ORIGINAL ARTICLE

Change in Overweight from Childhood to Early Adulthood and Risk of Type 2 Diabetes

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ABSTRACT

BACKGROUND
Childhood overweight is associated with an increased risk of type 2 diabetes in adulthood. We investigated whether remission of overweight before early adulthood reduces this risk.

METHODS
We conducted a study involving 62,565 Danish men whose weights and heights had been measured at 7 and 13 years of age and in early adulthood (17 to 26 years of age). Overweight was defined in accordance with Centers for Disease Control and Prevention criteria. Data on type 2 diabetes status (at age ≥30 years, 6710 persons) were obtained from a national health registry.

RESULTS
Overweight at 7 years of age (3373 of 62,565 men; 5.4%), 13 years of age (3418 of 62,565; 5.5%), or early adulthood (5108 of 62,565; 8.2%) was positively associated with the risk of type 2 diabetes; associations were stronger at older ages at overweight and at younger ages at diagnosis of type 2 diabetes. Men who had had remission of overweight before the age of 13 years had a risk of having type 2 diabetes diagnosed at 30 to 60 years of age that was similar to that among men who had never been overweight (hazard ratio, 0.96; 95% confidence interval [CI], 0.75 to 1.21). As compared with men who had never been overweight, 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 (hazard ratio, 1.47; 95% CI, 1.10 to 1.98), but their risk was lower than that among men with persistent overweight (hazard ratio [persistantly overweight vs. never overweight], 4.14; 95% CI, 3.57 to 4.79). An increase in body-mass index between 7 years of age and early adulthood was associated with an increased risk of type 2 diabetes, even among men whose weight had been normal at 7 years of age.

CONCLUSIONS
Childhood overweight at 7 years of age was associated with increased risks of adult type 2 diabetes only if it continued until puberty or later ages. (Funded by the European Union.)

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Lifestyle interventions that are aimed at weight loss in adults have been found to delay the onset of type 2 diabetes in persons who are at high risk for the condition.[1,2] In children, it is now well established that higher body-mass index (BMI) values, even at levels far below current overweight classifications, are associated with increased risks of type 2 diabetes in adulthood.[3] This raises the question of whether weight loss in children who are overweight or obese can reduce the risk of type 2 diabetes later in life. Not all studies have shown beneficial effects.[4-8]

Because more than 23% of children worldwide are overweight or obese,[9] it is important to know whether the adverse effects of childhood overweight on the risk of type 2 diabetes are reversible if remission to normal weight occurs before adulthood. Moreover, it is important to establish whether increases in weight that occur during the critical period of puberty — a period that is associated with a marked decrease in insulin sensitivity[10] — also play a central role in the later development of type 2 diabetes. Furthermore, since the risk of childhood obesity and the risk of diabetes in adulthood are inversely associated with socioeconomic status,[11-13] it is likely that associations between remission of overweight and the risk of type 2 diabetes are influenced by socioeconomic conditions.[4-8]

In this study, we investigated whether changes in weight status from childhood to early adulthood were associated with differences in the risk of type 2 diabetes and examined the modifying influences of socioeconomic indicators on these associations in a large cohort of Danish men.

METHODS

STUDY POPULATION

The Copenhagen School Health Record Register (CSHRR) is a database containing computerized information on almost all children attending public or private schools in Copenhagen who were born during the period from 1930 through 1989.[14] Children in this cohort underwent mandatory health examinations, and weights and heights were measured annually by school doctors or nurses.[14] Beginning in 1968, personal identification numbers were assigned to all Danish residents. With the use of this number, 73,877 boys in the CSHRR were linked to the Danish Conscription Database, which includes men born during the period from 1939 through 1959.[15] The Danish Conscription Database contains information on weights and heights measured by physicians at conscription examinations. Examinations were mandatory for all young Danish men, but a small number of exemptions were given for conditions that rendered men unable to enter military service (e.g., intellectual disability or epilepsy).[15] Cognitive ability was assessed with a validated psychological test of intelligence,[16] and scores were divided into three strata (Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org).[15] Educational level was reported by the men and categorized as short (7 to 10 years of primary school), medium (skilled training in industry, trade, or craft), or long (9 to 12 years of middle and secondary school or higher education).[15]

Vital status was obtained through linkage to the Danish Civil Registration System.[17] Inpatient and outpatient diagnoses of type 2 diabetes were obtained from the National Patient Register, which contains hospital discharge diagnoses from general hospitals since 1977 and from outpatient and emergency departments since 1995.[18] In Denmark, patients with type 2 diabetes who are treated in general practice are often included in the National Patient Register because they commonly receive treatment at specialized hospital-based clinics. The date of the first hospital admission was used to define the age at diagnosis.

Type 2 diabetes was defined in accordance with the *International Classification of Diseases, Eighth Revision*, until 1994 (code 250) and the *Tenth Revision* thereafter (codes E11 through E14). 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, we restricted the lower bound for the age at diagnosis of type 2 diabetes to 30 years, since type 1 diabetes generally is diagnosed at earlier ages.[19]

The inclusion criteria were the availability of information on BMI at 7 and 13 years of age; information on examination date, age, BMI, intelligence-test score, and educational level in early adulthood; and being alive and not having a diagnosis of diabetes before 30 years of age (Fig. S1 in the Supplementary Appendix). Follow-up started on January 1, 1977, or at the age of 30 years, whichever came later, and ended on the date of a type 2 diabetes diagnosis, death, emigration, loss to follow-up, or December 31, 2015, whichever came first. The project was approved by the Danish Data Protection Agency.

STATISTICAL ANALYSIS

Overweight and obesity were defined in accordance with Centers for Disease Control and Prevention (CDC) age-specific and sex-specific criteria (for overweight, a BMI [the weight in kilograms divided by the square of the height in meters] of ≥17.38 at the age of 7 years, ≥21.82 at the age of 13 years, and ≥25 in early adulthood; for obesity, a BMI of ≥19.12 at the age of 7 years, ≥25.14 at the age of 13 years, and ≥28.31 in early adulthood).[20] Patterns of overweight were defined as combinations of weight status in childhood (7 years), adolescence (13 years), and early adulthood (17 to 26 years). BMI was also categorized into seven groups on the basis of BMI percentiles from the CDC.

Associations between overweight at each age or patterns of overweight and adult type 2 diabetes were estimated with hazard ratios and 95% confidence intervals calculated by means of Cox proportional-hazards regression with age used as the time scale. Analyses were performed with and without adjustment for intelligence-test score, education, and age at conscription examination. Potential interactions with these factors were analyzed in nested models with and without cross-product terms. On the basis of tests of assumptions for Cox regression models (see the Supplementary Appendix), all analyses were performed separately for the risk of diabetes at 30 to 60 years of age and at more than 60 to 76 years of age. All analyses were stratified according to year of birth. In a subdistribution hazard regression model of death as a competing risk, the estimates were essentially similar (Table S2 in the Supplementary Appendix).[21] Our study was sufficiently powered to detect modest effects (Table S3 in the Supplementary Appendix). We applied Bonferroni corrections for multiple testing to the analysis of the hazard ratios for the development of type 2 diabetes associated with different patterns of overweight by defining this analysis as a family of tests. All other inferences are presented without adjustment for multiplicity, since it did not alter our conclusions (data not shown).

RESULTS

OVERALL PATTERNS OF OVERWEIGHT

Among the 62,565 men included in the study, 6710 (10.7%) received a diagnosis of type 2 diabetes during 1,969,165 person-years of follow-up. The prevalence of overweight increased from 5.4% (3373 of 62,565) at 7 years of age to 8.2% (5108 of 62,565) in early adulthood (Table 1). As expected, overweight at any age was positively associated with the risk of type 2 diabetes (Table S4 in the Supplementary Appendix). Men who had been overweight in early adulthood had the highest incidence of type 2 diabetes (Table S5 in the Supplementary Appendix).

Men who had been overweight at 7 years of age but had had remission of overweight by 13 years of age and had remained at a normal weight as young men had a risk of having type 2 diabetes diagnosed at 30 to 60 years of age that was similar to that among men who had never been overweight (hazard ratio, 0.96; 95% confidence interval [CI], 0.75 to 1.21) (Fig. 1, and Table S2 in the Supplementary Appendix). Men who had been overweight only at 13 years of age or only at 7 and 13 years of age had a risk of having type 2 diabetes diagnosed at 30 to 60 years of age that was lower than that among men who had been persistently overweight but higher than that among men who had never been overweight (overweight only at 7 and 13 years of age vs. never overweight: hazard ratio, 1.47 [95% CI, 1.10 to 1.98]; persistently overweight vs. never overweight: hazard ratio, 4.14 [95% CI, 3.57 to 4.79]). Men who had been overweight at 13 years of age and in early adulthood had a risk of type 2 diabetes that was higher than that among men who had been overweight only as young adults and similar to that among men

Table 1. Patterns of Overweight and Body-Mass Index Values in the Study Population.*

Pattern of Overweight	No. of Men (%) (N=62,565)	Mean	Range
Overweight			
At age 7 yr	3,373 (5.4)		
At age 13 yr	3,418 (5.5)		
In early adulthood	5,108 (8.2)		
Pattern of overweight			
Normal weight at all ages	54,529 (87.2)		
BMI at age 7 yr		15.2±0.9	11.7–17.4
BMI at age 13 yr		17.6±1.5	12.5–21.8
BMI in early adulthood		21.0±1.8	14.2–25.0
Overweight only at 7 yr of age	1,437 (2.3)		
BMI at age 7 yr		17.9±0.5	17.4–22.4
BMI at age 13 yr		20.0±1.1	15.6–21.8
BMI in early adulthood		22.6±1.4	16.9–25.0
Overweight only at 13 yr of age	900 (1.4)		
BMI at age 7 yr		16.3±0.7	13.4–17.4
BMI at age 13 yr		22.8±1.0	21.8–28.2
BMI in early adulthood		23.0±1.3	17.3–25.0
Overweight only at 7 and 13 yr of age	591 (0.9)		
BMI at age 7 yr		18.5±1.0	17.4–24.5
BMI at age 13 yr		23.4±1.5	21.8–30.3
BMI in early adulthood		23.2±1.3	17.7–25.0
Overweight only in early adulthood	2,807 (4.5)		
BMI at age 7 yr		15.9±0.9	11.8–17.4
BMI at age 13 yr		19.7±1.4	13.5–21.8
BMI in early adulthood		26.5±1.6	25.0–38.5
Overweight only at 7 yr of age and in early adulthood	374 (0.6)		
BMI at age 7 yr		18.0±0.6	17.4–22.2
BMI at age 13 yr		20.8±0.8	17.3–21.8
BMI in early adulthood		26.7±1.8	25.0–36.9
Overweight only at 13 yr of age and in early adulthood	956 (1.5)		
BMI at age 7 yr		16.4±0.7	13.1–17.4
BMI at age 13 yr		23.4±1.3	21.8–29.6
BMI in early adulthood		27.9±2.5	25.0–39.3
Overweight at all ages	971 (1.6)		
BMI at age 7 yr		18.8±1.3	17.4–25.5
BMI at age 13 yr		24.5±2.2	21.8–35.1
BMI in early adulthood		28.6±3.0	25.0–41.6

* Plus–minus values are means ±SD. Overweight was defined with the use of age-specific cutoff values for body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) proposed by the Centers for Disease Control and Prevention for boys (for age 7 years, ≥17.38; 13 years, ≥21.82; and early adulthood, ≥25).

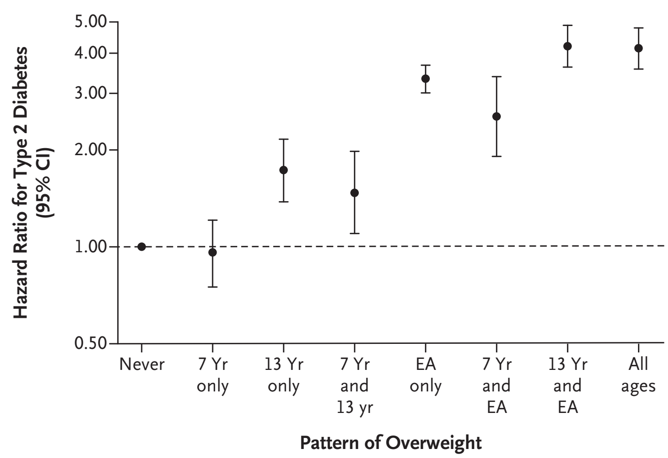

Figure 1. **Patterns of Overweight at 7 Years of Age, 13 Years of Age, and Early Adulthood (EA) and the Risk of Type 2 Diabetes at 30 to 60 Years of Age.**
In the calculation of hazard ratios for the development of type 2 diabetes, men who had not been overweight at any of the ages examined were used as the reference group. When Bonferroni corrections were applied, overweight only at the ages of 7 and 13 years was no longer significantly associated with an increased risk of type 2 diabetes (unadjusted P=0.01; number of tests, 7; P=0.07 with Bonferroni correction applied [7×0.01]), whereas all other significant associations remained significant. CI denotes confidence interval.

who had been overweight at all the ages examined. The relationships between patterns of overweight and the risk of having type 2 diabetes diagnosed after 60 years of age were similar to those described above, although for all patterns of overweight, the estimated risks were higher for a diagnosis before rather than after 60 years of age (Fig. 1, and Table S2 and Fig. S2 in the Supplementary Appendix). Intelligence-test scores and educational levels did not modify these associations (P>0.79 for all tests of interaction), and adjustment for these two variables and for age at conscription examination only minimally changed the results (Table 2, and Table S6 in the Supplementary Appendix).

Patterns of Overweight According to Percentile of BMI

Among the 2872 men who had been overweight (i.e., with a BMI in 85th to 94th percentiles) at 7 years of age, by early adulthood 1023 (35.6%) remained overweight or had become obese and 1849 (64.4%) had had remission of overweight (Table 3). Among the men who had had remission, those whose BMI had decreased to below the 75th percentile in early adulthood had risks of type 2 diabetes similar to those among men whose BMI had remained in the 25th to 49th percentiles, which indicated that the effects of overweight during childhood were reversible (Table 4). Increases in BMI between 7 years of age and early adulthood were associated with an increased risk of type 2 diabetes. Within adult BMI groups, there was a tendency for the risk of type 2 diabetes to be higher among men in whom the BMI had been lower at 7 years of age. Associations were similar for type 2 diabetes diagnosed before and after 60 years of age, although the associations were weaker at older ages (Table S7 in the Supplementary Appendix). Adjustment for intelligence-test scores, education, and age at conscription examination minimally changed the results (Tables S8 and S9 in the Supplementary Appendix).

Among the 501 men who had been obese at 7 years of age (BMI in the ≥95th percentile), by early adulthood 166 (33.1%) remained obese, 156 (31.1%) had become overweight, and 179 (35.7%) had a BMI within the normal range (Table 3). As compared with men who had been obese at all ages, those who reduced their BMI to overweight by early adulthood halved their risk of type 2 diabetes, and men who reduced their BMI to within the normal range had even lower risks. Among most groups, however, there were too few cases to reliably estimate risks (Table 4). Obesity in early adulthood was associated with very high risks of type 2 diabetes, irrespective of BMI at 7 years of age.

Discussion

This large-scale longitudinal study showed that men who had remission of overweight between 7 and 13 years of age and had subsequently maintained a normal weight in early adulthood had a risk of type 2 diabetes similar to that among men with normal weights at all of these ages. Men who had had remission of overweight between 13 years of age and early adulthood had a risk of type 2 diabetes that was higher than that among men who had never been overweight but lower than that among men who had been overweight at all the ages examined.

Thus, our data showed that in this study population, men who had been overweight in childhood had a lower risk of type 2 diabetes if they had had remission of overweight before puberty (i.e., before 13 years of age). Remission of overweight after that age but before early adulthood was associated with a risk of type 2 diabetes that was markedly lower than that among men who had been overweight at every age. Overweight around puberty and early adulthood was associated with higher risks of type 2 diabetes than was overweight only in early adulthood. Since overweight during puberty appears to be a particularly important factor involved in increasing the risk of type 2 diabetes in middle and late adulthood, normalization of BMI before these ages may reduce this risk.

The results of our study documenting changes in BMI throughout puberty based on measured weights and heights are supported by other studies, but direct comparisons are difficult.[4,5] Two other studies defined patterns of overweight during childhood and at two other ages.[4,5] However, one study included only women,[4] and the other lacked power to estimate associations with sufficient reliability.[5] Neither study examined risks beyond 58 years of age.[4,5] Those studies may have had bias due to the use of information reported by the participants and due to the use of overweight patterns that included adult BMI values measured close in time to the diagnosis of type 2 diabetes.[4,5] Other studies investigating whether child or adult BMI was a more important factor influencing the risk of type 2 diabetes in midlife have generally concluded that adult BMI matters more; however, those studies did not examine the effects of remission of overweight or obesity.[22-25] Thus, it has been unclear whether remission of overweight before puberty, a period suitable for preventive interventions in schools, could alter the positive association between childhood overweight and type 2 diabetes.

We found that men who had been obese at 7 years of age but only overweight in early adulthood had a risk of type 2 diabetes that was 3.5 times as high as that in men who had had stable BMIs in the 25th to 49th percentiles. Similarly, in a study involving a British cohort, remission of obesity between childhood (7 to 16 years of age) and adulthood (23 to 45 years of age) was associated with a risk of type 2 diabetes that was 5 times as high as that among persons who had never been obese.[8] In contrast, studies of remission of obesity between 4 to 19 years of age and adulthood have shown a nonsignificant difference in the risk of type 2 diabetes (relative risk, 1.3 [95% CI, 0.4 to 4.1][6]; odds ratio, 1.4 [95% CI, 0.7 to 2.8][7]). Conversely, we found that an increase in BMI between 7 years and early adulthood increased the risk of type 2 diabetes. Within adult BMI groups, the risk tended to be higher among men who had had a lower BMI at 7 years of age than among men in whom the BMI had remained stable, which suggested that size and weight-gain patterns matter. Our results are in accord with studies that have shown that extreme weight gains from early infancy onward increase the risk of type 2 diabetes.[26,27]

Table 2. Adjusted Model of Patterns of Overweight from Childhood to Early Adulthood and the Risk of Type 2 Diabetes at 30 to 60 Years of Age.*

Variable	No. of Cases	Hazard Ratio for Type 2 Diabetes (95% CI)
Pattern of overweight†		
Never	2798	Reference
7 yr only	70	0.99 (0.78–1.25)
13 yr only	78	1.70 (1.35–2.12)
7 and 13 yr only	45	1.51 (1.13–2.03)
Early adulthood only	451	3.24 (2.93–3.58)
7 yr and early adulthood only	48	2.55 (1.92–3.39)
13 yr and early adulthood only	186	3.87 (3.33–4.49)
All ages	191	4.00 (3.45–4.63)
Intelligence-test score‡		
Low	1604	Reference
Medium	1319	0.86 (0.80–0.93)
High	944	0.70 (0.63–0.77)
Education§		
Short	1204	Reference
Medium	1508	0.84 (0.78–0.91)
Long	1155	0.75 (0.67–0.83)
Age at conscription	3867	0.93 (0.91–0.95)

* Data were stratified according to year of birth; in total, there were 62,565 observations and 3867 cases of type 2 diabetes diagnosed between 30 and 60 years of age. CI denotes confidence interval.

† Overweight was defined with the use of age-specific cutoff values for BMI proposed by the Centers for Disease Control and Prevention for boys (for age 7 years, ≥17.38; 13 years, ≥21.82; and early adulthood, ≥25).

‡ The intelligence-test scores were divided into three strata according to percentile.

§ Education was defined as short (7 to 10 years of primary school, with or without finals), medium (skilled training in industry, trade, or craft), or long (9 to 12 years of middle and secondary school or higher education).

Table 3. Cases of Type 2 Diabetes According to BMI Percentile Group at 7 Years of Age and in Early Adulthood.

BMI Percentile at 7 Yr and Measure of Diabetes Incidence	BMI Percentile in Early Adulthood							Total
	<5th	5th–24th	25th–49th	50th–74th	75th–84th	85th–94th	≥95th	
<5th								
No. of cases/total no.*	44/638	111/1,193	77/692	44/272	9/52	5/29	1/4	291/2,880
Person-yr of observation	19,522	36,862	21,709	8512	1546	795	121	89,067
Cases/1000 person-yr (95% CI)	2.25 (1.68–3.03)	3.01 (2.50–3.63)	3.55 (2.84–4.43)	5.17 (3.85–6.95)	5.82 (3.03–11.19)	6.29 (2.62–15.12)	8.27 (1.17–58.72)	3.27 (2.91–3.67)
5th–24th								
No. of cases/total no.*	44/806	320/4,098	416/4,590	325/2,380	73/381	55/202	10/32	1243/12,489
Person-yr of observation	24,491	128,683	145,970	75,319	11,679	5683	905	392,730
Cases/1000 person-yr (95% CI)	1.80 (1.34–2.41)	2.49 (2.23–2.77)	2.85 (2.59–3.14)	4.32 (3.87–4.81)	6.25 (4.97–7.86)	9.68 (7.43–12.61)	11.05 (5.94–20.53)	3.17 (2.99–3.35)
25th–49th								
No. of cases/total no.*	15/315	260/3,511	615/7,269	682/6,200	226/1,310	166/624	41/113	2005/19,342
Person-yr of observation	9806	110,962	231,902	197,364	40,512	18,349	2886	611,781
Cases/1000 person-yr (95% CI)	1.53 (0.92–2.54)	2.34 (2.08–2.65)	2.65 (2.45–2.87)	3.46 (3.21–3.72)	5.58 (4.90–6.36)	9.05 (7.77–10.53)	14.21 (10.46–19.30)	3.28 (3.14–3.42)
50th–74th								
No. of cases/total no.*	5/75	92/1,456	354/5,267	789/8,050	349/2,453	300/1,403	99/317	1988/19,021
Person-yr of observation	2183	45,919	167,630	257,527	77,298	42,154	8586	601,297
Cases/1000 person-yr (95% CI)	2.29 (0.95–5.50)	2.00 (1.63–2.46)	2.11 (1.90–2.34)	3.06 (2.86–3.29)	4.52 (4.07–5.01)	7.12 (6.36–7.97)	11.53 (9.47–14.04)	3.31 (3.16–3.45)
75th–84th								
No. of cases/total no.*	2/6	11/151	56/795	219/2,310	165/1,159	151/816	70/223	674/5,460
Person-yr of observation	142	4706	25,287	73,209	36,413	24,677	6388	170,822
Cases/1000 person-yr (95% CI)	14.09 (3.52–56.33)	2.34 (1.29–4.22)	2.21 (1.70–2.88)	2.99 (2.62–3.42)	4.53 (3.89–5.28)	6.12 (5.22–7.18)	10.96 (8.67–13.85)	3.95 (3.66–4.26)

85th–94th								
No. of cases/total no.*	0/3	1/34	14/242	76/932	87/638	131/703	101/320	410/2,872
Person-yr of observation	83	1077	7714	29,179	20,036	21,727	8954	88,769
Cases/1000 person-yr (95% CI)	0.00	0.93 (0.13–6.59)	1.81 (1.07–3.06)	2.60 (2.08–3.26)	4.34 (3.52–5.36)	6.03 (5.08–7.16)	11.28 (9.28–13.71)	4.62 (4.19–5.09)
≥95th								
No. of cases/total no.*	0/1	1/3	1/18	5/79	7/78	33/156	52/166	99/501
Person-yr of observation	25	91	545	2483	2424	4679	4451	14,700
Cases/1000 person-yr (95% CI)	0.00	10.93 (1.54–77.61)	1.83 (0.26–13.02)	2.01 (0.84–4.84)	2.89 (1.38–6.06)	7.05 (5.01–9.92)	11.68 (8.90–15.33)	6.73 (5.53–8.20)
Total								
No. of cases/total no.*	110/1,844	796/10,446	1533/18,873	2140/20,223	916/6,071	841/3,933	374/1,175	6710/62,565
Person-yr of observation	56,254	328,300	600,757	643,592	189,907	118,064	32,290	1,969,165
Cases/1000 person-yr (95% CI)	1.96 (1.62–2.36)	2.42 (2.26–2.60)	2.55 (2.43–2.68)	3.33 (3.19–3.47)	4.82 (4.52–5.15)	7.12 (6.66–7.62)	11.58 (10.47–12.82)	3.41 (3.33–3.49)

* Data in this row are the number of cases of type 2 diabetes diagnosed between 30 and 76 years of age and the total number of men with the given BMI pattern.

We observed that men who had been obese during childhood but had had subsequent remission of obesity and had been overweight as young men had a considerably lower risk of type 2 diabetes than did persistently obese men. Furthermore, if the men had a normal weight by early adulthood, their risk of type 2 diabetes was similar to that among men who had had stable BMIs in the 25th to 49th percentiles. Our results show a graded and reversible effect of child overweight and obesity and indicate that patterns of increases in BMI matter, findings that support increased vigilance in men with large increases in BMI from childhood onward to mitigate the risk of type 2 diabetes.

Although the inverse association between socioeconomic status and the risk of type 2 diabetes in adult life has been well established,[11,12] previous studies of remission of overweight and type 2 diabetes did not examine potential interactions.[4-8] Our results apply to all levels of cognitive ability and socioeconomic status, since we did not find interactions with intelligence-test scores or education. Moreover, despite strong inverse associations between indicators of socioeconomic status and type 2 diabetes, which has also been reported in other studies,[6] our results suggest that overweight increases the risk of type 2 diabetes through pathways that are unrelated to intelligence or education, since adjustment for these factors only minimally changed our results.

It is biologically plausible that excess weight in childhood leads to type 2 diabetes through the early development of insulin resistance.[28] Unsurprisingly, we found stronger associations between patterns of overweight and type 2 diabetes that was diagnosed at 30 to 60 years of age than between patterns of overweight and type 2 diabetes that was diagnosed in late adulthood (>60 to 76 years of age). This difference is probably attributable to a decrease in the correlation between child BMI and adult BMI as adult age increases.[29] Moreover, aging processes may outweigh the effects of BMI on the risk of type 2 diabetes at older ages.

Our study has several strengths, including the large sample size and mandatory examinations with weight and height measured at all ages, which limited the potential for information biases associated with recall of childhood body size.[30] In addition, the men were followed until ages at which the incidence of type 2 diabetes is high

Table 4. BMI Percentiles at 7 Years of Age and in Early Adulthood and the Risk of Type 2 Diabetes at 30 to 60 Years of Age.*

BMI Percentile at 7 Yr	BMI Percentile in Early Adulthood						
	<5th	5th–24th	25th–49th	50th–74th	75th–84th	85th–94th	≥95th
	hazard ratio for type 2 diabetes (95% CI)						
<5th	0.96 (0.64–1.43)	1.23 (0.93–1.61)	1.68 (1.24–2.28)	2.21 (1.47–3.32)	3.98 (1.97–8.04)	—	—
5th–24th	0.71 (0.47–1.08)	1.01 (0.84–1.22)	1.16 (0.97–1.38)	1.98 (1.65–2.37)	3.50 (2.62–4.68)	5.38 (3.88–7.45)	6.46 (3.20–13.04)
25th–49th	0.44 (0.19–0.98)	0.88 (0.72–1.08)	Reference	1.38 (1.18–1.61)	2.77 (2.28–3.37)	4.72 (3.81–5.85)	8.74 (6.10–12.52)
50th–74th	—	0.73 (0.54–1.00)	0.84 (0.70–1.01)	1.24 (1.07–1.44)	1.98 (1.66–2.37)	3.59 (3.00–4.30)	7.32 (5.74–9.35)
75th–84th	—	0.97 (0.43–2.17)	0.88 (0.60–1.28)	1.30 (1.05–1.61)	2.10 (1.67–2.64)	3.17 (2.53–3.97)	6.19 (4.61–8.31)
85th–94th	—	—	1.06 (0.58–1.94)	1.15 (0.84–1.58)	1.84 (1.36–2.50)	3.09 (2.43–3.91)	7.46 (5.88–9.46)
≥95th	—	—	—	—	1.72 (0.77–3.87)	3.53 (2.29–5.44)	6.87 (4.95–9.52)

* Data were stratified according to year of birth; in total, there were 62,565 observations and 3867 cases. 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.

and for more than 18 years longer than in previous studies.[4-8]

Our study has certain limitations. Although midlife and later-life factors are important in the underlying causes of type 2 diabetes,[31] information on later-life BMI was unavailable; however, it may be a mediator rather than a confounder. Information on potential early-life explanatory factors, such as pubertal timing and parental social class, was not available. We do not have information available about what caused the weight changes and cannot preclude that it was disease-driven weight loss; however, such weight loss is very rare at these ages. Although the analysis of missing data showed some significant differences between the men who were included in our analysis and those for whom data were missing (Table S10 in the Supplementary Appendix), the absolute differences were small and were probably due to procedural factors rather than to selection bias.[15]

The fact that we used registry-based information on type 2 diabetes means that patients who were treated exclusively in primary care and persons who had not received a diagnosis were not included in our study. Whereas the completeness of the National Patient Register over a 5-year period is moderate (sensitivity, 64%), the positive predictive value of a diabetes diagnosis is very high (97%).[32] In the context of the Danish system, the long study period increases the likelihood of capturing cases, since most persons with type 2 diabetes eventually appear in the hospital register. However, the recorded age at diagnosis may be delayed to an unknown degree, because the age at the first hospital admission is used as a proxy for the age at onset. Moreover, BMI is a proxy for adiposity,[33] so we do not know whether the changes in the risk of type 2 diabetes are due to changes in lean mass or fat mass. Furthermore, we had no pertinent anthropometric data on women. However, two smaller studies showed no differences according to sex in associations between overweight patterns from childhood through adulthood and the risk of type 2 diabetes.[5,7] Whether there are sex-related differences in the risk of type 2 diabetes after changes in weight status during childhood and adolescence remains to be investigated.

In Denmark, it is legally required that all young men be examined for conscription when they turn 18 years of age.[15] Hence, our results are representative of Danish men born during the study period. Contemporary populations who are exposed to more obesogenic environments have a higher prevalence of overweight than our study population, and remission rates may be lower.[34] Nonetheless, because the associations we found between patterns of overweight and the risk of type 2 diabetes were strong and applied to all men regardless of their cognitive abilities or educational levels, it is likely that our results apply to contemporary children with overweight who have remission of overweight before early adulthood.

Our results suggest that the adverse effects of childhood overweight at 7 years of age on the risk of type 2 diabetes are reduced by remission of overweight before puberty and maintenance of a normal weight until early adulthood, whereas the adverse effects of obesity at 7 years of age or overweight at 13 years of age are only partly reversible. Moreover, overweight during the period spanning puberty, from 13 years of age to early adulthood, irrespective of overweight at 7 years, is associated with a higher risk of type 2 diabetes than is development of overweight by early adulthood.

The opinions, results, and conclusions reported in this article are those of the authors and are independent from the funding source.

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