**Association of childhood fat mass and weight with adult-onset type 2 diabetes in Denmark** Authors: Mohammed T Hudda MSc\*1, Julie Aarestrup PhD2, Christopher G Owen PhD1, Derek G Cook PhD1, Thorkild I A Sørensen Dr Med Sci3,4, Alicja R Rudnicka PhD1, Jennifer L Baker PhD2,4, Peter H Whincup FRCP1 and Claire M Nightingale PhD1

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**Key Points**

**Question**

Is childhood fat mass (FM) more strongly associated with long-term type 2 diabetes risk in adulthood than childhood weight, independent of height?

**Findings**

In a population-based cohort study including more than 260,000 schoolchildren, height-independent associations between childhood FM and adult T2D risk (per kg) were stronger than those observed for childhood weight, which is used as the basis for current childhood obesity assessments in the form of BMI.

**Meaning**

Weight-based measures, currently used as the basis for childhood obesity assessment in the form of body mass index, are less strongly associated with adult T2D risk than childhood FM. Information on FM, rather than weight-based measures, focusses on the modifiable component of weight which is related to adult T2D risk.

**ABSTRACT**

**Importance**

Defining whether childhood fat mass (FM) is the driver of the associations between childhood obesity and adult type 2 diabetes (T2D) risk, where obesity is typically defined by cut-offs based upon the weight-based marker, body mass index.

**Objective**

Quantify and compare height-independent associations between childhood FM and weight with adult T2D risk in a historic Danish cohort

**Design**

Retrospective cohort-study

**Setting**

Population-based study of schoolchildren, born between 1930-1985, from the Copenhagen School Health Records Register with follow-up in adulthood through to 31st December 2015.

**Participants**

Analyses were based upon 269,913 schoolchildren aged 10y with 21,896 ascertained adult T2D cases, and 261,192 aged 13y with 21,530 ascertained adult T2D cases for whom childhood height and weight measurements, as well as predicted FM, were available.

**Exposures**

Childhood FM and weight at 10 and 13 years

**Main Outcomes and measures**

T2D diagnoses made for adults at least 30 years of age were ascertained by linkage to national disease registers. Sex-specific Cox regression quantified associations, adjusted for childhood height, within five birth-cohort groups. Group-specific results were pooled using random-effects meta-analyses accounting for heterogeneity across group-specific associations.

**Results**

Analyses contained 135,940 boys and 133,973 girls aged 10y with 21,896 ascertained adult T2D cases, and 131,025 boys and 130,167 girls aged 13y with 21,530 ascertained adult T2D cases. After adjusting for childhood height, increases in FM and weight (per kg) amongst 10-year-old boys were associated with elevated T2D risks at 50y of 12% (HR:1.12 [95%CI 1.10-1.14]) and 7% (HR:1.07 [95%CI 1.05-1.09) respectively, and amongst 10y girls of 15% (HR:1.15 [95%CI 1.13-1.17]) and 10% (HR:1.10 [95%CI 1.08-1.11]) respectively. Amongst 13-year-olds, increases in FM and weight (per kg) were associated with increased T2D risks at 50y of 10% (HR:1.10 [95%CI 1.09-1.10]) and 6% (HR:1.06 [95% CI 1.05-1.07]) respectively for boys, and of 10% (HR:1.10 [95%CI 1.10-1.11]) and 7% (HR:1.07 [95% CI 1.06-1.08]) for girls.

**Conclusions and Relevance**

A 1kg increase in childhood FM was more strongly associated with increased adult T2D risk than 1kg of weight, independent of childhood height. Information on FM, rather than weight-based measures, focusses on the modifiable component of weight which is related to adult T2D risk. These findings support the assessment of childhood FM in adiposity surveillance initiatives in the effort to reduce long-term T2D risk.

**INTRODUCTION**

Obesity is a major global public health issue, both in childhood and adulthood. The World Health Organization estimated that in 2016 worldwide there were over 340 million children and adolescents aged 5-19 1 affected by overweight (including obesity) and a further 41 million under 5 years of age.1 Overweight is a strong determinant of type 2 diabetes (T2D) risk; this association is apparent for overweight in childhood2 as well as in adulthood.3,4 Such reported associations have generally been based on childhood body mass index (BMI), a weight-for-height measure, which is widely used as a in clinical and public health practice. However, BMI has a number of limitations as a marker of body fatness (BF) in children,5-7 particularly its inability as a weight-based measure to discriminate between lean mass (fat free mass; FFM) and fat mass (FM), the balance of which can vary markedly in individuals with a given BMI.6 BMI is only moderately associated with childhood BF8,9 and is correlated with childhood height.8,10 Though it has been suggested that this correlation might reflect higher levels of BF in taller children11,12, short stature has been shown to be independently associated with adult T2D risk.13 It would be of considerable importance to establish whether childhood FM per se is more strongly associated with T2D risk than childhood weight-based measures, independent of height. Whilst previous studies in children and adolescents have shown significant cross-sectional associations between FM and cardiometabolic risk factors,14,15 which have been of comparable magnitude to those of BMI,14 there is little or no information on the long-term associations between fat-based measures in childhood and their associations with incident T2D in adulthood. This reflects the limited number of long-term cohort studies with information on childhood FM as well as ascertained adult T2D diagnoses. However, the recent development and extensively validated prediction equation for estimating FM based on height, weight and demographic factors of age, sex and ethnicity16 allows for retrospective BF estimation within historic datasets in which disease outcomes, including T2D. We therefore examined the height-independent associations between childhood FM and weight with adult T2D risk among a large Danish cohort of schoolchildren born between 1930 and 1985, measured in childhood and followed up for T2D incidence in adulthood.17

**METHODS**

**Study population**

This study was based on The Copenhagen School Health Records Register (CSHRR), a database containing information on almost every schoolchild in Copenhagen born between 1930 and 1985.17 Due to legal and procedural reasons, there were variations in the ages at which children were measured throughout the years included in the cohort. The cohort members had mandatory health examinations including height and weight measurements, which were recorded by school-based doctors or nurses.17

Using individual personal identification numbers, issued to Danish citizens alive or born after 1968, data from the CSHRR were linked with the Danish National Patient Register (NPR) to obtain inpatient and outpatient diagnoses of T2D. The NPR contains hospital discharge diagnoses from all hospitals since 1977 and from outpatient and emergency departments since 1995 18. The date of the first hospital registration was used to define the age at diagnosis. As the NPR only includes individuals who were referred to hospital-based clinics, and not patients who are diagnosed with T2D in general practice, the total population-level age-specific incidence of T2D will be underestimated in this study. However, as T2D in Denmark is treated using a “shared care” model, general practitioners often refer patients to treatment at specialized hospital outpatient clinics, so that even individuals with typical diabetes are frequently treated in a hospital setting and would be included within the NPR. As a result, the extent of underestimation, particularly with extended follow-up duration, is likely to be limited. The International Classification of Diseases, Eighth Revision, until 1994 (code 250) and the Tenth Revision thereafter (codes E11 through E14) were used to define T2D. In 1987, code 249 (insulin-dependent diabetes mellitus) was introduced in Denmark; previously, code 250 had included all forms of diabetes. To minimize the potential for misclassification, cases of insulin-dependent diabetes mellitus and diabetes diagnosed prior to 30 years of age were excluded, since type 1 diabetes is insulin-dependent and generally tends to be diagnosed at earlier ages.19

Of 316,340 individuals potentially eligible for this study, 11,282 emigrated, died or were untraceable before the initiation of follow-up on 1st January 1977 or 30 years of age (Supplemental figure 1). A total of 827 individuals diagnosed with diabetes prior to age 30 years or the start of follow-up were excluded, together with 5106 individuals missing childhood anthropometric data and 7 individuals with outlying values at all childhood ages (Supplementary figure 1). This study therefore included all individuals with complete information on height, weight, age, sex and date of the health examination for at least one childhood measurement at 7, 10 or 13 years of age and who were alive at the start of the diabetes follow-up period at age 30 years. Follow-up ended on the date of a T2D diagnosis, death, emigration, loss to follow-up or 31st December 2015, whichever was first.

**Statistical analysis**

Prediction of childhood FM

STATA version 15 was used for all analyses. The equation used to estimate childhood FFM and FM from height, weight, age and sex for this study was derived in a dataset of 2,375 UK children aged 4-15 years who had reference standard deuterium dilution measures of body composition.16 It was extensively validated both internally (to assess model overfitting) and externally (to assess model generalisability). External validation in UK children aged 11-12 years demonstrated promising model generalisability (R2 = 90.0%), good calibration of observed and predicted FM (calibration slope: 1.02 [95% CI: 0.97-1.07]) with a mean difference between observed and predicted fat mass of −1.29 kg.16 A comparison of the FM predictions obtained from the model with those obtained from DXA and bioelectrical impedance, found this equation to provide FM estimates at least as accurate as those of DXA and bioelectrical impedance.20 A supplementary file containing a Microsoft Excel based calculator was published alongside the original publication, to facilitate the quick and straightforward estimation of FFM and FM using this equation. This equation was used to estimate FFM (and FM by subtraction from weight measurement) within the CSHRR. Information on ethnicity was not available but was assumed to be white for all individuals as the proportion of children from a non-white European ethnic background was likely to be low due to migration patterns to Denmark at this time.17 Correlation coefficients were calculated between childhood FM, FFM, weight and height. Childhood measurements were also summarised using mean and standard deviations (SD), by adult T2D case status and birth-cohort group, within the study population.

Associations between childhood FM and weight with T2D

Cox proportional-hazards regression models were used to examine the respective associations between childhood FM and weight with adult T2D risk. The underlying timescale of the Cox models was age, where follow-up began at 30 years. At each childhood age of 7, 10 and 13 years of age, sex-specific models were fitted for each of the two childhood exposures (FM and weight) and adjusting for childhood height (as a continuous variable), a potential confounder of the associations of interest. To account for potential heterogeneity in associations across the wide range of birth years, the above models were also all fitted separately within five birth-cohort groups (1930-39, 1940-49, 1950-59, 1960-69 and 1970-85).

Model assumptions

The linearity assumption within the sex- and birth-cohort specific- Cox models described above (i.e. assuming a log-linear association between the exposures of interest (FM and weight) at each childhood age and adult T2D risk) was tested by re-fitting each Cox model and including a non-linear restricted cubic spline term with 3 knots for the childhood exposure of interest (either FM or weight) as well as for height. The likelihood ratio test was used to determine the statistical significance (p<0.05) of the non-linear cubic spline terms. Results of tests for the significance of cubic spline terms (data not presented) suggested largely log-linear patterns at both 10 and 13 years for both FM and weight associations, but not at 7 years. Therefore, analyses in this study focussed on quantifying the FM and weight associations at 10 and 13 years of age. The proportional-hazards assumption was assessed by testing the statistical significance (Wald test at the 5% significance level) of time-varying coefficients, interaction terms between adult age and the main exposure (FM or weight) within each of the Cox models fitted. There was evidence to suggest the assumption was violated (i.e. associations between childhood FM or weight and T2D risk were not constant across the range of adult ages) and therefore time-varying coefficients were retained within final sex- and birth-cohort specific models.

Hazard ratios (and 95% CIs) were therefore estimated from the Cox models, adjusting for childhood height (as a continuous variable) and including time-varying coefficients, for a range of adult ages including 30, 40, 50, 60 and 70 years. This was done for each birth-cohort group without extrapolation beyond the greatest adult age in the birth-cohort group; hence, associations at older adult ages were not quantified for more recent birth-cohort groups where individuals had not yet reached these ages. Due to the low levels of meaningful heterogeneity between associations from birth-cohort groups at given ages, hazard ratios from each of the five birth-cohort groups were averaged using random-effects meta-analysis to provide a pooled estimate of the associations of interest across birth-cohort groups for each age group. As FM and weight are measured on the same scale, we present the effect sizes per kg increase in the childhood adiposity markers. Effect sizes were also presented per SD increase in exposure variables. However, as weight can be partitioned into FM and FFM and it follows by definition that the SD of weight is a combination of the SDs of FM and FFM, comparisons on the SD scale of effect sizes for weight with those of FM should be interpreted with caution as they provide a different perspective on the effect of childhood body composition on long-term T2D risk. As the SDs of FM and weight differed by birth-cohort group, the SDs used to transform the effect sizes onto the Sd scale were calculated within birth-cohort, and therefore results were not pooled across groups as was done for the per kg analysis.

**RESULTS**

Childhood measurements of weight, height and predicted FM and FFM contained no missing data and were available across the five birth-cohort groups in 269,913 children aged 10 years (135,940 boys and 133,973 girls)and in 261,192 children aged 13 years (131,025 boys and 130,167 girls). Mean levels and SDs for each variable at both 10 and 13 years of age in boys and girls are presented by adult T2D diagnosis status in Tables 1 & 2 and overall in Supplementary Table 1. Average levels of each variable increased in more recent birth cohorts at both 10 and 13 years of age (Supplementary Table 1). At 10 years of age, across all birth cohort groups, the average weight was similar amongst girls (31.6kg) and boys (31.9kg), as well as the height (boys:1.38m, girls: 1.37m), but girls had higher average levels of FM (8.2kg) compared to boys (7.1kg) (Supplementary Table 1). While average childhood height was very similar amongst those with future T2D compared with those who did not develop T2D, average FM and weight levels were higher amongst those who went on to develop T2D (Tables 1 & 2). This difference, which was observed at 10 and 13 years amongst both sexes, was more marked in more recent birth-cohort groups. Furthermore, the percentage of weight attributed to FM was greater in more recent birth-cohort groups, than those earlier (Tables 1 & 2, Supplementary Table 1). A strong correlation was observed between height and both FFM and weight in childhood at 10 and 13 years of age, while FM was only moderately correlated with childhood height (Supplementary Table 2).

Associations between childhood FM and weight with T2D

Analyses were based upon 269,913 children aged 10 years, spanning 7,501,643 person-years, with 21,896 T2D diagnoses (13,262 men and 8,634 women) and 261,192 children aged 13 years, spanning 7,920,050 person-years, with 21,530 T2D diagnoses (13,000 men and 8,530 women).

Sex-specific associations, adjusted for childhood height, between childhood FM and weight (per kg increase in exposure) with T2D risk across a range of adult ages, are presented in Tables 3 and 4 for 10- and 13-year olds respectively. At ages 10 and 13 years, FM was more strongly associated with higher adult T2D risk than weight, independent of childhood height (Tables 3&4). The strengths of these associations with adult T2D risk did not appear to vary appreciably between birth-cohort groups, were systematically higher amongst girls than boys at 10 years, but not at 13 years, and diminished with increasing adult age.

Estimates pooled across birth-cohort groups (Tables 3&4, Figure 1) suggested that for children aged 10 years, a 1 kg increase in FM was associated with increased risk of T2D at age 50 of 12% (HR: 1.12 [95%CI 1.10-1.14%]) for boys and 15% (HR:1.15 [95%CI 1.13-1.17%]) for girls. In comparison, a 1 kg increase in weight at 10 years of age was associated with an increased risk of T2D risk at age 50 of 7% for boys (HR: 1.07 [95% CI 1.05-1.09%]) and 10% for girls (HR:1.10 [95% CI 1.08-1.11%]) (Tables 3&4, Figure 1). Pooled estimates of the associations at 13 years of age (Tables 3&4, Figure 1) suggested that a 1 kg increase in childhood FM was associated with an increased risk of T2D at age 50 of 10% (HR:1.10 [95%CI 1.09-1.10%]) for boys and 10% (HR: 1.10 [95%CI 1.10-1.11%]) for girls. In comparison, a 1 kg increase in childhood weight at 13 years of age was associated with an increased risk of T2D at age 50 of 6% for boys (HR:1.06 [95% CI 1.05-1.07%]) and 7% for girls (HR:1.07 [95% CI 1.06-1.08%]) (Tables 3&4, Figure 1).

Unadjusted associations between childhood FM and weight with T2D risk across a range of adult ages, presented in Supplementary Tables 3 and 4 for 10- and 13-year olds respectively, show similar findings to the height-adjusted results with stronger associations between childhood FM and adult T2D risk, than weight.

Height-adjusted associations between childhood FM and weight with T2D risk, per SD increase in the respective adiposity markers, are presented in Supplementary Tables 5 and 6 for 10- and 13-year-olds respectively. As would be expected, due to the SD of FM being approximately half that of weight (Supplementary Table 1), the magnitude of the effect sizes on the SD scale for weight were greater than those of FM, particularly in more recent birth-cohort groups. However, the associated 95% CIs for childhood FM (for boys and girls at both childhood ages) and childhood weight were overlapping (Supplementary Table 1).

Sensitivity analyses, conducted to investigate the influence of elderly onset T2D on the observed FM and weight associations by repeating the Cox regression analyses including censoring at 60 years of age, did not materially affect the results (Supplementary Tables 7&8).

**DISCUSSION**

In this large cohort study, we showed that after adjusting for childhood height, a 1kg increase in childhood FM levels was more strongly associated with adult T2D risk than childhood weight. Furthermore, height-adjusted associations for childhood weight presented per SD increase (where the SD of childhood FM was approximately half that of weight) were stronger than childhood FM, albeit with largely overlapping 95%CIs.

The very large sample size and long period of follow-up allowed for the quantification of associations across a wide range of adult ages with high levels of precision. The quantified associations rely upon the validity of the equations used to estimate childhood FM in this population. Notably, the pooled datasets used to derive the equation contain a wide range of anthropometric characteristics, which remain reasonably consistent with those of the CSHRR cohort. Moreover, the relationship between natural log-transformed FFM (the outcome of the prediction equation) and the predictors is unlikely to have changed over this time period suggesting that our weight-height prediction method works equally well across the ranges of FM in this cohort. Although derived on UK children, the derivation dataset also contained children of other European origins, which strengthens generalisability of the equation to the Danish CSHRR cohort. Furthermore, the diagnoses of adult T2D, as obtained via data linkage with national registries, was not subject to recall bias.

Previous investigations into the association between childhood adiposity and T2D risk have predominantly been based on BMI, rather than on weight or FM and FFM, due to the lack of historic cohorts with information on both childhood body composition and adult T2D diagnoses. Several studies, including earlier analyses based on the present cohort, demonstrated that increases in childhood BMI were associated with elevated T2D risks in adulthood.21-23 However, childhood BMI was not independent of height (both r ~ 0.3) in this cohort suggesting the power of 2 used to standardise weight for height was inadequate. This is problematic as childhood height has been shown previously within this cohort to be independently associated with long-term T2D risk, with shorter stature being associated with an increased risk of adult T2D risk,13 and therefore the residual correlation with height is likely to have inflated estimated associations between childhood BMI and adult T2D risk. Therefore, comparing associations based upon childhood BMI with the associations of FM and weight in this study would not be comparing like with like. The analysis undertaken in this study, quantifying and comparing the height-adjusted associations between childhood FM and adult T2D risk with those of weight, allows us to go back to first principles by focussing on weight itself, which BMI is based upon. Our findings, demonstrating positive associations between childhood weight and T2D risk, are consistent with previous studies, which found positive correlations between childhood weight and risk markers of T2D in adulthood.24-26 These studies found higher childhood weight to be associated with an increase in levels of fasting insulin,24,25 whilst another found an inverse association between childhood weight and attenuated insulin-stimulated glucose utilization in adulthood and a reduction in the ability to metabolise glucose in adulthood.26 Furthermore, studies comparing the associations between adult body weight and T2D to those of adult FM have reported that higher BF levels were more indicative of higher T2D risk than body weight.27,28

**Limitations**

The present study had a number of limitations. Only individuals who were referred to hospital-based clinics are included in the NPR registry and therefore the age-specific T2D incidence is likely to be underestimated in this study. However, the study data are likely to provide a reasonable coverage of the occurrence of T2D in this population. A validation study, which included only 5 years of follow-up, previously estimated the sensitivity of the NPR to be 64% 29 suggesting, 36% of the patients treated by GPs were not identified in the NPR in that study. We find it likely that the completeness in capturing the cases with at least one diagnosis in the NPR would be higher in our study, where the individuals were followed for an average of 28 years for males and 30 years for females. Additionally, previous work based on the CSHRR cohort has demonstrated similar findings when obtaining ascertained T2D cases via linkage to the Danish National Diabetes Register as opposed to the NPR used in this study.21 The prediction equation was derived upon children born later (1985-2010) than those within this cohort (1930-1985), which may have impacted the estimates of childhood FM. While ethnicity information was not available within the CSHRR, the Danish population was predominantly of white ethnic origins at this time and therefore this has an impact on the generalisability of the results to more ethnically diverse populations. Although the results from this study may be more robust in a single ethnic group, further work examining these associations in ethnically diverse populations would be of value in establishing the generalizability of the findings, particularly considering the established ethnic differences in childhood of both FM and emerging T2D risk 30-34. The impact on FM predictions by assuming that children with this missing predictor are of white ethnicity was investigated and shown to be low in the original report.16 Direct measurements or linked information on other established risk factors of T2D in adulthood, such as adult weight and height, diet or physical activity, were not available in this study. However, it is unlikely that the relative strengths of the associations would be altered by adjustment for other T2D risk factors, some of which may in fact be mediators and not confounders.

**Implications**

BMI has a number of limitations as a marker of childhood BF and when used to classify children as overweight or obese. As a weight-based measure, it does not discriminate between FM and FFM, which can vary markedly in individuals with a given BMI. In this study we have demonstrated that when compared on a per kg basis, childhood FM is more strongly associated with T2D risk in adulthood than childhood weight, suggesting that childhood FM, rather than weight, could be a more precise marker of the influence of childhood adiposity on long-term T2D risk. The presentation of effect sizes per kg increase in childhood body composition has been favoured because each of the markers are on the same scale of measurement. While hazard ratios are greater per SD increase in weight compared with FM effects per SD, the SD of weight is almost double that of FM, hence giving rise to a potentially inflated HR for weight. We believe that in this situation, comparisons of effect sizes per kg increase in body composition markers are likely to allow for a fairer and more robust comparison of associations with prospective outcomes. The results presented show childhood FM (rather than FFM) to be the component of weight influencing adult T2D risk and therefore using weight-based measures to assess childhood adiposity fails to focus on this crucial modifiable component of weight. These findings suggest that the assessment of FM could be particularly helpful for the surveillance and monitoring of childhood adiposity in the effort to reduce long-term adverse health outcomes including T2D risk. This could affect the interpretation of childhood adiposity surveillance initiatives, such as the English National Child Measurement Programme and the U.S. National Health and Nutrition Examination Survey, where non-invasive methods for FM assessment could be particularly useful in this context alongside established thresholds for defining adverse childhood FM levels 35-37 which can be used to aid discussions between clinicians, parent/guardian(s) and child. In particular, the prediction equation used in this report could be of particular value as it relies upon information already collected as part of these routine surveillance initiatives and would not require additional measurements to be collected.16 A Microsoft Excel based calculator is available to facilitate the quick and straightforward estimation of FM in clinical and public health practice.

**Figure Legend**

**Figure 1: Adjusted hazard ratios (95%CI) for associations between fat mass and weight (per kilogram increase) at ages 10 and 13 years and risk of type 2 diabetes (T2D) between 30 and 70 years: by sex**

**Conflict of Interests:** The authors declare no conflict of interests

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**Author Contributions:** Study design – MTH, CGO, DGC, TIAS ARR, JLB, PHW, CMN. Data acquisition – The Copenhagen School Health Record Register was initiated and planned by TIAS, and was built by the staff of the former Institute of Preventive Medicine of the Copenhagen Health Services. Data analysis – MTH, JA. Data interpretation – all authors. Drafting manuscript – MTH, CGO, PHW, CMN. Critical evaluation and revision of manuscript – all authors. The corresponding author, MTH, attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. This publication is the work of the authors who will serve as guarantors for the contents of this paper. MTH affirms that the manuscript is an honest, accurate, and transparent account of the study being reported with adherence to the STROBE reporting guidelines for cohort studies; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

**Access to Data statement:** MTH had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis

**REFERENCES**

1. World Health Organisation. Obesity and overweight. 2018; <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>, 2020.

2. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ.* 2000;320(7244):1240-1243.

3. Shaper AG, Wannamethee SG, Walker M. Body weight: implications for the prevention of coronary heart disease, stroke, and diabetes mellitus in a cohort study of middle aged men. *BMJ.* 1997;314(7090):1311-1317.

4. Whitlock G, Lewington S, Sherliker P, et al. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet.* 2009;373(9669):1083-1096.

5. Hall DM, Cole TJ. What use is the BMI? *Arch Dis Child.* 2006;91(4):283-286.

6. Wells JC. A Hattori chart analysis of body mass index in infants and children. *Int J Obes Relat Metab Disord.* 2000;24(3):325-329.

7. Wells JC, Fewtrell MS. Measuring body composition. *Arch Dis Child.* 2006;91(7):612-617.

8. Nightingale CM, Rudnicka AR, Owen CG, Cook DG, Whincup PH. Patterns of body size and adiposity among UK children of South Asian, black African-Caribbean and white European origin: Child Heart And health Study in England (CHASE Study). *International Journal of Epidemiology.* 2011;40(1):33-44.

9. Frontini MG, Bao W, Elkasabany A, Srinivasan SR, Berenson G. Comparison of weight-for-height indices as a measure of adiposity and cardiovascular risk from childhood to young adulthood: the Bogalusa heart study. *J Clin Epidemiol.* 2001;54(8):817-822.

10. Freedman DS, Thornton JC, Mei Z, et al. Height and Adiposity among Children. *Obesity research.* 2004;12(5):846-853.

11. Metcalf BS, Hosking J, Fremeaux AE, Jeffery AN, Voss LD, Wilkin TJ. BMI was right all along: taller children really are fatter (implications of making childhood BMI independent of height) EarlyBird 48. *International journal of obesity (2005).* 2011;35(4):541-547.

12. Lazarus R, Baur L, Webb K, Blyth F. Adiposity and body mass indices in children: Benn's index and other weight for height indices as measures of relative adiposity. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity.* 1996;20(5):406-412.

13. Bjerregaard LG, Jensen BW, Baker JL. Height at Ages 7-13 Years in Relation to Developing Type 2 Diabetes Throughout Adult Life. *Paediatric and perinatal epidemiology.* 2017;31(4):284-292.

14. Steinberger J, Jacobs DR, Raatz S, Moran A, Hong CP, Sinaiko AR. Comparison of body fatness measurements by BMI and skinfolds vs dual energy X-ray absorptiometry and their relation to cardiovascular risk factors in adolescents. *International journal of obesity (2005).* 2005;29(11):1346-1352.

15. Lindsay RS, Hanson RL, Roumain J, Ravussin E, Knowler WC, Tataranni PA. Body mass index as a measure of adiposity in children and adolescents: relationship to adiposity by dual energy x-ray absorptiometry and to cardiovascular risk factors. *J Clin Endocrinol Metab.* 2001;86(9):4061-4067.

16. Hudda MT, Fewtrell MS, Haroun D, et al. Development and validation of a prediction model for fat mass in children and adolescents: meta-analysis using individual participant data. *BMJ.* 2019;366:l4293.

17. Baker JL, Olsen LW, Andersen I, Pearson S, Hansen B, Sorensen T. Cohort profile: the Copenhagen School Health Records Register. *Int J Epidemiol.* 2009;38(3):656-662.

18. Andersen TF, Madsen M, Jorgensen J, Mellemkjoer L, Olsen JH. The Danish National Hospital Register. A valuable source of data for modern health sciences. *Danish medical bulletin.* 1999;46(3):263-268.

19. The Danish Diabetes Association. Facts about diabetes in Denmark. 2018; <https://diabetes.dk/diabetesforeningen/in-english/facts-about-diabetes-in-denmark.aspx>.

20. Hudda MT, Owen CG, Rudnicka AR, Cook DG, Whincup PH, Nightingale CM. Quantifying childhood fat mass: comparison of a novel height-and-weight-based prediction approach with DXA and bioelectrical impedance. *International journal of obesity.* 2020.

21. Zimmermann E, Bjerregaard LG, Gamborg M, Vaag AA, Sorensen TIA, Baker JL. Childhood body mass index and development of type 2 diabetes throughout adult life-A large-scale danish cohort study. *Obesity (Silver Spring).* 2017;25(5):965-971.

22. Lawlor DA, Davey Smith G, Clark H, Leon DA. The associations of birthweight, gestational age and childhood BMI with type 2 diabetes: findings from the Aberdeen Children of the 1950s cohort. *Diabetologia.* 2006;49(11):2614-2617.

23. Petkeviciene J, Klumbiene J, Kriaucioniene V, Raskiliene A, Sakyte E, Ceponiene I. Anthropometric measurements in childhood and prediction of cardiovascular risk factors in adulthood: Kaunas cardiovascular risk cohort study. *BMC public health.* 2015;15(1):218.

24. Sinaiko Alan R, Donahue Richard P, Jacobs David R, Prineas Ronald J. Relation of Weight and Rate of Increase in Weight During Childhood and Adolescence to Body Size, Blood Pressure, Fasting Insulin, and Lipids in Young Adults. *Circulation.* 1999;99(11):1471-1476.

25. Steinberger J, Moran A, Hong C-P, Jacobs DR, Sinaiko AR. Adiposity in childhood predicts obesity and insulin resistance in young adulthood. *The Journal of pediatrics.* 2001;138(4):469-473.

26. Hulman S, Kushner H, Katz S, Falkner B. Can cardiovascular risk be predicted by newborn, childhood, and adolescent body size? An examination of longitudinal data in urban African Americans. *The Journal of pediatrics.* 1998;132(1):90-97.

27. Jo A, Mainous Iii AG. Informational value of percent body fat with body mass index for the risk of abnormal blood glucose: a nationally representative cross-sectional study. *BMJ Open.* 2018;8(4):e019200.

28. Solanki JD, Makwana AH, Mehta HB, Gokhale PA, Shah CJ. Body Composition in Type 2 Diabetes: Change in Quality and not Just Quantity that Matters. *Int J Prev Med.* 2015;6:122-122.

29. Kristensen JK, Drivsholm TB, Carstensen B, Steding-Jensen M, Green A. [Validation of methods to identify known diabetes on the basis of health registers]. *Ugeskrift for laeger.* 2007;169(18):1687-1692.

30. Nightingale CM, Rudnicka AR, Owen CG, et al. Influence of adiposity on insulin resistance and glycemia markers among U.K. Children of South Asian, black African-Caribbean, and white European origin: child heart and health study in England. *Diabetes Care.* 2013;36(6):1712-1719.

31. Whincup PH, Gilg JA, Papacosta O, et al. Early evidence of ethnic differences in cardiovascular risk: cross sectional comparison of British South Asian and white children. *BMJ.* 2002;324(7338):635.

32. Whincup PH, Gilg JA, Owen CG, Odoki K, Alberti KG, Cook DG. British South Asians aged 13-16 years have higher fasting glucose and insulin levels than Europeans. *Diabet Med.* 2005;22(9):1275-1277.

33. Ehtisham S, Crabtree N, Clark P, Shaw N, Barrett T. Ethnic differences in insulin resistance and body composition in United Kingdom adolescents. *J Clin Endocrinol Metab.* 2005;90(7):3963-3969.

34. Klein DJ, Aronson Friedman L, Harlan WR, et al. Obesity and the development of insulin resistance and impaired fasting glucose in black and white adolescent girls: a longitudinal study. *Diabetes Care.* 2004;27(2):378-383.

35. Weber DR, Moore RH, Leonard MB, Zemel BS. Fat and lean BMI reference curves in children and adolescents and their utility in identifying excess adiposity compared with BMI and percentage body fat. *Am J Clin Nutr.* 2013;98(1):49-56.

36. McCarthy HD, Cole TJ, Fry T, Jebb SA, Prentice AM. Body fat reference curves for children. *International journal of obesity.* 2006;30(4):598-602.

37. Wells JC, Williams JE, Chomtho S, et al. Body-composition reference data for simple and reference techniques and a 4-component model: a new UK reference child. *Am J Clin Nutr.* 2012;96(6):1316-1326.

**TABLES**

**Table 1: Mean (SD) of weight, fat mass, fat-free mass and height amongst boys, by adult type 2 diabetes status and birth-cohort group**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **10 Years** | | | | | **13 Years** | | | | | |
|  | **Birth-cohort group** | **N (%)** | **Weight (kg)** | **Fat Mass (kg)** | **Fat-free Mass (kg)** | **Height (m)** | **N (%)** | **Weight (kg)** | **Fat Mass (kg)** | **Fat-free Mass (kg)** | **Height (m)** |
| Those who develop type 2 diabetes | 1930-39 | 4,588 (34.6) | 30.6 (4.2) | 6.7 (1.9) | 23.9 (2.5) | 1.36 (0.06) | 4,410 (33.9) | 41.5 (7.0) | 8.7 (3.2) | 32.8 (4.4) | 1.51 (0.07) |
| 1940-49 | 5,554 (41.9) | 32.3 (4.9) | 7.5 (2.5) | 24.9 (2.8) | 1.38 (0.06) | 5,508 (42.4) | 44.3 (8.0) | 9.7 (3.8) | 34.6 (4.9) | 1.54 (0.08) |
| 1950-59 | 2,317 (17.5) | 33.0 (5.5) | 7.7 (2.9) | 25.2 (2.9) | 1.39 (0.06) | 2,299 (17.7) | 45.7 (8.9) | 10.2 (4.5) | 35.5 (5.2) | 1.55 (0.08) |
| 1960-69 | 684 (5.2) | 34.4 (6.2) | 8.4 (3.3) | 26.1 (3.3) | 1.40 (0.06) | 686 (5.3) | 48.1 (9.6) | 11.1 (4.9) | 37.0 (5.7) | 1.57 (0.09) |
| 1970-85 | 119 (0.9) | 37.5 (9.4) | 10.4 (5.4) | 27.2 (4.3) | 1.41 (0.07) | 97 (0.7) | 52.8 (13.2) | 13.8 (7.0) | 39.0 (7.3) | 1.58 (0.09) |
| *Overall* | *13,262 (100)* | *32.0 (5.1)* | *7.3 (2.5)* | *24.7 (2.8)* | *1.38 (0.06)* | *13,000 (100)* | *43.8 (8.3)* | *9.6 (3.9)* | *34.3 (5.0)* | *1.53 (0.08)* |
| Those who do not develop type 2 diabetes | 1930-39 | 25,329 (20.1) | 30.4 (3.9) | 6.6 (1.8) | 23.8 (2.4) | 1.36 (0.06) | 24,345 (20.6) | 40.7 (6.4) | 8.2 (2.8) | 32.4 (4.2) | 1.51 (0.07) |
| 1940-49 | 38,265 (31.2) | 31.8 (4.5) | 7.1 (2.2) | 24.7 (2.6) | 1.38 (0.06) | 38,040 (32.2) | 42.8 (7.2) | 8.8 (3.2) | 34.0 (4.7) | 1.53 (0.07) |
| 1950-59 | 26,826 (21.9) | 31.9 (4.8) | 7.0 (2.4) | 24.9 (2.8) | 1.39 (0.06) | 26,636 (22.6) | 42.9 (7.8) | 8.6 (3.5) | 34.3 (5.0) | 1.54 (0.08) |
| 1960-69 | 18,683 (15.2) | 32.4 (5.0) | 7.2 (2.5) | 25.3 (2.9) | 1.40 (0.06) | 18,618 (15.8) | 44.2 (8.1) | 8.9 (3.7) | 35.3 (5.2) | 1.56 (0.08) |
| 1970-85 | 13,575 (11.1) | 33.9 (6.1) | 8.0 (3.3) | 25.9 (3.2) | 1.40 (0.06) | 10,386 (8.8) | 47.1 (10.1) | 10.3 (5.0) | 36.8 (6.0) | 1.57 (0.08) |
| *Overall* | *122,678 (100)* | *31.8 (4.8)* | *7.1 (2.4)* | *24.8 (2.8)* | *1.38 (0.06)* | *118,025 (100)* | *43.0 (7.8)* | *8.8 (3.5)* | *34.2 (5.0)* | *1.54 (0.08)* |

**Table 2: Mean (SD) of weight, fat mass, fat-free mass and height amongst girls, by adult type 2 diabetes status and birth-cohort group**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **10 Years** | | | | | **13 Years** | | | | | |
|  | **Birth-cohort group** | **N (%)** | **Weight (kg)** | **Fat Mass (kg)** | **Fat-free Mass (kg)** | **Height (m)** | **N (%)** | **Weight (kg)** | **Fat Mass (kg)** | **Fat-free Mass (kg)** | **Height (m)** |
| Those who develop type 2 diabetes | 1930-39 | 3,223 (37.3) | 30.5 (4.8) | 8.0 (2.5) | 22.5 (2.6) | 1.35 (0.06) | 3,177 (37.2) | 44.2 (7.7) | 11.7 (4.1) | 32.6 (4.3) | 1.52 (0.07) |
| 1940-49 | 3,375 (39.1) | 32.4 (5.6) | 8.9 (3.0) | 23.5 (2.8) | 1.37 (0.06) | 3,358 (39.4) | 46.8 (8.6) | 12.7 (4.8) | 34.1 (4.5) | 1.55 (0.07) |
| 1950-59 | 1,440 (16.7) | 33.0 (6.2) | 9.1 (3.4) | 23.9 (3.1) | 1.38 (0.06) | 1,434 (16.8) | 48.1 (9.4) | 13.2 (5.4) | 34.9 (4.7) | 1.56 (0.07) |
| 1960-69 | 492 (5.7) | 35.1 (7.3) | 10.3 (4.3) | 24.9 (3.3) | 1.39 (0.06) | 496 (5.8) | 51.3 (10.8) | 14.9 (6.4) | 36.4 (5.2) | 1.58 (0.07) |
| 1970-85 | 104 (1.2) | 38.8 (9.4) | 12.6 (5.5) | 26.2 (4.3) | 1.40 (0.08) | 65 (0.8) | 55.6 (13.7) | 18.2 (8.1) | 37.4 (6.3) | 1.56 (0.08) |
| *Overall* | *8,634 (100)* | *32.0 (5.8)* | *8.7 (3.1)* | *23.3 (2.9)* | *1.37 (0.06)* | *8,530 (100)* | *46.4 (8.9)* | *12.5 (4.9)* | *33.8 (4.7)* | *1.54 (0.07)* |
| Those who do not develop type 2 diabetes | 1930-39 | 25,963 (20.7) | 30.1 (4.3) | 7.7 (2.2) | 22.4 (2.4) | 1.35 (0.06) | 25,893 (21.3) | 43.1 (7.1) | 10.9 (3.6) | 32.2 (4.1) | 1.52 (0.07) |
| 1940-49 | 40,008 (31.9) | 31.4 (4.9) | 8.2 (2.5) | 23.2 (2.6) | 1.37 (0.06) | 39,831 (32.7) | 44.7 (7.5) | 11.2 (3.9) | 33.5 (4.3) | 1.55 (0.07) |
| 1950-59 | 27,055 (21.6) | 31.6 (5.2) | 8.2 (2.7) | 23.4 (2.8) | 1.38 (0.06) | 26,987 (22.2) | 45.1 (7.9) | 11.1 (4.2) | 34.0 (4.4) | 1.56 (0.07) |
| 1960-69 | 18,800 (15.0) | 32.1 (5.4) | 8.3 (2.8) | 23.8 (2.9) | 1.39 (0.06) | 18,771 (15.4) | 46.1 (8.3) | 11.4 (4.4) | 34.7 (4.6) | 1.57 (0.07) |
| 1970-85 | 13,513 (10.8) | 33.8 (6.6) | 9.2 (3.6) | 24.6 (3.3) | 1.40 (0.07) | 10,155 (8.3) | 48.8 (9.8) | 12.9 (5.5) | 35.9 (5.1) | 1.58 (0.07) |
| *Overall* | *125,339 (100)* | *31.5 (5.2)* | *8.2 (2.7)* | *23.3 (2.8)* | *1.37 (0.06)* | *121,637 (100)* | *45.0 (8.0)* | *11.3 (4.2)* | *33.7 (4.5)* | *1.55 (0.07)* |

**Table 3:** **Adjusted hazard ratios (95%CI) for associations between fat mass and weight (per kilogram increase) at age 10 years and risk of type 2 diabetes between 30 and 70 years, by sex, birth-cohort group and overall**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Birth-cohort group (N, cases)** | | | | |  |
| **Adult Age (years)** | **Adiposity marker** | **1930-39**  **(29917, 4588)** | **1940-49**  **(43819, 5554)** | **1950-59**  **(29143, 2317)** | **1960-69**  **(19367, 684)** | **1970-85**  **(13694, 119)** | ***Pooled*** |
| **Boys** | |  |  |  |  |  |  |
| 30 | Fat Mass | 1.13 (1.08 - 1.20) | 1.19 (1.15 - 1.23) | 1.20 (1.15 - 1.24) | 1.21 (1.15 - 1.28) | 1.20 (1.13 - 1.27) | 1.19 (1.16 - 1.21) |
|  | Weight | 1.06 (1.03 - 1.09) | 1.10 (1.08 - 1.12) | 1.11 (1.09 - 1.14) | 1.13 (1.10 - 1.17) | 1.14 (1.09 - 1.18) | 1.11 (1.08 - 1.13) |
| 40 | Fat Mass | 1.11 (1.07 - 1.15) | 1.15 (1.13 - 1.18) | 1.16 (1.14 - 1.19) | 1.17 (1.14 - 1.20) | 1.19 (1.14 - 1.24) | 1.16 (1.14 - 1.18) |
|  | Weight | 1.05 (1.03 - 1.07) | 1.09 (1.07 - 1.10) | 1.10 (1.08 - 1.12) | 1.11 (1.10 - 1.13) | 1.13 (1.10 - 1.17) | 1.10 (1.07 - 1.12) |
| 50 | Fat Mass | 1.09 (1.06 - 1.12) | 1.12 (1.10 - 1.13) | 1.13 (1.12 - 1.15) | 1.14 (1.10 - 1.17) |  | 1.12 (1.10 - 1.14) |
|  | Weight | 1.04 (1.03 - 1.06) | 1.07 (1.06 - 1.08) | 1.09 (1.08 - 1.10) | 1.09 (1.07 - 1.12) |  | 1.07 (1.05 - 1.09) |
| 60 | Fat Mass | 1.06 (1.04 - 1.08) | 1.08 (1.07 - 1.10) | 1.10 (1.08 - 1.13) |  |  | 1.08 (1.06 - 1.10) |
|  | Weight | 1.04 (1.02 - 1.05) | 1.06 (1.05 - 1.06) | 1.07 (1.06 - 1.09) |  |  | 1.05 (1.04 - 1.07) |
| 70 | Fat Mass | 1.04 (1.02 - 1.06) | 1.05 (1.03 - 1.07) |  |  |  | 1.04 (1.03 - 1.06) |
|  | Weight | 1.03 (1.02 - 1.04) | 1.04 (1.03 - 1.05) |  |  |  | 1.03 (1.02 - 1.05) |
|  |  |  |  |  |  |  |  |
| **Girls** | | **1930-39**  **(29186, 3223)** | **1940-49**  **(43383, 3375)** | **1950-59**  **(28495, 1440)** | **1960-69**  **(19292, 492)** | **1970-85**  **(13617, 104)** | ***Pooled*** |
| 30 | Fat Mass | 1.20 (1.14 - 1.27) | 1.19 (1.15 - 1.23) | 1.20 (1.15 - 1.25) | 1.24 (1.18 - 1.30) | 1.29 (1.22 - 1.37) | 1.22 (1.18 - 1.25) |
|  | Weight | 1.10 (1.07 - 1.14) | 1.11 (1.09 - 1.13) | 1.13 (1.10 - 1.16) | 1.16 (1.12 - 1.19) | 1.20 (1.15 - 1.25) | 1.14 (1.11 - 1.16) |
| 40 | Fat Mass | 1.17 (1.12 - 1.21) | 1.16 (1.14 - 1.19) | 1.17 (1.14 - 1.20) | 1.22 (1.19 - 1.25) | 1.28 (1.22 - 1.35) | 1.19 (1.16 - 1.23) |
|  | Weight | 1.09 (1.06 - 1.11) | 1.10 (1.08 - 1.12) | 1.11 (1.09 - 1.13) | 1.14 (1.12 - 1.17) | 1.20 (1.15 - 1.24) | 1.12 (1.10 - 1.15) |
| 50 | Fat Mass | 1.13 (1.10 - 1.16) | 1.14 (1.12 - 1.16) | 1.14 (1.12 - 1.16) | 1.19 (1.15 - 1.23) |  | 1.15 (1.13 - 1.17) |
|  | Weight | 1.07 (1.06 - 1.09) | 1.09 (1.08 - 1.10) | 1.10 (1.08 - 1.11) | 1.13 (1.11 - 1.16) |  | 1.10 (1.08 - 1.11) |
| 60 | Fat Mass | 1.10 (1.08 - 1.12) | 1.12 (1.10 - 1.13) | 1.11 (1.09 - 1.14) |  |  | 1.11 (1.10 - 1.12) |
|  | Weight | 1.06 (1.05 - 1.07) | 1.08 (1.07 - 1.09) | 1.08 (1.06 - 1.10) |  |  | 1.07 (1.06 - 1.08) |
| 70 | Fat Mass | 1.07 (1.05 - 1.09) | 1.09 (1.07 - 1.12) |  |  |  | 1.08 (1.05 - 1.11) |
|  | Weight | 1.05 (1.03 - 1.06) | 1.07 (1.06 - 1.08) |  |  |  | 1.06 (1.04 - 1.08) |

FOOTNOTE: Hazard Ratios + 95% CIs estimated from Cox proportional hazards models fitted within each of the five birth-cohort groups, adjusting for childhood height at age 10 years. The resulting estimates were averaged using a random-effects meta-analysis approach to provide an overall estimate of the effect of fat mass and weight on type 2 diabetes risk in adulthood. Birth-cohort groups from 1950-59, 1960-69 and 1970-85 contain some empty cells as individuals within these groups were not yet old enough to provide estimates, without extrapolation, at these adult ages.

**Table 4:** **Adjusted hazard ratios (95%CI) for associations between fat mass and weight (per kilogram increase) at age 13 years and risk of type 2 diabetes between 30 and 70 years, by sex, birth-cohort group and overall**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Birth-cohort group (N, cases)** | | | | |  |
| **Adult Age (years)** | **Adiposity marker** | **1930-39**  **(28755, 4410)** | **1940-49**  **(43548, 5508)** | **1950-59**  **(28935, 2299)** | **1960-69**  **(19304, 686)** | **1970-85**  **(10483, 97)** | ***Pooled*** |
| **Boys** | |  |  |  |  |  |  |
| 30 | Fat Mass | 1.13 (1.10 - 1.17) | 1.13 (1.11 - 1.16) | 1.14 (1.12 - 1.17) | 1.14 (1.10 - 1.18) | 1.09 (1.04 - 1.14) | 1.13 (1.12 - 1.15) |
|  | Weight | 1.06 (1.05 - 1.08) | 1.08 (1.06 - 1.09) | 1.08 (1.07 - 1.10) | 1.09 (1.07 - 1.11) | 1.07 (1.04 - 1.10) | 1.08 (1.07 - 1.08) |
| 40 | Fat Mass | 1.11 (1.09 - 1.14) | 1.11 (1.10 - 1.13) | 1.12 (1.11 - 1.14) | 1.12 (1.10 - 1.14) | 1.13 (1.09 - 1.16) | 1.12 (1.11 - 1.13) |
|  | Weight | 1.06 (1.04 - 1.07) | 1.07 (1.06 - 1.08) | 1.07 (1.06 - 1.08) | 1.08 (1.07 - 1.09) | 1.08 (1.06 - 1.11) | 1.07 (1.06 - 1.08) |
| 50 | Fat Mass | 1.09 (1.08 - 1.11) | 1.09 (1.08 - 1.10) | 1.10 (1.09 - 1.11) | 1.11 (1.08 - 1.13) |  | 1.10 (1.09 - 1.10) |
|  | Weight | 1.05 (1.04 - 1.06) | 1.06 (1.05 - 1.06) | 1.07 (1.06 - 1.07) | 1.07 (1.06 - 1.09) |  | 1.06 (1.05 - 1.07) |
| 60 | Fat Mass | 1.07 (1.06 - 1.08) | 1.07 (1.07 - 1.08) | 1.08 (1.07 - 1.10) |  |  | 1.08 (1.07 - 1.08) |
|  | Weight | 1.05 (1.04 - 1.05) | 1.05 (1.05 - 1.06) | 1.06 (1.05 - 1.07) |  |  | 1.05 (1.04 - 1.06) |
| 70 | Fat Mass | 1.05 (1.04 - 1.07) | 1.06 (1.04 - 1.07) |  |  |  | 1.06 (1.05 - 1.06) |
|  | Weight | 1.04 (1.03 - 1.05) | 1.04 (1.04 - 1.05) |  |  |  | 1.04 (1.04 - 1.05) |
|  |  |  |  |  |  |  |  |
| **Girls** | | **1930-39**  **(29070, 3177)** | **1940-49**  **(43189, 3358)** | **1950-59**  **(28421, 1434)** | **1960-69**  **(19267, 496)** | **1970-85**  **(10220, 65)** | ***Pooled*** |
| 30 | Fat Mass | 1.16 (1.12 - 1.19) | 1.11 (1.09 - 1.14) | 1.15 (1.12 - 1.18) | 1.17 (1.14 - 1.20) | 1.13 (1.07 - 1.19) | 1.14 (1.12 - 1.17) |
|  | Weight | 1.08 (1.06 - 1.10) | 1.07 (1.06 - 1.08) | 1.10 (1.08 - 1.11) | 1.11 (1.09 - 1.13) | 1.09 (1.06 - 1.13) | 1.09 (1.07 - 1.10) |
| 40 | Fat Mass | 1.13 (1.11 - 1.16) | 1.11 (1.09 - 1.12) | 1.13 (1.11 - 1.15) | 1.14 (1.12 - 1.16) | 1.17 (1.13 - 1.21) | 1.13 (1.11 - 1.15) |
|  | Weight | 1.07 (1.06 - 1.09) | 1.07 (1.06 - 1.08) | 1.08 (1.07 - 1.09) | 1.10 (1.08 - 1.11) | 1.11 (1.09 - 1.14) | 1.08 (1.07 - 1.10) |
| 50 | Fat Mass | 1.11 (1.09 - 1.13) | 1.10 (1.09 - 1.11) | 1.11 (1.09 - 1.12) | 1.11 (1.09 - 1.13) |  | 1.10 (1.10 - 1.11) |
|  | Weight | 1.06 (1.05 - 1.07) | 1.06 (1.06 - 1.07) | 1.07 (1.06 - 1.08) | 1.08 (1.07 - 1.09) |  | 1.07 (1.06 - 1.08) |
| 60 | Fat Mass | 1.08 (1.07 - 1.10) | 1.09 (1.08 - 1.10) | 1.08 (1.07 - 1.10) |  |  | 1.09 (1.08 - 1.09) |
|  | Weight | 1.05 (1.05 - 1.06) | 1.06 (1.05 - 1.07) | 1.06 (1.05 - 1.07) |  |  | 1.06 (1.05 - 1.06) |
| 70 | Fat Mass | 1.06 (1.05 - 1.07) | 1.08 (1.07 - 1.09) |  |  |  | 1.07 (1.05 - 1.09) |
|  | Weight | 1.04 (1.04 - 1.05) | 1.06 (1.05 - 1.06) |  |  |  | 1.05 (1.04 - 1.06) |

FOOTNOTE: Hazard Ratios + 95% CIs estimated from Cox proportional hazards models fitted within each of the five birth-cohort groups, adjusting for childhood height at age 13 years. The resulting estimates were averaged using a random-effects meta-analysis approach to provide an overall estimate of the effect of fat mass and weight on type 2 diabetes risk in adulthood. Birth-cohort groups from 1950-59, 1960-69 and 1970-85 contain some empty cells as individuals within these groups were not yet old enough to provide estimates, without extrapolation, at these adult age

**Figure 1: Adjusted hazard ratios (95%CI) for associations between fat mass and weight (per kilogram increase) at ages 10 and 13 years and risk of type 2 diabetes between 30 and 70 years: by sex**



FOOTNOTE: Hazard Ratios + 95% CIs estimated from Cox proportional hazards models fitted within each of the five birth cohort groups, adjusting for childhood height. The resulting estimates were averaged using a random-effects meta-analysis approach to provide an overall estimate of the effect of fat mass and weight on type 2 diabetes risk in adulthood. Hazard ratios on the y-axis presented on the natural logarithmic scale. All estimates presented were highly statistically significant with p-values < 0.001. Hazard Ratios + 95% CIs presented can be found in Tables 3 & 4.