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The influence of birth weight and body mass in early adulthood on early coronary heart disease risk among Danish men born in 1953

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Abstract This study examines the joint and separate influence of birth weight and body mass in young adulthood on subsequent coronary heart disease (CHD) risk. A cohort of 9,143 men born in Copenhagen, Denmark, in 1953, for whom information on birth weight and body weight and height around age 19 years were retrieved from birth certificates and conscript records, respectively, were followed from 1978 until 2005 (between age 25 and 52 years) for incident fatal and non-fatal CHD. Data on CHD were obtained through record linkage to the Cause of Death Registry and the National Patient Registry. During follow-up, a total of 475 men had a CHD diagnosis. Men with low birth weight, high body mass index (BMI) at age 19, a father from the working class, and low educational level at age 19 had an increased risk for CHD. Birth weight was inversely associated with CHD only in men with BMI of 25 kg/m^2 or above. Adjustment for childhood social circumstances and educational status at age 19 had minor influence on the estimates. In conclusion, BMI in young adulthood seems to be strongly associated with the risk of CHD before age 52, and birth weight seem to modify the association. The risk estimates is highest for individuals with a combination of low birth weight and overweight in young adulthood.

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Abbreviations

CHD Coronary heart disease
BMI Body Mass Index

Introduction

A number of cohort studies have shown an inverse association between birth weight and coronary heart disease (CHD) [1–11], however, studies on the association of body weight in childhood and young adulthood with CHD risk are fewer and their results are diverse. Thus, in a Danish cohort of school children, higher BMI at age 7–13 years was associated with increased risk of CHD [11], while cohort studies from Finland [7] and UK [12] did not provide support for the contention that BMI in childhood is associated with future CHD risk [12]. Further, any effect modification by body proportion later in life on the weight-CHD risk association is unclear. In two studies from Finland [7, 8] and one from Hertfordshire, UK [1], low weight at age 1 year seemed to add to the increased risk of CHD associated with low birth weight in men. The studies from Finland also demonstrated that rapid increase in BMI from age 3 to 12 [7] or age 6 to 15 [8], respectively, was associated with an increased risk of CHD. The suggested mechanism for this association was that small babies who gain much weight later in childhood may have a disproportional high fat mass, which leads to insulin resistance. However, in the cohort of Danish school children [11], there was no statistical interaction between birth weight and BMI in childhood (7 through 13 years of age) on the

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risk of CHD in adulthood. Similarly, in a study from Aberdeen, UK, weight at school entry did not modify the inverse relation between birth weight and CHD risk [10]. However, it has not been investigated whether weight in young adulthood, influence the relation between birth weight and CHD.

In the present study, we use data from a population-based cohort with measures of birth weight and weight at to analyse the joint and separate influence of birth weight and BMI in young adulthood on the risk of fatal and non-fatal CHD, in Danish men born in 1953.

Material and methods

Study population

This birth cohort consists of all 11,532 men born in the Copenhagen metropolitan area, who were alive and living in Denmark in 1968, and for whom data from birth-certificates were abstracted in 1965 [13]. This information include birth weight and length, whether the child was a singleton or not, and fathers' occupational status at time of delivery. All Danish men are at age of 18 years required to register with the conscription board and undergo a health examination by a medical doctor [14]. In 2004, the results of these tests were collected manually from all Danish conscript district registers for the cohort members who were alive and living in Denmark in 1971. The median age of examination was 19 year among these men. A total of 2,389 cohort members were excluded from the analyses because they were twins or triplets ($n = 227$), had missing information on birth weight ($n = 396$) or BMI at conscription ($n = 1,566$), had died ($n = 113$) or emigrated ($n = 87$) before 1978 where follow-up started. Thus, the sample included in the analyses presented here consists of 9,143 men.

Assessment of variables

From the birth records, we used information on birth weight and father's occupational social class at the time of delivery. *Birth weight* was recorded in 100-g groups and was analysed as a continuous variable and initially in five categories (<2,500; 2,500–2,900; 3,000–3,400; 3,500–3,900; and 4,000+ g), respectively. The initial data analyses showed very equal estimates in the categories from 2,500 to 3,900 g, and consequently these categories were collapsed. *Father's occupation at participant's birth* was recorded in 23 categories and re-coded into three categories: self-employed/salaried employed/civil servants; unskilled/skilled workers; and unknown. Body height and weight at the conscript board examination was used for calculation of *Body Mass Index (BMI)* as weight in kg divided by height in meters squared. BMI was analysed in 4 categories: <20; 20–24.9; 25–29.9; and 30+ kg/m^2 and in z scores. Information on *Educational attainment* was also obtained from the conscript records. Since, in most cases, conscription occurs before entry to higher education, educational attainment was categorised into three groups, ranging from primary and lower secondary school (up to 9 years of schooling) to at least 'studenter' exam (equivalent to the British Advanced (A) level qualifications).

Assessment of outcome

The Metropolit cohort was linked with the Central Person Registry to determine the vital status of participants. If the person was not alive or no longer living in Denmark, we got information on date of death or date of emigration/disappearance. Since 1977, the National Patient Registry has computerized data on all admissions to somatic hospitals in Denmark. Information on date of admission to somatic hospital wards from 1978 to August 2005, and diagnosis on discharge for all hospital admissions, was obtained from this register. Furthermore, causes of death were identified from 1968 to January 2002 by record linkage with the Cause of Death Registry that unfortunately not was updated further than that.

Diagnoses were classified according to the 8th Revision of the International Classification of Diseases (ICD8) for the years from 1978 to 1993, and according to the 10th Revision (ICD10) from 1994 and onwards. Outcome of interest was defined as first hospital discharge or death from a main or contributory diagnosis of 410 to 414 (ICD-8) and I20–I25 (ICD 10).

Statistical analyses

Associations between birth weight and coronary heart disease were analysed using Cox's proportional hazards regression models with age as the underlying time scale. Entry time was age at 1.1 1978 (when the National Patient register was established), and the follow-up ended at the age of first admission for the outcome of interest, death from other causes ($n = 808$), emigration ($n = 306$), or January 1, 2005, whichever came first. Statistical interaction between birth weight and other covariates (BMI at conscription, father's social class and own education) was examined by adding an interaction term between birth weight and each covariate in the regression model. Models with and without the interaction term were compared using likelihood ratio tests. Proportionality assumptions were assessed by inspection of cumulative incident plots; and there was no evidence of any violation. All analyses were conducted using STATA version 8.0 (Stata corporation, Texas 2002).

Results

The 9,143 study participants contributed with 231,662 person-years of risk during the follow-up period. In total, 475 subjects were diagnosed with a first incident of fatal or non-fatal CHD, giving a rate of 19.5 per 10,000 person years (95% CI: 18.7–20.4). Of these, 41 had a fatal first CHD attack (33 died outside a hospital and 8 died within 28 days after the first diagnosis of CHD in the National Patient Register).

Table 1 shows the unadjusted associations between birth weight, BMI at age 19 years, father's occupational social class, and own education, respectively, and CHD. Birth weight displayed a U-shaped relation with risk of CHD, while BMI was associated with a gradually increasing risk of CHD. The estimate for BMI displayed a hazard ratio of 1.25 (1.15–1.34) for each unit increase in z-score. Children of working class fathers, or fathers with unknown occupation, were also at greater risk of CHD in adulthood, as compared to those who were self-employed/employee/civil servants. Moreover, men with lower educational attainment at age 19 had an increased risk of CHD. Although low birth weight and high BMI was associated with low socioeconomic status (Table 1), adjustment for father's occupational social class and educational attainment at conscription had very little impact on the associations. Tests for statistical interaction between BMI in four categories and birth weight in three categories were significant ($P < 0.01$). The number of cases in some of the strata was small but the estimates supported that the categories of BMI below 25 kg/m^2 or more, respectively, could be represented by one category as reported in Table 2. Birth weight was inversely associated with CHD risk ($P = 0.04$) in men with BMI equal to or above 25 kg/m^2. In men with BMI below 25 kg/m^2 at conscription, a birth weight of 4,000 g or more was associated with a significantly higher risk of CHD as compared to those with birth weights between 2,500 and 3,500 g (Table 2). All analyses were repeated for the 434 non-fatal CHD events, only. This gave risk estimates in a similar direction to those based on all incident events; and, although based on fewer cases, the Hazard Ration for non fatal CHD was 1.52 (1.01–2.28) for a birth weight below 2,500 g compared to birth weights between 2,500 and 3,900 g.

Table 1 Birth weight and young adult weight in relation to number of coronary heart disease (CHD) events at age 25–52 years, in 9,143 Danish men born in the metropolitan area of Copenhagen, in 1953

Characteristics	Number (%)	BW <2,500 (%)	BMI >25 (%)	CHD events	CHD rate per 10,000	Crude HR	Adjusted HR
Birth weight in kg							
<2,500 g	370 (4.0)		5.4	25	26.8 (18.1–39.7)	1.41 (0.97–2.11)	1.49 (0.99–2.23)
2,500–3,999 g	7,456 (81.5)		8.3*	370	19.5 (17.6–21.7)	1	1
4,000 g	1,317 (14.3)		12.3*	80	22.1 (19.2–29.7)	1.22 (0.95–1.56)	1.18 (0.92–1.52)
BMI in kg/m^2 at age 19							
<20	2,748 (30.0)	5.2		102	14.6 (12.4–17.8)	1	1
20–24.9	5,595 (61.2)	3.6*		300	21.4 (18.2–23.6)	1.44 (1.15–1.80)	1.44 (1.13–1.83)
25–29.9	687 (7.5)	2.5*		63	36.1 (28.2–46.3)	2.45 (1.79–3.36)	2.08 (1.54–2.79)
30–	113 (1.2)	2.7		10	35.3 (19.0–65.6)	2.48 (1.29–4.75)	2.44 (1.27–4.69)
z score						1.25 (1.15–1.34)	1.25 (1.14–1.36)
Father's occupational social class							
Self-employed/employee, civil servant	4,109 (44.9)	3.2	7.6	162	15.5 (13.2–18.1)	1	1
Skilled and unskilled worker	4,484 (49.0)	4.9*	9.8*	271	23.8 (21.1–26.8)	1.53 (1.26–1.86)	1.32 (1.07–1.63)
Outside/unknown	550 (6.0)	6.4*	9.1	42	31.0 (22.9–42.0)	2.10 (1.49–2.94)	1.76 (1.22–2.53)
Educational attainment at age 19							
Highest school exam	2,241 (24.5)	3.2	7.3	72	12.5 (9.8–15.7)	1	1
Secondary school	4,922 (53.8)	3.9	8.7	276	22.2 (19.5–24.8)	1.75 (1.35–2.27)	1.52 (1.16–2.01)
Basic school	1,910 (20.9)	5.5*	10.7*	127	26.6 (22.9–31.8)	2.14 (1.60–2.87)	1.77 (1.29–2.43)
Total	9,143			475	19.5 (18.7–20.4)		

95% Confidence intervals in parentheses

* $P < 0.05$ in chi-square test of marked category versus first variable category

Table 2 Adjusted[a] HR for coronary heart disease at age 25–52 years, in 9,143 Danish men, according to birth weight and to BMI at age 19

	Birth weight in g		
	<2,500	2,500–3,900	4,000+
BMI <25 kg/m^2 at age 19 years	1.21 (0.84–2.04)	1	1.38 (1.07–1.78)
	[22.6 (14.6–35.2)][b]	[17.9 (16.0–20.1)][b]	[24.5 (19.5–30.9)][b]
	[20; 350][c]	[310; 6838][c]	[72; 1155][c]
BMI ≥25 kg/m^2 at age 19 years	5.19 (2.13–12.62)	2.06 (1.56–2.71)	1.04 (0.52–2.14)
	[100.4 (41.8–241.2)][b]	[38.4 (29.2–49.6)][b]	[19.3 (9.6–38.6)][b]
	[5; 20][c]	[60; 618][c]	[8; 160][c]

95% Confidence intervals in parentheses

[a] Adjusted for father's social class at birth and educational level at age 19

[b] [Rate per 10,000 py]

[c] [Number of cases; number at risk]

Discussion

This study examined the association between birth weight and the risk of non-fatal and fatal CHD in early adulthood. The study showed that birth weight was inversely associated with CHD risk in men who had a BMI at age 19 years of 25 kg/m^2 or greater; while, for men with BMI less than 25 kg/m^2, the association seemed to be J-shaped. Adjustment for social circumstances during childhood and educational status at age 19 years had only a marginal influence on the estimates, suggesting that these did not explain the association. In accordance to the findings from a Danish cohort study of 276,835 school children aged 7 through 13 years of age, we found statistical evidence for a linear association between BMI at age 19 and CHD. Thus, we found an estimates for each unit increase in z-score of 1.25 (1.14–1.36), while the similar estimates for boys aged 13 years in the other Danish study was 1.20 (1.17–1.24) [11]. These finding contrasted to the findings in three cohort studies from the UK, where height and weight was measured at age 2–15, 9–18, and 16–22 years, respectively.

In an analysis with the three cohorts pooled, the adjusted hazard ratio pr SD increase in BMI was 1.09 (0.99–1.19). Some uncertainty remains because of the wide age range of the subjects. However, the relation between BMI and CHD risk did not vary by cohort or age.

Study strength and limitations

The present study includes all males born in a well-defined area (covering one-third of the Danish population) who survived to the age of 25 years. We had prospectively collected information on early life conditions and measures of BMI at the conscript board examination. By using the population-covering registers, we managed to get complete follow-up information for the period 1978–2005 (i.e., when participants were aged 25–52 years). We used both diagnoses from hospital discharge and death certificates, thus assuming that all new diagnoses of CHD were included. The age span of the men during the follow-up period (25–52 years) covered only the early coronary events. Misclassification (i.e., defining someone as not having CHD because they do not have a registered admission or cause of death) is likely to be infrequent and non-differential. We would also have liked more detailed data for some covariates. For instance, we had no information on gestational age in the birth register data, and thus could not take preterm birth into account. Further, we only had information on health behaviour for the 6,292 cohort members who participated in a follow-up survey in 2004. However, these data gave no evidence for a higher prevalence of ever smoking among those with the combination of high birth weight and BMI less than 25 kg/m^2 at age 19.

Our cohort consists of men only and therefore results are not necessarily generalisable to women. However, the larger Danish study suggest that for BMI the findings also apply to women [11].

Interpretation

The stronger association between low birth weight and risk of CHD among men with high BMI at age 19 is consistent with the findings in the two cohorts studies from Helsinki, Finland [7, 8], where weight gain in adolescence seemed to influence the relation between birth weight and CHD. The Finnish study suggests that the mechanism for the association works as follows: small babies who gain much weight later in childhood may have a disproportional high fat mass, which leads to insulin resistance. However, the large study among school children from Copenhagen showed no such interaction between birth weight and childhood BMI on the risk of CHD [11]. Among children born in Aberdeen, in the 1950s, BMI at school entry did not modify the inverse association between birth weight and CHD [10]. In that study, however, weight was only measured at around age 5. The findings in the present study are based on relatively few cases and might be due to chance. However, men with low birth weight and a high BMI at age 19 years might be those who experienced intrauterine growth retardation, partly due to maternal hypertensive disorder during pregnancy and, thus, might be genetically predisposed to CHD. Men with low birth weight and normal or low BMI at age 19, on the other hand, might be those who are genetically predisposed to a small body size. In line with the study from Finland [8], our study also suggests that men with a high birth weight (>4,000 g) but a BMI less than 25 kg/m^2 at age 19 are at greater risk of CHD. A decrease in relative weight between birth and young adulthood could reflect those who initiated smoking early in life, which might increase the risk of CHD later in adult life.

In conclusion, BMI in young adulthood seems to be strongly associated with the risk of CHD before age 52, and birth weight seem to modify the association. The risk estimates is highest for individuals with a combination of low birth weight and overweight in young adulthood.

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