# Possible modifiers of the association between change in weight status from child through adult ages and later risk of type 2 diabetes

Running title: BMI changes and type 2 diabetes meta-analysis

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ABSTRACT

Objective: We investigated the association between changes in weight status from childhood through adulthood and subsequent type 2 diabetes risks and whether educational attainment, smoking and leisure time physical activity (LTPA) modify this association.

Research design and methods: Using data from 10 Danish and Finnish cohorts including 25,283 individuals, childhood body mass index (BMI) at 7 and 12 years was categorised as normal or high using age- and sex-specific cut-offs (</≥85$^{th}$ percentile). Adult BMI (20-71 years) was categorised as non-obese or obese (</≥30.0 kg/m$^2$). Associations between BMI patterns and type 2 diabetes (989 women; 1370 men) were analysed using Cox proportional hazard regressions and meta-analysis techniques.

Results: Compared with individuals with a normal BMI at 7 years and without adult obesity, those with a high BMI at 7 years and adult obesity had higher type 2 diabetes risks (hazard ratio [HR]$_{girls}$: 5.04, 95%Confidence Interval [CI] 3.92-6.48; HR$_{boys}$: 3.78, 95%CI 2.68-5.33). Individuals with a high BMI at 7 years but without adult obesity did not have a higher risk (HR$_{girls}$: 0.74, 95%CI 0.52-1.06; HR$_{boys}$: 0.93, 95%CI 0.65-1.33). Education, smoking and LTPA were associated with diabetes risks, but did not modify or confound the associations with BMI changes. Results for age 12 years were similar.

Conclusions: A high BMI in childhood was associated with higher type 2 diabetes risks only if individuals also had obesity in adulthood. These associations were not influenced by educational and lifestyle factors, indicating that BMI is similarly related to the risk across all levels of these factors.

Even though child and adult body mass index (BMI; kg/m$^2$) are positively associated with the risk of developing type 2 diabetes, the effects of changes in weight status between childhood and adulthood are not well-understood. Previous studies indicate that children with overweight who remit from it before adulthood may reduce their risk of type 2 diabetes (1-6). Further, some studies find being persistently overweight from childhood to adulthood carries higher risk of type 2 diabetes than being overweight only in adulthood (1, 2, 4).

The development of childhood obesity has a strong social gradient (7) and in adult life, inverse associations between socioeconomic status and educational attainment and risks of obesity and type 2 diabetes are well-established (8, 9). It may be hypothesized that individuals of low socioeconomic status are more vulnerable to health risks associated with overweight. Yet, there is sparse evidence in this research area (10-12). Only one of the previous studies focusing on changes in weight status and type 2 diabetes evaluated a potential multiplicative interaction with educational attainment on these associations (4). Moreover, previous studies are limited by either including only one sex (1, 4, 5), having a low number of diabetes cases ($n<237$) (2, 3, 6), or ending follow-up in middle adulthood (3, 6). Further, smoking and lower levels of leisure time physical activity (LTPA) are associated with higher risks of developing type 2 diabetes (13, 14), but these were not investigated as modifying factors in the studies on changes in weight status and type 2 diabetes.

The aim of this study was to investigate the association between changes in weight status from childhood to adulthood and the risk of developing type 2 diabetes in Danish and Finnish cohorts and whether this association is modified by socioeconomic and lifestyle factors. It was hypothesized that high BMI at child and adult ages has stronger associations with type 2 diabetes among individuals with short educational attainment, smoking, and individuals with low levels of LTPA.

## RESEARCH DESIGN AND METHODS

### Study population

The study population was drawn from cohorts participating in the DynaHEALTH consortium that aims to build an empirical model of healthy ageing (15). To be eligible for this study, we required information on weight and height at ages 7 and 12 years and in adulthood (>18 years), as well as information on educational attainment, smoking and LTPA (Supplementary Table S1). Among the cohorts included in the DynaHEALTH consortium, 10 cohorts were eligible. Eight were subsamples of adult research studies (16-22) among whom the participants who were born from 1930 to 1981 were included in a Danish school cohort from Copenhagen (23) (N=19,717, Table S1). Additionally, the Northern Finland Birth Cohort 1966 (NFBC1966) was included. It includes individuals born in the two northernmost provinces of Finland in 1966 who participated in a clinical examination in adulthood (N=3985 included) (24-26). And finally, the Helsinki Birth Cohort Study (HBCS) contributed with individuals who were born between 1934 and 1944 at the Helsinki University Central Hospital, attended child welfare clinics in the city, went to school in the city of Helsinki and attended a clinical examination in adulthood (N=1581 included) (27). The cohorts are described in detail elsewhere (16-24, 27).

All studies were performed in accordance with the Helsinki 2 Declaration. The project was conducted on anonymous data, and it was approved by the Danish Data Protection Agency (Datatilsynet).

### Assessment of variables

Body height and weight were used for calculation of BMI ([weight (kg)]/[height $(m)^2$]) and were prospectively measured at school health examinations and recorded in health records. In the Danish cohorts, BMI at the exact ages of 7 and 12 years were obtained by interpolation between successive measurements around that age or by extrapolation always within ±12

months (28). In the Finnish cohorts, BMI from age ≥6.0 to <8 years and from ages ≥11.0 to <13 years was included as 7-year or 12-year measurements, respectively (29). In adulthood, weight and height were measured at clinical examinations in seven cohorts (18-22, 24) and self-reported in three cohorts (16, 17, 27). If individuals participated in more than one examination, we preferentially chose the one at the youngest adult age.

High BMI in childhood was defined as ≥85$^{th}$ BMI percentile at 7 or 12 years based on sex- and age-specific BMI percentiles for the Copenhagen cohorts, the NFBC1966 and HBCS, respectively (Table S2). Obesity in adulthood was defined in accordance with the World Health Organization criteria (BMI ≥30 kg/m$^2$) (30). Patterns of high BMI were defined as combinations of high BMI in childhood at 7 or 12 years and obesity in adulthood. Moreover, a BMI pattern with eight categories was defined according to combinations of high BMIs at 7 years (yes/no) and/or 12 years (yes/no) and/or adult obesity (yes/no).

At the time of the adult BMI assessment, information on educational attainment, current smoking (yes/no), and LTPA was obtained by questionnaire. Educational attainment was categorised into 0-7 (short), 8-10 (medium), or >10 (long) years of schooling. One cohort used categorizations of 7-9, 10, and >10 years, due to the definition in the questionnaire (17). The available information in each cohort consisted of either three to six levels of LTPA or energy expenditure, and it was categorized into three groups corresponding to low: <2 hours/week, medium: light physical activity 2-4 hours/week and high: light physical activity ≥4 hours/week or moderate activity ≥2 hours/week (HBCS: <2 times/week, 2-4 times/week, ≥4 times/week).

Assessment of type 2 diabetes

Information on type 2 diabetes was obtained by linking unique personal identification numbers (27, 31) of the cohort participants to computerized and comprehensive health registers. During

the follow-up period, <0.6% of the individuals emigrated, and they were censored on this date and no individuals were untraceable. Thus, loss to follow-up was minimal.

In the Danish cohorts, information on inpatient and outpatient diagnoses of type 2 diabetes (International Classification of Diseases [ICD] 8th revision code 250 and ICD-10 codes E11, E13, and E14) was obtained by linkage to the National Patient Register (NPR) (32) as previously described (4). In this register, whereas the completeness is moderate (sensitivity 64%), the positive predictive value of a diabetes diagnosis is very high (97%) when assessed against information from and verification of the diagnosis by general practitioners(33). In the NFBC1966 and the HBCS, in addition to hospital and prescription registers (34), clinical examination values (subsequent to obtaining the adult BMI) of plasma glucose≥7mmol/l and 2-hour plasma glucose≥11.1 mmol/l in a 2-hr 75 g oral glucose tolerance test were used to identify type 2 diabetes using WHO criteria (35). Furthermore, in the HBCS, HbA1c ≥6.5% or 48 mmol/mol was used to identify type 2 diabetes. Through the combination of these methods the sensitivity is likely very high, although a few individuals with type 2 diabetes may not be identified if they missed the clinical examination and were treated only with diet in general practice (36).

To achieve a baseline population free from diabetes, only individuals without type 2 diabetes at the adult BMI assessment were followed prospectively in registers from the age at the adult BMI measure – or from age 30 years for Danish individuals (4), whichever came last. As such, 266 individuals with type 2 diabetes were not included in this study from the Danish data, 172 from the HBCS and 8 from the NFBC1966. The follow-up ended at the date of a type 2 diabetes diagnosis, death, emigration, loss to follow-up, or at the end of the follow-up period, which was December 31, 2013 for the HBCS, and December 31, 2016 for the NFBC1966 and the Danish cohorts, whichever came first. Hence, the adult BMI measurement was collected

before information on type 2 diabetes to avoid potential reverse causality from effects of type 2 diabetes on weight gain or loss.

Statistical Methods

Associations between high BMI at each age or patterns of high BMI and adult type 2 diabetes were estimated with hazard ratios (HR) and 95% confidence intervals (CIs) using Cox proportional hazards regression. Age was used as the time scale, implying delayed entry at the time of BMI assessment, and stratified by year of birth. Specifically, researchers responsible for each cohort estimated the stratum-specific regression coefficients (SSRCs) and the corresponding standard errors by sex and these were pooled using random-effects meta-analyses techniques. As major differences between women and men exist in the prevalence, pathophysiology, treatment response, and outcome of type 2 diabetes (37), women and men were analysed separately.

The analyses were adjusted for age at adult BMI and additionally for educational attainment, smoking and LTPA. Potential heterogeneity in the associations in sub-groups of the following potential effect modifiers: sex, educational attainment, smoking, LTPA, birth cohort (1930-39, 1940-49 and 1950-89) and study was investigated using the $I^2$ statistic, the Cochran's Q test and meta-regression. To assess the proportional hazards assumption, we tested heterogeneity by categories of age-at-diagnosis divided into <70 and ≥70 years as graphs of the cumulative hazard from one weight category versus another showed that the slope changed at around this age (not shown). To assess the impact of self-reported BMI and reverse causality, we performed sensitivity analyses omitting the three cohorts in which BMI was self-reported and by omitting the first 3 years of follow-up after the adult BMI measure.

Additionally, we performed an analysis of adult BMI adjusted for child BMI and summarised the results in a meta-analysis. An investigation of non-linearity by modelling the

mutually adjusted associations using cubic splines with 7 knot points showed changes in the slope of the associations at approximately the 90th percentile for child BMIs and at 30 kg/m$^2$ for adult BMI. Therefore, the associations were estimated using a linear spline regression with knot points inserted at the sex and region specific 90th percentile for child BMIs and at 30 kg/m$^2$ for adult BMI. Hazard ratios for specific linear combinations of child and adult BMI are reported. All statistical analyses were performed using Stata (version 14.2; StataCorp, College Station, TX).

## RESULTS

Among the 12,277 women and 13,006 men included in the study, 989 women (8.1%) and 1370 men (10.5%), respectively, were diagnosed with type 2 diabetes from 1978 through 2016. The ages at diagnosis ranged from 30-85 years over an average follow-up time of 18.8 years (475,056 total person-years). We found similar associations between the BMI patterns and risk of type 2 diabetes in women and men, and these were not different in the meta-regression analyses ($p>0.33$; data not shown).

Smokers, individuals with long education or high levels of LTPA were more often in the groups who never had a high BMI or had a high BMI only as a child (Table 1 and Supplementary Table S3). Among women and men, high child BMI and adult obesity were each positively associated with risks of type 2 diabetes (Table 2). As expected, men and smokers had higher risks of type 2 diabetes and educational attainment and LTPA were inversely associated with risks of type 2 diabetes (Table 2).

Figure 1 shows the association between the BMI pattern and type 2 diabetes by levels of the potential effect modifiers. At higher educational levels in women and men, there was a tendency for the HR for persistently high BMI from age 7 years to adulthood or only high adult BMI and type 2 diabetes to be higher than those for women and men who never had a high

BMI (Figure 1, Panels A & B). These tendencies, however, were generally not supported by the subgroup meta-analysis and the meta-regression analyses (Supplementary Table S4). In women, smoking minimally influenced the associations between BMI patterns and type 2 diabetes (Figure 1, Panel C). Non-smoking men who only had a high BMI in childhood had a lower risk of type 2 diabetes than non-smoking men who never had a high BMI, but associations in men with persistently high BMI or high adult BMI were positive in both smokers and non-smokers (Figure 1, Panel D and Supplementary Table S4). In women and men, the associations between BMI patterns and type 2 diabetes remained similar across levels of LTPA in the sub-group analyses and the meta-regression (Figure 1, Panels E & F and Supplementary Table S4).

Women and men who had a high BMI only as a child had a similar risk of type 2 diabetes to that among women and men who never had a high BMI (women: HR: 0.74, 95% CI 0.52-1.06; men: HR: 0.93, 95% CI 0.65-1.33; Figure 2). Women and men with a persistently high BMI or a high BMI only as an adult had higher risks of type 2 diabetes compared with women and men who never had a high BMI (HR range: 3.78 to 5.27; Figure 2). Notably, adjustment for educational attainment, smoking and LTPA minimally changed the estimates and the confidence intervals. In women, the $I^2$ ranged from 0 to 41% indicating low to moderate heterogeneity across cohorts. Among men, the $I^2$ ranged from 26.9 to 53.2% (Supplementary Appendix 1). Similar results were observed for weight status at age 12 years combined with adulthood (Supplementary Figure S1).

In sub-group analyses investigating the effects of diabetes diagnosed at <70 years, we observed stronger associations for persistently high BMI and high adult BMI with type 2 diabetes diagnosed at <70 years than after this age (Supplementary Figure S2). However, the confidence intervals for diagnoses after 70 years were wide and the overall conclusions were the same. In analyses investigating potential birth cohort effects, associations between high

BMIs and type 2 diabetes were stronger in later birth cohorts, but the patterns of associations were the same in all birth cohorts (Supplementary Figure S3). Omission of the two cohorts with self-reported weight and height or restriction of follow-up time to from 3 years after the BMI assessment and onwards minimally changed the results (Supplementary Figures S4 & S5).

Women who had a high BMI at 7 years and did not have obesity as an adult, irrespective of their childhood BMI status at 12 years, had a similar risk of type 2 diabetes as women who never had a high BMI at ages 7, 12 and in adulthood (Supplementary Figure S6). In contrast, women who had a high BMI at age 12 but not at 7 and who did not have obesity in adulthood had a higher risk of type 2 diabetes (HR: 1.55, 95% CI 1.12-2.13). Women who were obese as adults had a higher risk of type 2 diabetes irrespective of their childhood BMI status. Although most results were similar for men, there was an exception. Men who had a high BMI at 12 years but not at 7 years and who did not have obesity in adulthood had a similar risk of type 2 diabetes as men who never had a high BMI. Adjustment for educational attainment, smoking and LTPA minimally changed the results (Supplementary Figure S6).

The regression coefficients for childhood and adult BMI from the linear spline model generally were similar across levels of education, smoking and LTPA in the meta-analysis (Supplementary Table S5). Based upon these results, the point estimate for children who had a BMI at the 95$^{th}$ percentile at 7 years and an adult BMI of 30 kg/m$^2$ (corresponding approximately to the 86$^{th}$ percentile) showed they had a 5-fold risk of type 2 diabetes compared with children who had a stable BMI at the 50$^{th}$ percentile at 7 years and an adult BMI of 22 kg/m$^2$ (Supplementary Table S6). If a child with a BMI at the 95$^{th}$ percentile moved towards lower percentiles and had an adult BMI of 25 kg/m$^2$ (corresponding to the 50$^{th}$ percentile), the risk was much lower although still above that of the reference group. The highest risk was observed among individuals who started at the 25$^{th}$ BMI percentile in childhood and ended at

a BMI of 35 kg/m$^2$, i.e. individuals who increased their degree of adiposity the most (Supplementary Table S6). Adjustment for educational attainment, smoking and LTPA minimally changed the results (Supplementary Table S6).

## CONCLUSIONS

This study showed that in 10 Danish and Finnish cohorts associations between BMI patterns and risk of type 2 diabetes were virtually not confounded or modified by educational attainment, smoking in women and LTPA. Apart from smoking which influenced one of the associations in men, the results were similar for men and women. This study confirmed that a high BMI in childhood combined with obesity in adulthood is associated with higher risks of type 2 diabetes, whereas a high childhood BMI combined with non-obesity in adulthood is not.

Individuals who developed obesity in adulthood had about the same risk of having type 2 diabetes as those who had a high BMI in childhood and obesity in adulthood. We also found that the BMI trajectory associated with the highest risk was the one that started at the 25$^{th}$ BMI percentile in childhood and ended at an adult BMI of 35 kg/m$^2$; in other words, among individuals who increased the most in adiposity. These findings are supported by a large women-only study (38) that reported that those who were lean at 8 years and who had a sharp increase in self-reported body shape at puberty and thereafter had an almost 3-fold higher risk of developing type 2 diabetes compared with women whose body shape stayed in the mid-range. This risk tended to be even higher compared with always having a large body shape (38).

Conversely, a decrease in BMI percentile from childhood to adulthood was associated with a lower, although still increased, risk of type 2 diabetes. This finding corresponds those from a British study in which remission of obesity between childhood (7 to 16 years of age) and adulthood (23 to 45 years of age) was associated with a higher risk of type 2 diabetes

compared with individuals who had never been obese (6). Other studies show that remission of overweight at 8 years (5) and obesity between 4 to 19 years of age (3) and adulthood, is not associated with a difference in the risk of type 2 diabetes. Together, these findings indicate that the adverse effect of a high child BMI is at least partly reversible by remission of high BMI in men and women.

Even when socioeconomic and lifestyle factors were accounted for, the associations between BMI patterns and type 2 diabetes changed little. Thus, the group with a high child BMI only did not have a higher risk at any level of education and LTPA, and those who had a persistently high BMI or developed obesity had consistently higher risk at all levels of education and LTPA. This suggests that BMI changes affect the risk of type 2 diabetes in the same way across levels of these factors. These results are in accord with our previous findings in men (4) and the current study extends these to women. We have not identified any studies reporting on potential interactions between LTPA and patterns of overweight from childhood to adulthood on risks of type 2 diabetes. In middle aged individuals, a large case-cohort study in the European Prospective Investigation into Cancer and Nutrition cohort reported an interaction between physical activity and BMI measured at middle age only in women on the risk of type 2 diabetes ($p=0.008$ in women). The higher risk of type 2 diabetes associated with lower levels of physical activity was evident in normal-weight and overweight women, but not in obese women (13).

Our analyses revealed a difference in the associations between the BMI pattern and type 2 diabetes in adulthood by current smoking status in men. Non-smoking men with high child BMI only had a lower risk of type 2 diabetes than the non-smoking men who never had a high BMI. We did not identify any other studies examining an interaction between smoking and the overweight pattern from childhood to adulthood. In adults, a large meta-analysis reported an interaction between smoking and overweight on the risk of type 2 diabetes such that the effects

of smoking were stronger in overweight or obese individuals as compared with effects in normal-weight individuals ($p<0.001$) (14).

When using a pattern of three BMI values, we found that men and women who had a high BMI at 7 and 12 years had a higher risk of developing type 2 diabetes only if obesity was present in adulthood. This finding is in accord with results from a study in three British birth cohorts followed into middle-age (2). Our previous study yielded a slightly different result as we found that men who had been overweight at 7 and 13 years of age but not during early adulthood had a higher risk of type 2 diabetes as compared with men who had never been overweight (4). Moreover, a large women-only study found that women with overweight (by somatotype) at 10 and 18 years of age but not at 34 years had a slightly higher risk of type 2 diabetes than women who had never been overweight (1). It is possible that these differences are due to size of the studies as the two largest studies showed evidence of an increased risk among those with overweight in childhood and adolescence (1, 4).

The strengths of this study are that we had measured weights and heights in seven (70%) of the cohorts limiting the potential for recall bias, we included men and women and information on lifestyle factors, and we were able to follow individuals to late adult ages. Rather than searching for published studies, we included eligible cohorts in the DynaHEALTH consortium (15), which circumvented the potential for publication bias usually encountered in meta-analysis on previously published results. The random effect meta-analysis model allowed any potential heterogeneity in the associations across cohorts to occur around a normally distributed mean effect. Moreover, a wide range of birth cohorts were included. We found slightly stronger associations in post-war generations, but the overall patterns were the same. This suggests that the results are applicable to multiple generations, including contemporary populations as some individuals in the study were born as recently as 1981. Further, sensitivity analyses examining the effects of self-reported weight and height and potential effects of

reverse causality did not change these associations. Nevertheless, further studies are needed to investigate whether the findings are generalisable to other settings.

The study has some limitations. The sample sizes may in some strata have been too small to show effect modification. The estimates for some categories were imprecise, but this reflects that certain groups such as high child BMI only have a limited risk of developing type 2 diabetes. We did not have information on pubertal status, LTPA was self-reported, and we used BMI as an indicator of adiposity. BMI is a proxy for adiposity (39), so we do not know whether the changes in the risk of type 2 diabetes are due to changes in lean or fat mass or the location of the fat mass. This is important as people without obesity also develop diabetes, dependent on their fat mass (40). Moreover, the study populations included only few children with severe obesity and, due to the racial composition of Denmark and Finland at these times, were predominantly of Caucasian descent. Whether the associations differ in groups with severe obesity, by race or by ethnicity requires further evaluations. Lastly, similar to other studies, we did not have the age at onset of obesity.

In conclusion, in the ten Danish and Finnish cohorts studied, a high BMI in childhood combined with obesity in adulthood was associated with higher risks of developing type 2 diabetes, whereas a high childhood BMI combined with non-obesity in adulthood was not. These associations were virtually similar across levels of educational and lifestyle factors suggesting that BMI affects the risk of type 2 diabetes in the same way across levels of these other risk factors. Thus, public health initiatives should focus on preventing the continuation of adiposity from childhood into adulthood irrespective of educational level and individuals of all levels of physical activity may benefit from health promoting interventions.

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CONFLICTS OF INTEREST

The authors declared no conflicts of interest.

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AUTHOR CONTRIBUTIONS

The authors' responsibilities were as follows: LGB, TIAS, MRJ, JGE, SS, and JLB conceived the study and all authors were involved in the design of the study; KKH, GBJ, ELM, MO,

KO, TS, AT, TIAS, MRJ, JGE, SS and JLB provided data; LGB, NW, RN and SS analysed data; all authors were involved in the data interpretation; LGB and JLB drafted the manuscript; all authors contributed to revision and approval of the final manuscript. LGB, NW, RN and JLB are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

## PRIOR PRESENTATION

This study was presented at the European congress on Obesity, Glasgow, Scotland, 28 April-1 May 2019.

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TABLES

Table 1. Number of individuals in the study population by patterns of BMI and educational attainment, smoking and LTPA, presented with N and row percentages.*

| | Women | | | | Men | | | |
|---|---|---|---|---|---|---|---|---|
| | Never high BMI | High child BMI | High adult BMI | Persistently high BMI | Never high BMI | High child BMI | High adult BMI | Persistently high BMI |
| | N (%) | N (%) | N (%) | N (%) | N (%) | N (%) | N (%) | N (%) |
| Education† | | | | | | | | |
| Short | 1803 (71.6) | 248 (9.8) | 351 (13.9) | 116 (4.6) | 2365 (72.1) | 286 (8.7) | 448 (13.7) | 180 (5.5) |
| Medium | 5340 (75.7) | 737 (10.4) | 667(9.5) | 310 (4.4) | 5296 (76.3) | 755 (10.9) | 604 (8.7) | 284 (4.1) |
| Long | 2107 (77.9) | 342 (12.6) | 168 (6.2) | 88 (3.3) | 2185 (78.4) | 350 (12.6) | 156 (5.6) | 97 (3.5) |
| Current smoking | | | | | | | | |
| No | 5604 (75.1) | 713 (9.6) | 839 (11.2) | 304 (4.1) | 5190 (75.2) | 685 (9.9) | 715 (10.4) | 315 (4.6) |
| Yes | 3646 (75.7) | 614 (12.7) | 347 (7.2) | 210 (4.4) | 4656 (76.3) | 706 (11.6) | 493 (8.1) | 246 (4.0) |
| LTPA‡ | | | | | | | | |
| Low | 2469 (73.2) | 352 (10.4) | 378 (11.2) | 175 (5.2) | 2543 (74.6) | 355 (10.4) | 343 (10.1) | 166 (4.9) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Medium | 4463 (76.0) | 627 (10.7) | 553 (9.4) | 227 (3.9) | 4513 (75.0) | 656 (10.9) | 581 (9.7) | 267 (4.4) |
| High | 2318 (76.4) | 348 (11.5) | 255 (8.4) | 112 (3.7) | 2790 (77.9) | 380 (10.6) | 284 (7.9) | 128 (3.6) |

LTPA: leisure time physical activity.

* The patterns of BMI were defined as follows: 1) Never high BMI: <85$^{th}$ percentile in childhood and <30 kg/m$^2$ in adulthood, 2) High child BMI: ≥85$^{th}$ percentile in childhood and <30 kg/m$^2$ in adulthood, 3) High adult BMI: <85$^{th}$ percentile in childhood and ≥30 kg/m$^2$ in adulthood and 4) Persistently high BMI: ≥85$^{th}$ percentile in childhood and ≥30 kg/m$^2$ in adulthood.

† Educational attainment was categorised into years of school 0-7 years, 8-10 years, or >10 years. One cohort used categorizations of 7-9 years, 10 years, and >10 years, due to the definition of the questionnaire (17).

‡ Leisure time physical activity was defined as low: <2 hours/week, medium: light physical activity 2-4 hours/week and high: light physical activity ≥4 hours/week or moderate activity >2 hours/week (Helsinki: <2 times/week, 2-4 times/week, ≥4 times/week).

Table 2. Meta-analysis of hazard ratios and 95% confidence intervals for the risk of type 2 diabetes for women and men with a high BMI at 7 years, 12 years or in adulthood and for educational attainment, smoking and LTPA.*

| | Women | (N=12,277)† | Men | (N=13,006)‡ |
|---|---|---|---|---|
| Variable | N (%) | Hazard ratio (95% CI) | N (%) | Hazard ratio (95% CI) |
| High child BMI, 7 years | | | | |
| No | 10,436 (85) | Reference | 11,054 (85) | Reference |
| Yes | 1841 (15) | 1.30 (1.10-1.53) | 1952 (15) | 1.28 (0.97-1.69) |
| High child BMI, 12 years | | | | |
| No | 10,435 (85) | Reference | 11,056 (85) | Reference |
| Yes | 1842 (15) | 1.92 (1.54-2.39) | 1950 (15) | 1.55 (1.36-1.78) |
| Obesity, adulthood | | | | |
| No | 10,577 (86.2) | Reference | 11,237 (86.4) | Reference |
| Yes | 1700 (13.8) | 5.25 (4.38-6.29) | 1769 (13.6) | 4.21 (3.45-5.14) |
| Education§ | | | | |
| Short | 2518 (20.5) | 1.17 (1.01-1.38) | 3279 (25.2) | 1.19 (0.96-1.48) |
| Medium | 7054 (57.4) | Reference | 6939 (53.4) | Reference |
| Long | 2705 (22.0) | 0.78 (0.54-1.12) | 2788 (21.4) | 0.84 (0.68-1.04) |
| Current smoking | | | | |
| No | 7460 (60.8) | Reference | 6905 (53.1) | Reference |
| Yes | 4817 (39.2) | 1.30 (1.14-1.48) | 6101 (46.9) | 1.29 (1.16-1.44) |
| LTPA‖ | | | | |
| Low | 3374 (27.5) | 1.34 (1.16-1.56) | 3407 (26.2) | 1.29 (1.13-1.48) |
| Medium | 5870 (47.8) | Reference | 6017 (46.3) | Reference |
| High | 3033 (24.7) | 0.90 (0.76-1.06) | 3582 (27.5) | 0.92 (0.80-1.05) |

LTPA: leisure time physical activity.

* The results for high child BMI, overweight and obesity are adjusted for age at adult BMI, educational attainment, smoking and LTPA and the results for educational attainment, smoking and LTPA are mutually adjusted.

† Among women, low heterogeneity among the cohorts was observed for the associations between high child BMI or adult obesity and type 2 diabetes ($I^2$=0.0%-34.1%; all $P_Q$-values>0.10).

‡ Among men, moderate to high heterogeneity was observed for the associations of a high BMI at 7 years ($I^2$=59.3%; $P_Q$<0.01) and obesity in adulthood ($I^2$=43.1%; $P_Q$=0.04).

§ Educational attainment was categorised into years of school 0-7 years, 8-10 years, or >10 years. One cohort used categorizations of 7-9 years, 10 years, and >10 years, due to the definition of the questionnaire (17).

‖ Leisure time physical activity was defined as low: <2 hours/week, medium: light physical activity 2-4 hours/week and high: light physical activity ≥4 hours/week or moderate activity >2 hours/week (Helsinki: <2 times/week, 2-4 times/week, ≥4 times/week).

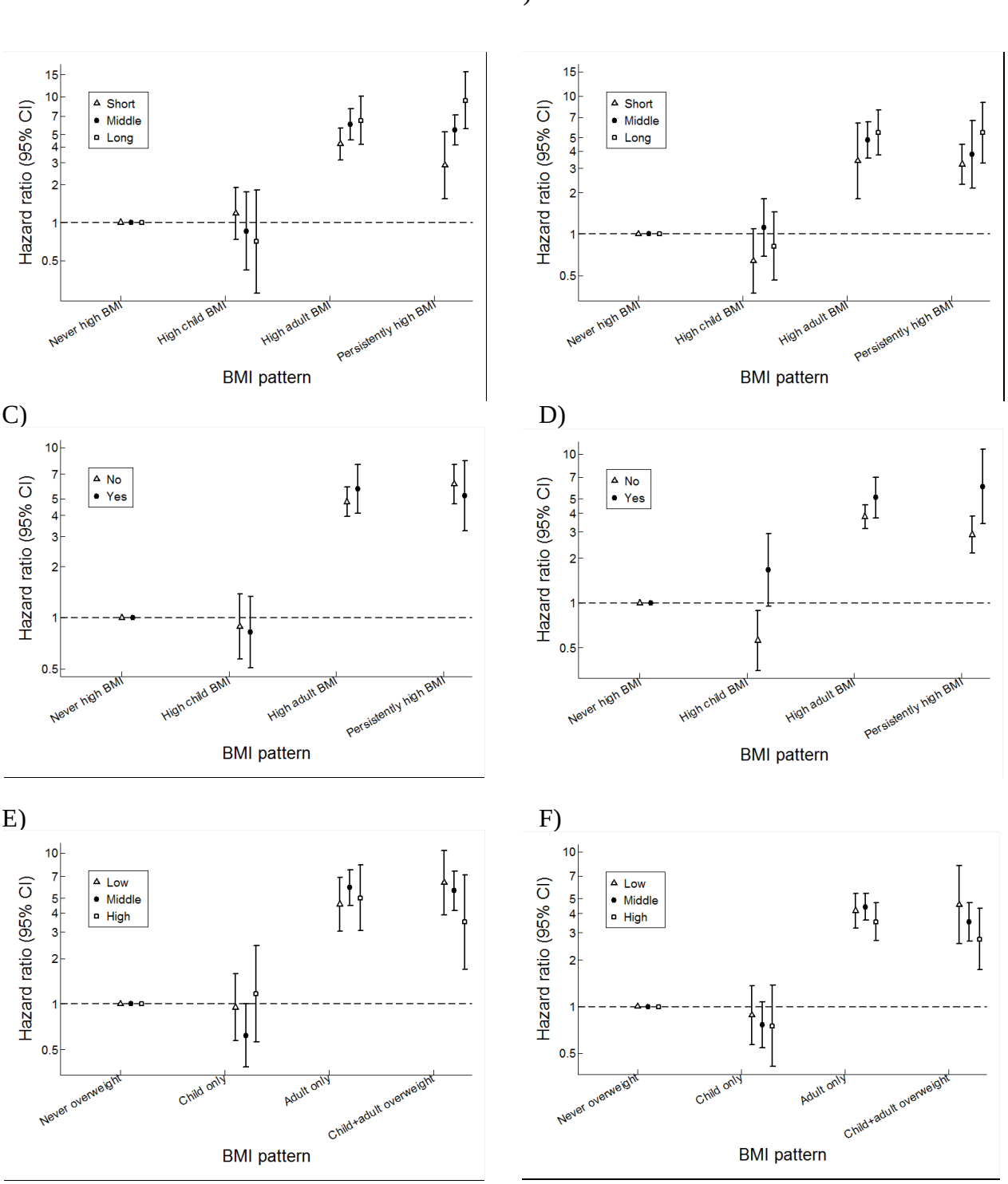
FIGURE LEGENDS

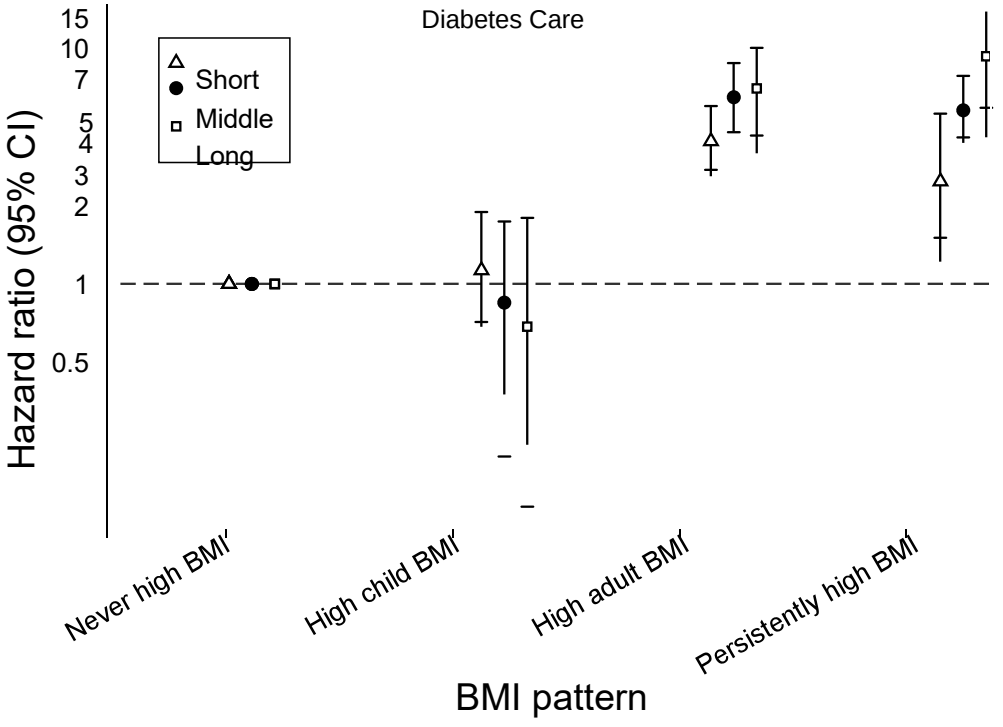
Figure 1. Meta-analysis of hazard ratios and 95% confidence intervals by levels of education (top row), smoking (middle row) and LTPA (bottom row) for the association between the weight pattern from age 7 years to adulthood and the risk of type 2 diabetes in women and men. (A) women, by educational attainment; (B) men, by educational attainment; (C) women, by smoking; (D) men, by smoking; (E) women, by LTPA; (F) men, by LTPA. A high childhood BMI is defined by the 85$^{th}$ BMI percentile. The results are adjusted for age at adult BMI, educational attainment, smoking and LTPA (unless stratified on the factor).

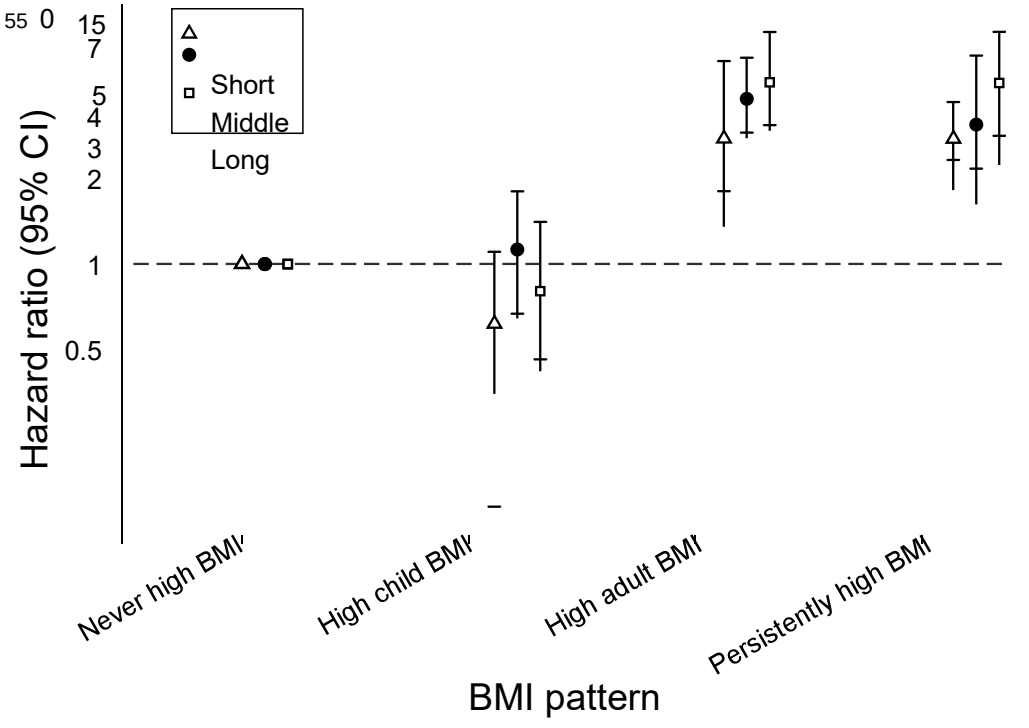
Figure 2. Meta-analysis of hazard ratios and 95% confidence intervals for the risk of type 2 diabetes for women (A) and men (B) with a high BMI at 7 years, obesity in adulthood or a high BMI at 7 years and obesity in adulthood, respectively, compared with individuals with a BMI below the cut-off for high BMI at 7 years and in adulthood. A high childhood BMI is defined by the 85$^{th}$ BMI percentile. The results are adjusted for age at adult BMI (open dots) or for age at adult BMI, educational attainment, smoking and LTPA (filled dots).

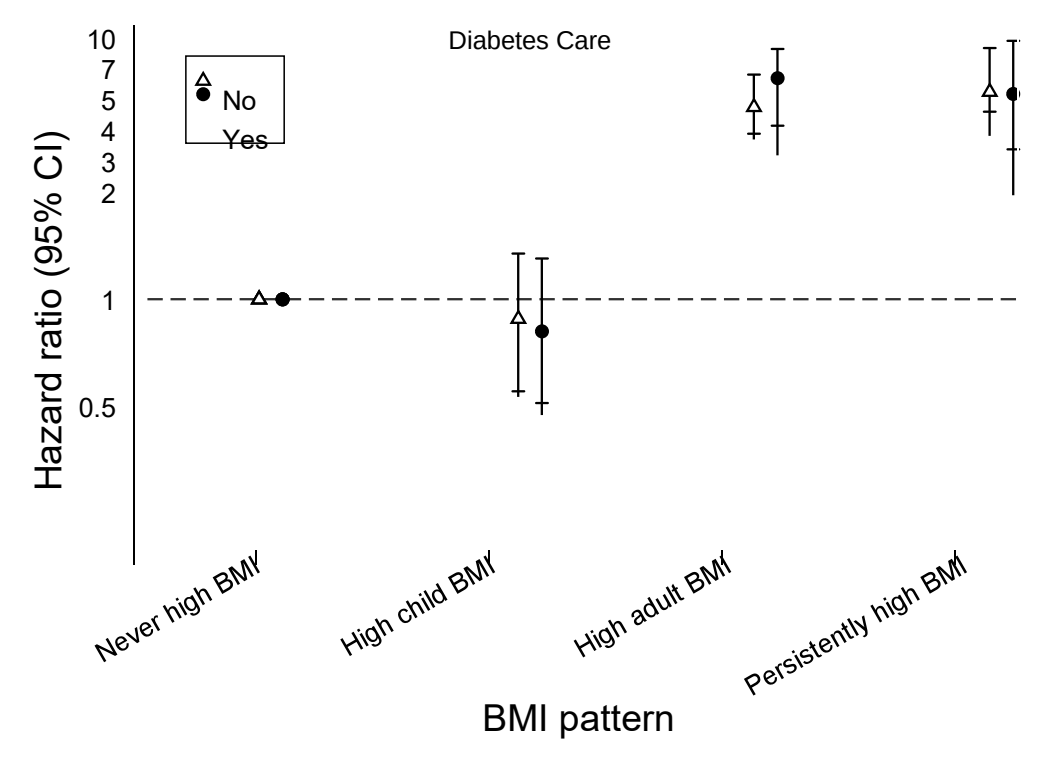
## FIGURES

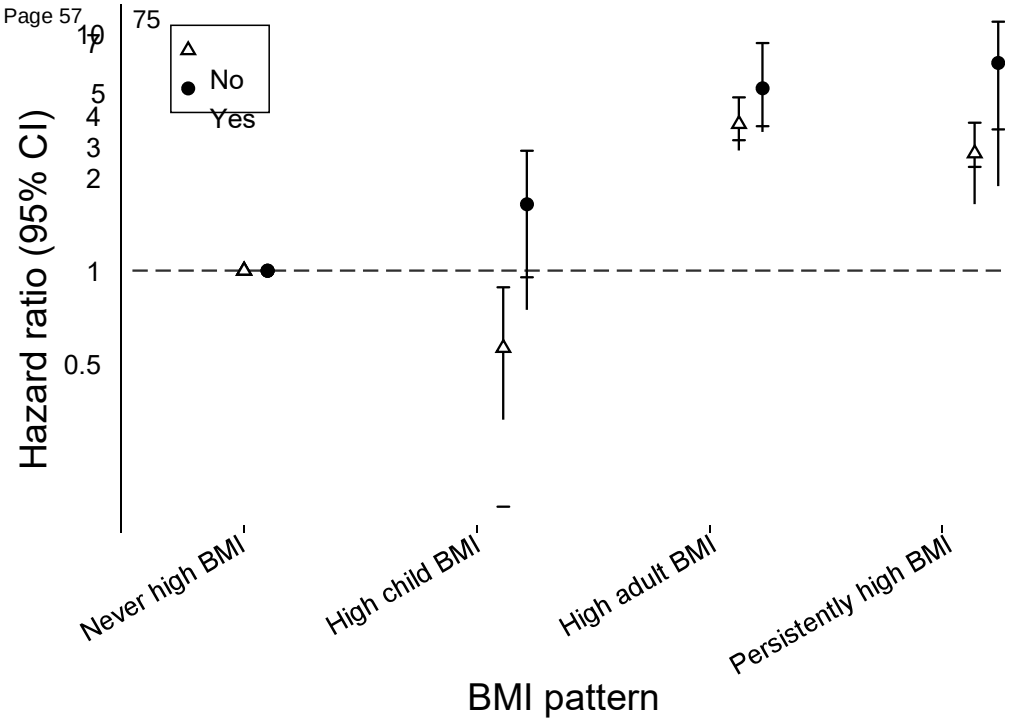
**Figure 1**. Meta-analysis of hazard ratios and 95% confidence intervals by levels of education (top row), smoking (middle row) and LTPA (bottom row) for the association between the weight pattern from age 7 years to adulthood and the risk of type 2 diabetes in women and men. (A) women, by educational attainment; (B) men, by educational attainment; (C) women, by smoking; (D) men, by smoking; (E) women, by LTPA; (F) men, by LTPA. A high childhood BMI is defined by the 85$^{th}$ BMI percentile. The results are adjusted for age at adult BMI, educational attainment, smoking and LTPA (unless stratified on the factor).

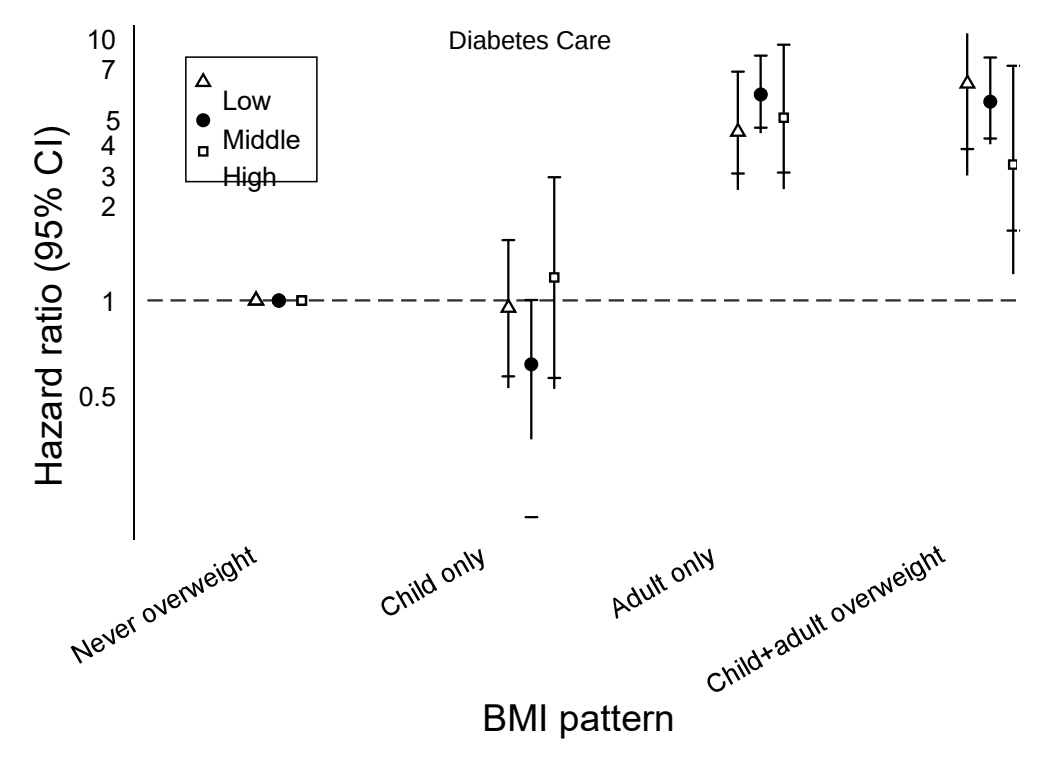



Diabetes Care
Short
Middle
Long
Hazard ratio (95% CI)
15
10
7
5
4
3
2
1
0.5
Never high BMI
High child BMI
High adult BMI
Persistently high BMI
BMI pattern


55 0
15
7
5
4
3
2
1
0.5
Short
Middle
Long
Hazard ratio (95% CI)
Never high BMI
High child BMI
High adult BMI
Persistently high BMI
BMI pattern


Diabetes Care
No
Yes
10
7
5
4
3
2
1
0.5
Hazard ratio (95% CI)
Never high BMI
High child BMI
High adult BMI
Persistently high BMI
BMI pattern


75
10
7
5
4
3
2
1
0.5
No
Yes
Hazard ratio (95% CI)
Never high BMI
High child BMI
High adult BMI
Persistently high BMI
BMI pattern


Diabetes Care
Low
Middle
High
Hazard ratio (95% CI)
10
7
5
4
3
2
1
0.5
Never overweight
Child only
Adult only
Child+adult overweight
BMI pattern

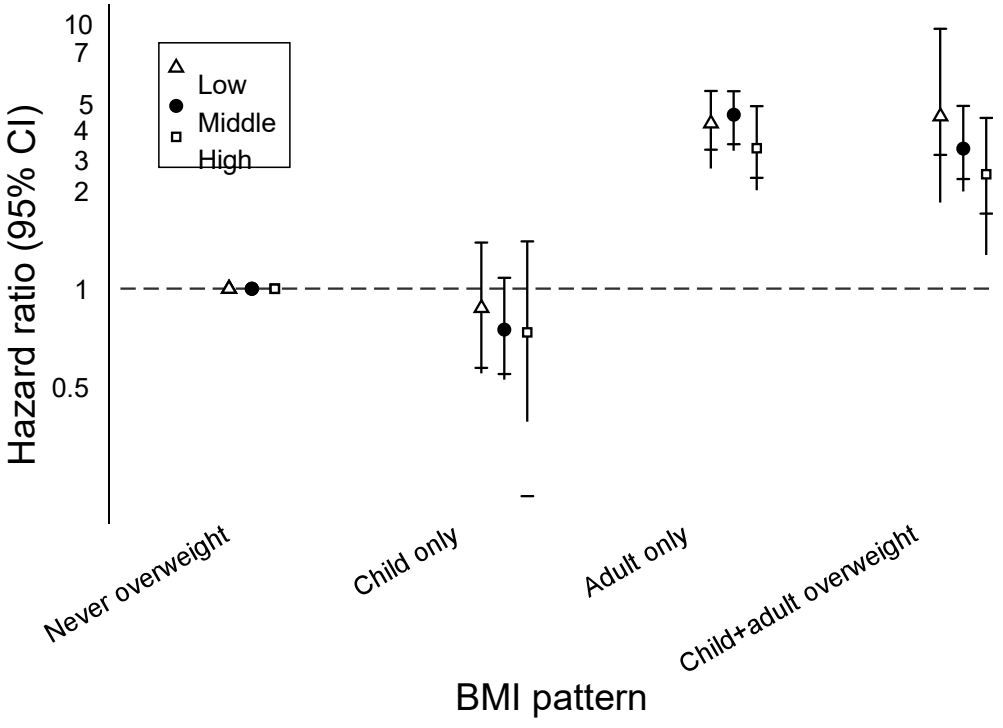
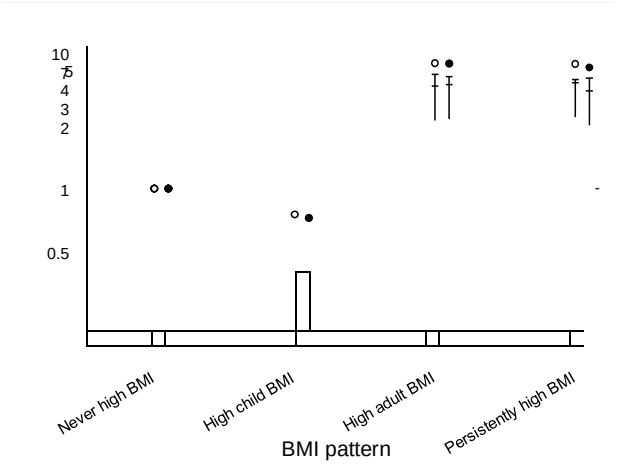
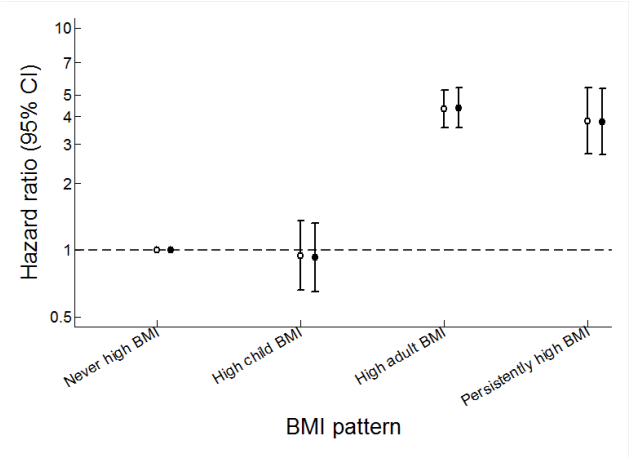

Hazard ratio (95% CI)
10
7
5
4
3
2
1
0.5
Low
Middle
High
Never overweight
Child only
Adult only
Child+adult overweight
BMI pattern

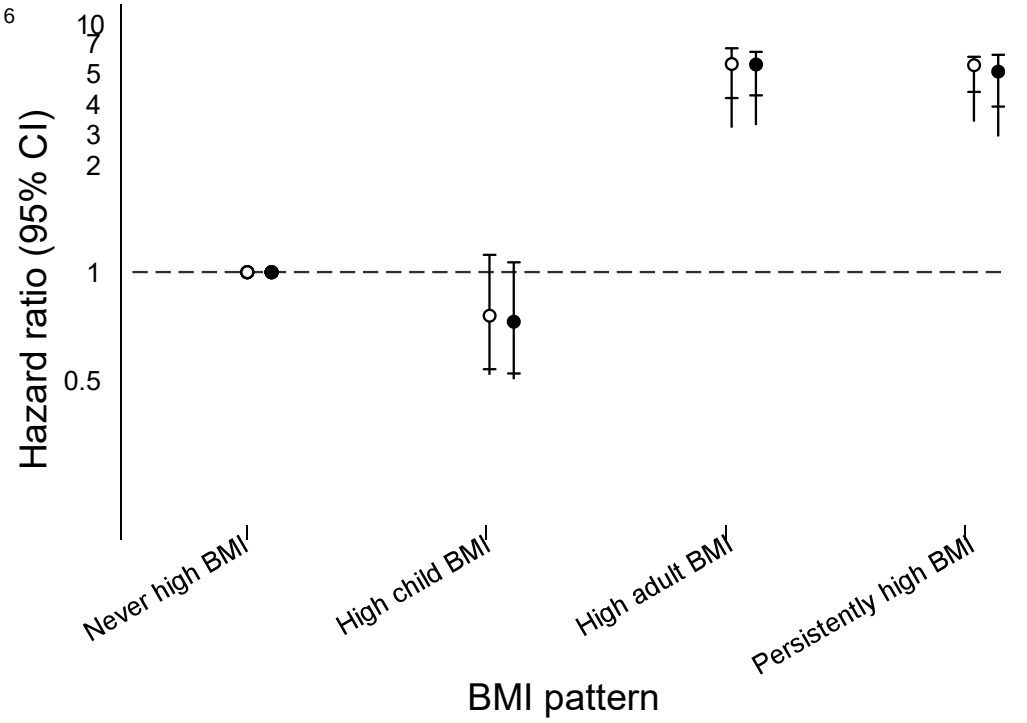
**Figure 2.**

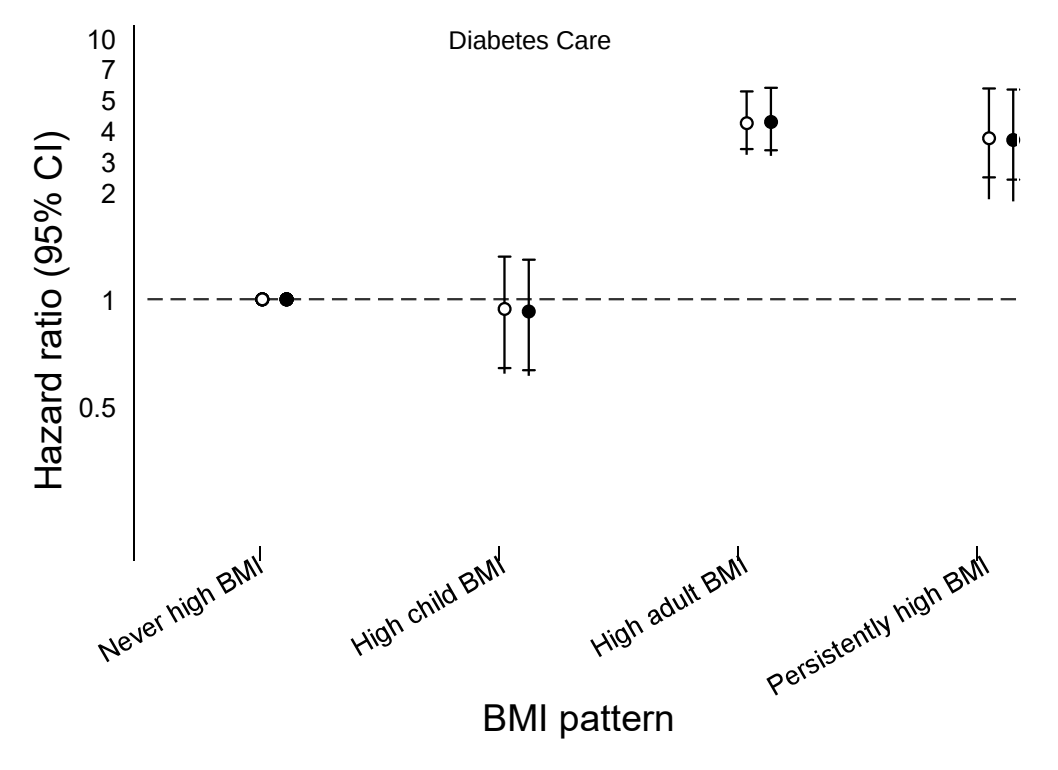
A)


10
7
5
4
3
2
1
0.5
Never high BMI
High child BMI
High adult BMI
Persistently high BMI
BMI pattern

B)


Hazard ratio (95% CI)
10
7
5
4
3
2
1
0.5
Never high BMI
High child BMI
High adult BMI
Persistently high BMI
BMI pattern


Hazard ratio (95% CI)
10
7
5
4
3
2
1
0.5
Never high BMI
High child BMI
High adult BMI
Persistently high BMI
BMI pattern


Diabetes Care
Hazard ratio (95% CI)
10
7
5
4
3
2
1
0.5
Never high BMI
High child BMI
High adult BMI
Persistently high BMI
BMI pattern

**SUPPLEMENTARY MATERIAL**

## Appendix 1. Heterogeneity

In women, the $I^2$ ranged from 0 to 41% indicating low to moderate heterogeneity across cohorts, and the hypothesis of homogeneity was not rejected ($P_Q$-values>0.10). Among men, the $I^2$ ranged from 26.9 to 53.2%, and the Q test indicated heterogeneity across cohorts in the associations for the groups of high BMI in childhood only ($P_Q$=0.05) and for persistently high BMI ($P_Q$=0.02). It is likely that the heterogeneity for the high child BMI only group was driven by the Danish Diet, Cancer and Health cohort in which there was a statistically significant and inverse association with type 2 diabetes. In all other cohorts the associations were variable in direction and not statistically significant (not shown). Although there was heterogeneity for the pattern of persistently high BMI in men, the HRs for all cohorts were far greater than 1 in all but the Conscript Sub-study (not shown).

**Table S1.** Cohorts included in the meta-analysis of change in BMI and type 2 diabetes

| | | | Women | | | | Men | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Country and study** | **Birth year(s)** | **Age at adult assessment (years)[a]** | **N** | **Mean Adult BMI[b]** | **% obese, adult** | **T2D, N (%)[c]** | **N** | **Mean Adult BMI[b]** | **% obese, adult** | **T2D, N (%)[c]** |
| *Denmark* | | | | | | | | | | |
| Diet, Cancer and Health(20) | 1930-1947 | 50.1-65.4 | 6407 | 25.8 (4.4) | 20.7 | 534 (8.3) | 5781 | 26.7 (3.7) | 16.2 | 673 (11.6) |
| Conscript Sub-study (19) | 1930-1959 | 23-63.2 | 0 | - | - | - | 293 | 25.1 (3.5) | 7.9 | 33 (11.3) |
| Copenhagen City Heart Study (21, 22) | 1930-1981 | 20.6-71.8 | 1163 | 24.0 (4.6) | 9.6 | 111 (9.5) | 1,170 | 25.3 (3.9) | 10.9 | 172 (14.7) |
| MONICAI-III (18) | 1931-1961 | 29.6-62.1 | 638 | 24.0 (4.4) | 9.6 | 47 (7.4) | 649 | 25.4 (3.4) | 10.8 | 67 (10.3) |
| Glostrup population Studies[d] (18) | 1936-1948 | 29.1-61.6 | 213 | 23.0 (3.6) | 6.1 | 29 (13.6) | 191 | 24.7 (3.3) | 6.3 | 29 (15.2) |
| Inter99 (18) | 1939-1970 | 30.1-60.9 | 609 | 26.4 (5.5) | 20.7 | 37 (6.1) | 566 | 27.1 (4.1) | 19.7 | 38 (6.7) |
| Metropolit (17)[e] | 1953 | 51.1-52.5 | 0 | - | - | - | 1,335 | 26.0 (3.7) | 12.5 | 77 (5.8) |
| Copenhagen Perinatal Cohort (16, 39)[e] | 1959-1961 | 40.2-44.0 | 384 | 24.5 (46.3) | 13.5 | 18 (4.7) | 318 | 25.7 (3.6) | 12.6 | 12 (3.77) |
| *Finland* | | | | | | | | | | |
| Northern Finland Birth Cohort 1966 (24) | 1966 | 31.2 | 2073 | 24.0 (4.4) | 9.3 | 106 (5.1) | 1912 | 25.1 (3.5) | 8.0 | 126 (6.6) |
| Helsinki Birth[e] Cohort Study (40) | 1934-1944 | 57-68 | 790 | 26.9 (4.9) | 21.1 | 107 (13.5) | 791 | 26.7 (4.1) | 16.5 | 143 (18.0) |

BMI: Body mass index; T2D: Type 2 diabetes.

[a] Age where weight, height, educational attainment, smoking and LTPA were assessed. [b] Numbers in parentheses, standard deviation. [c] Among all women and men in the cohorts. [d] 1936 cohort and the Health 78 study. [e] Self-reported weight and height.

**Table S2.** Childhood BMI 85th percentiles values used for the definition of high BMI.

| | **Girls** | | **Boys** | |
|---|---|---|---|---|
| **Region** | 7 years | 12 years | 7 years | 12 years |
| **Copenhagen** | 16.54 | 19.74 | 16.52 | 19.13 |
| **Northern Finland** | 17.19 | 20.42 | 16.91 | 19.91 |
| **Helsinki** | 16.90 | 20.45 | 16.71 | 19.74 |

**Table S3.** Number of individuals with type 2 diabetes in the study population by patterns of BMI and educational attainment, smoking and LTPA, presented with n and row percentages.*

| | Women | | | | Men | | | |
|---|---|---|---|---|---|---|---|---|
| | **Never high BMI** | **High child BMI** | **High adult BMI** | **Persistently high BMI** | **Never high BMI** | **High child BMI** | **High adult BMI** | **Persistently high BMI** |
| | **n (%)** | **n (%)** | **n (%)** | **n (%)** | **n (%)** | **n (%)** | **n (%)** | **n (%)** |
| **Education †** | | | | | | | | |
| **Short** | 143 (52.2) | 22 (8.0) | 84 (30.7) | 25 (9.1) | 240 (54.5) | 21 (4.8) | 130 (29.5) | 49 (11.1) |
| **Medium** | 299 (52.3) | 25 (4.4) | 172 (30.1) | 76 (13.3) | 432 (61.5) | 48 (6.8) | 164 (23.3) | 59 (8.4) |
| **Long** | 77 (53.8) | 6 (4.2) | 36 (25.2) | 24 (16.8) | 138 (60.8) | 16 (7.0) | 50 (22.0) | 23 (10.1) |
| **Current smoking** | | | | | | | | |
| **No** | 266 (48.9) | 23 (4.2) | 183 (33.6) | 72 (13.2) | 390 (59.1) | 23 (3.5) | 187 (28.3) | 60 (9.1) |
| **Yes** | 253 (56.9) | 30 (6.7) | 109 (24.5) | 53 (11.9) | 420 (59.2) | 62 (8.7) | 157 (22.1) | 71 (10.0) |
| **LTPA‡** | | | | | | | | |
| **Low** | 149 (47.6) | 18 (5.8) | 95 (30.4) | 51 (16.3) | 213 (54.8) | 26 (6.7) | 104 (26.7) | 46 (11.8) |
| **Medium** | 244 (52.7) | 20 (4.3) | 141 (30.5) | 58 (12.5) | 363 (57.9) | 39 (6.2) | 163 (26.0) | 62 (9.9) |
| **High** | 126 (59.2) | 15 (7.0) | 56 (26.3) | 16 (7.5) | 234 (66.1) | 20 (5.6) | 77 (21.8) | 23 (6.5) |

LTPA: leisure time physical activity.

* The patterns of BMI were defined as follows: 1) Never high BMI: <85$^{th}$ percentile in childhood and <30 kg/m$^2$ in adulthood, 2) High child BMI: ≥85$^{th}$ percentile in childhood and <30 kg/m$^2$ in adulthood, 3) High adult BMI: <85$^{th}$ percentile in childhood and ≥30 kg/m$^2$ in adulthood and 4) Persistently high BMI: ≥85$^{th}$ percentile in childhood and ≥30 kg/m$^2$ in adulthood.

† Educational attainment was categorised into years of school 0-7 years, 8-10 years, or >10 years. One cohort used categorizations of 7-9 years, 10 years, and >10 years, due to the definition of the questionnaire (17).

‡ Leisure time physical activity was defined as low: <2 hours/week, medium: light physical activity 2-4 hours/week and high: light physical activity ≥4 hours/week or moderate activity >2 hours/week (Helsinki: <2 times/week, 2-4 times/week, ≥4 times/week).

**Table S4.** Results of meta-regressions analyses for the influence of educational attainment, smoking and LTPA on the association between the BMI pattern and type 2 diabetes

| | | | Women | | | | | Men | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Effect modifier** | **Comparison for the HR** | **BMI pattern category** | **HR** | **95% CI** | **p[a]** | **Sub-group heterogeneity p-value** | | **HR** | **95% CI** | **p[a]** | **Sub-group heterogeneity p-value** |
| **Education** | | | | | | | | | | | |
| | Per higher level of education | High child BMI | 0.74 | 0.40-1.37 | 0.31 | 0.37 | | 1.03 | 0.58-1.81 | 0.92 | 0.43 |
| | | High adult BMI | 1.30 | 0.96-1.80 | 0.08 | 0.18 | | 1.25 | 0.91-1.73 | 0.15 | 0.16 |
| | | Persistently high BMI | 1.70 | 1.15-2.53 | 0.01 | 0.008 | | 1.20 | 0.73-1.97 | 0.79 | 0.22 |
| **Smoking** | | | | | | | | | | | |
| | Smoking vs. non-smoking | High child BMI | 0.89 | 0.39-2.02 | 0.76 | 0.73 | | 3.01 | 0.93-9.77 | 0.07 | 0.006 |
| | | High adult BMI | 1.13 | 0.69-1.86 | 0.53 | 0.54 | | 1.25 | 0.85-1.87 | 0.23 | 0.17 |
| | | Persistently high BMI | 0.73 | 0.44-1.19 | 0.18 | 0.25 | | 1.94 | 0.89-4.24 | 0.09 | 0.01 |
| **LTPA** | | | | | | | | | | | |
| | Per higher level of LTPA | High child BMI | 1.05 | 0.65-1.71 | 0.83 | 0.27 | | 0.90 | 0.61-1.33 | 0.58 | 0.79 |
| | | High adult BMI | 1.05 | 0.70-1.56 | 0.81 | 0.38 | | 0.92 | 0.74-1.14 | 0.44 | 0.44 |
| | | Persistently high BMI | 0.70 | 0.47-1.05 | 0.08 | 0.08 | | 0.78 | 0.52-1.18 | 0.23 | 0.27 |

BMI: Body mass index; CI: Confidence interval; HR: Hazard Ratio; LTPA: leisure time physical activity

[a] Represents the test for the significance of the effect modification across strata of the effect modifier for the association between the specific BMI pattern and type 2 diabetes corresponding to estimates shown in figure 1 ('Never high BMI' is the reference group in all comparisons).

**Table S5.** Results of meta-regressions analyses for the influence of education on the association between child and adult BMI mutually adjusted and type 2 diabetes.

| | | | Women | | | | | Men | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Effect modifier** | **Comparison for the HR** | **BMI pattern category** | **HR** | **95% CI** | **p[a]** | **Sub-group heterogeneity p-value** | | **HR** | **95% CI** | **p[a]** | **Sub-group heterogeneity p-value** |
| **Education** | | | | | | | | | | | |
| | Per higher level of education | Child BMI <90th | 0.96 | 0.84-1.08 | 0.45 | 0.57 | | 0.96 | 0.82-1.13 | 0.62 | 0.95 |
| | | Child BMI >90th | 1.01 | 0.83-1.23 | 0.92 | 0.90 | | 0.92 | 0.73-1.17 | 0.49 | 0.91 |
| | | Adult BMI <30 kg/m$^2$ | 0.98 | 0.93-1.03 | 0.45 | 0.34 | | 0.97 | 0.93-1.02 | 0.24 | 0.46 |
| | | Adult BMI >30 kg/m$^2$ | 1.05 | 1.01-1.10 | 0.03 | 0.003 | | 1.06 | 1.01-1.12 | 0.03 | 0.14 |
| **Smoking** | _ | _ | _ | _ | _ | _ | _ | _ | _ | _ | |
| | Smoking vs. non-smoking | Child BMI <90th | 1.02 | 0.88-1.19 | 0.74 | 0.73 | | 1.26 | 0.996-1.60 | 0.053 | 0.05 |
| | | Child BMI >90th | 0.93 | 0.73-1.18 | 0.52 | 0.50 | | 1.00 | 0.76-1.32 | 0.995 | 0.995 |
| | | Adult BMI <30 kg/m$^2$ | 0.98 | 0.93-1.04 | 0.52 | 0.51 | | 0.98 | 0.92-1.04 | 0.49 | 0.46 |
| | | Adult BMI >30 kg/m$^2$ | 0.99 | 0.94-1.04 | 0.58 | 0.53 | | 1.03 | 0.98-1.09 | 0.17 | 0.15 |
| **LTPA** | _ | _ | _ | _ | _ | _ | _ | _ | _ | _ | |
| | Per higher level of LTPA | Child BMI <90th | 0.90 | 0.79-1.02 | 0.09 | 0.009 | | 0.95 | 0.85-1.05 | 0.29 | 0.25 |
| | | Child BMI >90th | 1.07 | 0.88-1.33 | 0.45 | 0.25 | | 0.92 | 0.76-1.11 | 0.37 | 0.49 |
| | | Adult BMI <30 kg/m$^2$ | 1.03 | 0.99-1.07 | 0.19 | 0.08 | | 1.00 | 0.95-1.06 | 0.90 | 0.04 |
| | | Adult BMI >30 kg/m$^2$ | 0.99 | 0.96-1.03 | 0.69 | 0.91 | | 1.03 | 0.98-1.08 | 0.25 | 0.28 |

BMI: Body mass index; CI: Confidence interval; HR: Hazard Ratio; LTPA: leisure time physical activity

[a] Represents the test for the significance of the effect modification across strata.

**Table S6.** Child and adult BMI mutually adjusted.

The associations were investigated by a linear spline regression with knot points inserted at the sex and city specific 90th percentile for child BMIs and at 30 kg/m2 for adult BMI. The reference was BMI at 7 years at the 50th percentile and adult BMI of 22 kg/m$^2$. Risks of type 2 diabetes for individuals with specific linear combinations of childhood BMIs at age 7 and corresponding to the 25th, 50th, 85th and 95th percentile and adult BMI at 22, 25, 30 and 35 kg/m$^2$ are reported in women and men. Few events of type 2 diabetes were observed at BMI <22 kg/m$^2$. The results are adjusted for age at adult BMI (upper panel) or for age at adult BMI, education, smoking and LTPA (lower panel).

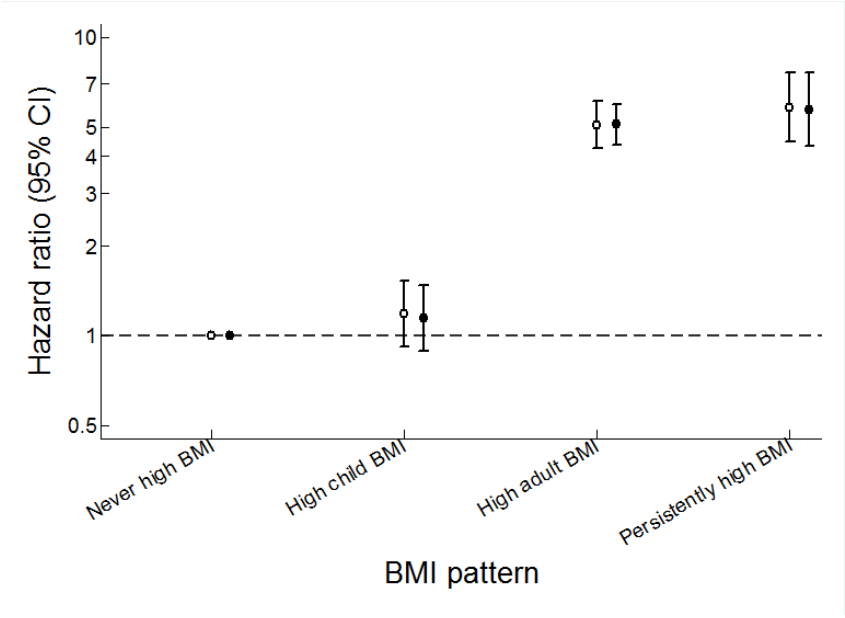
| | **Adjusted for age at adult BMI** | | | |
|---|---|---|---|---|
| **BMI percentile at 7 years** | **BMI in adulthood** | | | |
| | **22 kg/m$^2$** | **25 kg/m$^2$** | **30 kg/m$^2$** | **35 kg/m$^2$** |
| **Women** | *Hazard ratio for type 2 diabetes (95% CI)* | | | |
| **25th** | 1.18 (1.10–1.26) | 2.64 (2.31–3.02) | 10.04 (7.63–13.22) | 16.29 (13.08–20.29) |
| **50th** | Reference | 2.23 (2.05–2.43) | 8.47 (6.76–10.63) | 13.89 (11.38–16.95) |
| **85th** | – | 1.66 (1.44–1.91) | 6.28 (5.06–7.78) | 10.30 (8.46–12.53) |
| **95th** | – | 1.50 (1.22–1.84) | 5.83 (4.45–7.64) | 9.28 (7.57–11.37) |
| **Men** | *Hazard ratio for type 2 diabetes (95% CI)* | | | |
| **25th** | 1.24 (1.18–1.30) | 2.66 (2.30–3.07) | 9.59 (6.92–13.29) | 19.82 (14.92–26.33) |
| **50th** | Reference | 2.16 (1.93–2.42) | 7.79 (5.77–10.52) | 16.25 (12.30–21.47) |
| **85th** | – | 1.49 (1.36–1.64) | 5.43 (4.15–7.11) | 11.52 (8.58–15.47) |
| **95th** | – | 1.39 (1.24–1.55) | 5.00 (3.85–6.50) | 10.52 (7.95–12.93) |

| | **Adjusted for age at adult BMI, education, smoking and LTPA** | | | |
|---|---|---|---|---|
| **BMI percentile at 7 years** | **BMI in adulthood** | | | |
| | **22 kg/m$^2$** | **25 kg/m$^2$** | **30 kg/m$^2$** | **35 kg/m$^2$** |
| **Women** | *Hazard ratio for type 2 diabetes (95% CI)* | | | |
| **25th** | 1.19 (1.13–1.26) | 2.65 (2.34–3.01) | 10.02 (7.46–13.46) | 16.86 (13.63–20.85) |
| **50th** | Reference | 2.22 (2.00–2.46) | 8.37 (6.37–11.01) | 14.19 (11.70–17.22) |
| **85th** | – | 1.59 (1.38–1.84) | 5.99 (4.57–7.84) | 10.24 (8.47–12.38) |
| **95th** | – | 1.42 (1.18–1.70) | 5.41 (4.03–7.27) | 9.01 (7.30–11.12) |
| **Men** | *Hazard ratio for type 2 diabetes (95% CI)* | | | |
| **25th** | 1.25 (1.18–1.32) | 2.77 (2.38–3.21) | 10.37 (7.41–14.51) | 21.49 (15.86–29.11) |
| **50th** | Reference | 2.21 (1.97–2.48) | 8.29 (6.07–11.32) | 17.42 (12.89–23.55) |
| **85th** | – | 1.51 (1.34–1.69) | 5.63 (4.21–7.52) | 12.16 (8.78–16.83) |
| **95th** | – | 1.38 (1.23–1.54) | 5.16 (3.91–6.82) | 10.52 (8.10–13.66) |

BMI: Body mass index; CI, Confidence intervals; LTPA: leisure time physical activity
A dash indicates that a hazard ratio was not calculated for the category because there were fewer than five diagnoses of type 2 diabetes in the group.

**Figure S1.** Meta-analysis of hazard ratios and 95% confidence intervals for the risk of type 2 diabetes for women (Panel A) and men (Panel B) with a high BMI at 12 years, obesity in adulthood or a high BMI at 12 years and obesity in adulthood, respectively, compared with individuals with a BMI below the cut-off for high BMI at 12 years and in adulthood. A high childhood BMI is defined by the 85th BMI percentile. The results are adjusted for age at adult BMI (open dots) or for age at adult BMI, education, smoking and LTPA (filled dots).

A)




B)

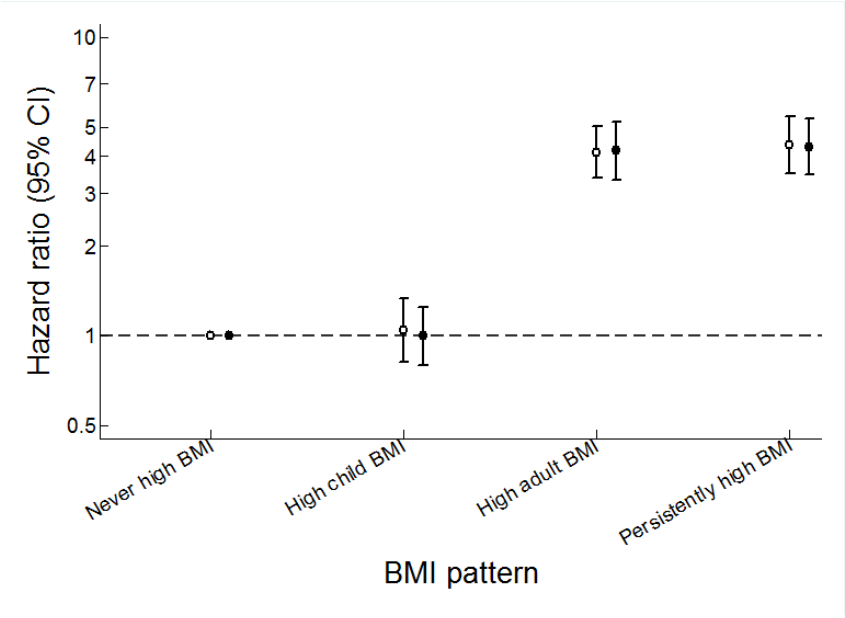
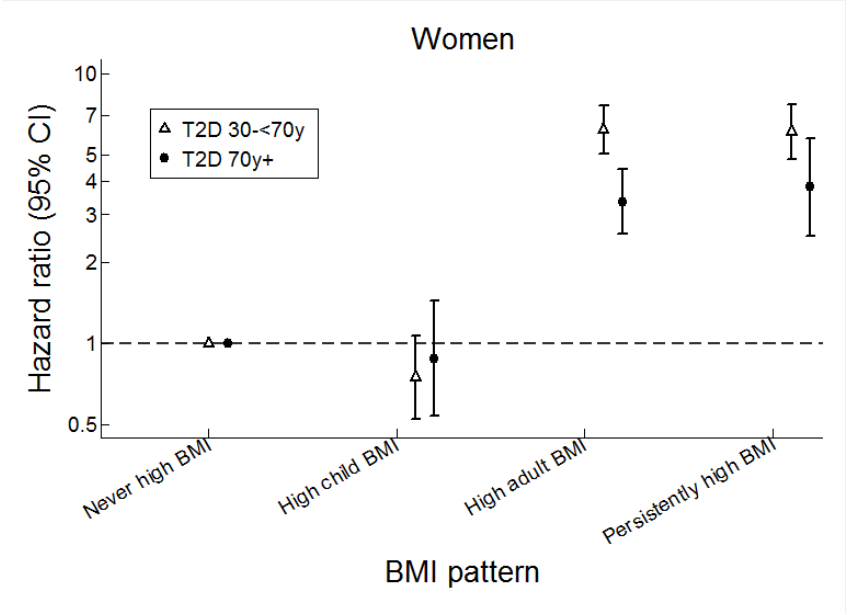


**Figure S2.** Meta-analysis of hazard ratios and 95% confidence intervals for the association between the weight pattern from age 7 years to adulthood and the risk of type 2 diabetes at 30 to 70 years of age (open triangles) and at age >70 to 85 years (filled dots) in women (Panel A) and men (Panel B). A high childhood BMI is defined by the 85$^{th}$ BMI percentile. The results are adjusted for age at adult BMI, education, smoking and LTPA.

A)




B)

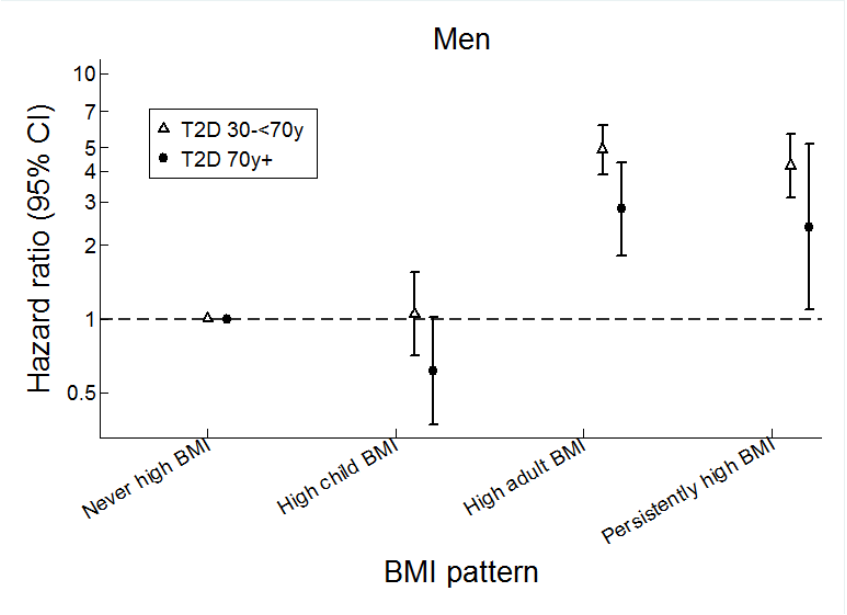
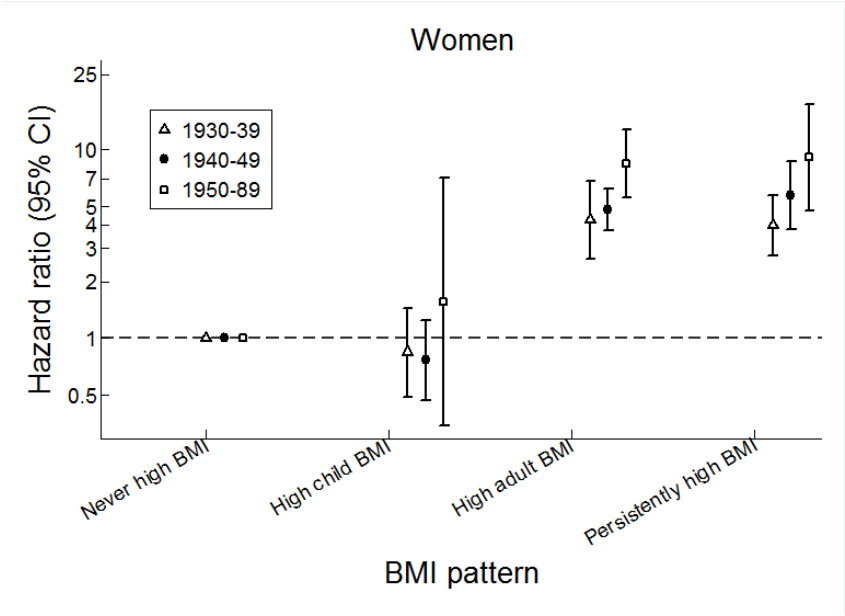


**Figure S3**. Meta-analysis of hazard ratios and 95% confidence intervals by birth cohorts for the association between the weight pattern from age 7 years to adulthood and the risk of type 2 diabetes in women (Panel A) and men (Panel B). A high childhood BMI is defined by the 85$^{th}$ BMI percentile. The results are adjusted for age at adult BMI, education, smoking and LTPA.

A)




B)

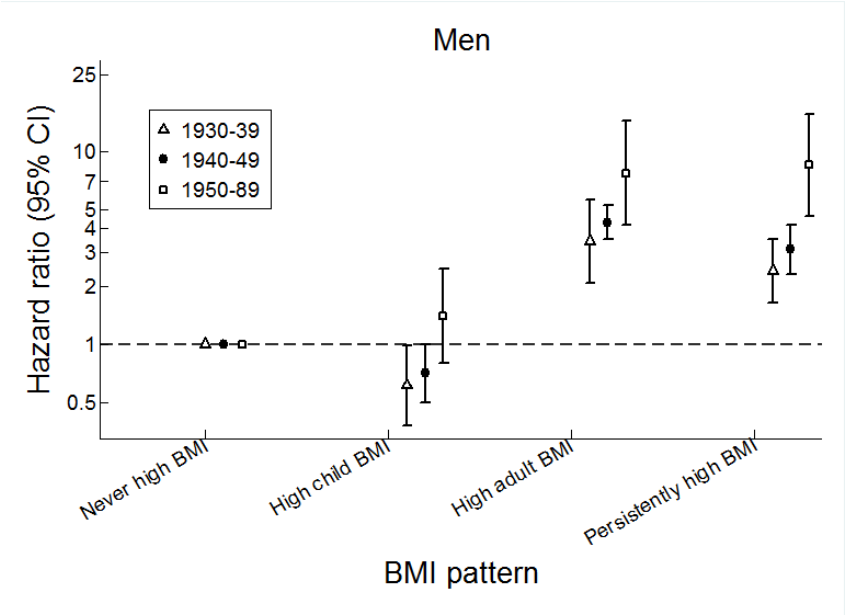
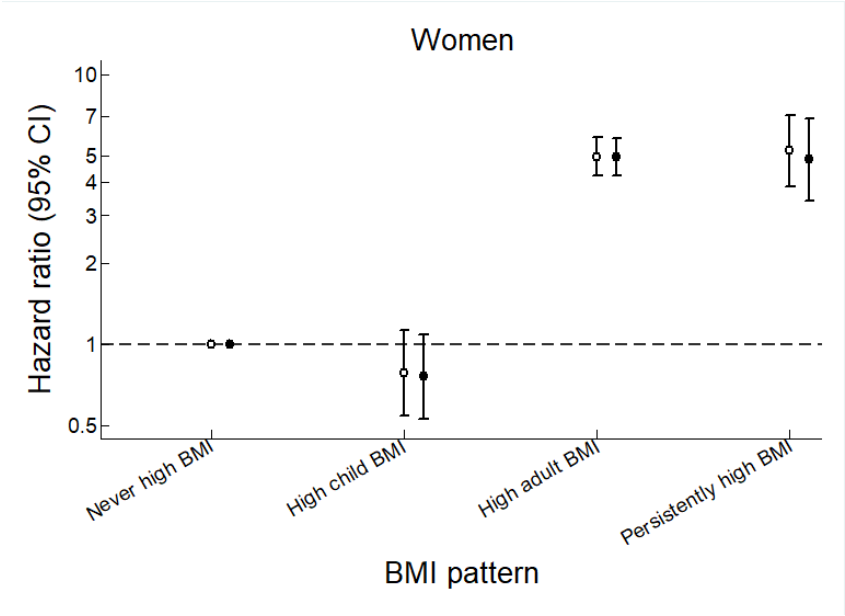
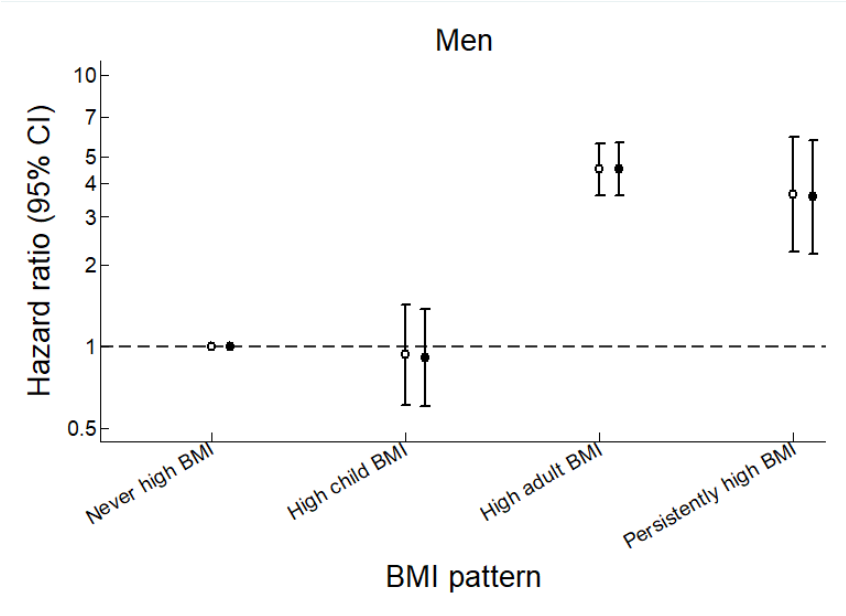


**Figure S4**. Meta-analysis of hazard ratios and 95% confidence intervals for the association between the weight pattern from age 7 years to adulthood and the risk of type 2 diabetes in cohorts with measured weight and height in women[1] (Panel A) and men[2] (Panel B). A high childhood BMI is defined by the 85th BMI percentile. The results are adjusted for age at adult BMI (open dots) or for age at adult BMI, education, smoking and LTPA (filled dots).

A)



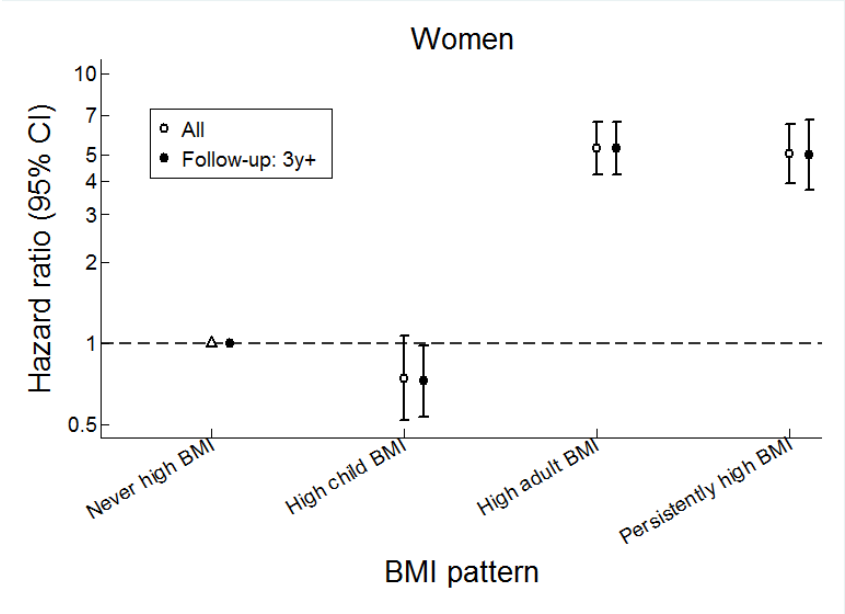

B)




[1] Two cohorts excluded due to self-reported weight and height (CPC & HBCS).
[2] Three cohorts excluded due to self-reported weight and height (CPC, Metropolit & HBCS).

**Figure S5**. Meta-analysis of hazard ratios and 95% confidence intervals for the association between the weight pattern from age 7 years to adulthood and the risk of type 2 diabetes diagnosed three years or more after the BMI assessment in women (Panel A) and men (Panel B). A high childhood BMI is defined by the 85th BMI percentile. The results are adjusted for age at adult BMI, education, smoking and LTPA.

A)




B)

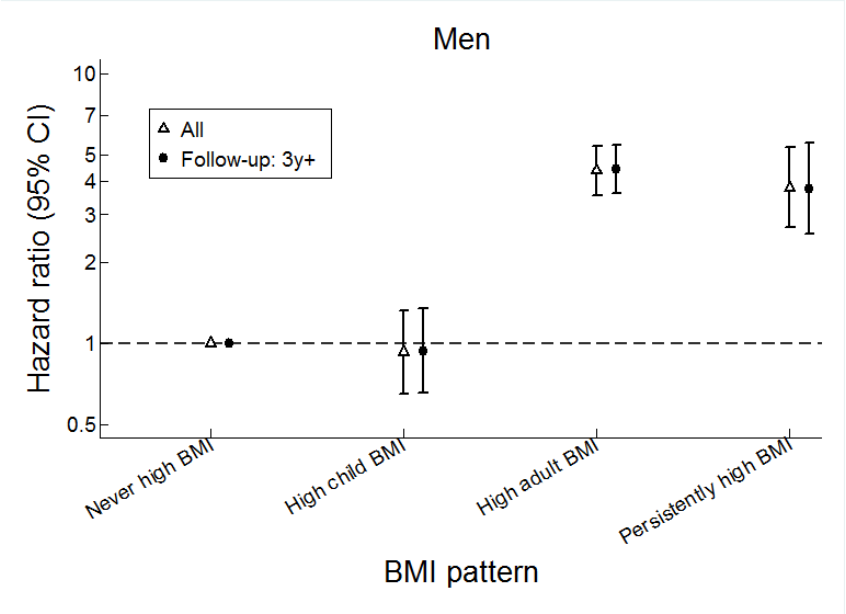
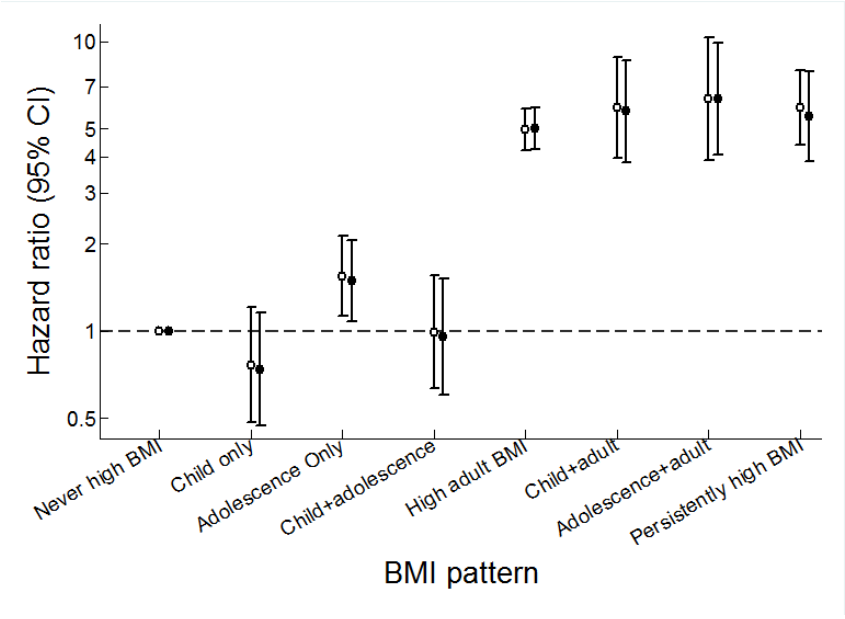


**Figure S6**. Meta-analysis of hazard ratios and 95% confidence intervals for the risk of type 2 diabetes for women (Panel A) and men (Panel B) with a BMI at 7 or 12 years above the 85th percentile and/or obesity in adulthood and combinations of these. The results are adjusted for age at adult BMI only (open dots) or for age at adult BMI, education, smoking and LTPA (filled dots).

A)




B)