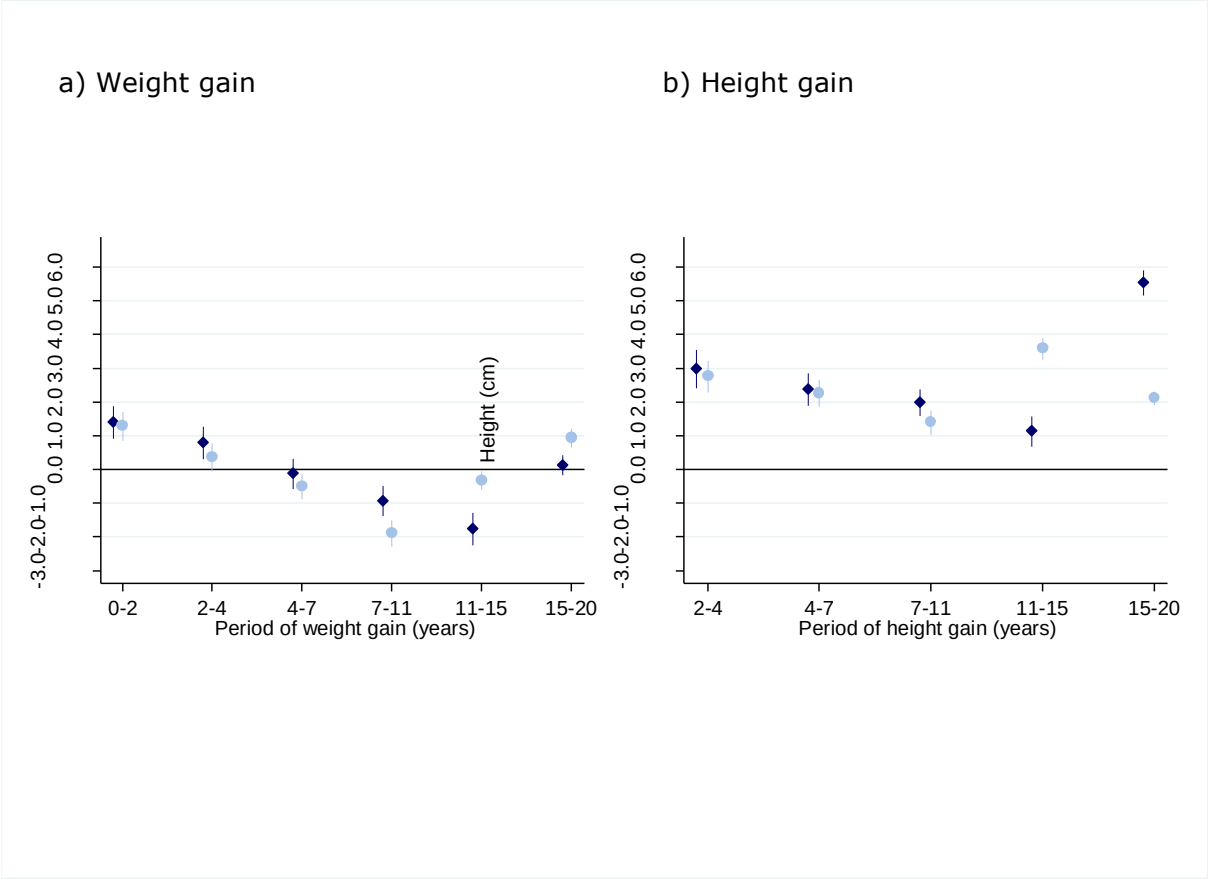
Note: analyses were restricted those with valid data for body composition outcomes

Appendix 12. Mean differences (95% confidence intervals, P-value) in (a) weight and (b) height gain velocity (standard deviation score) between the lowest and highest childhood socioeconomic position in childhood (paternal occupational class at 4 years)—the slope index of inequality

| a) Weight gain (years) | Males | Females |
|---|---|---|
| 0-2 | -0.37(-0.66, -0.09), 0.01 | -0.34(-0.61, -0.07), 0.01 |
| 2–4 | -0.10(-0.37, 0.17), 0.48 | 0.09(-0.17, 0.35), 0.51 |
| 4–7 | 0.01(-0.26, 0.27), 0.96 | 0.08(-0.17, 0.34), 0.52 |
| 7–11 | 0.13(-0.11, 0.37), 0.29 | 0.17(-0.06, 0.39), 0.15 |
| 11–15 | 0.20(-0.02, 0.43), 0.08 | 0.16(-0.11, 0.43), 0.25 |
| 15-20 | 0.43(0.18, 0.68), <0.001 | 0.19(-0.10, 0.47), 0.21 |
| b) Height gain (years) | | |
| 2–4 | -0.26(-0.48, -0.03), 0.02 | -0.29(-0.52, -0.06), 0.01 |
| 4–7 | -0.19(-0.43, 0.05), 0.12 | -0.27(-0.51, -0.04), 0.02 |
| 7–11 | -0.08(-0.36, 0.19), 0.55 | -0.19(-0.44, 0.06), 0.13 |
| 11–15 | 0.02(-0.23, 0.26), 0.90 | -0.24(-0.47, 0.00), 0.05 |
| 15-20 | -0.39(-0.58, -0.19), <0.001 | 0.08(-0.21, 0.37), 0.59 |

Note: models in a) are adjusted for concurrent height gain and weight and height at the beginning of each period (except for weight gain from 0–2 years, adjusted for birth weight and height at 2 years only); models in b) are adjusted for concurrent weight gain and weight and height at the beginning of each period; sample sizes in the different periods were (male/female): 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549); analyses were restricted those with valid data for weight and height at each age, paternal occupational class, and body composition outcomes

Appendix 13. Mean differences in adult height (with 95% confidence intervals) per 1 standard deviation increase in a) weight gain velocity, adjusted for weight and height at the beginning of each period and concurrent height gain, and b) height gain velocity, adjusted for height and weight at the beginning of each period and concurrent weight gain




Note: males=dark blue diamonds; females=light blue circles. Sample sizes in the different periods were (male/female): 0–2 (574/603); 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549); weight gain from 0–2 years was adjusted for height at 2 years and birth weight only; analyses were restricted those with valid data for height and weight at each age, paternal occupational class, and body composition outcomes

Appendix 14. P-values for tests of sex interaction for periods of a) weight gain (adjusted for weight and height at the beginning of each period and concurrent height gain), and b) height gain velocity (adjusted for weight and height at the beginning of each period and concurrent height gain) regressed against body composition outcomes.

| a) Weight gain (years) | Fat mass (kg) | Lean mass (kg) | App. lean mass (kg) | Fat: lean mass ratio | Android: gynoid ratio |
|---|---|---|---|---|---|
| 0-2 | 0.60 | 0.01 | 0.02 | 0.59 | 0.79 |
| 2–4 | 0.04 | 0.54 | 0.31 | 0.09 | 0.54 |
| 4–7 | 0.18 | <0.01 | <0.01 | 0.33 | 0.45 |
| 7–11 | 0.39 | 0.96 | 0.72 | 0.10 | 0.14 |
| 11–15 | 0.66 | 0.91 | 0.38 | 0.88 | 0.13 |
| 15-20 | 0.55 | <0.01 | <0.01 | 0.17 | 0.44 |
| b) Height gain (years) | | | | | |
| 2–4 | 0.50 | 0.74 | 0.69 | 0.71 | 0.43 |
| 4–7 | 0.04 | 0.38 | 0.67 | 0.17 | 0.44 |
| 7–11 | 0.61 | 0.56 | 0.40 | 0.41 | 0.92 |
| 11–15 | 0.01 | <0.01 | <0.01 | 0.74 | 0.71 |
| 15-20 | 0.24 | <0.01 | <0.01 | 0.65 | 0.02 |

Note: sample sizes in the different periods were (male/female): 2–4 (554/570); 4–7 (567–608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549); weight gain from 0–2 years was adjusted for birth weight and height at 2 years only; analyses were restricted those with valid data for weight and height at each age, paternal occupational class, and body composition outcomes

Appendix 15. Mean differences in android and gynoid fat mass (kg) (95% confidence intervals, P-value) by sex per 1 standard deviation increase in weight and height gain velocity, adjusted for weight and height at the beginning of each period and concurrent weight and height gain

| Period (years) | Weight gain | | Height gain | |
|---|---|---|---|---|
| Android fat mass (kg) | Males | Females | Males | Females |
| 0-2 | 0.07(-0.01, 0.15), 0.10 | -0.01(-0.09, 0.08), 0.85 | | |
| 2–4 | 0.00(-0.09, 0.09), 0.97 | 0.11(0.01, 0.20), 0.02 | -0.12(-0.23, -0.01), 0.03 | -0.05(-0.16, 0.06), 0.37 |
| 4–7 | 0.23(0.14, 0.32), <0.01 | 0.07(-0.02, 0.16), 0.11 | -0.03(-0.13, 0.07), 0.53 | 0.08(-0.02, 0.17), 0.12 |
| 7–11 | 0.18(0.09, 0.28), <0.01 | 0.26(0.16, 0.36), <0.01 | -0.02(-0.10, 0.06), 0.66 | -0.04(-0.14, 0.05), 0.36 |
| 11–15 | 0.20(0.09, 0.30), <0.01 | 0.13(0.05, 0.22), <0.01 | -0.11(-0.20, -0.01), 0.04 | 0.04(-0.06, 0.14), 0.43 |
| 15-20 | 0.20(0.10, 0.30), <0.01 | 0.22(0.14, 0.31), <0.01 | -0.04(-0.16, 0.09), 0.58 | -0.03(-0.12, 0.06), 0.48 |
| Gynoid fat mass (kg) | | | | |
| 0-2 | 0.12(0.03, 0.21), 0.01 | 0.06(-0.07, 0.18), 0.36 | | |
| 2–4 | 0.02(-0.07, 0.12), 0.62 | 0.19(0.05, 0.32), 0.01 | -0.07(-0.18, 0.05), 0.26 | 0.06(-0.10, 0.21), 0.48 |
| 4–7 | 0.26(0.17, 0.36), <0.01 | 0.09(-0.04, 0.22), 0.16 | -0.06(-0.16, 0.05), 0.28 | 0.23(0.09, 0.36), <0.01 |
| 7–11 | 0.18(0.08, 0.28), <0.01 | 0.24(0.09, 0.38), <0.01 | 0.02(-0.06, 0.11), 0.58 | 0.00(-0.13, 0.14), 0.99 |
| 11–15 | 0.18(0.07, 0.30), <0.01 | 0.25(0.13, 0.37), <0.01 | -0.14(-0.24, -0.04), 0.01 | 0.16(0.02, 0.30), 0.02 |
| 15-20 | 0.26(0.15, 0.36), <0.01 | 0.29(0.17, 0.42), <0.01 | 0.10(-0.03, 0.23), 0.12 | -0.04(-0.17, 0.08), 0.50 |

Note: sample sizes in the different periods were (male/female): model a) 0–2 (574/603); 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549); weight gain from 0–2 years was adjusted for birth weight and height at 2 years only; analyses were restricted those with valid data for weight and height at each age, paternal occupational class, and body composition outcomes

Appendix 16. Mean differences in fat and lean mass (95% confidence intervals, P-value) per 1 standard deviation increase in weight gain velocity: a) adjusted for weight at the beginning of each period; b) identical to model a with additional adjustment for height at the beginning of each period, height gain in the same period, pubertal timing, and maternal body mass index and height; c) identical to model a with additional adjustment for height at the beginning of each period and height gain in the same period

| Period (years) | Males a) | b) | c) | Females a) | b) | c) |
|---|---|---|---|---|---|---|
| Fat mass (kg) | | | | | | |
| 0-2 | 0.65(0.05, 1.24), 0.03 | 0.53(-0.16, 1.23), 0.13 | 0.51(-0.30, 1.33), 0.22 | 0.48(-0.25, 1.21), 0.20 | -0.07(-0.94, 0.81), 0.88 | 0.45(-0.60, 1.51), 0.40 |
| 2–4 | 0.03(-0.58, 0.64), 0.93 | -0.01(-0.83, 0.80), 0.97 | 0.40(-0.56, 1.36), 0.41 | 1.32(0.56, 2.07), <0.01 | 0.79(-0.15, 1.73), 0.10 | 1.01(-0.09, 2.12), 0.07 |
| 4–7 | 1.33(0.75, 1.91), <0.01 | 1.58(0.81, 2.35), <0.01 | 2.06(1.15, 2.98), <0.01 | 1.25(0.52, 1.97), <0.01 | 0.17(-0.74, 1.07), 0.72 | 0.90(-0.23, 2.02), 0.12 |
| 7–11 | 1.53(0.85, 2.21), <0.01 | 1.75(0.94, 2.55), <0.01 | 2.32(1.35, 3.28), <0.01 | 1.94(1.13, 2.74), <0.01 | 1.86(0.82, 2.90), <0.01 | 1.56(0.30, 2.81), 0.02 |
| 11–15 | 0.65(0.02, 1.28), 0.05 | 1.47(0.58, 2.36), <0.01 | 1.78(0.75, 2.81), <0.01 | 1.70(1.00, 2.40), <0.01 | 1.34(0.56, 2.11), <0.01 | 1.29(0.27, 2.32), 0.01 |
| 15-20 | 1.91(1.25, 2.57), <0.01 | 1.51(0.71, 2.32), <0.01 | 2.14(1.27, 3.01), <0.01 | 2.06(1.31, 2.82), <0.01 | 2.19(1.22, 3.17), <0.01 | 2.52(1.60, 3.44), <0.01 |
| Lean mass (kg) | | | | | | |
| 0-2 | 1.90(1.37, 2.44), <0.01 | 1.61(1.00, 2.22), <0.01 | 1.57(0.84, 2.30), <0.01 | 1.09(0.67, 1.50), <0.01 | 0.38(-0.12, 0.88), 0.14 | 0.66(0.06, 1.26), 0.03 |
| 2–4 | 1.67(1.13, 2.21), <0.01 | 1.47(0.78, 2.17), <0.01 | 1.65(0.80, 2.49), <0.01 | 1.42(1.01, 1.84), <0.01 | 0.99(0.47, 1.51), <0.01 | 1.04(0.42, 1.65), <0.01 |
| 4–7 | 2.18(1.69, 2.67), <0.01 | 1.91(1.26, 2.55), <0.01 | 1.92(1.14, 2.70), <0.01 | 1.35(0.95, 1.74), <0.01 | 0.67(0.17, 1.17), 0.01 | 0.74(0.13, 1.35), 0.02 |
| 7–11 | 0.75(0.17, 1.33), 0.01 | 0.59(-0.10, 1.27), 0.10 | 0.94(0.10, 1.78), 0.03 | 0.64(0.20, 1.08), <0.01 | 0.70(0.13, 1.26), 0.02 | 0.48(-0.20, 1.15), 0.17 |
| 11–15 | 0.80(0.25, 1.35), <0.01 | 1.06(0.29, 1.83), 0.01 | 1.21(0.29, 2.13), 0.01 | 1.26(0.87, 1.65), <0.01 | 0.93(0.51, 1.35), <0.01 | 0.77(0.23, 1.31), 0.01 |
| 15-20 | 3.28(2.75, 3.81), <0.01 | 2.37(1.75, 3.00), <0.01 | 2.37(1.67, 3.07), <0.01 | 1.66(1.27, 2.06), <0.01 | 1.49(0.98, 2.00), <0.01 | 1.51(1.03, 1.99), <0.01 |
| Appendicular lean mass (kg) | | | | | | |
| 0-2 | 0.92(0.67, 1.18), <0.01 | 0.75(0.46, 1.05), <0.01 | 0.70(0.35, 1.05), <0.01 | 0.54(0.34, 0.74), <0.01 | 0.23(-0.01, 0.47), 0.06 | 0.36(0.08, 0.64), 0.01 |
| 2–4 | 0.90(0.65, 1.16), <0.01 | 0.76(0.42, 1.09), <0.01 | 0.86(0.46, 1.27), <0.01 | 0.69(0.49, 0.88), <0.01 | 0.49(0.24, 0.73), <0.01 | 0.48(0.20, 0.77), <0.01 |
| 4–7 | 1.06(0.83, 1.30), <0.01 | 0.94(0.63, 1.25), <0.01 | 0.87(0.49, 1.24), <0.01 | 0.62(0.43, 0.80), <0.01 | 0.30(0.06, 0.54), 0.01 | 0.36(0.08, 0.65), 0.01 |
| 7–11 | 0.31(0.04, 0.58), 0.03 | 0.24(-0.08, 0.57), 0.14 | 0.38(-0.02, 0.79), 0.06 | 0.29(0.08, 0.50), 0.01 | 0.36(0.09, 0.62), 0.01 | 0.21(-0.11, 0.52), 0.20 |
| 11–15 | 0.25(-0.01, 0.52), 0.06 | 0.38(0.01, 0.74), 0.05 | 0.45(0.00, 0.89), 0.05 | 0.61(0.43, 0.80), <0.01 | 0.47(0.27, 0.66), <0.01 | 0.36(0.10, 0.61), 0.01 |
| 15-20 | 1.58(1.32, 1.84), <0.01 | 1.09(0.78, 1.39), <0.01 | 0.99(0.65, 1.34), <0.01 | 1.66(1.27, 2.06), <0.01 | 0.67(0.43, 0.91), <0.01 | 0.66(0.43, 0.88), <0.01 |

| Period (years) | Males a) | b) | c) | Females a) | b) | c) |
|---|---|---|---|---|---|---|
| Fat: lean ratio | | | | | | |
| 0-2 | -0.33(-1.25, 0.59), 0.48 | -0.36(-1.45, 0.72), 0.51 | -0.33(-1.59, 0.92), 0.60 | -1.05(-2.56, 0.46), 0.17 | -1.00(-2.83, 0.83), 0.28 | -0.29(-2.42, 1.84), 0.79 |
| 2–4 | -1.31(-2.24, -0.37), 0.01 | -1.25(-2.51, 0.01), 0.05 | -0.63(-2.10, 0.85), 0.41 | 0.33(-1.25, 1.91), 0.68 | -0.32(-2.29, 1.65), 0.75 | 0.12(-2.12, 2.36), 0.91 |
| 4–7 | 0.57(-0.34, 1.48), 0.22 | 1.22(0.01, 2.42), 0.05 | 2.07(0.65, 3.50), <0.01 | 0.42(-1.10, 1.94), 0.59 | -1.07(-2.96, 0.81), 0.27 | 0.86(-1.45, 3.17), 0.47 |
| 7–11 | 2.17(1.11, 3.23), <0.01 | 2.74(1.48, 3.99), <0.01 | 3.56(2.05, 5.08), <0.01 | 3.75(2.06, 5.44), <0.01 | 3.49(1.30, 5.68), <0.01 | 3.18(0.59, 5.78), 0.02 |
| 11–15 | 0.61(-0.41, 1.63), 0.24 | 1.80(0.38, 3.23), 0.01 | 2.26(0.62, 3.90), 0.01 | 1.56(0.07, 3.06), 0.04 | 1.25(-0.43, 2.93), 0.15 | 1.50(-0.67, 3.66), 0.18 |
| 15-20 | 0.59(-0.50, 1.69), 0.29 | 0.67(-0.66, 2.01), 0.32 | 1.82(0.37, 3.27), 0.01 | 1.83(0.18, 3.47), 0.03 | 2.59(0.48, 4.71), 0.02 | 3.40(1.41, 5.39), <0.01 |
| Android: gynoid ratio | | | | | | |
| 0-2 | -0.62(-1.87, 0.63), 0.33 | -0.25(-1.70, 1.19), 0.73 | 0.48(-1.17, 2.13), 0.57 | -0.48(-1.47, 0.51), 0.35 | -0.63(-1.81, 0.55), 0.30 | -0.76(-2.17, 0.66), 0.29 |
| 2–4 | -1.47(-2.75, -0.19), 0.02 | -0.53(-2.22, 1.16), 0.54 | 0.08(-1.87, 2.03), 0.93 | 0.05(-0.99, 1.08), 0.93 | 0.16(-1.11, 1.42), 0.81 | 0.23(-1.25, 1.71), 0.76 |
| 4–7 | 0.78(-0.48, 2.03), 0.23 | 1.36(-0.30, 3.01), 0.11 | 1.80(-0.09, 3.70), 0.06 | 0.13(-0.85, 1.11), 0.80 | -0.01(-1.23, 1.21), 0.99 | -0.04(-1.57, 1.50), 0.96 |
| 7–11 | 1.04(-0.44, 2.52), 0.17 | 1.32(-0.43, 3.07), 0.14 | 3.37(1.32, 5.43), <0.01 | 2.62(1.56, 3.68), <0.01 | 2.44(1.04, 3.83), <0.01 | 3.08(1.38, 4.79), <0.01 |
| 11–15 | 1.24(-0.14, 2.62), 0.08 | 1.56(-0.38, 3.51), 0.12 | 2.40(0.21, 4.60), 0.03 | 0.13(-0.82, 1.08), 0.79 | 0.47(-0.59, 1.53), 0.38 | 0.38(-1.06, 1.81), 0.61 |
| 15-20 | -0.35(-1.86, 1.16), 0.65 | 1.03(-0.82, 2.88), 0.28 | 1.73(-0.22, 3.68), 0.08 | 1.42(0.37, 2.48), 0.01 | 1.49(0.15, 2.84), 0.03 | 1.68(0.35, 3.00), 0.01 |

Note: pubertal timing (derived as previously described), maternal height and BMI all entered into regression model as linear terms; sample sizes in the different periods were (male/female):
Model a) 0–2 (574/603); 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549)
Model b) 0–2 (467/483) ; 2–4 (453/457; 4–7 (484/515); 7–11 (493/534); 11–15 (493/535); 15–20 (452/478)
Model c) males=341; females=360 in all periods
All analyses were restricted to those with valid data for body composition outcomes

Appendix 17. Mean differences in fat and lean mass (95% confidence intervals, P-value) per 1 standard deviation increase in height gain velocity adjusted for height at the beginning of each period; b) identical to model a with additional adjustment for weight at the beginning of each period and weight gain in the same period

| Period (years) | Males a) | b) | Females a) | b) |
|---|---|---|---|---|
| Fat mass (kg) | | | | |
| 2–4 | -0.25(-0.97, 0.46), 0.49 | -0.72(-1.76, 0.33), 0.18 | 0.65(-0.17, 1.48), 0.12 | 0.02(-1.20, 1.23), 0.98 |
| 4–7 | 0.83(0.22, 1.44), 0.01 | -0.60(-1.57, 0.37), 0.22 | 1.63(0.88, 2.39), <0.01 | 1.48(0.33, 2.63), 0.01 |
| 7–11 | 0.73(0.14, 1.32), 0.02 | -0.41(-1.22, 0.41), 0.33 | 0.78(0.07, 1.50), 0.03 | 0.14(-0.95, 1.24), 0.80 |
| 11–15 | 0.05(-0.57, 0.67), 0.89 | -0.70(-1.65, 0.25), 0.15 | 1.09(0.25, 1.92), 0.01 | 0.90(-0.24, 2.05), 0.12 |
| 15-20 | 1.00(0.12, 1.88), 0.03 | 0.10(-1.01, 1.20), 0.87 | -0.13(-0.93, 0.67), 0.75 | -0.19(-1.19, 0.80), 0.71 |
| Lean mass (kg) | | | | |
| 2–4 | 1.88(1.22, 2.54), <0.01 | 0.46(-0.46, 1.37), 0.33 | 1.38(0.93, 1.83), <0.01 | 0.76(0.09, 1.43), 0.03 |
| 4–7 | 2.11(1.58, 2.65), <0.01 | 0.38(-0.45, 1.21), 0.37 | 1.63(1.22, 2.04), <0.01 | 1.22(0.60, 1.84), <0.01 |
| 7–11 | 0.99(0.48, 1.51), <0.01 | -0.04(-0.75, 0.66), 0.90 | 0.66(0.27, 1.04), <0.01 | 0.61(0.02, 1.20), 0.04 |
| 11–15 | 0.13(-0.41, 0.68), 0.63 | -0.77(-1.62, 0.08), 0.08 | 1.44(0.99, 1.89), <0.01 | 1.46(0.86, 2.06), <0.01 |
| 15-20 | 3.22(2.48, 3.96), <0.01 | 2.33(1.43, 3.22), <0.01 | 0.55(0.13, 0.98), 0.01 | 0.41(-0.10, 0.93), 0.12 |
| Appendicular lean mass (kg) | | | | |
| 2–4 | 1.00(0.68, 1.31), <0.01 | 0.29(-0.15, 0.73), 0.20 | 0.72(0.51, 0.94), <0.01 | 0.38(0.07, 0.69), 0.02 |
| 4–7 | 1.06(0.81, 1.32), <0.01 | 0.29(-0.10, 0.69), 0.15 | 0.74(0.55, 0.93), <0.01 | 0.55(0.26, 0.84), <0.01 |
| 7–11 | 0.46(0.21, 0.70), <0.01 | -0.02(-0.36, 0.32), 0.89 | 0.28(0.10, 0.47), <0.01 | 0.25(-0.02, 0.53), 0.07 |
| 11–15 | -0.03(-0.29, 0.23), 0.83 | -0.44(-0.85, -0.03), 0.04 | 0.72(0.51, 0.94), <0.01 | 0.69(0.41, 0.98), <0.01 |
| 15-20 | 1.69(1.33, 2.04), <0.01 | 1.36(0.92, 1.80), <0.01 | 0.25(0.05, 0.45), 0.01 | 0.27(0.03, 0.51), 0.03 |

| Period (years) | Males a) | b) | Females a) | b) |
|---|---|---|---|---|
| Fat: lean ratio | | | | |
| 2–4 | -2.04(-3.14, -0.94), <0.01 | -1.71(-3.32, -0.10), 0.04 | -1.02(-2.73, 0.69), 0.24 | -1.16(-3.61, 1.29), 0.35 |
| 4–7 | -0.20(-1.14, 0.74), 0.67 | -1.30(-2.81, 0.21), 0.09 | 0.83(-0.75, 2.41), 0.30 | 1.25(-1.11, 3.62), 0.30 |
| 7–11 | 0.51(-0.40, 1.43), 0.27 | -0.70(-1.98, 0.58), 0.28 | 0.62(-0.87, 2.11), 0.42 | -0.98(-3.24, 1.29), 0.40 |
| 11–15 | 0.05(-0.92, 1.02), 0.92 | -0.47(-1.98, 1.04), 0.54 | -0.27(-2.01, 1.48), 0.76 | -0.77(-3.19, 1.66), 0.54 |
| 15-20 | -1.01(-2.39, 0.36), 0.15 | -1.88(-3.72, -0.04), 0.05 | -1.37(-3.02, 0.27), 0.10 | -1.35(-3.49, 0.80), 0.22 |
| Android: gynoid ratio | | | | |
| 2–4 | -2.31(-3.81, -0.80), <0.01 | -2.83(-4.96, -0.71), 0.01 | -1.16(-2.28, -0.04), 0.04 | -0.98(-2.60, 0.65), 0.24 |
| 4–7 | 0.67(-0.62, 1.97), 0.31 | 0.10(-1.90, 2.11), 0.92 | -0.12(-1.13, 0.89), 0.82 | 1.03(-0.54, 2.60), 0.20 |
| 7–11 | -0.35(-1.61, 0.91), 0.58 | -2.23(-3.96, -0.49), 0.01 | 0.44(-0.51, 1.38), 0.37 | -1.04(-2.53, 0.44), 0.17 |
| 11–15 | 0.88(-0.42, 2.19), 0.18 | 0.44(-1.58, 2.47), 0.67 | -0.74(-1.85, 0.37), 0.19 | -0.88(-2.49, 0.72), 0.28 |
| 15-20 | -2.95(-4.83, -1.07), <0.01 | -3.56(-6.03, -1.08), 0.01 | 0.07(-0.99, 1.12), 0.90 | -0.33(-1.77, 1.10), 0.65 |

Note: sample sizes in the different periods were (male/female):
Model a) 0–2 (574/603); 2–4 (554/570); 4–7 (567/608); 7–11 (566/614); 11–15 (536/582); 15–20 (493/549)
Model b) males=341; females=360 in all periods
All analyses were restricted those with valid data for body composition outcomes

Appendix 18. Formulae used to calculate total physical activity energy expenditure (PAEE) using the Actiheart at 60–64 years:

PAEE [J/min/kg] = 14.08 - 0.138 * age + 0.39 * sex + 0.0021 * SHR + 0.51 * betablocker) * HRaS + 0.94 * age + 5.41 * sex - 0.76 * SHR - 0.0 * SHR *sex + 12.3 * betablocker - 84.1

Note: age in years, sex coded as 1 for men and 0 for women; betablocker coded as 1 for yes and 0 for no; HR=heart rate in beats per minute; SHR=sleeping HR; HRaS=HR above SHR in beats per minute

Appendix 19. Models compared when using the structured life course models

Fully saturated model:

$E(Y)= \alpha + \beta_1 Pa_{36} + \beta_2 Pa_{43} + \beta_3 Pa_{53} + \beta_4 Pa_{63} + \theta_{12} Pa_{36} Pa_{43} + \theta_{23} Pa_{43} Pa_{53} + \theta_{13} Pa_{36} Pa_{53} + \theta_{14} Pa_{36} Pa_{63} + \theta_{242} Pa_{43} Pa_{63} + \theta_{34} Pa_{53} Pa_{63} + \theta_{1234} Pa_{36} Pa_{43} Pa_{53} Pa_{63}$

Compared with:

(1) Critical/sensitive period model

$E(Y)= \alpha + \beta_1 Pa_{36}$

constraints: $\beta_2= \beta_3= \beta_4=0$; $\theta_{12}=\theta_{23}=\theta_{13}=\theta_{14}=\theta_{24}=\theta_{34}=\theta_{1234}=0$

(2) Accumulation model: summed score (assuming similar effect sizes at each age)

$E(Y)= \alpha +\beta \Sigma jPaj$

constraints: $\beta_1=\beta_2=\beta_3=\beta_4$; $\theta_{12}=\theta_{23}=\theta_{13}=\theta_{14}=\theta_{24}=\theta_{34}=\theta_{1234}=0$

(3) Accumulation model: mutually adjusted (allowing for differences in effect size at each age)

$E(Y)= \alpha + \beta_1 Pa_{36} + \beta_2 Pa_{43} + \beta_3 Pa_{53} + \beta_4 Pa_{63}$

constraints: $\beta_1 \neq \beta_2 \neq \beta_3 \neq \beta_4$; $\theta_{12}=\theta_{23}=\theta_{13}=\theta_{14}=\theta_{24}=\theta_{34}=\theta_{1234}=0$

Notes: Pa=physical activity at age 36, 43, 53, and 63 (60–64) years.

Appendix 20. Correlations between objectively assessed measures of physical activity measures

a) Males (n=564)

| | | | |
|---|---|---|---|
| Light | -0.89 | | |
| Moderate-vigorous | -0.70 | 0.31 | |
| Total PAEE | -0.88 | 0.61 | 0.90 |
| | Sedentary | Light | Moderate-vigorous |

b) Females (n=598)

| | | | |
|---|---|---|---|
| Light | -0.92 | | |
| Moderate-vigorous | -0.68 | 0.33 | |
| Total PAEE | -0.89 | 0.67 | 0.86 |
| | Sedentary | Light | Moderate-vigorous |

Notes: METs=metabolic equivalent; sedentary=≤1.5 METs; Light=>1.5–3 METs; Moderate-vigorous=>3 METs; total PAEE=total physical energy expenditure in kj/kg/day; analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 21. Cross-tabulations of self-reported physical activity at 36, 43, 53 and 60–64 years

a) Males

| | 43 years | | | 53 years | | | 60-64 years | | |
|---|---|---|---|---|---|---|---|---|---|
| | Inactive | Moderately | Most active | Inactive | Moderately | Most active | Inactive | Moderately | Most active |
| 36 years | | | | | | | | | |
| Inactive | 107 (44.40) | 36 (25.17) | 23 (12.43) | 94 (41.59) | 33 (23.91) | 39 (19.02) | 136 (39.42) | 18 (20.93) | 12 (8.70) |
| Moderately | 72 (29.88) | 48 (33.57) | 41 (22.16) | 57 (25.22) | 43 (31.16) | 61 (29.76) | 101 (29.28) | 24 (27.91) | 36 (26.09) |
| Most active | 62 (25.73) | 59 (41.26) | 121 (65.41) | 75 (33.19) | 62 (44.93) | 105 (51.22) | 108 (31.3) | 44 (51.16) | 90 (65.22) |
| 43 years | | | | | | | | | |
| Inactive | | | | 140 (61.95) | 48 (34.78) | 53 (25.85) | 184 (53.33) | 32 (37.21) | 25 (18.12) |
| Moderately | | | | 41 (18.14) | 41 (29.71) | 61 (29.76) | 79 (22.90) | 25 (29.07) | 39 (28.26) |
| Most active | | | | 45 (19.91) | 49 (35.51) | 91 (44.39) | 82 (23.77) | 29 (33.72) | 74 (53.62) |
| 53 years | | | | | | | | | |
| Inactive | | | | | | | 181 (52.46) | 23 (26.74) | 22 (15.94) |
| Moderately | | | | | | | 68 (19.71) | 34 (39.53) | 36 (26.09) |
| Most active | | | | | | | 96 (27.83) | 29 (33.72) | 80 (57.97) |

b) Females

| | 43 years | | | 53 years | | | 60-64 years | | |
|---|---|---|---|---|---|---|---|---|---|
| | Inactive | Moderately | Most active | Inactive | Moderately | Most active | Inactive | Moderately | Most active |
| 36 years | | | | | | | | | |
| Inactive | 160 (51.12) | 42 (25.00) | 25 (15.53) | 128 (46.72) | 47 (35.61) | 52 (22.03) | 155 (42.47) | 38 (33.33) | 34 (20.86) |
| Moderately | 80 (25.56) | 61 (36.31) | 39 (24.22) | 74 (27.01) | 38 (28.79) | 68 (28.81) | 108 (29.59) | 30 (26.32) | 42 (25.77) |
| Most active | 73 (23.32) | 65 (38.69) | 97 (60.25) | 72 (26.28) | 47 (35.61) | 116 (49.15) | 102 (27.95) | 46 (40.35) | 87 (53.37) |
| 43 years | | | | | | | | | |
| Inactive | | | | 183 (66.79) | 56 (42.42) | 74 (31.36) | 218 (59.73) | 40 (35.09) | 55 (33.74) |
| Moderately | | | | 55 (20.07) | 38 (28.79) | 75 (31.78) | 97 (26.58) | 33 (28.95) | 38 (23.31) |
| Most active | | | | 36 (13.14) | 38 (28.79) | 87 (36.86) | 50 (13.70) | 41 (35.96) | 70 (42.94) |
| 53 years | | | | | | | | | |
| Inactive | | | | | | | 213 (58.36) | 28 (24.56) | 33 (20.25) |
| Moderately | | | | | | | 64 (17.53) | 33 (28.95) | 35 (21.47) |
| Most active | | | | | | | 88 (24.11) | 53 (46.49) | 95 (58.28) |

Note: cells show N (%); in all cross-tabulations, P-values from chi-squared tests were <0.001; activity at each age was coded as inactive (no participation), moderately active (participated one to four times) and most active (participated five or more times), in the previous month (36 years), per month (43 years) and in the previous 4 weeks (53 and 60-64 years); analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 22. Mean difference in physical activity outcomes (standard deviation score [95% confidence interval]) in those who were moderately and most active (compared with inactive) at 60-64 years

a) Males (n=621)

| | Total PAEE | Sedentary | Light | Moderate-vigorous |
|---|---|---|---|---|
| 60-64 years | | | | |
| Inactive | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 0.08(-0.16, 0.33) | -0.04(-0.28, 0.20) | -0.03(-0.27, 0.21) | 0.09(-0.15, 0.34) |
| Most active | 0.11(-0.09, 0.30) | 0.03(-0.17, 0.23) | -0.10(-0.30, 0.09) | 0.14(-0.06, 0.34) |
| P* | 0.53 | 0.88 | 0.58 | 0.37 |
| P (sex interaction) | 0.14 | 0.09 | 0.11 | 0.35 |

b) Females (n=681)

| | Total PAEE | Sedentary | Light | Moderate-vigorous |
|---|---|---|---|---|
| 60-64 years | | | | |
| Inactive | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 0.05(-0.17, 0.27) | 0.05(-0.17, 0.27) | -0.01(-0.24, 0.21) | -0.04(-0.27, 0.18) |
| Most active | 0.36(0.17, 0.55) | -0.24(-0.44, -0.05) | 0.18(-0.01, 0.38) | 0.27(0.08, 0.47) |
| P* | <0.01 | 0.03 | 0.14 | 0.01 |

Notes: *P-values show overall test of association (likelihood ratio test comparing models with and without physical activity included); sedentary=≤1.5 metabolic equivalent (METs); Light=>1.5–3 METs; Moderate-vigorous=>3 METs; total PAEE=total physical energy expenditure in kj/kg/day; analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 23. Mean difference (95% CI) in total physical energy expenditure (kj/kg/day) standard deviation score by potential confounders (indicators of socioeconomic position and limiting illness)

| Paternal occupational class (4 years) | Males (n=564) | Females (n=598) |
|---|---|---|
| I/II Highest | 0.00 | 0.00 |
| III Non manual | -0.05(-0.30, 0.19) | 0.08(-0.15, 0.31) |
| III Manual | -0.09(-0.32, 0.14) | -0.06(-0.28, 0.16) |
| IV/V Lowest | 0.01(-0.23, 0.25) | -0.13(-0.36, 0.10) |
| P* | 0.83 | 0.35 |
| P# | 0.50 | |
| Own Educational attainment (26 years) | | |
| Highest | 0.00 | 0.00 |
| Intermediate | 0.10(-0.11, 0.32) | -0.07(-0.26, 0.12) |
| None | 0.14(-0.06, 0.34) | -0.02(-0.24, 0.19) |
| P* | 0.33 | 0.78 |
| P# | 0.50 | |
| Self-reported long-term illness, health problem or disability that limits activities or work (60–64 years) | | |
| No | 0.00 | 0.00 |
| Yes | -0.47(-0.68, -0.27) | -0.49(-0.69, -0.28) |
| P* | <0.001 | <0.001 |
| P# | 0.71 | |

Notes: *P-values show overall test of association (likelihood ratio test comparing models with and without the potential confounder included; #test of sex interaction; educational attainment was categorised as none (none attempted), intermediate (GCE 'O' level or Burnam C or lower) or highest (GCE A level or Burnam B or higher); analyses restricted to those with valid data for paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 24. Associations between potential confounders (indicators of socioeconomic position and health status) and self-reported physical activity levels across adulthood, N (%)

iii) Paternal occupational class at 4 years (Registrar General's classification)

| | Males | | | | Females | | | |
|---|---|---|---|---|---|---|---|---|
| | I/II Highest | III Non manual | III Manual | IV/V Lowest | I/II Highest | III Non manual | III Manual | IV/V Lowest |
| 36 years | | | | | | | | |
| Inactive | 36 (24.16) | 29 (23.77) | 46 (29.49) | 55 (38.73) | 45 (26.16) | 42 (28.97) | 74 (41.11) | 66 (45.52) |
| Moderately | 42 (28.19) | 41 (33.61) | 43 (27.56) | 35 (24.65) | 43 (25) | 48 (33.1) | 51 (28.33) | 38 (26.21) |
| Most active | 71 (47.65) | 52 (42.62) | 67 (42.95) | 52 (36.62) | 84 (48.84) | 55 (37.93) | 55 (30.56) | 41 (28.28) |
| P* | 0.08 | | | | 0.08 | | | |
| 43 years | | | | | | | | |
| Inactive | 55 (36.91) | 38 (31.15) | 73 (46.79) | 75 (52.82) | 69 (40.12) | 64 (44.14) | 104 (57.78) | 76 (52.41) |
| Moderately | 43 (28.86) | 41 (33.61) | 31 (19.87) | 28 (19.72) | 47 (27.33) | 46 (31.72) | 36 (20) | 39 (26.9) |
| Most active | 51 (34.23) | 43 (35.25) | 52 (33.33) | 39 (27.46) | 56 (32.56) | 35 (24.14) | 40 (22.22) | 30 (20.69) |
| P* | 0.01 | | | | <0.01 | | | |
| 53 years | | | | | | | | |
| Inactive | 46 (30.87) | 42 (34.43) | 67 (42.95) | 71 (50) | 57 (33.14) | 55 (37.93) | 85 (47.22) | 77 (53.1) |
| Moderately | 36 (24.16) | 33 (27.05) | 41 (26.28) | 28 (19.72) | 43 (25) | 28 (19.31) | 41 (22.78) | 20 (13.79) |
| Most active | 67 (44.97) | 47 (38.52) | 48 (30.77) | 43 (30.28) | 72 (41.86) | 62 (42.76) | 54 (30) | 48 (33.1) |
| P* | <0.01 | | | | 0.01 | | | |
| 60-64 years | | | | | | | | |
| Inactive | 86 (57.72) | 62 (50.82) | 102 (65.38) | 95 (66.9) | 85 (49.42) | 76 (52.41) | 112 (62.22) | 92 (63.45) |
| Moderately | 20 (13.42) | 23 (18.85) | 24 (15.38) | 19 (13.38) | 33 (19.19) | 31 (21.38) | 31 (17.22) | 19 (13.1) |
| Most active | 43 (28.86) | 37 (30.33) | 30 (19.23) | 28 (19.72) | 54 (31.4) | 38 (26.21) | 37 (20.56) | 34 (23.45) |
| P* | 0.09 | | | | <0.001 | | | |

ii) Own educational attainment (26 years)

| | Males | | | Females | | |
|---|---|---|---|---|---|---|
| | Highest | Intermediate | None | Highest | Intermediate | None |
| 36 years | | | | | | |
| Inactive | 77 (25.58) | 35 (28.23) | 54 (37.5) | 66 (25.98) | 92 (39.15) | 69 (45.1) |
| Moderately | 87 (28.9) | 32 (25.81) | 42 (29.17) | 72 (28.35) | 66 (28.09) | 42 (27.45) |
| Most active | 137 (45.51) | 57 (45.97) | 48 (33.33) | 116 (45.67) | 77 (32.77) | 42 (27.45) |
| P* | <0.001 | | | <0.001 | | |
| 43 years | | | | | | |
| Inactive | 115 (38.21) | 47 (37.9) | 79 (54.86) | 93 (36.61) | 130 (55.32) | 90 (58.82) |
| Moderately | 81 (26.91) | 34 (27.42) | 28 (19.44) | 78 (30.71) | 58 (24.68) | 32 (20.92) |
| Most active | 105 (34.88) | 43 (34.68) | 37 (25.69) | 83 (32.68) | 47 (20) | 31 (20.26) |
| P* | <0.001 | | | <0.001 | | |
| 53 years | | | | | | |
| Inactive | 94 (31.23) | 51 (41.13) | 81 (56.25) | 74 (29.13) | 110 (46.81) | 90 (58.82) |
| Moderately | 85 (28.24) | 32 (25.81) | 21 (14.58) | 58 (22.83) | 50 (21.28) | 24 (15.69) |
| Most active | 122 (40.53) | 41 (33.06) | 42 (29.17) | 122 (48.03) | 75 (31.91) | 39 (25.49) |
| P* | 0.03 | | | <0.001 | | |
| 60-64 years | | | | | | |
| Inactive | 155 (51.5) | 77 (62.1) | 113 (78.47) | 122 (48.03) | 128 (54.47) | 115 (75.16) |
| Moderately | 58 (19.27) | 17 (13.71) | 11 (7.64) | 58 (22.83) | 44 (18.72) | 12 (7.84) |
| Most active | 88 (29.24) | 30 (24.19) | 20 (13.89) | 74 (29.13) | 63 (26.81) | 26 (16.99) |
| P* | 0.04 | | | <0.001 | | |

iii) Self-reported long-term illness, health problem or disability that limits activities or work (60–64 years; no/yes)

| | Males | | Females | |
|---|---|---|---|---|
| | No | Yes | No | Yes |
| 36 years | | | | |
| Inactive | 128 (28.13) | 38 (33.33) | 180 (35.09) | 47 (36.43) |
| Moderately | 136 (29.89) | 25 (21.93) | 149 (29.04) | 31 (24.03) |
| Most active | 191 (41.98) | 51 (44.74) | 184 (35.87) | 51 (39.53) |
| P* | 0.22 | | 0.51 | |
| 43 years | | | | |
| Inactive | 188 (41.32) | 53 (46.49) | 242 (47.17) | 71 (55.04) |
| Moderately | 114 (25.05) | 29 (25.44) | 146 (28.46) | 22 (17.05) |
| Most active | 153 (33.63) | 32 (28.07) | 125 (24.37) | 36 (27.91) |
| P* | 0.49 | | 0.03 | |
| 53 years | | | | |
| Inactive | 167 (36.7) | 59 (51.75) | 213 (41.52) | 61 (47.29) |
| Moderately | 118 (25.93) | 20 (17.54) | 106 (20.66) | 26 (20.16) |
| Most active | 170 (37.36) | 35 (30.7) | 194 (37.82) | 42 (32.56) |
| P* | 0.01 | | 0.45 | |
| 60-64 years | | | | |
| Inactive | 271 (59.56) | 74 (64.91) | 284 (55.36) | 81 (62.79) |
| Moderately | 67 (14.73) | 19 (16.67) | 89 (17.35) | 25 (19.38) |
| Most active | 117 (25.71) | 21 (18.42) | 140 (27.29) | 23 (17.83) |
| P* | 0.26 | | 0.09 | |

Notes: *P(chi-squared test); educational attainment was categorised as none (none attempted), intermediate (GCE 'O' level or Burnam C or lower) or highest (GCE A level or Burnam B or higher); maximum available sample size used with each indicator; activity at each age was coded as inactive (no participation), moderately active (participated one to four times) and most active (participated five or more times), in the previous month (36 years), per month (43 years) and in the previous 4 weeks (53 and 60-64 years); analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 25. Mean differences in body composition outcomes per standard deviation increase in hours spent sedentary, in light and moderate-vigorous physical activity at 60-64 years adjusted for paternal occupation class (4y) own educational attainment (26y) and limiting illness (60-64y)

| | Total physical activity energy expenditure | | | | |
|---|---|---|---|---|---|
| | Males (n=564) | | Females (n=598) | | |
| Outcome models | β (95% CI) | P | β (95% CI) | P | P (sex interaction) |
| Fat mass index (kg/m$^2$) | -0.76(-1.05, -0.47) | <0.001 | -1.67(-2.04, -1.30) | <0.001 | <0.001 |
| Lean mass index (kg/m$^2$) | -0.15(-0.31, 0.02) | 0.08 | -0.33(-0.48, -0.18) | <0.001 | 0.11 |
| Fat: lean mass ratio | -2.39(-3.29, -1.49) | <0.001 | -5.95(-7.30, -4.61) | <0.001 | <0.001 |
| Android: gynoid fat mass ratio | -1.97(-3.23, -0.71) | <0.01 | -1.99(-2.93, -1.04) | <0.001 | 0.91 |
| Appendicular lean mass index (kg/m$^2$) | -0.03(-0.10, 0.05) | 0.53 | -0.13(-0.20, -0.06) | <0.001 | 0.03 |
| Appendicular lean mass index (kg/m$^2$) + fat mass index (kg/m$^{1.2}$) | 0.08(0.01, 0.15) | 0.03 | 0.07(0.02, 0.13) | <0.01 | 0.81 |

Note: analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 26. Mean differences in body composition outcomes per standard deviation increase in hours spent sedentary, in light intensity and moderate-vigorous physical activity at 60-64 years adjusted for paternal occupation class (4y) own educational attainment (26y) and limiting illness (60-64y)

a) Males (n=564)

| | Sedentary | | | Light | | | Moderate-vigorous | | |
|---|---|---|---|---|---|---|---|---|---|
| Outcome models | β (95% CI) | P | P# | β (95% CI) | P | P# | β (95% CI) | P | P# |
| Fat mass index (kg/m$^2$) | 0.33(0.03, 0.64) | 0.03 | <0.001 | -0.33(-0.64, -0.03) | 0.03 | <0.001 | -0.22(-0.52, 0.07) | 0.14 | 0.38 |
| Lean mass index (kg/m$^2$) | -0.02(-0.19, 0.14) | 0.78 | 0.09 | -0.06(-0.22, 0.11) | 0.50 | 0.04 | 0.16(0.00, 0.33) | 0.06 | 0.97 |
| Fat: lean mass ratio | 1.28(0.36, 2.21) | <0.01 | <0.001 | -1.10(-2.02, -0.17) | 0.02 | <0.001 | -1.19(-2.10, -0.29) | 0.01 | 0.72 |
| Android: gynoid ratio | 0.57(-0.71, 1.86) | 0.38 | 0.60 | -0.49(-1.77, 0.79) | 0.45 | 0.29 | -0.52(-1.78, 0.75) | 0.42 | 0.28 |
| Appen. lean mass index (kg/m$^2$) | -0.04(-0.12, 0.04) | 0.34 | 0.03 | -0.02(-0.10, 0.06) | 0.70 | 0.02 | 0.12(0.04, 0.20) | <0.01 | 0.54 |
| Appen. lean mass index (kg/m$^2$) + fat mass index (kg/m$^{1.2}$) | -0.08(-0.15, -0.01) | 0.02 | 1.00 | 0.03(-0.04, 0.10) | 0.43 | 0.51 | 0.15(0.08, 0.22) | <0.001 | 0.16 |

b) Females (n=598)

| | Sedentary | | Light | | Moderate-vigorous | |
|---|---|---|---|---|---|---|
| Outcome models | β (95% CI) | P | β (95% CI) | P | β (95% CI) | P |
| Fat mass index (kg/m$^2$) | 1.17(0.79, 1.55) | <0.001 | -1.49(-1.86, -1.12) | <0.001 | 0.07(-0.32, 0.46) | 0.73 |
| Lean mass index (kg/m$^2$) | 0.16(0.01, 0.30) | 0.04 | -0.28(-0.42, -0.13) | <0.001 | 0.17(0.02, 0.31) | 0.03 |
| Fat: lean mass ratio | 4.42(3.04, 5.81) | <0.001 | -5.15(-6.51, -3.79) | <0.001 | -0.60(-2.03, 0.82) | 0.41 |
| Android: gynoid ratio | 0.89(-0.07, 1.85) | 0.07 | -1.27(-2.22, -0.32) | <0.01 | 0.45(-0.51, 1.40) | 0.36 |
| Appen. lean mass index (kg/m$^2$) | 0.06(-0.01, 0.13) | 0.08 | -0.13(-0.20, -0.06) | <0.001 | 0.10(0.03, 0.17) | <0.01 |
| Appen. lean mass index (kg/m$^2$) + fat mass index (kg/m$^{1.2}$) | -0.08(-0.14, -0.03) | <0.01 | 0.05(0.00, 0.11) | 0.05 | 0.09(0.04, 0.14) | <0.001 |

Notes: #P-value for sex interaction term**;** analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 27. Mean difference in body composition outcomes (95% confidence intervals) in those who were moderately and most active (compared with inactive) at 36, 43, 53 and 60-64 years

| a) Males | N (%) | Fat mass index (kg/m$^2$) | Lean mass index (kg/m$^2$) | Fat: lean ratio | Android: gynoid ratio | Appen. lean mass index (kg/m$^2$) | Appen. lean mass index (kg/m2) + FMI |
|---|---|---|---|---|---|---|---|
| 36 years | | | | | | | |
| Inactive | 166 (29.17) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 161 (28.3) | 0.33(-0.45, 1.12) | 0.12(-0.31, 0.56) | 0.84(-1.59, 3.27) | 1.25(-2.13, 4.62) | 0.01(-0.19, 0.21) | -0.03(-0.21, 0.15) |
| Most active | 242 (42.53) | 0.29(-0.43, 1.00) | 0.41(0.02, 0.81) | -0.12(-2.33, 2.09) | -0.28(-3.36, 2.79) | 0.14(-0.05, 0.32) | 0.10(-0.06, 0.26) |
| P* | | 0.65 | 0.10 | 0.67 | 0.61 | 0.25 | 0.23 |
| P# | | <0.01 | 0.02 | 0.03 | 0.61 | 0.08 | 0.60 |
| 43 years | | | | | | | |
| Inactive | 241 (42.36) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 143 (25.13) | 0.32(-0.43, 1.07) | 0.34(-0.08, 0.75) | 0.19(-2.12, 2.51) | -0.72(-3.94, 2.50) | 0.19(0.00, 0.38) | 0.15(-0.02, 0.32) |
| Most active | 185 (32.51) | -0.18(-0.87, 0.52) | 0.11(-0.27, 0.49) | -1.05(-3.20, 1.09) | -2.06(-5.04, 0.92) | 0.10(-0.08, 0.28) | 0.12(-0.04, 0.28) |
| P* | | 0.46 | 0.27 | 0.52 | 0.40 | 0.15 | 0.15 |
| P# | | <0.01 | 0.05 | <0.01 | 0.83 | 0.06 | 0.37 |
| 53 years | | | | | | | |
| Inactive | 226 (39.72) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 138 (24.25) | -0.14(-0.91, 0.62) | 0.20(-0.22, 0.63) | -1.18(-3.54, 1.18) | -1.47(-4.76, 1.82) | 0.16(-0.04, 0.36) | 0.18(0.00, 0.35) |
| Most active | 205 (36.03) | -0.82(-1.50, -0.13) | -0.05(-0.42, 0.33) | -3.10(-5.20, -0.99) | -2.51(-5.45, 0.43) | 0.05(-0.13, 0.22) | 0.15(-0.01, 0.30) |
| P* | | 0.05 | 0.50 | 0.02 | 0.24 | 0.29 | 0.07 |
| P# | | 0.07 | 0.22 | 0.03 | 0.87 | 0.08 | 0.36 |
| 60-64 years | | | | | | | |
| Inactive | 345 (60.63) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 86 (15.11) | -0.25(-1.11, 0.60) | 0.41(-0.07, 0.88) | -1.85(-4.47, 0.77) | -2.04(-5.71, 1.63) | 0.22(0.00, 0.44) | 0.25(0.06, 0.45) |
| Most active | 138 (24.25) | -0.81(-1.52, -0.09) | 0.12(-0.28, 0.51) | -3.73(-5.92, -1.54) | -3.01(-6.08, 0.06) | 0.10(-0.09, 0.28) | 0.20(0.04, 0.36) |
| P* | | 0.09 | 0.23 | <0.01 | 0.13 | 0.12 | <0.01 |
| P# | | 0.03 | 0.09 | <0.01 | 0.99 | 0.02 | 0.06 |

| b) Females | N (%) | Fat mass index (kg/m$^2$) | Lean mass index (kg/m$^2$) | Fat: lean ratio | Android: gynoid ratio | Appen. lean mass index (kg/m$^2$) | Appen. lean mass index (kg/m2) + FMI |
|---|---|---|---|---|---|---|---|
| 36 years | | | | | | | |
| Inactive | 227 (35.36) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 180 (28.04) | -0.49(-1.47, 0.50) | -0.18(-0.55, 0.19) | -0.78(-4.34, 2.78) | -0.53(-2.91, 1.84) | 0.00(-0.18, 0.17) | 0.05(-0.07, 0.18) |
| Most active | 235 (36.6) | -1.66(-2.58, -0.74) | -0.33(-0.67, 0.01) | -5.57(-8.90, -2.25) | -1.92(-4.13, 0.30) | -0.11(-0.28, 0.05) | 0.08(-0.04, 0.20) |
| P* | | <0.01 | 0.16 | <0.01 | 0.22 | 0.30 | 0.40 |
| 43 years | | | | | | | |
| Inactive | 313 (48.75) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 168 (26.17) | -0.99(-1.93, -0.05) | -0.30(-0.65, 0.05) | -3.27(-6.66, 0.12) | -0.56(-2.83, 1.72) | -0.09(-0.26, 0.07) | 0.03(-0.10, 0.15) |
| Most active | 161 (25.08) | -2.11(-3.07, -1.15) | -0.32(-0.67, 0.04) | -8.17(-11.61, -4.73) | -3.08(-5.38, -0.77) | -0.11(-0.28, 0.06) | 0.14(0.02, 0.27) |
| P* | | <0.001 | 0.11 | <0.001 | 0.03 | 0.35 | 0.08 |
| 53 years | | | | | | | |
| Inactive | 274 (42.68) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 132 (20.56) | -1.46(-2.51, -0.42) | -0.31(-0.70, 0.08) | -5.41(-9.15, -1.67) | -2.54(-5.06, -0.03) | -0.15(-0.33, 0.03) | 0.02(-0.11, 0.16) |
| Most active | 236 (36.76) | -1.92(-2.79, -1.04) | -0.22(-0.55, 0.10) | -8.03(-11.17, -4.89) | -2.70(-4.81, -0.59) | -0.09(-0.25, 0.06) | 0.14(0.02, 0.25) |
| P* | | <0.001 | 0.22 | <0.001 | 0.02 | 0.23 | 0.06 |
| 60-64 years | | | | | | | |
| Inactive | 365 (56.85) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 114 (17.76) | -1.75(-2.81, -0.70) | -0.27(-0.66, 0.12) | -6.78(-10.54, -3.02) | -1.71(-4.26, 0.84) | -0.19(-0.37, 0.00) | 0.02(-0.11, 0.16) |
| Most active | 163 (25.39) | -2.11(-3.03, -1.19) | 0.01(-0.34, 0.36) | -9.83(-13.13, -6.53) | -3.06(-5.30, -0.82) | 0.02(-0.14, 0.18) | 0.28(0.16, 0.40) |
| P* | | <0.001 | 0.37 | <0.001 | 0.02 | 0.10 | <0.001 |

Notes: *overall test of association (likelihood ratio test comparing models with and without physical activity included); #P-value for sex interaction term; activity at each age was coded as inactive (no participation), moderately active (participated one to four times) and most active (participated five or more times), in the previous month (36 years), per month (43 years) and in the previous 4 weeks (53 and 60-64 years)**;** analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 28. Mean difference in body composition outcomes (95% confidence intervals) in those who were moderately and most active (compared with inactive) at 36, 43, 53 and 60-64 years, adjusted for paternal occupation class (4y) own educational attainment (26y) and limiting illness (60-64y)

| a) Males | N (%) | Fat mass index (kg/m$^2$) | Lean mass index (kg/m$^2$) | Fat: lean ratio | Android: gynoid ratio | Appen. lean mass index (kg/m$^2$) | Appen. lean mass index (kg/m2) + FMI |
|---|---|---|---|---|---|---|---|
| 36 years | | | | | | | |
| Inactive | 166 (29.17) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 161 (28.3) | 0.48(-0.31, 1.27) | 0.24(-0.19, 0.68) | 1.20(-1.23, 3.63) | 1.85(-1.52, 5.21) | 0.05(-0.16, 0.25) | -0.01(-0.19, 0.17) |
| Most active | 242 (42.53) | 0.47(-0.24, 1.19) | 0.54(0.15, 0.93) | 0.36(-1.85, 2.57) | 0.53(-2.54, 3.59) | 0.18(0.00, 0.37) | 0.12(-0.04, 0.29) |
| P* | | 0.36 | 0.02 | 0.60 | 0.53 | 0.12 | 0.17 |
| P# | | <0.01 | 0.02 | 0.04 | 0.69 | 0.07 | 0.07 |
| 43 years | | | | | | | |
| Inactive | 241 (42.36) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 143 (25.13) | 0.53(-0.23, 1.29) | 0.48(0.07, 0.90) | 0.72(-1.62, 3.06) | 0.22(-3.01, 3.46) | 0.24(0.05, 0.44) | 0.18(0.00, 0.35) |
| Most active | 185 (32.51) | 0.04(-0.66, 0.73) | 0.23(-0.15, 0.61) | -0.50(-2.65, 1.65) | -1.16(-4.14, 1.82) | 0.14(-0.04, 0.32) | 0.13(-0.02, 0.29) |
| P* | | 0.33 | 0.07 | 0.61 | 0.65 | 0.04 | 0.09 |
| P# | | <0.01 | 0.03 | <0.01 | 0.90 | 0.04 | 0.04 |
| 53 years | | | | | | | |
| Inactive | 226 (39.72) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 138 (24.25) | 0.18(-0.61, 0.96) | 0.41(-0.02, 0.84) | -0.43(-2.84, 1.98) | -0.03(-3.38, 3.32) | 0.22(0.02, 0.43) | 0.20(0.02, 0.38) |
| Most active | 205 (36.03) | -0.54(-1.24, 0.15) | 0.16(-0.22, 0.54) | -2.45(-4.59, -0.30) | -1.10(-4.09, 1.88) | 0.11(-0.07, 0.30) | 0.18(0.02, 0.34) |
| P* | | 0.13 | 0.17 | 0.06 | 0.72 | 0.09 | 0.03 |
| P# | | 0.04 | 0.15 | 0.02 | 0.83 | 0.06 | 0.06 |
| 60-64 years | | | | | | | |
| Inactive | 345 (60.63) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 86 (15.11) | -0.01(-0.87, 0.86) | 0.51(0.04, 0.99) | -1.14(-3.79, 1.51) | -1.17(-4.85, 2.52) | 0.26(0.04, 0.48) | 0.26(0.06, 0.46) |
| Most active | 138 (24.25) | -0.50(-1.22, 0.23) | 0.31(-0.09, 0.70) | -2.94(-5.16, -0.72) | -1.75(-4.84, 1.34) | 0.16(-0.03, 0.35) | 0.22(0.06, 0.39) |
| P* | | 0.37 | 0.06 | 0.03 | 0.50 | 0.04 | <0.01 |
| P# | | 0.02 | 0.10 | <0.01 | 0.97 | 0.02 | 0.02 |

| b) Females | N (%) | Fat mass index (kg/m$^2$) | Lean mass index (kg/m$^2$) | Fat: lean ratio | Android: gynoid ratio | Appen. lean mass index (kg/m$^2$) | Appen. lean mass index (kg/m2) + FMI |
|---|---|---|---|---|---|---|---|
| 36 years | | | | | | | |
| Inactive | 227 (35.36) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 180 (28.04) | -0.18(-1.17, 0.81) | -0.13(-0.50, 0.24) | 0.62(-2.94, 4.18) | 0.04(-2.36, 2.44) | 0.00(-0.18, 0.18) | 0.02(-0.11, 0.15) |
| Most active | 235 (36.6) | -1.38(-2.31, -0.44) | -0.31(-0.66, 0.04) | -4.06(-7.41, -0.71) | -1.23(-3.49, 1.03) | -0.13(-0.29, 0.04) | 0.04(-0.08, 0.16) |
| P* | | <0.01 | 0.21 | 0.01 | 0.46 | 0.23 | 0.81 |
| 43 years | | | | | | | |
| Inactive | 313 (48.75) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 168 (26.17) | -0.62(-1.57, 0.33) | -0.25(-0.61, 0.10) | -1.65(-5.06, 1.76) | -0.14(-2.44, 2.17) | -0.09(-0.26, 0.08) | -0.01(-0.14, 0.11) |
| Most active | 161 (25.08) | -1.91(-2.88, -0.95) | -0.33(-0.69, 0.03) | -6.93(-10.39, -3.48) | -2.53(-4.86, -0.19) | -0.13(-0.31, 0.04) | 0.10(-0.03, 0.23) |
| P* | | <0.001 | 0.14 | <0.001 | 0.08 | 0.27 | 0.23 |
| 53 years | | | | | | | |
| Inactive | 274 (42.68) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 132 (20.56) | -1.21(-2.26, -0.16) | -0.28(-0.67, 0.12) | -4.16(-7.92, -0.40) | -2.13(-4.67, 0.41) | -0.16(-0.34, 0.03) | -0.01(-0.15, 0.13) |
| Most active | 236 (36.76) | -1.60(-2.49, -0.71) | -0.18(-0.51, 0.16) | -6.51(-9.70, -3.31) | -2.26(-4.42, -0.09) | -0.10(-0.26, 0.06) | 0.09(-0.02, 0.21) |
| P* | | <0.01 | 0.33 | <0.001 | 0.08 | 0.21 | 0.19 |
| 60-64 years | | | | | | | |
| Inactive | 365 (56.85) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 114 (17.76) | -1.60(-2.66, -0.53) | -0.24(-0.64, 0.16) | -5.90(-9.69, -2.12) | -1.63(-4.21, 0.95) | -0.20(-0.39, -0.01) | 0.00(-0.14, 0.14) |
| Most active | 163 (25.39) | -1.82(-2.76, -0.89) | 0.07(-0.28, 0.42) | -8.59(-11.92, -5.26) | -2.83(-5.10, -0.56) | 0.03(-0.14, 0.20) | 0.25(0.13, 0.38) |
| P* | | <0.001 | 0.36 | <0.001 | 0.04 | 0.07 | <0.001 |

Notes: *overall test of association (likelihood ratio test comparing models with and without physical activity included);#P-value for sex interaction term; activity at each age was coded as inactive (no participation), moderately active (participated one to four times) and most active (participated five or more times), in the previous month (36 years), per month (43 years) and in the previous 4 weeks (53 and 60-64 years); analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 29. Mean difference in body composition outcomes (95% confidence intervals) in those who were moderately and most active (compared with inactive) at 36, 43 and 53 years, adjusted for activity levels at 60–64 years

a) Males

| | N (%) | Fat mass index (kg/m$^2$) | Lean mass index (kg/m$^2$) | Fat: lean ratio | Android: gynoid ratio | Appendicular lean mass index (kg/m$^2$) | Appendicular lean mass index (kg/m$^2$), adjusted for fat mass index |
|---|---|---|---|---|---|---|---|
| 36 years | | | | | | | |
| Inactive | 166 (29.17) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 161 (28.3) | 0.50(-0.30, 1.30) | 0.11(-0.33, 0.55) | 1.55(-0.89, 3.99) | 1.83(-1.59, 5.24) | -0.01(-0.21, 0.20) | -0.03(-0.21, 0.15) |
| Most active | 242 (42.53) | 0.61(-0.15, 1.37) | 0.39(-0.03, 0.81) | 1.26(-1.06, 3.59) | 0.85(-2.41, 4.10) | 0.10(-0.09, 0.30) | 0.10(-0.06, 0.26) |
| P* | | 0.26 | 0.15 | 0.41 | 0.57 | 0.44 | 0.19 |
| P# | | <0.01 | 0.02 | <0.01 | 0.50 | 0.08 | 0.08 |
| 43 years | | | | | | | |
| Inactive | 241 (42.36) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 143 (25.13) | 0.48(-0.28, 1.24) | 0.31(-0.11, 0.73) | 0.92(-1.42, 3.26) | -0.19(-3.47, 3.08) | 0.17(-0.03, 0.37) | 0.15(-0.02, 0.32) |
| Most active | 185 (32.51) | 0.09(-0.65, 0.82) | 0.08(-0.33, 0.48) | 0.12(-2.12, 2.36) | -1.23(-4.37, 1.90) | 0.08(-0.11, 0.26) | 0.12(-0.04, 0.28) |
| P* | | 0.44 | 0.34 | 0.72 | 0.72 | 0.23 | 0.11 |
| P# | | <0.01 | 0.05 | <0.01 | 0.87 | 0.07 | 0.07 |
| 53 years | | | | | | | |
| Inactive | 226 (39.72) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 138 (24.25) | -0.01(-0.80, 0.78) | 0.12(-0.31, 0.56) | -0.44(-2.87, 1.98) | -0.81(-4.22, 2.59) | 0.12(-0.09, 0.32) | 0.18(0.00, 0.35) |
| Most active | 205 (36.03) | -0.63(-1.35, 0.09) | -0.10(-0.50, 0.30) | -2.14(-4.35, 0.08) | -1.72(-4.83, 1.38) | 0.01(-0.17, 0.20) | 0.15(-0.01, 0.30) |
| P* | | 0.16 | 0.59 | 0.14 | 0.55 | 0.49 | 0.06 |
| P# | | 0.07 | 0.22 | 0.03 | 0.85 | 0.08 | 0.08 |

b) Females

| | N (%) | Fat mass index (kg/m$^2$) | Lean mass index (kg/m$^2$) | Fat: lean ratio | Android: gynoid ratio | Appendicular lean mass index (kg/m$^2$) | Appendicular lean mass index (kg/m$^2$), adjusted for fat mass index |
|---|---|---|---|---|---|---|---|
| 36 years | | | | | | | |
| Inactive | 227 (35.36) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 180 (28.04) | -0.34(-1.31, 0.64) | -0.19(-0.56, 0.18) | -0.04(-3.53, 3.46) | -0.30(-2.68, 2.07) | -0.01(-0.18, 0.17) | 0.05(-0.07, 0.18) |
| Most active | 235 (36.6) | -1.21(-2.15, -0.28) | -0.35(-0.70, 0.01) | -3.42(-6.76, -0.07) | -1.27(-3.54, 1.01) | -0.12(-0.29, 0.04) | 0.08(-0.04, 0.20) |
| P* | | 0.03 | 0.15 | 0.08 | 0.52 | 0.28 | 0.19 |
| 43 years | | | | | | | |
| Inactive | 313 (48.75) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 168 (26.17) | -0.81(-1.75, 0.13) | -0.29(-0.65, 0.06) | -2.46(-5.82, 0.89) | -0.35(-2.63, 1.93) | -0.08(-0.25, 0.08) | 0.03(-0.10, 0.15) |
| Most active | 161 (25.08) | -1.49(-2.49, -0.49) | -0.32(-0.69, 0.06) | -5.30(-8.86, -1.73) | -2.31(-4.73, 0.12) | -0.10(-0.28, 0.08) | 0.14(0.02, 0.27) |
| P* | | 0.01 | 0.13 | 0.01 | 0.16 | 0.44 | 0.03 |
| 53 years | | | | | | | |
| Inactive | 274 (42.68) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Moderately | 132 (20.56) | -1.03(-2.09, 0.03) | -0.30(-0.69, 0.10) | -3.49(-7.28, 0.30) | -2.05(-4.64, 0.53) | -0.14(-0.32, 0.05) | 0.02(-0.11, 0.16) |
| Most active | 236 (36.76) | -1.30(-2.23, -0.36) | -0.23(-0.58, 0.12) | -5.15(-8.48, -1.82) | -1.92(-4.18, 0.35) | -0.09(-0.26, 0.08) | 0.14(0.02, 0.25) |
| P* | | 0.02 | 0.27 | <0.01 | 0.16 | 0.32 | 0.02 |

Notes: *overall test of association (likelihood ratio test comparing models with and without physical activity included); #P-value for sex interaction term; activity at each age was coded as inactive (no participation), moderately active (participated one to four times) and most active (participated five or more times), in the previous month (36 years), per month (43 years) and in the previous 4 weeks (53 and 60-64 years); analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 30**.** A series of different life course models that relate physical activity measures (at 36, 43, 53 and 60–64 years) with body composition outcomes, in comparison with a fully saturated model (which incorporates all parameters)

| Life course model | Fat mass index (kg/m$^2$) | Lean mass index (kg/m$^2$) | Fat: lean ratio | Android: gynoid Ratio | Appendicular lean mass index (kg/m$^2$) | Appendicular lean mass index (kg/m$^2$), adjusted for fat mass index |
|---|---|---|---|---|---|---|
| Males (n=569) | | | | | | |
| No effect (at any age) | <0.001 | 0.14 | <0.001 | 0.21 | 0.23 | 0.03 |
| Accumulation (36 to 60–64y)[a] | <0.01 | 0.15 | <0.01 | 0.38 | 0.33 | 0.16 |
| Accumulation (36 to 60–64y)[b] | <0.01 | 0.14 | 0.01 | 0.30 | 0.15 | 0.08 |
| Sensitive period at 60–64y | <0.01 | 0.12 | 0.01 | 0.40 | 0.27 | 0.17 |
| Sensitive period at 53y | <0.01 | 0.10 | <0.01 | 0.31 | 0.18 | 0.05 |
| Sensitive period at 43y | <0.001 | 0.11 | <0.001 | 0.24 | 0.24 | 0.04 |
| Sensitive period at 36y | <0.001 | 0.31 | <0.001 | 0.16 | 0.30 | 0.03 |
| | | | | | | |
| Females (n=642) | | | | | | |
| No effect (at any age) | <0.001 | 0.06 | <0.001 | 0.07 | 0.18 | <0.001 |
| Accumulation (36 to 60–64y)[a] | 0.86 | 0.12 | 0.51 | 0.73 | 0.23 | 0.06 |
| Accumulation (36 to 60–64y)[b] | 0.70 | 0.08 | 0.68 | 0.50 | 0.12 | 0.10 |
| Sensitive period at 60–64y | 0.02 | 0.04 | 0.02 | 0.34 | 0.13 | 0.20 |
| Sensitive period at 53y | <0.01 | 0.07 | <0.001 | 0.26 | 0.19 | <0.01 |
| Sensitive period at 43y | <0.01 | 0.12 | <0.001 | 0.25 | 0.21 | <0.01 |
| Sensitive period at 36y | <0.001 | 0.12 | <0.001 | 0.10 | 0.21 | <0.01 |

Note: activity at each age was coded as inactive (no participation), moderately active (participated one to four times) and most active (participated five or more times), in the previous month (36 years), per month (43 years) and in the previous 4 weeks (53 and 60-64 years), and included as linear terms; cells show P-values which compare each particular model against a fully saturated model; [a]model assumes similar effect sizes at each age; [b]model allows for differences in effect size at each age; analyses restricted to those with valid data for physical activity measures, paternal occupational class, own educational attainment, limiting illness, and body composition outcomes

Appendix 31. Mean body composition measures by socioeconomic position category in a) childhood and b) adulthood
a) Childhood socioeconomic position

| | N (M/F) | Fat mass (kg) | | Lean mass (kg) | | Fat: lean mass ratio | |
|---|---|---|---|---|---|---|---|
| Paternal occupational class (4y) | | Males | Females | Males | Females | Males | Females |
| I professional | 55/58 | 23.07 (7.17) | 27.10 (9.24) | 53.67 (8.00) | 37.81 (4.75) | 43.07 (12.34) | 70.85 (19.10) |
| II intermediate | 133/149 | 22.79 (7.44) | 28.41 (9.86) | 53.44 (7.02) | 37.98 (5.36) | 42.25 (11.01) | 73.96 (19.26) |
| III skilled (Non-Manual) | 157/177 | 23.54 (6.76) | 27.55 (8.62) | 53.88 (6.47) | 36.57 (5.51) | 43.45 (10.41) | 74.99 (18.88) |
| III skilled (Manual) | 195/211 | 25.24 (7.54) | 29.72 (8.91) | 53.81 (7.28) | 37.01 (5.20) | 46.70 (11.24) | 79.66 (17.76) |
| IV partly skilled | 132/135 | 24.03 (6.94) | 30.53 (9.61) | 53.82 (7.16) | 37.24 (5.59) | 44.50 (10.51) | 81.30 (19.63) |
| V unskilled | 38/37 | 21.82 (6.84) | 30.78 (8.38) | 52.73 (6.55) | 37.75 (5.49) | 41.05 (10.81) | 80.98 (16.02) |
| | | | | | | | |
| Maternal educational attainment (6y) | | | | | | | |
| 2o and FE or higher | 99/115 | 23.45 (7.46) | 26.92 (9.46) | 54.06 (7.56) | 36.80 (5.36) | 43.30 (12.30) | 72.40 (19.51) |
| 2o only (or 1o & FE or higher) | 89/95 | 22.85 (6.55) | 27.97 (8.32) | 53.48 (8.02) | 37.06 (4.75) | 42.63 (9.66) | 74.95 (17.47) |
| 1o and FE(no quals) | 121/102 | 23.79 (7.53) | 28.78 (10.32) | 53.50 (6.67) | 37.50 (5.11) | 44.19 (11.61) | 75.56 (20.02) |
| 1o only | 359/409 | 24.35 (7.31) | 29.92 (9.10) | 53.88 (6.74) | 37.18 (5.60) | 44.92 (11.04) | 80.00 (18.71) |
| | | | | | | | |
| Paternal educational attainment (6y) | | | | | | | |
| 2o and FE or higher | 131/144 | 23.92 (7.05) | 26.05 (7.93) | 54.09 (6.92) | 36.61 (4.61) | 44.17 (11.60) | 70.86 (17.96) |
| 2o only (or 1o & FE or higher) | 98/115 | 23.04 (7.29) | 28.55 (9.40) | 53.93 (7.11) | 37.38 (5.32) | 42.46 (10.81) | 75.78 (19.70) |
| 1o and FE(no quals) | 117/92 | 22.97 (6.15) | 28.99 (10.12) | 52.72 (6.51) | 37.65 (6.28) | 43.50 (9.78) | 75.80 (18.16) |
| 1o only | 314/367 | 24.54 (7.75) | 30.33 (9.30) | 54.17 (7.22) | 37.23 (5.47) | 44.97 (11.60) | 80.88 (18.77) |

Note: tabulations restricted to those with valid body composition outcome data

| | N (M/F) | Appendicular lean mass (kg) | | Android: gynoid ratio | |
|---|---|---|---|---|---|
| Paternal occupational class (4y) | | Males | Females | Males | Females |
| I professional | 55/58 | 24.84 (3.86) | 16.64 (2.29) | 59.38 (14.85) | 43.44 (12.67) |
| II intermediate | 133/149 | 24.61 (3.31) | 16.55 (2.52) | 62.11 (16.76) | 41.88 (11.27) |
| III skilled (Non-Manual) | 157/177 | 24.76 (3.17) | 15.98 (2.56) | 65.57 (15.48) | 44.31 (13.17) |
| III skilled (Manual) | 195/211 | 24.52 (3.53) | 16.09 (2.50) | 68.89 (14.49) | 45.78 (11.16) |
| IV partly skilled | 132/135 | 24.57 (3.40) | 16.01 (2.65) | 67.61 (13.86) | 47.02 (12.34) |
| V unskilled | 38/37 | 24.37 (3.10) | 16.25 (2.60) | 63.97 (15.75) | 46.72 (13.19) |
| | | | | | |
| Maternal educational attainment (6y) | | | | | |
| 2o and FE or higher | 99/115 | 25.00 (3.70) | 16.22 (2.52) | 60.95 (14.61) | 41.56 (12.06) |
| 2o only (or 1o & FE or higher) | 89/95 | 24.81 (3.99) | 16.15 (2.38) | 62.66 (15.13) | 43.63 (11.57) |
| 1o and FE(no quals) | 121/102 | 24.53 (3.20) | 16.28 (2.47) | 67.84 (16.65) | 44.05 (12.56) |
| 1o only | 359/409 | 24.60 (3.22) | 16.11 (2.63) | 67.35 (14.92) | 45.93 (12.03) |
| | | | | | |
| Paternal educational attainment (6y) | | | | | |
| 2o and FE or higher | 131/144 | 24.93 (3.31) | 16.12 (2.17) | 62.55 (15.43) | 40.22 (11.03) |
| 2o only (or 1o & FE or higher) | 98/115 | 24.95 (3.56) | 16.37 (2.51) | 63.70 (15.09) | 43.81 (11.99) |
| 1o and FE(no quals) | 117/92 | 24.10 (3.20) | 16.27 (2.86) | 65.77 (16.08) | 43.83 (13.05) |
| 1o only | 314/367 | 24.76 (3.46) | 16.11 (2.63) | 68.07 (15.19) | 46.99 (12.07) |

b) Adult socioeconomic position

| | N (M/F) | Fat mass (kg) | | Lean mass (kg) | | Fat: lean ratio | |
|---|---|---|---|---|---|---|---|
| Own educational attainment (26y) | | Males | Females | Males | Females | Males | Males |
| Degree or higher | 132/61 | 23.16 (6.75) | 27.74 (9.61) | 53.77 (7.49) | 38.57 (5.62) | 42.79 (9.80) | 70.94 (16.72) |
| GCE A level or Burnam B | 232/240 | 23.23 (7.10) | 28.09 (8.75) | 53.82 (7.02) | 37.04 (5.08) | 42.92 (10.73) | 75.27 (18.78) |
| GCE 'O' level or Burnam C | 108/218 | 23.76 (7.64) | 29.03 (9.62) | 53.56 (6.79) | 37.34 (5.36) | 44.15 (12.10) | 77.05 (18.79) |
| Sub GCE or sub Burnham C | 40/70 | 23.66 (6.27) | 29.30 (8.76) | 50.07 (5.95) | 36.80 (5.90) | 47.24 (11.32) | 79.05 (18.50) |
| None attempted | 192/182 | 24.96 (7.51) | 30.26 (8.83) | 54.49 (6.99) | 37.10 (5.49) | 45.58 (11.35) | 81.04 (18.22) |
| | | | | | | | |
| Home ownership (26y) | | | | | | | |
| Owned at 26 years | 332/422 | 23.93 (7.51) | 28.74 (8.59) | 54.24 (6.84) | 37.11 (5.08) | 43.77 (11.34) | 76.92 (17.65) |
| …Renting or living at home | 332/322 | 23.79 (6.92) | 29.42 (10.06) | 53.07 (7.13) | 37.47 (5.74) | 44.68 (10.66) | 77.75 (20.27) |
| | | | | | | | |
| Own RGSC occ. class (53y) | | | | | | | |
| I professional | 101/16 | 22.95 (6.63) | 26.35 (7.09) | 53.65 (6.93) | 37.44 (5.67) | 42.54 (9.71) | 70.68 (18.22) |
| II intermediate | 344/345 | 24.02 (7.08) | 28.40 (9.31) | 53.91 (7.18) | 37.52 (5.55) | 44.36 (10.80) | 75.02 (18.73) |
| III skilled (Non-Manual) | 83/280 | 24.70 (7.55) | 28.96 (8.82) | 52.51 (6.59) | 36.88 (4.91) | 46.73 (11.71) | 78.05 (18.78) |
| III skilled (Manual) | 155/49 | 24.07 (7.62) | 31.31 (9.18) | 54.30 (7.05) | 37.74 (4.79) | 44.08 (11.55) | 82.23 (17.71) |
| IV partly skilled | 46/75 | 21.89 (7.06) | 31.57 (9.52) | 53.16 (7.21) | 38.22 (5.95) | 40.81 (10.98) | 81.72 (17.92) |
| V unskilled | 10/24 | 23.63 (5.21) | 28.09 (11.22) | 50.69 (6.64) | 35.56 (5.96) | 46.60 (8.23) | 77.71 (22.15) |
| | | | | | | | |
| H of H RGSC occ. class (53y) | | | | | | | |
| I professional | 114/86 | 22.95 (6.55) | 26.29 (7.62) | 53.77 (7.15) | 36.67 (4.93) | 42.46 (9.60) | 71.28 (16.93) |
| II intermediate | 376/424 | 24.00 (7.07) | 29.16 (9.59) | 53.81 (6.96) | 37.71 (5.51) | 44.41 (10.85) | 76.62 (19.09) |
| III skilled (Non-Manual) | 139/186 | 23.64 (7.12) | 28.79 (8.39) | 52.93 (6.94) | 36.51 (5.02) | 44.47 (11.11) | 78.52 (18.33) |
| III skilled (Manual) | 83/53 | 24.96 (8.52) | 31.90 (10.65) | 54.58 (7.27) | 37.92 (4.85) | 45.33 (12.98) | 83.01 (20.26) |
| IV partly skilled | 22/34 | 22.43 (7.31) | 31.68 (8.50) | 53.51 (8.02) | 37.97 (5.91) | 41.62 (11.02) | 82.92 (16.72) |
| V unskilled | 5/6 | 22.42 (5.40) | 26.30 (9.27) | 52.75 (8.97) | 34.63 (8.04) | 42.27 (5.06) | 74.50 (18.16) |
| Own NS-SEC occ. class (53y) | | | | | | | |
| I Managerial & professional | 378/298 | 23.58 (6.86) | 28.07 (9.23) | 53.79 (7.12) | 37.40 (5.29) | 43.62 (10.47) | 74.42 (19.04) |
| II Intermediate | 172/303 | 23.75 (6.82) | 29.25 (8.54) | 53.35 (7.12) | 37.10 (4.96) | 44.41 (10.66) | 78.50 (18.66) |
| III Routine and manual | 182/197 | 24.39 (8.19) | 30.39 (10.16) | 53.97 (6.95) | 37.56 (5.97) | 44.83 (12.30) | 79.83 (18.81) |

| | N (M/F) | Fat mass (kg) | | Lean mass (kg) | | Fat: lean ratio | |
|---|---|---|---|---|---|---|---|
| Household income (60-64y) | | | | | | | |
| 1 (highest) | 292/233 | 23.13 (6.48) | 28.01 (8.37) | 53.93 (7.16) | 37.30 (5.17) | 42.68 (9.55) | 74.66 (17.99) |
| 2 | 172/200 | 23.45 (6.91) | 28.49 (8.52) | 53.85 (7.02) | 37.50 (5.63) | 43.39 (10.75) | 75.53 (16.57) |
| 3 | 171/211 | 24.47 (7.56) | 30.21 (10.52) | 53.07 (7.27) | 37.41 (5.64) | 45.88 (11.77) | 79.83 (20.45) |
| 4 (lowest) | 76/126 | 24.55 (8.37) | 30.12 (9.41) | 53.00 (6.42) | 36.80 (5.02) | 45.83 (12.70) | 81.05 (20.49) |

| | N (M/F) | Appendicular lean mass (kg) | | Android: gynoid ratio | |
|---|---|---|---|---|---|
| Own educational attainment (26y) | | Males | Females | Males | Females |
| Degree or higher | 132/61 | 24.96 (3.62) | 17.00 (2.60) | 62.82 (16.29) | 41.99 (12.24) |
| GCE A level or Burnam B | 232/240 | 24.73 (3.42) | 16.16 (2.38) | 63.61 (14.55) | 43.95 (12.45) |
| GCE 'O' level or Burnam C | 108/218 | 24.51 (3.35) | 16.23 (2.58) | 66.54 (15.15) | 45.74 (12.63) |
| Sub GCE or sub Burnham C | 40/70 | 22.69 (3.06) | 15.76 (2.74) | 67.40 (17.20) | 45.17 (12.18) |
| None attempted | 192/182 | 24.81 (3.24) | 16.05 (2.61) | 68.76 (14.24) | 45.65 (12.07) |
| | | | | | |
| Home ownership (26y) | | | | | |
| Owned at 26 years | 332/422 | 24.95 (3.29) | 16.15 (2.46) | 66.17 (15.47) | 44.33 (11.75) |
| …Renting or living at home | 332/322 | 24.30 (3.44) | 16.27 (2.67) | 65.44 (15.39) | 45.05 (12.88) |
| | | | | | |
| Own RGSC occ. class (53y) | | | | | |
| I professional | 101/16 | 24.81 (3.32) | 16.50 (2.62) | 64.11 (16.37) | 42.03 (8.98) |
| II intermediate | 344/345 | 24.71 (3.53) | 16.38 (2.57) | 65.00 (15.31) | 43.87 (12.06) |
| III skilled (Non-Manual) | 83/280 | 24.06 (3.15) | 16.00 (2.37) | 68.10 (16.26) | 44.75 (13.25) |
| III skilled (Manual) | 155/49 | 24.80 (3.29) | 16.25 (2.46) | 67.67 (14.56) | 47.22 (10.89) |
| IV partly skilled | 46/75 | 24.38 (3.44) | 16.62 (2.85) | 62.19 (12.69) | 47.82 (11.72) |
| V unskilled | 10/24 | 23.23 (2.80) | 15.22 (2.79) | 77.36 (13.10) | 43.97 (12.76) |
| | | | | | |

| H of H RGSC occ. class (53y) | | Appendicular lean mass (kg) | | Android: gynoid ratio | |
|---|---|---|---|---|---|
| I professional | 114/86 | 24.87 (3.39) | 15.97 (2.31) | 63.92 (16.41) | 41.26 (11.36) |
| II intermediate | 376/424 | 24.65 (3.41) | 16.44 (2.60) | 65.62 (15.11) | 44.77 (12.19) |
| III skilled (Non-Manual) | 139/186 | 24.29 (3.34) | 15.81 (2.33) | 66.02 (15.03) | 44.34 (13.40) |
| III skilled (Manual) | 83/53 | 24.74 (3.33) | 16.38 (2.59) | 68.96 (14.99) | 47.45 (10.88) |
| IV partly skilled | 22/34 | 24.80 (3.88) | 16.54 (2.77) | 60.33 (13.47) | 50.83 (10.08) |
| V unskilled | 5/6 | 24.38 (3.57) | 14.44 (3.47) | 84.59 (12.87) | 45.33 (20.22) |
| | | | | | |
| Own NS-SEC occ. class (53y) | | | | | |
| I Managerial & professional | 378/298 | 24.68 (3.41) | 16.32 (2.48) | 64.80 (16.23) | 43.66 (11.89) |
| II Intermediate | 172/303 | 24.48 (3.43) | 16.13 (2.40) | 66.52 (14.47) | 45.14 (12.12) |
| III Routine and manual | 182/197 | 24.70 (3.36) | 16.26 (2.82) | 66.82 (14.02) | 46.12 (13.47) |
| | | | | | |
| Household income (60-64y) | | | | | |
| 1 (highest) | 292/233 | 24.76 (3.39) | 16.29 (2.39) | 64.64 (15.73) | 43.80 (12.53) |
| 2 | 172/200 | 24.70 (3.41) | 16.24 (2.63) | 65.09 (14.27) | 44.59 (12.42) |
| 3 | 171/211 | 24.28 (3.59) | 16.31 (2.76) | 66.42 (14.62) | 45.08 (12.60) |
| 4 (lowest) | 76/126 | 24.15 (2.92) | 15.95 (2.35) | 68.59 (17.09) | 46.43 (12.13) |

Appendix 32. Mean body composition measures (adjusted for adult height) by socioeconomic position category in a) childhood and b) adulthood

a) Childhood socioeconomic position

| | N (M/F) | Fat mass index (kg/m$^{1.20}$) | | Lean mass index (kg/m$^2$) | |
|---|---|---|---|---|---|
| Paternal occupational class (4y) | | Males | Females | Males | Females |
| I professional | 55/58 | 11.62 (3.59) | 14.96 (5.03) | 17.05 (1.99) | 14.05 (1.66) |
| II intermediate | 133/149 | 11.51 (3.79) | 15.81 (5.39) | 17.09 (2.05) | 14.31 (1.82) |
| III skilled (Non-Manual) | 157/177 | 11.94 (3.35) | 15.32 (4.74) | 17.40 (1.90) | 13.74 (1.86) |
| III skilled (Manual) | 195/211 | 12.97 (3.79) | 16.74 (4.96) | 17.74 (2.03) | 14.22 (1.80) |
| IV partly skilled | 132/135 | 12.33 (3.40) | 17.26 (5.41) | 17.72 (1.86) | 14.38 (1.97) |
| V unskilled | 38/37 | 11.32 (3.62) | 17.42 (4.58) | 17.63 (2.23) | 14.62 (1.62) |
| | | | | | |
| Maternal educational attainment (6y) | | | | | |
| 2o and FE or higher | 99/115 | 11.81 (3.76) | 15.00 (5.19) | 17.20 (2.06) | 13.90 (1.90) |
| 2o only (or 1o & FE or higher) | 89/95 | 11.49 (3.21) | 15.60 (4.62) | 16.98 (2.08) | 13.99 (1.64) |
| 1o and FE(no quals) | 121/102 | 12.16 (3.85) | 16.06 (5.67) | 17.46 (1.93) | 14.18 (1.68) |
| 1o only | 359/409 | 12.49 (3.67) | 16.84 (5.06) | 17.72 (1.96) | 14.26 (1.94) |
| | | | | | |
| Paternal educational attainment (6y) | | | | | |
| 2o and FE or higher | 131/144 | 12.05 (3.58) | 14.48 (4.34) | 17.20 (1.94) | 13.76 (1.58) |
| 2o only (or 1o & FE or higher) | 98/115 | 11.71 (3.73) | 15.92 (5.13) | 17.42 (2.11) | 14.15 (1.84) |
| 1o and FE(no quals) | 117/92 | 11.80 (3.13) | 16.14 (5.52) | 17.35 (1.88) | 14.20 (2.01) |
| 1o only | 314/367 | 12.56 (3.87) | 17.10 (5.20) | 17.75 (2.00) | 14.32 (1.93) |

Note: tabulations restricted to those with valid body composition outcome data

b) Adult socioeconomic position

| | N (M/F) | Fat mass index (kg/m$^{1.2}$) | | Lean mass index (kg/m$^2$) | |
|---|---|---|---|---|---|
| Own educational attainment (26y) | | Males | Females | Males | Females |
| Degree or higher | 132/61 | 11.64 (3.36) | 15.33 (5.23) | 17.06 (2.06) | 14.37 (1.81) |
| GCE A level or Burnam B | 232/240 | 11.79 (3.51) | 15.69 (4.87) | 17.39 (1.99) | 14.02 (1.79) |
| GCE 'O' level or Burnam C | 108/218 | 12.13 (3.88) | 16.20 (5.23) | 17.46 (1.87) | 14.12 (1.80) |
| Sub GCE or sub Burnham C | 40/70 | 12.33 (3.26) | 16.51 (4.88) | 16.89 (1.85) | 14.15 (1.99) |
| None attempted | 192/182 | 12.85 (3.79) | 17.10 (4.93) | 18.02 (1.93) | 14.33 (1.89) |
| Home ownership (26y) | | | | | |
| Owned at 26 years | 332/422 | 12.18 (3.74) | 16.10 (4.80) | 17.64 (1.96) | 14.11 (1.75) |
| …Renting or living at home | 332/322 | 12.17 (3.51) | 16.45 (5.54) | 17.33 (2.01) | 14.23 (1.96) |
| Own RGSC occ. class (53y) | | | | | |
| I professional | 101/16 | 11.61 (3.28) | 14.73 (3.77) | 17.25 (1.94) | 14.28 (2.04) |
| II intermediate | 344/345 | 12.19 (3.55) | 15.82 (5.12) | 17.42 (2.01) | 14.14 (1.87) |
| III skilled (Non-Manual) | 83/280 | 12.69 (3.81) | 16.25 (4.95) | 17.31 (1.90) | 14.05 (1.78) |
| III skilled (Manual) | 155/49 | 12.35 (3.85) | 17.72 (5.14) | 17.86 (1.95) | 14.60 (1.71) |
| IV partly skilled | 46/75 | 11.16 (3.57) | 17.76 (5.24) | 17.29 (2.12) | 14.66 (1.83) |
| V unskilled | 10/24 | 12.57 (2.73) | 15.90 (6.30) | 17.70 (2.00) | 13.81 (1.99) |
| H of H RGSC occ. class (53y) | | | | | |
| I professional | 114/86 | 11.61 (3.24) | 14.67 (4.18) | 17.28 (2.05) | 13.90 (1.69) |
| II intermediate | 376/424 | 12.21 (3.55) | 16.27 (5.30) | 17.44 (1.95) | 14.25 (1.88) |
| III skilled (Non-Manual) | 139/186 | 12.13 (3.55) | 16.18 (4.71) | 17.40 (1.95) | 13.96 (1.81) |
| III skilled (Manual) | 83/53 | 12.84 (4.35) | 18.11 (6.06) | 18.03 (1.96) | 14.73 (1.62) |
| IV partly skilled | 22/34 | 11.35 (3.74) | 17.73 (4.63) | 17.10 (2.24) | 14.44 (1.84) |
| V unskilled | 5/6 | 11.98 (2.54) | 14.86 (4.65) | 18.61 (2.24) | 13.59 (2.50) |
| Own NS-SEC occ. class (53y) | | | | | |
| I Managerial & professional | 378/298 | 11.97 (3.46) | 15.65 (5.10) | 17.37 (2.04) | 14.12 (1.82) |
| II Intermediate | 172/303 | 12.10 (3.41) | 16.38 (4.78) | 17.31 (1.88) | 14.09 (1.74) |
| III Routine and manual | 182/197 | 12.56 (4.10) | 17.10 (5.59) | 17.86 (1.96) | 14.42 (1.99) |

| | | Fat mass index (kg/m$^{1.2}$) | | Lean mass index (kg/m$^2$) | |
|---|---|---|---|---|---|
| Household income (60-64y) | | | | | |
| 1 (highest) | 292/233 | 11.71 (3.21) | 15.59 (4.62) | 17.37 (1.98) | 14.04 (1.76) |
| 2 | 172/200 | 12.00 (3.49) | 15.87 (4.65) | 17.60 (1.99) | 14.15 (1.86) |
| 3 | 171/211 | 12.53 (3.82) | 16.99 (5.81) | 17.40 (2.04) | 14.32 (1.95) |
| 4 (lowest) | 76/126 | 12.57 (4.17) | 16.99 (5.34) | 17.43 (1.95) | 14.16 (1.88) |

Appendix 33. Differences in body composition outcomes between the hypothetical lowest and highest socioeconomic position (slope index of inequality) in childhood, with each indicator mutually adjusted for one another

| | Fat mass index (kg/m$^{1.20}$) | | | | Lean mass index (kg/m$^2$) | | | |
|---|---|---|---|---|---|---|---|---|
| | Males | P | Females | P | Males | P | Females | P |
| Paternal occupational class (4y) | 0.60(-0.65, 1.85) | 0.35 | 0.71(-0.97, 2.39) | 0.41 | 0.63(-0.04, 1.30) | 0.07 | -0.05(-0.67, 0.56) | 0.86 |
| Maternal educational attainment (6y) | 0.74(-0.57, 2.06) | 0.27 | 1.03(-0.71, 2.78) | 0.25 | 0.42(-0.29, 1.13) | 0.24 | 0.13(-0.51, 0.77) | 0.69 |
| Paternal educational attainment (6y) | 0.35(-1.02, 1.73) | 0.62 | 2.71(0.77, 4.66) | 0.01 | 0.27(-0.47, 1.01) | 0.48 | 0.69(-0.02, 1.40) | 0.06 |

| | Fat: lean ratio | | | | Android: gynoid ratio | | | |
|---|---|---|---|---|---|---|---|---|
| | Males | P | Females | P | Males | P | Females | P |
| Paternal occupational class (4y) | 1.71(-2.11, 5.54) | 0.38 | 4.74(-1.46, 10.94) | 0.13 | 3.44(-1.78, 8.66) | 0.20 | 0.91(-3.03, 4.84) | 0.65 |
| Maternal educational attainment (6y) | 2.06(-1.96, 6.07) | 0.31 | 5.63(-0.81, 12.08) | 0.09 | 3.79(-1.68, 9.27) | 0.17 | 1.66(-2.43, 5.75) | 0.43 |
| Paternal educational attainment (6y) | 0.20(-3.99, 4.40) | 0.92 | 8.78(1.60, 15.95) | 0.02 | 4.57(-1.16, 10.29) | 0.12 | 8.42(3.87, 12.98) | <0.001 |

| | Appendicular lean mass index (kg/m$^2$)* | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Males | P | | P | Females | P | | P |
| | Model 1 | | Model 2 | | Model 1 | | Model 2 | |
| Paternal occupational class (4y) | 0.25(-0.07, 0.57) | 0.12 | 0.18(-0.10, 0.46) | 0.21 | -0.08(-0.38, 0.21) | 0.57 | -0.17(-0.39, 0.05) | 0.14 |
| Maternal educational attainment (6y) | 0.05(-0.29, 0.38) | 0.79 | -0.05(-0.34, 0.25) | 0.76 | 0.01(-0.29, 0.31) | 0.95 | -0.11(-0.34, 0.12) | 0.35 |
| Paternal educational attainment (6y) | 0.11(-0.24, 0.46) | 0.55 | 0.06(-0.24, 0.37) | 0.69 | 0.22(-0.12, 0.55) | 0.21 | -0.10(-0.35, 0.16) | 0.45 |

Note: sample sizes in all models were: males: n=594, females n=637; *Model 1: unadjusted; Model 2: Model 1 + adjusted for whole body fat mass index; analyses were restricted to those with valid data for all indicators of socioeconomic position and body composition outcomes

Appendix 34. Mean differences (95% confidence intervals, P-value) in birth weight and weight gain velocity standard deviation scores between the lowest and highest childhood socioeconomic position (the slope index of inequality)

| | | Paternal educational attainment (6y) | | | Own educational Attainment (26y) | |
|---|---|---|---|---|---|---|
| | N (M/F) | Males | Females | N (M/F) | Males | Females |
| Birth weight | 661/715 | -0.08(-0.36, 0.21), 0.61 | -0.17(-0.44, 0.10), 0.21 | 703/767 | | |
| 0-2 | 541/568 | -0.33(-0.64, -0.02), 0.04 | 0.09(-0.19, 0.38), 0.51 | 567/597 | -0.28(-0.54, -0.01), 0.04 | 0.03(-0.26, 0.33), 0.83 |
| 2–4 | 522/537 | 0.16(-0.12, 0.44), 0.26 | 0.06(-0.22, 0.33), 0.67 | 544/558 | -0.19(-0.44, 0.06), 0.13 | -0.17(-0.46, 0.12), 0.26 |
| 4–7 | 543/593 | 0.00(-0.27, 0.28), 0.98 | 0.17(-0.10, 0.43), 0.21 | 560/600 | -0.14(-0.38, 0.10), 0.24 | -0.07(-0.35, 0.20), 0.60 |
| 7–11 | 542/601 | -0.02(-0.27, 0.24), 0.89 | 0.37(0.14, 0.60), 0.00 | 560/606 | 0.05(-0.18, 0.28), 0.66 | 0.08(-0.16, 0.33), 0.51 |
| 11–15 | 510/556 | 0.34(0.10, 0.58), 0.01 | 0.09(-0.21, 0.38), 0.56 | 530/573 | 0.11(-0.11, 0.32), 0.33 | 0.27(-0.04, 0.57), 0.09 |
| 15-20 | 467/496 | 0.29(0.02, 0.56), 0.04 | 0.34(0.04, 0.65), 0.03 | 489/510 | 0.45(0.21, 0.69), 0.00 | 0.07(-0.25, 0.39), 0.68 |

Note: weight gain models (2–20 years) are adjusted for concurrent height gain and weight and height at the beginning of each period, except weight gain from 0–2 years (adjusted for height at 2 years and weight at birth); analyses were restricted to those with valid data for body composition outcomes

Appendix 35. Associations between indicators of socioeconomic position and self-reported physical activity levels across adulthood

i) Paternal educational attainment (6 years)

| | Males | | | | Females | | | |
|---|---|---|---|---|---|---|---|---|
| | 1 Highest | 2 | 3 | 4 Lowest | 1 Highest | 2 | 3 | 4 Lowest |
| 60-64 years | | | | | | | | |
| Inactive | 61 (47.29) | 51 (53.68) | 65 (57.52) | 207 (67.21) | 63 (44.37) | 64 (56.14) | 43 (47.25) | 230 (64.79) |
| Moderately | 23 (17.83) | 18 (18.95) | 15 (13.27) | 40 (12.99) | 35 (24.65) | 21 (18.42) | 21 (23.08) | 42 (11.83) |
| Most active | 45 (34.88) | 26 (27.37) | 33 (29.2) | 61 (19.81) | 44 (30.99) | 29 (25.44) | 27 (29.67) | 83 (23.38) |
| P* | <0.01 | | | | <0.001 | | | |
| 53 years | | | | | | | | |
| Inactive | 31 (25.62) | 39 (41.94) | 43 (39.09) | 134 (45.27) | 41 (29.5) | 39 (34.51) | 39 (44.32) | 185 (51.53) |
| Moderately | 33 (27.27) | 23 (24.73) | 25 (22.73) | 66 (22.3) | 31 (22.3) | 21 (18.58) | 19 (21.59) | 62 (17.27) |
| Most active | 57 (47.11) | 31 (33.33) | 42 (38.18) | 96 (32.43) | 67 (48.2) | 53 (46.9) | 30 (34.09) | 112 (31.2) |
| P* | 0.02 | | | | <0.001 | | | |
| 43 years | | | | | | | | |
| Inactive | 33 (25.78) | 36 (38.3) | 47 (41.96) | 153 (52.22) | 49 (35) | 44 (39.64) | 50 (59.52) | 191 (54.57) |
| Moderately | 41 (32.03) | 31 (32.98) | 25 (22.32) | 63 (21.5) | 43 (30.71) | 33 (29.73) | 19 (22.62) | 84 (24.00) |
| Most active | 54 (42.19) | 27 (28.72) | 40 (35.71) | 77 (26.28) | 48 (34.29) | 34 (30.63) | 15 (17.86) | 75 (21.43) |
| P* | <0.001 | | | | <0.001 | | | |
| 36 years | | | | | | | | |
| Inactive | 27 (23.08) | 23 (25) | 26 (23.42) | 94 (32.98) | 27 (20.77) | 32 (30.77) | 25 (29.07) | 156 (45.35) |
| Moderately | 28 (23.93) | 29 (31.52) | 43 (38.74) | 76 (26.67) | 41 (31.54) | 29 (27.88) | 22 (25.58) | 89 (25.87) |
| Most active | 62 (52.99) | 40 (43.48) | 42 (37.84) | 115 (40.35) | 62 (47.69) | 43 (41.35) | 39 (45.35) | 99 (28.78) |
| P* | 0.03 | | | | <0.001 | | | |

iii) Own occupational class at 53 years (Registrar General's classification)

| | Males | | | | Females | | | |
|---|---|---|---|---|---|---|---|---|
| | I/II Highest | III Non manual | III Manual | IV/V Lowest | I/II Highest | III Non manual | III Manual | IV/V Lowest |
| 60-64 years | | | | | | | | |
| Inactive | 202 (54.89) | 43 (58.9) | 99 (78.57) | 28 (59.57) | 152 (48.25) | 151 (61.38) | 32 (72.73) | 55 (67.07) |
| Moderately | 65 (17.66) | 12 (16.44) | 8 (6.35) | 9 (19.15) | 64 (20.32) | 40 (16.26) | 3 (6.82) | 11 (13.41) |
| Most active | 101 (27.45) | 18 (24.66) | 19 (15.08) | 10 (21.28) | 99 (31.43) | 55 (22.36) | 9 (20.45) | 16 (19.51) |
| P* | <0.001 | | | | <0.01 | | | |
| 53 years | | | | | | | | |
| Inactive | 118 (31.47) | 31 (42.47) | 75 (57.25) | 23 (47.92) | 106 (33.02) | 116 (46.03) | 27 (61.36) | 51 (60.71) |
| Moderately | 106 (28.27) | 17 (23.29) | 19 (14.5) | 10 (20.83) | 71 (22.12) | 49 (19.44) | 6 (13.64) | 12 (14.29) |
| Most active | 151 (40.27) | 25 (34.25) | 37 (28.24) | 15 (31.25) | 144 (44.86) | 87 (34.52) | 11 (25) | 21 (25) |
| P* | <0.001 | | | | <0.001 | | | |
| 43 years | | | | | | | | |
| Inactive | 138 (36.8) | 26 (35.62) | 78 (59.54) | 25 (52.08) | 139 (43.3) | 126 (50) | 24 (54.55) | 54 (64.29) |
| Moderately | 97 (25.87) | 22 (30.14) | 25 (19.08) | 12 (25) | 93 (28.97) | 67 (26.59) | 11 (25) | 17 (20.24) |
| Most active | 140 (37.33) | 25 (34.25) | 28 (21.37) | 11 (22.92) | 89 (27.73) | 59 (23.41) | 9 (20.45) | 13 (15.48) |
| P* | <0.001 | | | | 0.04 | | | |
| 36 years | | | | | | | | |
| Inactive | 102 (27.2) | 17 (23.29) | 48 (36.64) | 15 (31.25) | 97 (30.22) | 97 (38.49) | 19 (43.18) | 35 (41.67) |
| Moderately | 108 (28.8) | 20 (27.4) | 32 (24.43) | 19 (39.58) | 91 (28.35) | 69 (27.38) | 15 (34.09) | 21 (25) |
| Most active | 165 (44) | 36 (49.32) | 51 (38.93) | 14 (29.17) | 133 (41.43) | 86 (34.13) | 10 (22.73) | 28 (33.33) |
| P* | 0.12 | | | | 0.10 | | | |

iv) Household income at 60–64 years

| | Males | | | | Females | | | |
|---|---|---|---|---|---|---|---|---|
| | 1 Highest | 2 | 3 | 4 Lowest | 1 Highest | 2 | 3 | 4 Lowest |
| 60-64 years | | | | | | | | |
| Inactive | 116 (49.36) | 95 (62.91) | 99 (68.75) | 42 (72.41) | 99 (48.77) | 99 (54.4) | 107 (59.44) | 73 (69.52) |
| Moderately | 40 (17.02) | 26 (17.22) | 22 (15.28) | 3 (5.17) | 39 (19.21) | 35 (19.23) | 30 (16.67) | 12 (11.43) |
| Most active | 79 (33.62) | 30 (19.87) | 23 (15.97) | 13 (22.41) | 65 (32.02) | 48 (26.37) | 43 (23.89) | 20 (19.05) |
| P* | <0.001 | | | | 0.03 | | | |
| 53 years | | | | | | | | |
| Inactive | 76 (31.4) | 59 (38.82) | 69 (47.59) | 29 (48.33) | 59 (28.78) | 66 (36.07) | 91 (49.46) | 69 (63.3) |
| Moderately | 62 (25.62) | 37 (24.34) | 42 (28.97) | 7 (11.67) | 48 (23.41) | 33 (18.03) | 41 (22.28) | 18 (16.51) |
| Most active | 104 (42.98) | 56 (36.84) | 34 (23.45) | 24 (40) | 98 (47.8) | 84 (45.9) | 52 (28.26) | 22 (20.18) |
| P* | <0.001 | | | | <0.001 | | | |
| 43 years | | | | | | | | |
| Inactive | 74 (30.58) | 67 (44.08) | 76 (52.41) | 33 (55) | 78 (38.05) | 90 (49.18) | 93 (50.54) | 68 (62.39) |
| Moderately | 68 (28.1) | 40 (26.32) | 30 (20.69) | 13 (21.67) | 59 (28.78) | 54 (29.51) | 44 (23.91) | 22 (20.18) |
| Most active | 100 (41.32) | 45 (29.61) | 39 (26.9) | 14 (23.33) | 68 (33.17) | 39 (21.31) | 47 (25.54) | 19 (17.43) |
| P* | <0.001 | | | | <0.01 | | | |
| 36 years | | | | | | | | |
| Inactive | 56 (23.14) | 47 (30.92) | 49 (33.79) | 23 (38.33) | 51 (24.88) | 59 (32.24) | 73 (39.67) | 51 (46.79) |
| Moderately | 69 (28.51) | 45 (29.61) | 37 (25.52) | 19 (31.67) | 56 (27.32) | 60 (32.79) | 50 (27.17) | 26 (23.85) |
| Most active | 117 (48.35) | 60 (39.47) | 59 (40.69) | 18 (30) | 98 (47.8) | 64 (34.97) | 61 (33.15) | 32 (29.36) |
| P* | 0.08 | | | | <0.001 | | | |

Note: *P(chi-squared test); analyses were restricted to those with valid data for body composition outcomes

Appendix 36. Differences in android and gynoid fat mass (95% CI) between the hypothetical lowest and highest socioeconomic position (slope index of inequality)

| | | Android fat mass (kg) | | | | Gynoid fat mass (kg) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | N | Males | P | Females | P | Males | P | Females | P |
| Paternal occ. class (4y) | 1477 | 0.27(0.02, 0.52) | 0.03 | 0.48(0.23, 0.73) | <0.01 | -0.02(-0.28, 0.24) | 0.89 | 0.48(0.11, 0.84) | 0.01 |
| Maternal education (6y) | 1389 | 0.34(0.06, 0.62) | 0.02 | 0.55(0.27, 0.82) | <0.01 | 0.09(-0.21, 0.39) | 0.54 | 0.61(0.20, 1.01) | <0.01 |
| Paternal education (6y) | 1378 | 0.34(0.06, 0.62) | 0.02 | 0.75(0.48, 1.02) | <0.01 | 0.03(-0.27, 0.32) | 0.85 | 0.68(0.29, 1.08) | <0.01 |
| Own education (26y) | 1475 | 0.42(0.19, 0.65) | <0.01 | 0.37(0.10, 0.64) | <0.01 | 0.17(-0.08, 0.43) | 0.17 | 0.41(0.02, 0.81) | 0.04 |
| Home ownership (26y) | 1408 | -0.14(-0.44, 0.15) | 0.34 | 0.14(-0.16, 0.43) | 0.36 | -0.07(-0.38, 0.23) | 0.64 | 0.08(-0.35, 0.51) | 0.72 |
| Own RGSC occ. class (53y) | 1528 | 0.12(-0.11, 0.36) | 0.30 | 0.43(0.14, 0.72) | <0.01 | -0.05(-0.30, 0.20) | 0.69 | 0.46(0.05, 0.87) | 0.03 |
| Own NS-SEC occ. class (53y) | 1550 | 0.20(-0.05, 0.45) | 0.12 | 0.39(0.12, 0.66) | <0.01 | 0.08(-0.18, 0.35) | 0.53 | 0.45(0.06, 0.84) | 0.03 |
| H of H RGSC occ. class (53y) | 1530 | 0.18(-0.07, 0.43) | 0.16 | 0.46(0.19, 0.73) | <0.01 | 0.02(-0.24, 0.29) | 0.86 | 0.48(0.08, 0.88) | 0.02 |
| Household income (60-64y) | 1477 | 0.30(0.07, 0.54) | 0.01 | 0.42(0.17, 0.67) | <0.01 | 0.20(-0.05, 0.46) | 0.12 | 0.52(0.15, 0.89) | <0.01 |

Note: analyses were restricted to those with valid data for all body composition outcomes