

Supplementary Appendix

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Supplementary appendix

Change in overweight from childhood to early adulthood and type 2 diabetes

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Supplementary methods

Competing risk model analysis

The influence of competing risks due to death before a type 2 diabetes diagnosis was investigated in a sub-distribution hazard regression model.^{1,2} An updated outcome variable taking death into account (i.e. men censored from risk due to death) was created as: 0=no event, 1=case event, 2=death event.

The subdistribution hazard models were estimated using the *stcrreg* package in Stata 14 (StataCorp LP, College Station, Texas; www.stata.com). The hazard ratios obtained from the standard cause-specific Cox proportional hazards regression model and the subdistribution hazard ratios were virtually similar (Table S2). Thus, the two models lead to the same conclusions.

Note: Since the Cox regression stratification-option generally used for the analyses (allowing for strata-specific baseline hazards) was not available in the competing risk setting, we compared the results with those from a model that was not stratified by year-of-birth.

Testing of assumptions for the Cox regression models

First we tested the shape of the associations using a likelihood ratio test (linear vs. categorical BMI variables). These tests showed deviation from linearity. Therefore, we conducted the subsequent analyses based on a priori choices of BMI categorized into normal weight, overweight and obese and by categorizing BMI into 7 groups using CDC BMI percentiles (5th, 25th, 50th, 75th, 85th, 95th).

Second, we tested whether the proportional hazard assumption of the Cox model was fulfilled. To investigate potential non-proportionality we used several methods as each one gives a slightly different insight into how well the assumptions are fulfilled:

- Through a Cox regression model with a time-varying effect of overweight using the TVC option/stcox command.
 - o Results: The risk associated with overweight was attenuated with increasing age at diagnosis ($p < 0.0001$) for overweight (yes/no) at all ages.
- By letting the effects of the overweight patterns from ages 7 years and 13 years through early adulthood be constant within age-at-risk categories ($</>60$ years and by quartiles of the age-at-risk).

- Results: Likelihood ratio tests of interactions between the age categories and the overweight pattern from 7 years and 13 years through early adulthood were highly significant ($p < 0.0001$).
- We created graphs of the cumulative hazard from one weight category versus another for the overweight pattern from 7 years through early adulthood.
 - Results: These graphs showed that the slope changed at around age 60 years. Therefore, all analyses were performed separately for age-at-risk at 30-60 years and >60-76 years.

Note on statistical power

Due to the research question asked and the related analyses, several exposure groups who remitted from overweight or declined in BMI percentiles were expected to be protected against type 2 diabetes, and thus have a low number of type 2 diabetes cases. As seen in Table 3, there were few cases of type 2 diabetes in many of the groups that declined in BMI (lower left corner). This partly reflects that few boys declined a lot in BMI, but it also reflects that if they did, they rarely had a type 2 diabetes diagnosis. For instance, of the 932 men who were in the 85-94th percentile group at 7 years and in the 50-74th percentile group in early adulthood, only 76 men of 932 (8%) were later diagnosed with T2D, which is a similar proportion as the group of men who were stable in the 25–49th percentile group from childhood through adulthood.

To set the risk we found in perspective, we calculated least detectable effects (LDE) we could detect with our data with a power of 80%. In our case, these tests were post hoc, since we conducted a secondary analysis of an existing data source. Compared with the persistently normal weight men, the LDE based on the available number of cases among men with overweight at 7 years but not at later ages was a HR of 1.29 (or conversely a HR of 0.77) (Table S3). We also compared men with overweight at 7 years, but not at older ages, with men with persistent overweight. With our available number of cases we could detect a HR of 1.35 (or conversely a HR of 0.74).

In conclusion, we find that our derived LDEs indicate that our data had the potential to provide good power for detecting effects of a relatively modest size, especially for this kind of study where the purpose is to show reductions in risks.

Figure S1. Flow chart of eligible and included individuals in the study. BMI, body mass index; CSHRR, Copenhagen School Health Records Register; DCD, Danish Conscription Database.

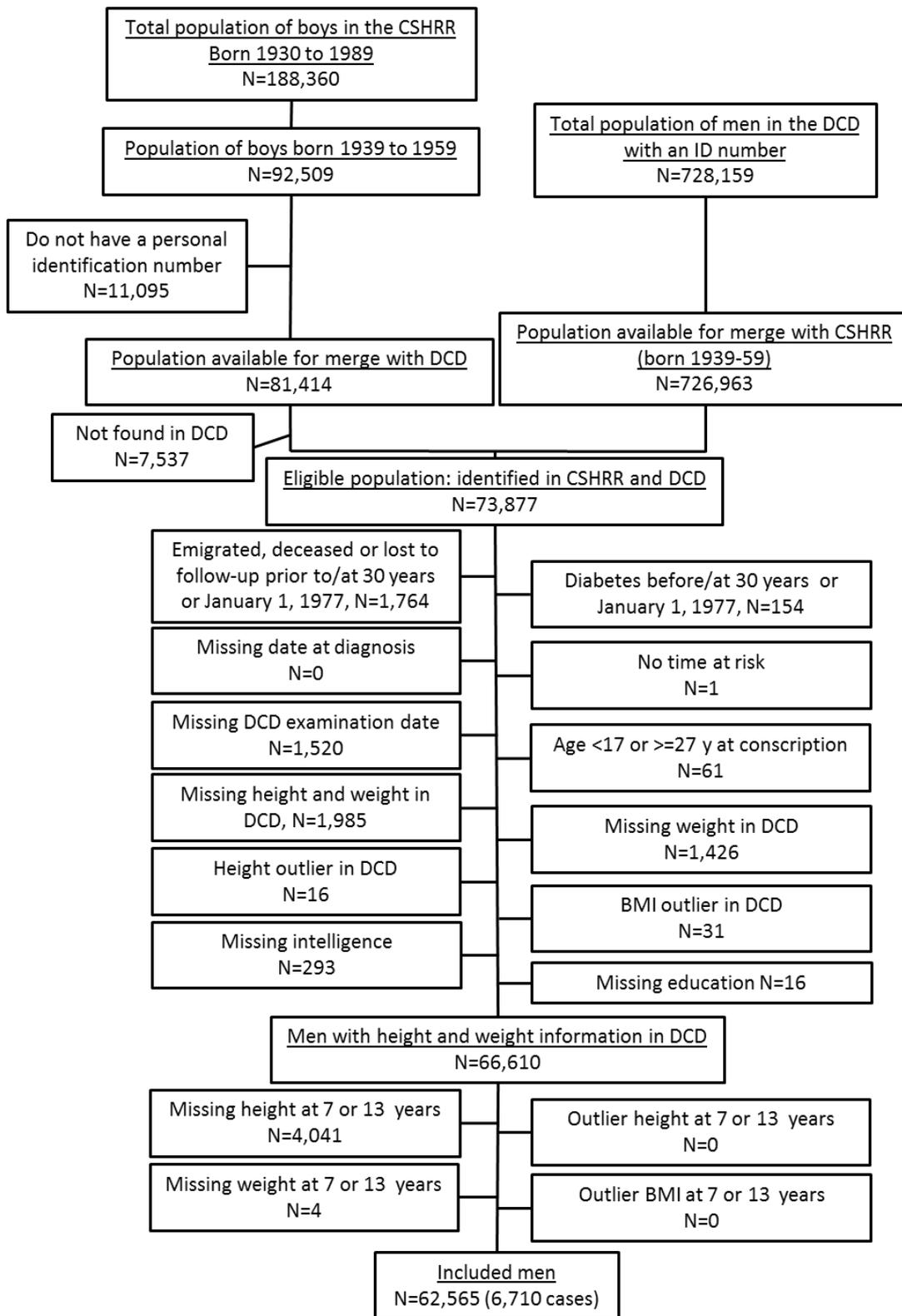
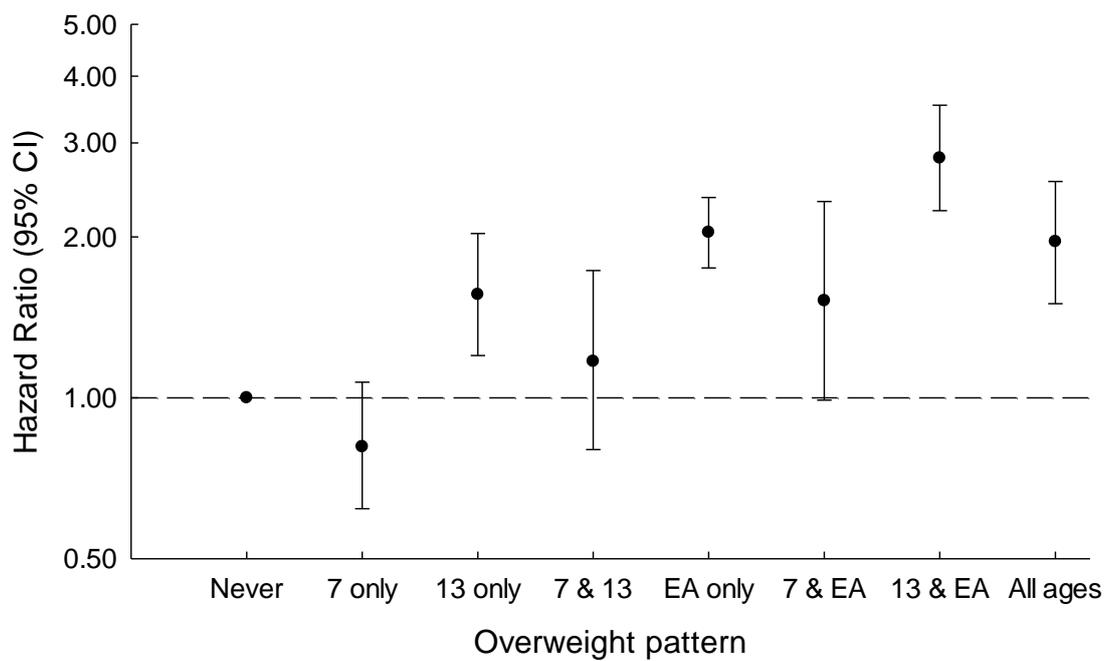


Figure S2. Overweight patterns from 7 through 13 years to early adulthood (EA) and risks of type 2 diabetes at ages >60-76 years.*



* When applying Bonferroni corrections all significant estimates remained so.

Table S1. Characteristics of the 62,565 men born between 1939 and 1959 included in this study

	n	Mean	SD	Range	
BMI					
Age 7 years	62,565	15.5	1.2	11.7	25.5
Age 13 years	62,565	18.1	2.1	12.5	35.1
Early adulthood	62,565	21.6	2.5	14.2	41.6
Intelligence test scores^a, n (%)		38.0	11.7	0	78
Low (scores: 0-32)	20,017 (32.0)				
Medium (scores: 33-43)	21,079 (33.7)				
High (scores: 44-78)	21,469 (34.3)				
Education^b, n (%)		3.7	1.4	1	6
Short	14,476 (23.1)				
Medium	22,833 (36.5)				
Long	25,256 (40.4)				
Age at conscription (years)	62,565	19.2	1.7	17.0	26.9

SD: Standard deviation

^a The intelligence test scores were divided into tertiles.

^b Education levels: Short: 7-10 years primary school with or without finals; medium: Skilled training in industry, trade and craft; and long: 9-12 years middle and secondary school, secondary school final, medium length or higher education.

Table S2. Overweight patterns from 7 through 13 years to early adulthood and risk of type 2 diabetes using the standard Cox proportional hazards regression model with or without stratification for year of birth and the subdistribution hazards model

Age at risk (years)	Overweight pattern ^b	Standard Cox regression with year-of-birth stratification	Standard Cox regression without year-of-birth stratification ^a	Subdistribution hazards model
		Hazard ratio (95% CI)	Hazard ratio (95% CI)	Subdistribution hazard ratio (95% CI)
30-60 ^c	Never	Reference	Reference	Reference
	7 years only	0.96 (0.75-1.21)	0.95 (0.75-1.21)	0.96 (0.76-1.21)
	13 years only	1.73 (1.38-2.16)	1.73 (1.38-2.16)	1.72 (1.37-2.15)
	7 and 13 years	1.47 (1.10-1.98)	1.49 (1.11-2.01)	1.51 (1.12-2.02)
	Early adulthood only	3.33 (3.01-3.67)	3.39 (3.07-3.75)	3.35 (3.04-3.71)
	7 years and early adulthood	2.54 (1.91-3.38)	2.58 (1.94-3.43)	2.63 (1.98-3.51)
	13 years and early adulthood	4.20 (3.62-4.88)	4.27 (3.68-4.95)	4.11 (3.54-4.77)
	7, 13 years and early adulthood	4.14 (3.57-4.79)	4.23 (3.65-4.90)	4.21 (3.63-4.88)
>60-76 ^d	Never	Reference	Reference	Reference
	7 years only	0.81 (0.62-1.07)	0.82 (0.62-1.09)	0.81 (0.61-1.07)
	13 years only	1.56 (1.20-2.03)	1.56 (1.20-2.03)	1.56 (1.19-2.03)
	7 and 13 years	1.17 (0.80-1.73)	1.17 (0.79-1.72)	1.14 (0.78-1.68)
	Early adulthood only	2.04 (1.75-2.37)	2.03 (1.75-2.36)	2.02 (1.74-2.35)
	7 years and early adulthood	1.52 (0.99-2.33)	1.52 (0.99-2.33)	1.46 (0.95-2.25)
	13 years and early adulthood	2.81 (2.24-3.53)	2.81 (2.24-3.52)	2.78 (2.21-3.50)
	7, 13 years and early adulthood	1.96 (1.50-2.54)	1.94 (1.49-2.52)	1.88 (1.44-2.44)

CI, Confidence intervals.

^a Not stratified by year of birth, since this option is not available in the subdistribution hazard model.

^b Overweight was defined using age-specific cut-points proposed by the Centers for Disease Control and Prevention for boys (age 7 years: BMI \geq 17.38, 13 years: BMI \geq 21.82 and in early adulthood: BMI \geq 25kg/m²).

^c 62,565 observations, 3,867 cases.

^d 43,091 observations, 2,843 cases.

Table S3. Least detectable effects

Reference	Exposure	N (reference + exposed)	Probability of event	SD	Estimated LDE (HR)	Alpha	Power
NW,NW,NW	OW, NW,NW	55,966	0.095	0.15	1.29	0.05	80
OW,OW,OW	OW, NW,NW	2,408	0.153	0.49	1.35	0.05	80

HR: Hazard ratio; LDE: least detectable effect; NW: Normal weight; OW: Overweight; SD: Standard deviation

Table S4. Overweight (yes/no) at 7 and 13 years and in early adulthood and risk of type 2 diabetes

Age	Age at risk (years) ^a	
	30-60 ^b	>60-76 ^c
	Hazard ratio (95% CI)	Hazard ratio (95% CI)
7 years	1.80 (1.61-2.01)	1.14 (0.97-1.34)
13 years	2.70 (2.46-2.96)	1.82 (1.58-2.09)
Early adulthood	3.52 (3.27-3.80)	2.10 (1.87-2.35)

CI, Confidence intervals.

^a Stratified by year of birth. Overweight was defined using age-specific cut-points proposed by the Centers for Disease Control and Prevention for boys (age 7 years: BMI \geq 17.38, 13 years: BMI \geq 21.82 and in early adulthood: BMI \geq 25kg/m²).

^b 62,565 observations, 3,867 cases.

^c 43,091 observations, 2,843 cases.

Table S5. Characteristics by overweight patterns from 7 through 13 years to early adulthood

Overweight patterns^a	N	Cases	Cumulative duration (person-years)	Incidence rates per 1000 person years
Never	54,529	5,169	1,727,220	2.99 (2.91-3.08)
7 years only	1,437	121	45,173	2.68 (2.24-3.20)
13 years only	900	134	27,932	4.80 (4.05-5.68)
7 and 13 years	591	71	18,485	3.84 (3.04-4.85)
Early adulthood only	2,807	635	83,069	7.64 (7.07-8.26)
7 years and early adulthood	374	69	11,528	5.99 (4.72-7.58)
13 years and early adulthood	956	263	27,475	9.57 (8.48-10.80)
7, 13 years and early adulthood	971	248	28,283	8.77 (7.74-9.93)
Total	62,565	6,710	1,969,165	3.41 (3.33-3.50)

^aOverweight was defined using age-specific cut-points proposed by the Centers for Disease Control and Prevention for boys (age 7 years: BMI \geq 17.38, 13 years: BMI \geq 21.82 and in early adulthood: BMI \geq 25kg/m²).

Table S6. Adjusted model of overweight patterns from 7 through 13 years to early adulthood and risk of type 2 diabetes at ages >60-76 years

Adjusted model	Cases	Hazard ratio (95% CI)^a
Overweight patterns^b		
Never	2,371	Reference
7 years only	51	0.83 (0.63-1.10)
13 years only	56	1.54 (1.18-2.01)
7 and 13 years	26	1.21 (0.82-1.78)
Early adulthood only	184	2.01 (1.73-2.33)
7 years and early adulthood	21	1.50 (0.97-2.30)
13 years and early adulthood	77	2.64 (2.10-3.31)
7, 13 years and early adulthood	57	1.87 (1.44-2.43)
Intelligence test scores^c		
Low (0-32)	1,156	Reference
Medium (33-43)	940	0.86 (0.79-0.95)
High (44-78)	747	0.77 (0.68-0.86)
Education^d		
Short	792	Reference
Medium	1,217	0.79 (0.72-0.86)
Long	834	0.65 (0.57-0.74)
Age at conscription (years)	2,843	0.95 (0.92-0.98)

CI, Confidence intervals.

^a Stratified by year of birth, 43,091 observations, 2,843 cases.

^b Overweight was defined using age-specific cut-points proposed by the Centers for Disease Control and Prevention for boys (age 7 years: BMI \geq 17.38, 13 years: BMI \geq 21.82 and in early adulthood: BMI \geq 25kg/m²).

^c The intelligence test scores were divided into tertiles.

^d Education levels: Short: 7-10 years primary school with or without finals; medium: Skilled training in industry, trade and craft; and long: 9-12 years middle and secondary school, secondary school final, medium length or higher education.

Table S7. BMI patterns from 7 years to early adulthood and risk of type 2 diabetes diagnosed at ages >60-76 years

		BMI groups by CDC percentiles ^a					
7 years	Early adulthood						
	<5 th	5-24 th	25-49 th	50-74 th	75-84 th	85-94 th	≥95 th
<5 th	0.95 (0.59-1.53)	1.25 (0.93-1.69)	1.12 (0.76-1.65)	1.97 (1.24-3.13)	- ^b	- ^b	- ^b
5-24 th	0.78 (0.50-1.23)	0.95 (0.78-1.15)	1.06 (0.88-1.26)	1.38 (1.13-1.70)	1.47 (0.93-2.34)	3.14 (1.84-5.36)	- ^b
25-49 th	0.90 (0.46-1.75)	0.93 (0.76-1.15)	Reference	1.27 (1.09-1.49)	1.64 (1.28-2.10)	2.80 (2.08-3.77)	3.97 (1.96-8.01)
50-74 th	2.70 (1.11-6.53)	0.85 (0.62-1.15)	0.76 (0.63-0.91)	1.05 (0.91-1.22)	1.52 (1.25-1.85)	2.25 (1.80-2.82)	2.48 (1.52-4.04)
75-84 th	- ^b	0.82 (0.34-1.99)	0.77 (0.52-1.14)	0.94 (0.75-1.18)	1.41 (1.08-1.83)	1.82 (1.35-2.46)	3.44 (2.14-5.54)
85-94 th	- ^b	- ^b	- ^b	0.86 (0.60-1.24)	1.47 (1.06-2.06)	1.70 (1.23-2.33)	1.75 (1.00-3.04)
≥95 th	- ^b	- ^b	- ^b	- ^b	- ^b	2.39 (1.31-4.36)	3.78 (2.07-6.91)

BMI, body mass index; CDC, Center for Disease Control and Prevention

^a Stratified by year of birth, 43,091 observations, 2,843 cases.

^b Hazard ratios were not calculated for these BMI categories owing to less than 5 events in these groups.

Table S8. Adjusted model of BMI patterns from 7 years to early adulthood and risk of type 2 diabetes diagnosed at ages 30-60 years

7 years	BMI groups by CDC percentiles ^a						
	<5 th	5-24 th	25-49 th	50-74 th	75-84 th	85-94 th	≥95 th
<5 th	0.98 (0.65-1.46)	1.23 (0.93-1.62)	1.67 (1.23-2.26)	2.34 (1.55-3.51)	4.01 (1.99-8.10)	- ^b	- ^b
5-24 th	0.73 (0.48-1.11)	1.01 (0.84-1.22)	1.15 (0.97-1.37)	2.00 (1.67-2.39)	3.56 (2.66-4.76)	5.15 (3.71-7.14)	6.66 (3.30-13.46)
25-49 th	0.47 (0.21-1.05)	0.88 (0.72-1.09)	Reference	1.39 (1.19-1.62)	2.77 (2.27-3.37)	4.57 (3.69-5.67)	8.13 (5.67-11.67)
50-74 th	- ^b	0.77 (0.56-1.05)	0.84 (0.70-1.01)	1.24 (1.07-1.44)	1.98 (1.66-2.37)	3.49 (2.92-4.18)	6.95 (5.44-8.89)
75-84 th	- ^b	1.03 (0.46-2.31)	0.93 (0.63-1.36)	1.30 (1.06-1.61)	2.08 (1.66-2.61)	3.12 (2.49-3.91)	5.90 (4.39-7.93)
85-94 th	- ^b	- ^b	1.14 (0.63-2.09)	1.19 (0.86-1.63)	1.85 (1.36-2.51)	3.06 (2.42-3.89)	7.13 (5.62-9.05)
≥95 th	- ^b	- ^b	- ^b	- ^b	1.92 (0.85-4.30)	3.55 (2.30-5.47)	6.79 (4.90-9.42)

BMI, body mass index; CDC, Centers for Disease Control and Prevention.

^a Adjusted for intelligence test scores, education and age at conscription examination. Stratified by year of birth, 62,565 observations, 3,867 cases.

^b Hazard ratios were not calculated for these BMI categories owing to less than 5 events in these groups.

Table S9. Adjusted model of BMI patterns from 7 years to early adulthood and risk of type 2 diabetes diagnosed at ages >60-76 years

7 years	BMI groups by CDC percentiles ^a						
	Early adulthood						
	<5 th	5-24 th	25-49 th	50-74 th	75-84 th	85-94 th	≥95 th
<5 th	0.96 (0.59-1.54)	1.26 (0.93-1.69)	1.11 (0.76-1.64)	2.07 (1.30-3.29)	- ^b	- ^b	- ^b
5-24 th	0.82 (0.52-1.29)	0.94 (0.78-1.15)	1.05 (0.87-1.25)	1.39 (1.13-1.70)	1.54 (0.97-2.45)	3.07 (1.80-5.26)	- ^b
25-49 th	0.95 (0.49-1.85)	0.94 (0.76-1.15)	Reference	1.27 (1.09-1.49)	1.63 (1.27-2.09)	2.75 (2.04-3.71)	3.44 (1.70-6.95)
50-74 th	2.93 (1.21-7.09)	0.87 (0.64-1.19)	0.75 (0.63-0.91)	1.04 (0.90-1.21)	1.50 (1.23-1.82)	2.18 (1.74-2.73)	2.37 (1.45-3.87)
75-84 th	- ^b	0.90 (0.37-2.17)	0.79 (0.54-1.18)	0.93 (0.74-1.17)	1.38 (1.06-1.80)	1.81 (1.34-2.44)	3.31 (2.06-5.34)
85-94 th	- ^b	- ^b	- ^b	0.88 (0.61-1.27)	1.46 (1.05-2.04)	1.64 (1.19-2.25)	1.60 (0.92-2.80)
≥95 th	- ^b	- ^b	- ^b	- ^b	- ^b	2.43 (1.33-4.44)	3.92 (2.15-7.16)

BMI, body mass index; CDC, Centers for Disease Control and Prevention

^a Adjusted for intelligence test scores, education and age at conscription examination. Stratified by year of birth, 43,091 observations, 2,843 cases.

^b Hazard ratios were not calculated for these BMI categories owing to less than 5 events in these groups.

Table S10. Specific test results and summary results of comparison of men who were excluded with those who were included

		Reason for exclusion									
		Not alive, emigrated or lost <30y or before January 1, 1977		Missing DCD date		Missing DCD-body size		Missing CSHRR- body size		All excluded	
N	%	1,764	2.4	1,520	2.1	3,411	4.6	4,045	5.5	11,321	15.3
Variables in analyses		P-value ^a	Difference ^b	P-value ^a	Difference ^b	P-value ^a	Difference ^b	P-value ^a	Difference ^b	P-value ^a	Difference ^b
Case-status		NA		0.17	-1.1%-point	0.63	-0.3%-point	0.04*	+ 1.0%-point	0.72	+0.1%-point
Z-Height at 7y		0.52	-0.02	0.04*	+ 0.05	0.73	-0.006	0.65	-0.01	0.72	-0.004
Z-BMI at 7y		0.23	0.03	0.004*	+ 0.07	0.42	+0.01	0.02*	+0.06	0.001*	+0.04
Z-Height at 13y		0.07	-0.05	0.007*	+ 0.07	0.96	-0.001	0.001*	-0.07	0.10	-0.02
Z-BMI at 13y		0.72	-0.01	0.08	+0.04	0.16	-0.02	<0.001*	-0.07	0.04*	-0.02
Height EA (cm)		0.07	-0.3	NA		<0.001*	-0.8	<0.001*	-0.4	<0.001*	-0.5
Z-BMI EA		0.74	-0.008	NA		NA		0.003*	-0.05	0.05*	-0.03
Education		<0.001*	Low edu. often excluded	NA		<0.001*	Low edu. often excluded	<0.001*	Low+high edu. often excluded	P<0.001*	Low+high edu. often excluded
Intelligence test score		<0.001*	- 1.0	NA		<0.001*	- 1.4	<0.001*	- 1.4	<0.001*	- 1.2
Summary – excluded vs. included		Not associated with body size.		Not associated with case status.		Not associated with case status or childhood body size. Excluded men had slightly lower education and intelligence scores. ^c		Slightly higher prevalence of T2D, slightly shorter and leaner in early adulthood and slightly lower intelligence test scores.		Not associated with case status or childhood height. Slightly heavier at 7 years, but slightly lighter at 13 years and in early adulthood, and slightly lower intelligence test scores ^c	

CSHRR: Copenhagen School health Record Register; DCD: Danish Conscription Database; EA: Early adulthood; edu: education; NA: not applicable.

* denotes p<0.05.

^a Chi-square test or linear regression. ^b Anthropometric variables in childhood and BMI in early adulthood included as z-scores.

^c Due to procedural reasons, weight was not systematically measured at all examinations in part of Western Denmark (Jutland). In this area, intelligence and education are generally lower than in the Eastern part of Denmark (Zealand, where the capital city, Copenhagen, is located)³

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