Abstract

While it is well documented that elevated body weight in middle- and older-aged populations is associated with multiple morbidities, the influence of childhood body weight on health endpoints other than coronary heart disease is not well understood. Accordingly, using a subsample of 4620 participants (2288 women) in the Scottish Mental Survey of 1947, we examined the association between body mass index measured at 11 years of age and future risk of nine independent health endpoints as ascertained from national hospital admissions and cancer registers up to 2014 (up to age 77 years). While there was some evidence of a relation between elevated childhood body mass index and increased rates of peripheral vascular disease (hazard ratio per one standard deviation increase in body mass index; 95% confidence interval: 1.21; 1.07, 1.37) and smoking-related cancers (1.09; 1.01, 1.17), there was no apparent association with coronary heart disease, stroke (including ischaemic stroke), heart failure, nor carcinoma of the colorectum, stomach, lung, prostate, and breast. In conclusion, a link between childhood body weight and later morbidity was largely lacking in the present study.

Keywords: Body weight, body mass index, cancer, cardiovascular disease, cohort study, life course, morbidity

Abbreviations: BMI, Body Mass Index, CVD, Cardiovascular Disease, SMS1947, Scottish Mental Survey 1947

Introduction

It is now well documented that obesity in middle- and older-aged populations is associated with multiple morbidities, including coronary heart disease,[1;2] stroke[1;2] and selected cancers.[1;3] The rapid secular increases in obesity prevalence in childhood and early adulthood over the last three decades has now brought into sharp focus the potential deleterious impact on health of higher body weight earlier in life.

There is a strong *prima facie* case for weight in childhood having a long term influence on adult health. First, body mass index (BMI) 'tracks' across the life course such that overweight and obese children have an increased likelihood of becoming overweight and obese adults.[4] Given the established relation between adult BMI and chronic disease, it is plausible that childhood overweight may, directly or indirectly, exert a similar influence. Second, in cross-sectional studies of children, obesity has been shown to be associated with blood pressure and cholesterol,[5] both of which predict selected health endpoints, such as cardiovascular disease (CVD), in later life.[6;7] Despite this biological plausibility, as exemplified by recent systematic reviews,[8] the evidence base for a link between childhood overweight and adult health is comparatively modest and findings are often discordant across studies. Thus, while higher levels of pre-adult body mass index tend to be related to an increased risk of total mortality and coronary heart disease, findings for all strokes combined are less clear and there are currently too few studies of other common presentations of cardiovascular disease (e.g., stroke sub-types, heart failure, peripheral vascular disease) and cancer (e.g., colorectal, stomach) to draw any clear conclusions about their link with pre-adult body weight.

Methodological shortcomings also complicate interpretation of some existing findings. These include a small sample size resulting in endpoint rarity, few studies of women, and a reliance by

some investigators on the distant recall of early life weight by middle- and older-aged study members[9;10] rather than direct measurement in early life. Thus, in a systematic review of childhood weight and prostate cancer rate, studies using directly measured body mass index revealed stronger associations than those utilising self-recall.[11] It is also the case that most studies use a single endpoint as the outcome, rather than explore the influence of body mass index across a range of chronic diseases, so limiting insights into specificity of association which is key in establishing causality when using observational data.[12]

Using data from the Scottish Mental Survey of 1947 (SMS1947) we address this paucity of data and methodological concerns by relating direct measurement of body mass index when the study members were 11 years of age to an array of chronic diseases up to 67 years later in a well characterised, nationally representative cohort of men and women.

Methods

On 4th June 1947, investigators on the SMS1947 attempted to measure the intelligence of every 11 years old child who was attending school on that day in Scotland; 88% of children responded (N = 70,805).[13;14] A subgroup of study members – the '36-Day Sample' – comprising children born on the first, second, and third days of each month of 1936, were selected by the then Scottish Council for Research in Education for further research participation. These were representative of the full SMS1947 in terms of sex, geographical location, size of family, and cognitive score.[15] The present analyses, comprising 5083 children (2561 girls) from that period, excludes those born on the first day of the even numbered months of 1936 who went on to take part in a more intensive longitudinal survey (the '6-Day Sample'). Our revitalisation of the SMS1947 as a cohort study was approved by

the Scotland-A Research Ethics Committee, the National Health Service Scotland Privacy Advisory Committee, and the Confidentiality Advisory Group of the Health Research Authority.[16]

For each study member, a head teacher populated a questionnaire (known as the 'sociological survey') pertaining to each pupil's physical attributes and socioeconomic circumstances, including: physical disability, father's occupational level, number of people in their home, and the number of rooms. Physical disability was denoted by a history of chorea, congenital paralysis, defective vision, deafness, encephalitis, epilepsy, or meningitis. Room occupancy was computed by dividing the number of people living in the dwelling by the number of rooms. The father's or main guardian's occupation was coded into one of five social class categorisations,[17] ranging from professional (highest prestige) to unskilled. Height (inches) and weight (stone/pounds) were directly measured. Conversion to metric units allowed us to compute body mass index using the standard formulae (weight[kg]/height^2[m^2]).

Morbidity ascertainment

We electronically traced study members resident in Scotland using the National Health Service Central Register, with those who had migrated to England and Wales being located using the Medical Research Information Service Integrated Database and Administration System. For those individuals not automatically matched, a manual search was conducted. Morbidity was ascertained using linkage to two sources: hospital admissions records (Scotland: 1980-2014; England and Wales: 1997-2013), and cancer registrations (Scotland: 1980-2014; England and Wales: 1984-2013). Irrespective of database, we used the first diagnosis of disease in our analyses, categorising them according to the International Classification of Disease (version 9 or 10) (see tables 1 and 2 for codes). We also grouped malignancies into those to have a known association with cigarette

smoking[18;19] and, by inference, those with no such relationship. In so doing, we attempted to circumvent the problem of an absence of confounding data on smoking in this study.

Statistical analyses

Among the initial group of 5083 study participants, 4826 (95%) were traced. Comparing the traced and untraced groups, there was essentially no difference in body mass index (16.7 vs. 16.9 kg/m^2; p-value for difference=0.39) and other baseline characteristics. Exclusion of people with missing data for BMI or covariates resulted in an analytical sample of 4620 (2288 females). In the main analyses we divided the body mass index data into quarters with the lowest weight group utilised as the referent; we also computed morbidity risk for a one standard deviation higher body mass index value. Cox proportional hazards regression analyses,[20] with age in years as the time scale, was used to compute hazard ratios with accompanying 95% confidence intervals to estimate the relationship between childhood BMI and later risk of morbidity. Study members were censored at age at hospitalisation, or age by the end of follow up period – which ever occurred first. In preliminary analyses conducted separately for males and females there was no evidence that gender modified the link between BMI and the major causes of morbidity. As such, data were pooled. Hazard ratios were first adjusted for sex, and then included the additional covariates of fathers' occupation, occupancy rate, height, and physical disability. All analyses were undertaken using the Statistical Package for the Social Sciences for Windows version 21.0 (IBM Corp., Armonk, NY).

Results

A maximum of 67 years of follow-up of the 4620 study members gave rise to 1778 (38.6%) CVD-related hospital admissions and 981 (21.3%) cancer diagnoses. In table 1 we present the association between childhood BMI and different CVD presentation. Childhood weight was essentially unrelated to risk of total CVD, coronary heart disease, myocardial infarction, stroke (including

ischaemic stroke), and heart failure. Peripheral vascular disease risk was elevated in the higher BMI category (fully adjusted hazard ratio for a one standard deviation higher BMI; 95% confidence interval: 1.21; 1.07, 1.37).

The results of the analyses for childhood BMI and subsequent risk of cancer are depicted in table 2. There were no apparent associations of weight with malignancy which included all cancers combined, colorectal, breast (women only), prostate, stomach and non-smoking related cancers. The only exception was smoking-related cancers where BMI was positively related to disease risk in selected analyses (1.09; 1.01, 1.17).

Discussion

Taking the results from the present study together, the main finding was that there was little evidence of a clear relationship between BMI measured at 11 years of age and nine independent morbidities assessed up to 67 years later. The occasional positive results that were apparent – smoking-related cancers and peripheral vascular disease – may have been generated by chance alone given the large number of models necessarily conducted in the course of our analyses.

Comparison with other studies

Our results accord with some existing findings. A systematic review in which the authors stratified studies into age at BMI assessment (<7, 7-17, 18-30 years) found that the positive relation with coronary heart disease was strongest in the older group (7 studies) and null in the youngest (3 studies), while the aggregated result in the intermediate age group (7 studies) for a one standard deviation increase in BMI (1.09; 1.00, 1.07) somewhat resembles our own (1.00; 0.94, 1.07).[21] In a separate review of eight studies featuring stroke as the outcome of interest,[8] in three studies null results were seen in keeping with our own. To the best of our knowledge, ours is the first

examination of the link between childhood BMI and other presentations of CVD, particularly heart failure and peripheral vascular disease. A few studies suggest a positive association between childhood BMI and colorectal cancers,[22;23] but null results have also been reported,[24] as they have for lung cancer.[23] The mean and standard deviations for BMI herein approximate those in other studies of similar era and age at BMI assessment,[25] including samples drawn from the UK.[26;27] These studies also revealed positive relations with coronary heart disease, therefore it is perhaps unlikely to be the narrow distribution of BMI in our cohort members, one that is very lean by more contemporary standards, that is responsible for the negative results.

Strengths and limitations

Although the present study has a series of strengths, including the unusually comprehensive range of health endpoints, the direct measurement of childhood BMI rather than adult recall, the high proportion of original study members traced, and the utilisation of a nationally-representative sample, it is of course not without its weaknesses. The previously described tracking of BMI between childhood and adulthood means that the apparent increased rates of peripheral vascular disease in study members with higher weight in early life may instead be ascribed to adult overweight. We had no repeat measurement of body mass index with which to test this hypothesis. Although we were able to analyse the relation of BMI with an array of health outcomes, there were too few cancer events to facilitate analyses for selected malignancies such as head and neck, and pancreatic. A further explanation for our generally negative results is that, unlike other published analyses, we utilised non-fatal endpoints only. However, there is evidence that, for at least BMI measured in middle-aged, similar findings are apparent for both CVD[28] and cancer[29] irrespective of whether the outcome is incidence (non-fatal events) or mortality. Consistent with our various ethical agreements, the morbidity and mortality data have been merged separately with the early life data, creating two distinct datasets. As such, it is not possible for us to ascertain if there is a different

relation of pre-adult BMI with the onset of a first event via hospitalisation (aetiology) or survival from it (prognosis). It is also the case that if an obese adult, who was also obese in childhood, died suddenly, without any recorded morbidities, that person might contribute to the finding of no association between childhood obesity and later morbidity risk. Again, however, the absence of linked morbidity and mortality data does not facilitate scrutiny of this hypothesis.

In conclusion, a link between pre-adult body weight and later morbidity was largely lacking in the present study.

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Table 1. Hazard ratios (95% confidence intervals) for the relation of childhood body mass index to cardiovascular disease diagnoses in the 1947 Scottish Mental Survey (1947-2014)

CVD event and model	BMI Quartile[a]								P value [trend]	HR per 1 SD increase in BMI	
	1 (*n* = 1,162)		2 (*n* = 1,152)		3 (*n* = 1,162)		4 (*n* = 1,144)				
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI		HR	95% CI
All CVD[b] (*n* = 1778)	38.6[c]		39.0		37.8		38.5				
Adjusted for sex	1.0	(Ref)	1.02	0.89, 1.16	0.97	0.85, 1.10	1.01	0.89. 1.15	0.95	1.02	0.97, 1.06
Adjusted for multiple covariates[d]	1.0		1.03	0.90, 1.17	0.97	0.85, 1.11	1.00	0.88, 1.14	0.80	1.01	0.97, 1.06
All Coronary Heart Disease[e] (*n*=920)	20.7		20.2		19.1		19.6				
Adjusted for sex	1.0		0.98	0.82, 1.17	0.91	0.76, 1.10	0.94	0.78, 1.12	0.35	1.01	0.94, 1.07
Adjusted for multiple covariates	1.0		0.98	0.82, 1.18	0.90	0.75, 1.09	0.94	0.78, 1.13	0.36	1.00	0.93, 1.07
Myocardial Infarction[f] (*n* = 383)	9.4		8.8		7.4		7.6				
Adjusted for sex	1.0		0.93	0.71, 1.22	0.77	0.58, 1.03	0.80	0.60, 1.06	0.065	0.97	0.88, 1.07
Adjusted for multiple covariates	1.0		0.94	0.71, 1.23	0.78	0.59, 1.03	0.81	0.61, 1.08	0.072	0.95	0.85, 1.06
All stroke[g] (*n* = 420)	9.9		9.7		8.0		8.7				
Adjusted for sex	1.0		0.99	0.76, 1.28	1.12	0.85, 1.47	0.91	0.69, 1.21	0.18	0.98	0.89, 1.08
Adjusted for multiple covariates	1.0		0.99	0.76, 1.28	0.80	0.61, 1.06	0.89	0.68, 1.17	0.20	0.99	0.90, 1.09
Ischaemic stroke[h] (*n* = 130)	2.8		3.5		2.8		2.2				
Adjusted for sex	1.0		1.27	0.80, 2.02	1.03	0.63, 1.68	0.79	0.47, 1.34	0.30	0.94	0.79, 1.13
Adjusted for multiple covariates	1.0		1.27	0.80, 2.03	1.05	0.65, 1.71	0.81	0.48, 1.36	0.33	0.94	0.78, 1.13
Peripheral vascular disease[i] (*n* = 191)	3.0		4.4		4.1		5.0				
Adjusted for sex	1.0		1.48	0.97, 2.28	1.38	0.89, 2.13	1.67	1.10, 2.55	0.033	1.21	1.07, 1.36
Adjusted for multiple covariates	1.0		1.49	0.97, 2.29	1.37	0.89, 2.13	1.71	1.12, 2.61	0.026	1.21	1.07, 1.37
Heart failure[j] (*n* = 314)	6.7		6.4		6.8		7.3				
Adjusted for sex	1.0		0.95	0.69, 1.31	1.00	0.73, 1.37	1.09	0.80, 1.48	0.55	1.10	0.99, 1.22
Adjusted for multiple covariates	1.0		0.96)	0.70, 1.32	0.98	0.72, 1.35	1.09	0.80, 1.48	0.58	1.10	0.98, 1.22

Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; CVD, Cardiovascular Disease; HR, Hazard Ratio; ICD, International Classification of Diseases; SD, Standard Deviation

[a] Range for ascending BMI (kg/m^2) quartiles for men (women): <15.85 (<15.46); 15.86-16.70 (15.46-16.38); 16.71-17.60 (16.39-17.51); ≥17.61 (17.52)

[b] ICD-10 codes for all CVD are I00.0-I78.9, I10X, I38X, I48X, I64X, G45.0-G45.9.

[c] Values are presented as percentages

[d] Adjustments were made for sex, occupancy rate, father's SES, height, and physical disability

[e] ICD-10 codes I11.0-I11.9 and I20.0-I25.9

[f] ICD-10 codes I21.0-I22.9

[g] ICD-10 codes I60.0-I69.9 and G45.0-G45.9

[h] ICD-10 codes I63.0-I63.9

[i] ICD-10 code I73.9

[j] ICD-10 codes I50.0-I50.9

Table 2. Hazard ratios (95% confidence intervals) for childhood body mass index in relation to selected cancer diagnoses in the 1947 Scottish Mental Survey (1947-2014)

Cancer diagnosis and model	BMI Quartile[a]								P value [trend]	HR per 1 SD increase in BMI	
	1 (*n* = 1,162)		2 (*n* = 1,152)		3 (*n* = 1,162)		4 (*n* = 1,144)				
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI		HR	95% CI
All malignant neoplasms[b] (*n* = 981)	20.5[c]		20.4		22.5		21.5				
Unadjusted	1.0	(Ref)	1.00	0.83, 1.19	1.11	0.93, 1.33	1.07	0.89, 1.28	0.29	1.05	0.98, 1.11
Adjusted for multiple covariates[d]	1.0		1.00	0.84, 1.20	1.10	0.92, 1.31	1.06	0.88, 1.26	0.37	1.06	1.00, 1.13
Breast,[e] females (*n*=150)	7.1		6.4		4.1		6.5				
Unadjusted	1.0		0.90	0.59, 1.39	0.57	0.35, 0.92	0.93	0.61, 1.42	0.37	1.02	0.88, 1.18
Adjusted for multiple covariates	1.0		0.88	0.57, 1.36	0.58	0.35, 0.94	0.97	0.63, 1.49	0.51	1.03	0.88, 1.20
Prostate[f] (*n* = 109)	4.0		4.4		6.04		3.2				
Unadjusted	1.0		1.09	0.64, 1.88	1.50	0.90, 2.49	0.80	0.44, 1.43	0.82	0.96	0.78,1.17
Adjusted for multiple covariates	1.0		1.10	0.64, 1.90	1.48	0.89, 2.46	0.79	0.44, 1.42	0.82	0.97	0.80, 1.18
Colorectal[g] (*n* = 127)	2.7		3.0		2.5		2.8				
Unadjusted	1.0		1.14	0.70, 1.85	0.94	0.56, 1.55	1.05	0.64, 1.72	0.95	0.99	0.84, 1.18
Adjusted for multiple covariates	1.0		1.15	0.71, 1.86	0.92	0.55, 1.53	1.02	0.62, 1.68	0.85	1.01	0.85, 1.20
Stomach[h] (*n* = 49)	1.2		1.3		1.1		0.6				
Unadjusted	1.0		1.08	0.52, 2.24	0.93	0.44, 1.98	0.51	0.21, 1.26	0.15	0.82	0.61, 1.11
Adjusted for multiple covariates	1.0		1.09	0.52, 2.26	0.96	0.45, 2.04	0.53	0.21, 1.31	0.18	0.80	0.58, 1.11
Lung[i] (*n* = 192)	3.5		4.0		4.9		4.2				
Unadjusted	1.0		1.13	0.74, 1.78	1.40	0.94, 2.09	1.20	0.79, 1.81	0.26	1.11	0.97, 1.26
Adjusted for multiple covariates	1.0		1.14	0.75, 1.73	1.38	0.92, 2.06	1.21	0.80, 1.84	0.25	1.12	0.98, 1.29
Smoking-related[j] (*n* = 633)	12.4		13.2		15.0		14.2				
Unadjusted	1.0		1.07	0.85, 1.34	1.23	0.99, 1.53	1.17	0.93, 1.46	0.091	1.07	0.99, 1.15
Adjusted for multiple covariates	1.0		1.07	0.85, 1.35	1.20	0.97, 1.50	1.17	0.93, 1.46	0.11	1.09	1.01, 1.17
Non-smoking-related (*n* = 384)	8.8		8.2		8.3		7.9				
Unadjusted	1.0		0.94	0.71, 1.24	0.95	0.72, 1.25	0.90	0.68, 1.19	0.48	0.97	0.88, 1.07
Adjusted for multiple covariates	1.0		0.94	0.71, 1.24	0.94	0.71, 1.24	0.88	0.66, 1.17	0.42	0.97	0.88, 1.08

Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; CVD, Cardiovascular Disease; HR, Hazard Ratio; ICD, International Classification of Diseases; SD, Standard Deviation

[a] Range for ascending BMI (kg/m^2) quartiles for men (women): <15.85 (<15.46); 15.86-16.70 (15.46-16.38); 16.71-17.60 (16.39-17.51); ≥17.61 (17.52)

[b] ICD-10 codes for all malignant neoplasms are C000-C439, C450-C979

[c] Values are presented as percentages

[d] Adjustments were made for sex, occupancy rate, father's SES, height, and physical disability.

[e] ICD-10 codes are C500-C509

[f] ICD-10 codes are C610-C619 and C61

[g] ICD-10 codes are C180-C218

[h] ICD-10 codes are C160-C169

[i] ICD-10 codes are C330-C349

[j] Categorisation based on existing knowledge about tobacco-related malignancies[18;19]