Birthweight, lifetime obesity and physical functioning in mid-adulthood: a nationwide birth cohort study.

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Abstract

Background

Evidence is scant on long-term implications of childhood obesity and BMI gains over the life-course for poor physical functioning (PF). The objective was to establish whether i) birthweight and body mass index (BMI) across the life-course; ii) BMI gains at specific life-stages and iii) age of obesity onset were associated with PF at 50y.

Methods

In the 1958 British birth cohort (N=8,674), BMI (kg/m^2) was calculated using height and weight (measured (7, 11, 16, 33 and 45y); self-reported (23 and 50y)). PF was assessed at 50y using the validated PF subscale of the Short-form 36 survey; the bottom (gender-specific) 10% was classified as poor PF. Missing data were imputed via multiple imputation. Associations were examined using logistic regression, adjusting for health and social factors.

Results

Birthweight was not associated with PF. At each adult age, odds of poor PF were highest for obese (vs normal) e.g. for 23y obesity the $OR_{adjusted}$ for poor PF was 2.28(1.34,3.91) and 2.67(1.72,4.14) in males and females respectively. BMI gains were associated with poor PF, e.g. for females, $OR_{adjusted}$ per SD in BMI gain 16-23y was 1.28(1.13,1.46); for BMI gains 45-50y it was 1.36(1.11,1.65). Longer duration of obesity was associated with poor PF, e.g. in males, $OR_{adjusted}$ was 2.32(1.26,4.29) for childhood obesity onset and 1.50(1.16, 1.96) for mid-adulthood onset (vs never obese, p-trend<0.001).

Conclusions

Obesity, BMI gains, and earlier obesity onset were associated with poor PF in mid-adulthood reinforcing the importance of preventing and delaying obesity onset.

Key words: Body Mass Index, obesity, overweight, life-course, physical functioning, ageing, birth cohort

Key messages

- Obesity at any age in adulthood was associated with approximately two-fold higher odds of poor physical functioning at 50y.
- BMI gains over much of the life-course (from 16y in males; 7y in females) were associated with poor physical functioning at 50y, with weaker associations for childhood than adult BMI gains.
- There was a trend between longer duration of obesity and increasing odds of poor physical functioning, such that onset in childhood/adolescence (vs never) was associated with approximately two-fold higher odds of poor physical functioning; this trend was most likely due to the higher BMI at 50y for those with earlier obesity onset.
- Findings, in particular those relating to long duration of obesity, are important given the increasing prevalence of childhood obesity, which tends to track into adulthood.
- Study implications include preventing and delaying obesity onset to mitigate the risk of poor functioning in mid-adulthood.

Introduction

Maintaining physical functioning is of prime importance in an ageing population[1,2]. Physical functioning (PF), the ability to undertake the physical tasks of daily living, such as carrying groceries or climbing stairs, allows older individuals to remain independent, actively engage in family and community activities[3] and increases the likelihood of extending working lives and volunteering after retirement[4]. Poor PF predicts numerous adverse health outcomes including fractures, cognitive decline, hospitalisation and nursing home admission[5–7]. Moreover, poor PF in mid-adulthood is associated with higher risk of premature death[8], highlighting its relevance to public health even at relatively young ages. Thus, consideration of the determinants of PF is valuable in planning effective public health policy interventions that aim to increase independence at older ages[9].

One risk factor associated with PF is adiposity[10–13], and against the backdrop of the current global obesity epidemic[14,15] understanding associations between excess body weight and PF is important. A few prospective studies have demonstrated associations between adiposity, usually assessed by Body Mass Index (BMI) and poor PF in mid-adulthood and through to older ages[10–13]. Yet, much of the evidence is limited because previous studies have relied on retrospective recall of body size[10–13], BMI measures restricted to adulthood[10,11,13], or examined only two measures 35-54 years apart[11]. While adiposity is associated with poor PF[10–13], it is unclear whether adiposity at specific life-stages are particularly detrimental. One study suggested that adiposity in adolescence was associated with poor PF at 65y, even after accounting for adult body size[12], while another demonstrated that young adult adiposity was associated with poor PF at older ages (60-79y), mainly via concurrent adiposity[11]. Knowledge is limited regarding changes in body size from early-life onwards and PF and so it is unclear whether there are sensitive periods of BMI gain for subsequent PF. Moreover, there is some evidence linking longer duration of obesity to poor PF[10,11,13] but these studies rely on recalled body size in adulthood. Thus a knowledge gap exists on the relationship between onset of obesity in childhood/adolescence and subsequent PF. Finally, evidence is limited on links between birthweight, subsequent BMI gains and adult PF[16,17].

To address research gaps on the importance of particular life-stages, timing of weight gain and duration of exposure to obesity we used longitudinal data from the 1958 British Birth Cohort, followed from birth to 50y, to establish whether there are sensitive periods of the life-course when BMI (and BMI gains) are particularly important for PF in mid-adulthood. Specifically, we assessed the

following in relation to poor PF i) birthweight and BMI at different childhood and adult ages to 50y, ii) gains in BMI during different periods of the life-course and iii) age of onset of obesity from 7y to mid-adulthood.

Methods

The 1958 cohort study contains prospective information on all born during one week of March 1958 (>17,000 individuals) and followed-up at 7y, 11y, 16y, 23y, 33y, 42y, 45y and 50y[18]. Ethical approval was given, including at 50y by the London multi-centre Research Ethics Committee; informed consent was obtained from participants at various ages. Respondents in mid-adulthood are broadly representative of the surviving cohort[19]. This study consists of those who took part in the 50y survey with a valid measure of PF (4,173 males and 4,501 females).

Measures

PF at 50y was assessed using the validated PF subscale of the Short-form 36 (SF-36) survey[20] which is an extensively used instrument for general and older populations[21–23]. The 10-item scale covers a range of activities that require mild to moderate physical abilities to carry out daily tasks including lifting, carrying groceries, climbing stairs, bending, kneeling, stooping, and walking moderate distances. Participants indicated how able they were to perform each item by using a three-point scale (limited 'a lot', 'a little', or 'not at all'). The ten items were summed and linearly transformed to a scale ranging from 0 to 100, with lower scores representing poor PF. As used elsewhere, poor PF was defined as the lowest gender-specific 10th centile of the PF scale[24].

Birthweight, BMI and obesity duration: Birthweight was converted into kilograms from pounds and ounces and standardized by adjusting for gestational age. Height and weight were measured at 7y, 11y, 16y, 33y and 45y and self-reported at 23y and 50y. BMI was calculated as weight/height^2 (kg/m^2). BMIs were categorised as normal, overweight or obese using standard cut-points for childhood[25,26] and adulthood (<25 (normal), 25-29.99 (overweight) and ≥30 (obese)[27]). As in previous

work[28], age of obesity onset (to represent obesity duration) was identified as the first age when BMI was defined as obese (details in table 4 footnotes).

Covariates were identified as risk factors for poor PF[9] and were determined *a priori*. They included social class at birth and at 50y (4 categories: professional/managerial to unskilled); breastfed status (<one month; ≥month); 7y physical impairment (parent report: yes/no), 42y physical activity frequency (4 categories: no exercise in a week to ≥3 times/week)[29], 42y smoking status (current, ex, never); adult educational attainment (4 categories: no qualifications to degree or higher).

Statistical analysis

At each data collection, heights and weights were measured over a range of ages (e.g. 7.11y to 8.66y at the 7y follow-up). Therefore, BMI was centred at 7y, 11y, etc. for all individuals by using predictions from linear regression models that assumed a linear age trend over short periods. A unit of BMI has different implications in childhood and adulthood, hence to enable comparison of BMI's at different ages, BMI was converted to gender-specific standard deviation (SD) scores (i.e. zBMI). zBMIs were calculated by subtracting mean BMI from the individual's BMI and dividing by SD of BMI at a given age. Thus, an individual's zBMI represents their rank on a standardized scale at a particular age. Similarly, we calculated gender-specific birthweight SD scores.

Our analysis consisted of three main phases. First, we used logistic regression models to examine whether birthweight, zBMI and BMI categories (normal, overweight and obese) at specific ages were associated with poor PF at 50y. Second, we assessed associations between changes in zBMI during defined age intervals (i.e. 7-11y; 11-16y etc.) and 50y PF. Since zBMI changes may be partly determined by previous (i.e. 'baseline') zBMI, all models controlled for 'baseline' zBMI; e.g. the relationship between change in zBMI from 7y to 11y and PF at 50y was adjusted for 7y zBMI. To determine whether associations between BMI and PF at 50y were modified by birthweight or BMI at younger ages, we tested interactions between 50y zBMI and (i) birthweight and (ii) zBMI at 7y and 11y. Finally, we assessed the relationship between age of obesity onset (from childhood) and 50y PF. All analyses were conducted separately by gender.

Sensitivity analyses were conducted using an alternative cut-point for PF, i.e. we repeated the analyses described above using the lowest gender-specific 25th centile of the SF-36 PF score[30,31]. Further sensitivity analysis was performed to examine the relationship between age of overweight/obesity onset and 50y PF. We also explored whether those lost to follow-up had different levels of adiposity to the included analytic sample and found broadly similar mean BMI and prevalence of overweight and obesity across the life-course in the two groups (Table S1). Missing data ranged from 0% (adult educational attainment) to 28% (16y weight). To

minimize data loss, missing data were imputed using multiple imputation chained equations. Following guidelines[32], imputation models included all model variables, plus main predictors of missingness (7-year internalising and externalising behaviours and cognitive ability)[19]. Regression analyses were run across 20 imputed datasets and overall estimates were obtained. Imputed results were broadly similar to those obtained using observed values; the former are presented.

Results

Mean BMI increased with age in the population (Table 1). Obesity prevalence was low during childhood, but increased by mid-adulthood e.g. in males at 7y and 45y obesity prevalence was 1.8% and 25.3% respectively. Individuals with poor PF were less likely to: be from a professional/managerial class at birth and in adulthood, have a higher educational qualification and be a never smoker (Table S2). Of those with poor PF, 58% reported that they were 'limited a lot' bending, kneeling or stooping, 44% lifting or carrying groceries; and 27% bathing or dressing themselves (data not shown).

Birthweight, BMI, overweight and obesity at specific ages and poor PF at 50y

In both genders, birthweight was not associated with 50y PF (Table 2); however, at all ages from 11y, zBMI was associated with poor PF and associations were stronger with increasing age; e.g. in males, per SD increment in BMI, the $OR_{adjusted}$ of poor PF was 1.13(1.02,1.25) at age 11y and 1.34(1.22,1.47) at 50y. At each age from 16y in males and 23y in females $OR_{adjusted}$ for poor PF were highest for the obese, ranging from 1.77 to 2.28 (males) and from 2.42 to 2.67 (females) (Table 2).

BMI gains between specific ages

In females, BMI gains during all age intervals from 7y were associated with poor 50y PF (Table 3). The strongest association was observed for BMI gain 33-45y ($OR_{adjusted}$=1.50 (1.30,1.73) per SD gain, conditional on 33y zBMI). $OR_{adjusted}$ for BMI gain in the intervals 11-16y and 45-50y were similar. In males, BMI gains in young and mid-adulthood (i.e. 16-23y, 23-33y, and 33-45y) were associated with poor PF with ORs ranging from 1.21 to 1.32. In both genders, gains in standardised units from birth to 7y were not associated with 50y poor PF. The association between 50y BMI and PF was not modified by birthweight or early-life (i.e. 7y or 11y) BMI ($p_{interaction}$>0.05 for all ages and both genders).

Age of obesity onset

Mean BMI at 50y increased with earlier onset of obesity; e.g. in females, from 31.9 kg/m^2 for mid-adult onset to 37.3kg/m^2 for child/adolescent onset (Table 4). Obesity in childhood/adolescence that did not carry through to adulthood was rare (<1% in both genders); and was not associated with poor PF. Approximately 67% of individuals were never obese, while 20% became obese in mid-adulthood. There was a relationship between earlier age of obesity onset and increasing odds of poor PF at 50y, e.g. in males, $OR_{adjusted}$ ranged from 1.50 (1.16,1,96) for mid-adulthood onset to 2.32 (1.26,4.29) for childhood/adolescence onset (p_{trend}<0.0001); in females, $OR_{adjusted}$ were 1.78 (1.39,2.28) and 1.98 (1.19,3.31) respectively (p_{trend}<0.0001). When models were further adjusted for 50y BMI, associations between obesity onset and poor PF were no longer present (p_{trend}=0.07 and 0.50 for males and females respectively, data not shown). The trend for earlier onset was also observed in sensitivity analysis for overweight/obesity and poor PF at 50y (p_{trend}<0.0001; Table S3).

In sensitivity analysis using the bottom 25th centile of the SF-36 to define poor PF, associations for BMI, BMI gains and obesity onset were broadly similar to those observed for the 10thcentile (Tables S4-S6).

Discussion

In this nationwide general population sample followed from birth to 50y, we identified three important findings. First, obesity at any age in adulthood was associated with approximately two-fold higher odds of poor PF in mid-life; for example, 23y obesity (vs normal), in males, was associated with a 2.3 higher odds of poor PF. Second, BMI gains over much of the life-course (16y to 45y in males and 7y to 50y in females) were associated with poor functioning, with weaker associations for childhood than adult BMI gains. Third, there was a trend of increasing odds of poor functioning with longer duration from obesity onset, such that childhood/adolescence onset (vs never obese) was associated with approximately two-fold higher odds of poor PF and this trend was explained by differences in 50y BMI. We also found that both birthweight and obesity in childhood/adolescence that did not progress into adulthood were not associated with poor 50y PF.

Methodological considerations

Our study has a number of strengths including its large prospective design with multiple follow-up time-points over five decades of life. In addition to repeat, prospectively measured birthweight and BMI, our study benefited from prospectively collected information on socioeconomic and lifestyle covariates. The SF-36 based measure of PF has been widely used in general and older populations[21–23] and validated against objective assessments of physical performance (e.g. grip strength[33]) and chronic conditions including multiple sclerosis[34]; nonetheless it is self-reported. Other study limitations are acknowledged. Height and weight were measured at all but two ages (23y and 50y), when they were self-reported. BMI is a widely used indicator, but does not completely reflect body fatness and longitudinal data on other measures, e.g. waist circumference, were not available. Since the study is observational uncontrolled covariates could account for some of the observed associations. Finally, there has been attrition of the study sample over time with under-representation of certain groups by mid-adulthood (e.g. those with childhood cognitive and behavioural problems). However respondents in mid-adulthood were broadly representative of the surviving cohort with respect to childhood social class, housing tenure, physical and maternal factors and key adult characteristics[19], including adiposity levels across the life-course. Furthermore, we used multiple imputation to avoid further reductions in the sample due to missing information.

Interpretation and comparison with previous studies

To our knowledge, this is the first study to examine life-course BMI from childhood through to 50y and physical functioning in mid-adulthood. Our results consistently show links between higher BMI (from 11y) across the life-course (up to 50y) and poor PF in mid-adulthood with stronger associations for more recent ages. For example, we found that compared to a woman of average height (1.62cm) and weight at 23y, an 8kg higher weight was associated with a 32% elevated odds of poor PF at 50y. While previous literature linking early-life BMI and adult PF is scant, our findings for adult BMI are in line with previous studies that demonstrate higher BMI at various adult life-stages is related to poor PF from mid-adulthood through to older ages[10–13]. For example, we found 23y obesity in males to be associated with a 2.3 higher odds of poor PF, which is comparable to a previous study showing a 2.4 higher odds of functional limitations at 60-79y in relation to 25y obesity[11].

Our results for BMI and BMI gains at different life-stages inform on whether there are sensitive periods of the life-course for PF in mid-adulthood. Whilst associations were observed for BMI from 11y and for BMI gains over much of the life-course (16y to 45y in males; 7y to 50y in females) the magnitude of associations provides little support for sensitive periods for adiposity in relation to mid-life PF. However, childhood BMI gains showed generally weaker associations than those seen

for adulthood gains. These findings are consistent with literature demonstrating that gains from 7y to 11y have stronger associations with poor PF in early old age than gains from earlier life[16] and that weight gain among ageing employees associates with worse and declining PF[35]. Our null findings for birthweight and gains in body size, birth to 7y, suggest that size in early-life is not a main factor in relation to mid-adult PF. These results are consistent with previous work showing that early-life BMI gains (till 7y) are not associated with PF in the early 60's[16], although our null finding for birthweight contrasts with previous studies[16]. Given the lack of association between birthweight and childhood BMI with mid-life PF in our study population, it is unsurprising that 50y BMI and PF associations were not modified by these factors.

A particularly novel finding relates to our examination of duration of obesity and poor PF. Few studies have focussed on this link, perhaps due to the lack of repeat measures of BMI across the life-course. We found that longer duration of obesity was associated with increased risk of poor PF, with higher odds seen for obesity onset in childhood compared to midlife onset. Thus, our study extends previous work that showed longer durations of obesity in adulthood were associated with mobility limitations[13,36] and poor physical performance[10,37]. BMI in earlier life is correlated with later life BMI[38,39] and, in this[28], and other cohorts[13], longer duration of obesity across the life-course is related to higher BMI in adulthood. The high BMI at 50y for those with childhood obesity onset is likely to explain our finding for duration of obesity given that the association with PF was no longer present after accounting for midlife BMI. Such findings suggest that magnitude of adiposity is the key factor in relation to PF, with the highest levels of BMI particularly detrimental. This argument is supported by observations in this population that it is obesity, less so overweight, that increases the risk of poor PF. Furthermore, a recent intervention study has shown that loss of body mass, particularly fat mass, by intentional weight loss leads to improvements in mobility, disability and walking speed in overweight and obese older adults[40]. Also, we found no risk of poor PF for childhood obesity that did not carry through into adulthood. Weight loss has been shown to decrease levels of circulating inflammatory markers[41] which may be involved in some aspects of functioning (e.g. walking limitations, mobility-disability[42,43]), but not others (e.g. grip strength[37]). Obesity causally influences inflammation as indicated with specific markers[44] which in turn have been postulated to lead to muscle weakness and sarcopenia[42]. Hence, excessive obesity may result in persistently elevated inflammatory profiles, which could ultimately lead to decreased functional capacity even in midlife. This is in line with previous observations that prolonged and heightened periods of inflammation in midlife increases the risk of subsequent frailty[45]. It is also possible that a persistent state of obesity may lead to increased joint wear and tear and reduced physical activity[46–48], contributing to muscle weakness and ultimately increased risk of disability[49].

Conclusions and implications

In conclusion, we found that obesity at any adult age was associated with an approximate doubling of the odds of poor PF in mid-adulthood and that earlier onset of obesity was detrimental for PF. Given that obesity tends to track into adulthood[50], our findings relating to longer duration of obesity, from this generation when it was uncommon, are important in the context of increasing childhood obesity prevalence[14,15]. Physical functioning in mid-adulthood is an important life-stage at which prevention of poor functioning could potentially alleviate adverse health outcomes including premature death[8]. While the aging population[3] and increasing obesity prevalence warrant the need for future studies to understand underlying mechanisms linking adiposity to PF, our findings highlight the importance of preventing and delaying obesity onset to mitigate the risk of poor functioning in mid-adulthood.

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Contributors

SMPP and CP conceptualised the study. NTR carried out all analysis and drafted the manuscript. SMPP and CP commented on the manuscript. All authors have read and approved the final version.

Declaration of interests

We declare no competing interests.

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References

1. Kuh D. A Life Course Approach to Healthy Aging, Frailty, and Capability. *Journals Gerontol Ser A Biol Sci Med Sci*. 2007;62(7):717–721.

2. Freedman VA, Martin LG, Schoeni RF. Recent Trends in Disability and Functioning Among Older Adults in the United States. *JAMA*. 2002;288(24):3137.

3. Government Office for Science. Future of an ageing population. 2016;

4. Stafford M, Cooper R, Cadar D, et al. Physical and cognitive capability in mid-adulthood as determinants of retirement and extended working life in a British cohort study. *Scand J Work Environ Health*. 2017;43(1):15–23.

5. Cooper R, Kuh D, Cooper C, et al. Objective measures of physical capability and subsequent health: a systematic review. *Age Ageing*. 2011;40(1):14–23.

6. Cawthon PM, Fox KM, Gandra SR, et al. Do Muscle Mass, Muscle Density, Strength, and Physical Function Similarly Influence Risk of Hospitalization in Older Adults? *J Am Geriatr Soc*. 2009;57(8):1411–1419.

7. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol*. 1994;49(2):M85-94.

8. Cooper R, Strand BH, Hardy R, Patel K V, Kuh D. Physical capability in mid-life and survival over 13 years of follow-up: British birth cohort study. *BMJ*. 2014;348:g2219.

9. Kuh D, Karunananthan S, Bergman H, Cooper R. A life-course approach to healthy ageing: maintaining physical capability. *Proc Nutr Soc*. 2014;73(2):237–48.

10. Houston DK, Ding J, Nicklas BJ, et al. The association between weight history and physical performance in the Health, Aging and Body Composition study. *Int J Obes*. 2007;31(11):1680–1687.

11. Dowd JB, Zajacova A. Long-term obesity and physical functioning in older Americans. *Int J Obes*. 2015;39(3):502–507.

12. Vasunilashorn S, Martinson ML. Weight status in adolescence is associated with later life functional limitations. *J Aging Health*. 2013;25(5):758–75.

13. Stenholm S, Rantanen T, Alanen E, Reunanen A, Sainio P, Koskinen S. Obesity History as a Predictor of Walking Limitation at Old Age. *Obesity*. 2007;15(4):929–938.

14. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2014;384(9945):766–81.

15. Lobstein T, Jackson-Leach R, Moodie ML, et al. Child and adolescent obesity: part of a bigger picture. *Lancet*. 2015;385(9986):2510–20.

16. Bonsdorff MB von, Rantanen T, Sipila S, et al. Birth Size and Childhood Growth as

Determinants of Physical Functioning in Older Age: The Helsinki Birth Cohort Study. *Am J Epidemiol*. 2011;174(12):1336–1344.

17. Kuh D, Hardy R, Butterworth S, et al. Developmental Origins of Midlife Physical Performance: Evidence from a British Birth Cohort. *Am J Epidemiol*. 2006;164(2):110–121.

18. Power C, Elliott J. Cohort profile: 1958 British birth cohort (National Child Development Study). *Int J Epidemiol*. 2006;35(1):34–41.

19. Atherton K, Fuller E, Shepherd P, Strachan DP, Power C. Loss and representativeness in a biomedical survey at age 45 years: 1958 British birth cohort. *J Epidemiol Community Health*. 2008;62(3):216–23.

20. Archer G, Pinto Pereira S, Power C. Child maltreatment as a predictor of adult physical functioning in a prospective British birth cohort. *BMJ Open*. 2017;7(10).

21. Ware JE, Kosinski M, Dewey JE, Gandek B. SF-36 health survey: manual and interpretation guide. Quality Metric Inc; 2000.

22. Ware J, Sherbourne JE, Donald C. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Med Care*. 1992;473–483.

23. Brazier JE, Harper R, Jones NM, et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ*. 1992;305(6846):160–4.

24. Palumbo AJ, Roos AJ De, Cannuscio C, et al. Work Characteristics Associated with Physical Functioning in Women. *Int J Environ Res Public Health*. 2017;14(4).

25. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. *BMJ*. 2007;335(7612):194.

26. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ*. 2000;320(7244):1240–3.

27. World Health Organization. World Health Organisiation. Report of a WHO consultation on obesity.Obesity: preventing and managing the global epidemic. Geneva. *WHO* World Health Organization; 1998.

28. Power C, Thomas C. Changes in BMI, duration of overweight and obesity, and glucose metabolism: 45 years of follow-up of a birth cohort. *Diabetes Care*. 2011;34(9):1986–91.

29. Parsons TJ, Power C, Manor O. Longitudinal Physical Activity and Diet Patterns in the 1958 British Birth Cohort. *Med Sci Sport Exerc*. 2006;38(3):547–554.

30. Robinson SM, Jameson KA, Syddall HE, et al. Clustering of Lifestyle Risk Factors and Poor Physical Function in Older Adults: The Hertfordshire Cohort Study. *J Am Geriatr Soc*. 2013;61(10):1684–1691.

31. Wilson LF, Pandeya N, Byles J, Mishra GD. Hysterectomy and perceived physical function in middle-aged Australian women: a 20-year population-based prospective

cohort study. *Qual Life Res*. 2018;27(6):1501–1511.

32. Sterne JAC, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ*. 2009;338.

33. Syddall HE, Martin HJ, Harwood RH, Cooper C, Aihie Sayer A. The SF-36: a simple, effective measure of mobility-disability for epidemiological studies. *J Nutr Health Aging*. 2009;13(1):57–62.

34. Dallmeijer A, Groot V de, Roorda L, et al. Cross-diagnostic validity of the SF-36 physical functioning scale in patients with stroke, multiple sclerosis and amyotrophic lateral sclerosis: A study using rasch analysis. *J Rehabil Med*. 2007;39(2):163–169.

35. Svärd A, Lahti J, Roos E, et al. Obesity, change of body mass index and subsequent physical and mental health functioning: a 12-year follow-up study among ageing employees. *BMC Public Health*. 2017;17(1):744.

36. Houston DK, Ding J, Nicklas BJ, et al. Overweight and Obesity Over the Adult Life Course and Incident Mobility Limitation in Older Adults: The Health, Aging and Body Composition Study. *Am J Epidemiol*. 2009;169(8):927–936.

37. Stenholm S, Sallinen J, Koster A, et al. Association between obesity history and hand grip strength in older adults--exploring the roles of inflammation and insulin resistance as mediating factors. *J Gerontol A Biol Sci Med Sci*. 2011;66(3):341–8.

38. Rooney BL, Mathiason MA, Schauberger CW. Predictors of Obesity in Childhood, Adolescence, and Adulthood in a Birth Cohort. *Matern Child Health J*. 2011;15(8):1166–1175.

39. Power C, Lake JK, Cole TJ. Body mass index and height from childhood to adulthood in the 1958 British born cohort. *Am J Clin Nutr*. Oxford University Press; 1997;66(5):1094–1101.

40. Beavers KM, Miller ME, Rejeski WJ, Nicklas BJ, Krichevsky SB, Kritchevsky SB. Fat mass loss predicts gain in physical function with intentional weight loss in older adults. *J Gerontol A Biol Sci Med Sci*. 2013;68(1):80–6.

41. Selvin E, Paynter NP, Erlinger TP. The Effect of Weight Loss on C-Reactive Protein. *Arch Intern Med*. 2007;167(1):31.

42. Stenholm S, Rantanen T, Heliovaara M, Koskinen S. The Mediating Role of C-Reactive Protein and Handgrip Strength Between Obesity and Walking Limitation. *J Am Geriatr Soc*. 2008;56(3):462–469.

43. Ferrucci L, Harris TB, Guralnik JM, et al. Serum IL-6 Level and the Development of Disability in Older Persons. *J Am Geriatr Soc*. 1999;47(6):639–646.

44. Timpson NJ, Nordestgaard BG, Harbord RM, et al. C-reactive protein levels and body mass index: elucidating direction of causation through reciprocal Mendelian randomization. *Int J Obes (Lond)*. 2011;35(2):300–8.

45. Walker KA, Walston J, Gottesman RF, Kucharska-Newton A, Palta P, Windham BG.

Midlife Systemic Inflammation Is Associated With Frailty in Later Life: The ARIC Study. *Journals Gerontol Ser A*. 2018;00:1–7.

46. Richmond RC, Davey Smith G, Ness AR, Hoed M den, McMahon G, Timpson NJ. Assessing Causality in the Association between Child Adiposity and Physical Activity Levels: A Mendelian Randomization Analysis. *PLoS Med*. 2014;11(3).

47. Golubic R, Ekelund U, Wijndaele K, et al. Rate of weight gain predicts change in physical activity levels: a longitudinal analysis of the EPIC-Norfolk cohort. *Int J Obes*. 2013;37(3):404–9.

48. Bauman AE, Reis RS, Sallis JF, et al. Correlates of physical activity: Why are some people physically active and others not? *Lancet*. 2012;380(9838):258–271.

49. Roubenoff R, Hughes VA. Sarcopenia: Current Concepts. *Journals Gerontol Ser A Biol Sci Med Sci*. 2000;55(12):M716–M724.

50. Simmonds M, Llewellyn A, Owen CG, Woolacott N. Predicting adult obesity from childhood obesity: A systematic review and meta-analysis. *Obes Rev*. 2016;17(2):95–107.