Lifelong patterns of BMI and cardiovascular phenotype in individuals aged 60–64 years in the 1946 British birth cohort study: an epidemiological study

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Lancet Diabetes Endocrinol 2014; 2: 648–54

Published Online May 21, 2014 http://dx.doi.org/10.1016/S2213-8587(14)70103-2

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Summary

Background Excess body fat is associated with an increase in risk of type 2 diabetes and hypertension in adulthood and these risks can adversely affect progression of arterial disease. We aimed to assess the impact of lifelong patterns of adiposity on cardiovascular risk factors and carotid intima media thickness (cIMT) in later life in participants in the 1946 British birth cohort study.

Methods The National Survey of Health and Development Study was a nationally representative sample of 5362 singleton births to married parents in England, Scotland, and Wales, stratified by social class, during 1 week in March 1946. Our present study is based on the 60% of participants still alive and with a known present address in England, Scotland, or Wales who attended a clinic assessment after invitation aged 60–64 years. We included participants with lifetime adiposity measures, cardiovascular risk factors, and cIMT measured at 60–64 years. Participants were classified as normal weight or overweight or obese at each age (36, 43, 53, and 60–64 years) in adulthood, and childhood overweight was defined. Patterns of BMI change were identified and we used BMI to define adiposity status. We used multivariable linear regression to establish the cross-sectional association of BMI category at age 60–64 years with cIMT, adjusted for various confounders.

Findings We included 1273 (45%) of 2856 participants eligible in 2006–10 (at age 60–64 years) in this study. Compared with normal weight, overweight and obesity were associated with higher cIMT (0·029 mm, 95% CI 0·014–0·043) and systolic blood pressure (7·95 mm Hg, 5·86–10·0). Increased cIMT, systolic blood pressure, leptin, prevalence of diabetes, and reduced adiponectin were all associated with duration of exposure to adult adiposity ($p<0·0001$ for all). We noted little additional effect of childhood overweight. Individuals who dropped a BMI category in adulthood had lower cIMT (–0·034 mm, –0·056 to –0·013) and leptin concentrations (–0·4 ng/mL, –0·47 to –0·32), even when this change was not maintained, than did those who never lost weight.

Interpretation Longer exposure to high adiposity in adulthood had a cumulative adverse effect on cardiovascular phenotype in later life. Reductions in BMI category, even if not sustained, were associated with decreases in cIMT and improvements in cardiovascular risk-factor profile, suggesting that weight loss, at any age in adulthood, is worthwhile because it might result in long-term cardiovascular benefit.

Funding Medical Research Council and the British Heart Foundation.

Introduction

The upward trend in prevalence of overweight and obesity is a worldwide problem and is estimated that about 1 billion people are now overweight and more than 300 million people are obese.[1,2] Excess body fat is associated with increased risk of type 2 diabetes and hypertension in adulthood, and accumulating evidence shows that these risks adversely affect progression of arterial disease.[1,3–7] Reductions in weight achieved by lifestyle interventions have been associated with improvements in cardiovascular risk factors,[8,9] although not necessarily with cardiovascular outcomes.[10] However, sustained weight loss is challenging and most people maintain or regain their overweight or obese status in the long term.[11]

The Medical Research Council National Survey of Health and Development (NSHD) study, established at the beginning of the modern welfare state, is the longest prospective British cohort study to provide information about developmental and environmental influences from birth through to early old age. The cohort underwent detailed cardiovascular phenotyping between the ages of 60 and 64 years, which provided a unique opportunity to assess the effect of lifetime exposure to adiposity on cardiovascular risk factors and arterial phenotype at this age. The many recordings of weight and BMI obtained over the lifecourse of patients in the NSHD study enabled us to investigate the effect of lifetime patterns of weight change, and specifically, to examine any cardiovascular health benefit from reduction in BMI at different ages.

Methods

Study design and participants

The NSHD study was a nationally representative sample of 5362 singleton births to married parents in England, Scotland, and Wales, stratified by social class, during

1 week in March 1946. The cohort has been followed-up 23 times since birth.[12] Study members still alive and with a known present address in England, Scotland, or Wales were invited for either an assessment at one of six clinical research facilities or for home visitation from a research nurse at the ages of 60–64 years. Our present study is based on the 60% of participants who attended for a clinic assessment. Participants in this study had some differences in their clinical characteristics compared with the original cohort, with lower levels of adiposity and lifetime smoking exposure, and higher levels of physical activity.[13,14]

Ethics approval was obtained from the Greater Manchester and the Scotland Research Ethics Committees. Participants provided written informed consent.

Procedures

We measured carotid intima media thickness (cIMT) in the right and left common carotid artery of participants using a high resolution scanner (Vivid I [12MHz probe]; GE Healthcare).[15] 10s cineloops were recorded in Digital Imaging and Communications in Medicine format and downloaded for offline analysis in the core laboratory (Vascular Physiology Unit, University College of London) with the Carotid Analyser software package (version 5.8.1). Three end-diastolic frames from the lateral views were analysed for mean cIMT. All images were analysed by two trained readers who were masked to participants' characteristics; intra-reader and inter-reader reproducibility were assessed on a subset of ten randomly selected images. Intra-class and inter-class correlations were more than 0·9. Carotid plaques were defined as cIMTs of greater than 1·5 mm, with abnormal shape, and with an abnormal wall texture. In 13 people, carotid plaque was identified in the area where the cIMT measurement was done and cIMT measurements were unreliable, so they were excluded from the analysis.

Weight and height were measured during childhood (at ages 2, 4, 6, 7, and 11 years) and adulthood (at ages 36, 43, 53 and 60–64 years): BMI was calculated as weight (kg) divided by height (m²). Waist circumference was measured at the same ages in adulthood. BMI was used to define adiposity status (BMI <25 kg/m² normal weight, 25–29 kg/m² overweight, and ≥30 kg/m² obese) at each age in adulthood. Adults who did not have BMI recorded were not included in the longitudinal analysis. In childhood, overweight and obesity were defined with age-specific and sex-specific BMI thresholds proposed by the International Obesity Taskforce.[16] Participants were defined as overweight or obese in childhood if their BMI was in that category on at least one of the five measurements in childhood.

Blood pressure was measured twice at ages 36, 43, 53, and 60–64 years, with the participant in a seated position. We used the second reading for the analysis. Hypertension in adulthood was defined as a blood pressure of 140/90 mm Hg or more. We classed people as ever hypertensive if their blood pressure had been greater than 140/90 mm Hg at any time since age 36 years. We identified smoking status from self-reported questionnaires completed between ages 60 and 64 years; individuals were categorised into present smokers, ex-smokers, and non-smokers. Participants were asked if they were receiving lipid or blood-pressure-lowering drugs.

Non-fasting blood samples were obtained during home visits at age 53 years and overnight fasting blood samples were obtained at age 60–64 years.[12] Details of the biochemical assay used to estimate total cholesterol, HDL cholesterol, and triglycerides have been previously published.[17] HbA_{1c} was measured with high-performance liquid chromatography using the Tosoh A1c 2.2 analyser (Tosoh, Tokyo, Japan). C-reactive protein was measured colorimetrically with a Siemens Dimension Xpand analyser at the Medical Research Council Human Nutrition Research laboratory in Cambridge. Concentrations of leptin, adiponectin, and high-sensitivity interleukin-6 were measured with ELISA (R&D systems, Abingdon, UK).

We assessed physical activity in leisure time at ages 36, 43, 53, and 60–64 years with self-reported activity questionnaires: the Minnesota Leisure-Time Physical Activity Questionnaire at 36 years, and more basic non-validated questions, as previously described, at 43, 53, and 60–64 years and older.[18] We generated a long-term single activity score that distinguished those who were active (more than one to five times a month) at every age from those who were active on at least one occasion and those who were inactive at all ages. Participants' occupational social class at age 53 years (grouped into six categories according to the UK Registrar General's classification) was used as a measure of adult socioeconomic position because many individuals were retired at the time of the clinic visit.

Statistical analysis

We made comparisons between individuals who were normal weight, overweight, and obese for cardiovascular risk factors and cIMT by ANOVA for parametric measures and Kruskal Wallis test for non-parametric measures. Potential confounding and mediating variables were sex, systolic blood pressure at age 60–64 years, occupational social class at age 53 years, and other cardiovascular risk factors (heart rate and smoking status at age 60–64 years) and physical activity score in adulthood, and those associated with intima media thickness and obesity at $p<0·05$. We used multivariable linear regression to establish the cross-sectional association of BMI category at age 60–64 years with cIMT, adjusted for various confounders. Confounders were either selected a priori—eg, sex and occupational social class—or were those variables that were associated with both cIMT and obesity in univariable models ($p<0·05$).

We compared the mean cIMT for children categorised as overweight or obese with that of normal weight children, then added overweight or obese adults (60–64 years) to the model to assess whether overweight or obesity in childhood was independently related to cIMT. Mean cIMT was then compared across four groups of individuals: those who were of normal weight in childhood and adulthood (60–64 years); those who were of normal weight in childhood, but were overweight or obese in adulthood; those who were overweight or obese in childhood but were of normal weight in adulthood; and those who were overweight or obese in both periods. Additionally, we assessed whether overweight or obesity in childhood modified the effect of the adult condition by testing the interaction term.

We grouped individuals according to seven different patterns of BMI change across adulthood: (a) those who maintained normal weight; (b) those who were overweight at age 36 years and did not subsequently drop a weight category (from obese to overweight or overweight to obese); groups c–e were the same as for b, but included individuals first recorded as overweight or obese at age 43, 53, or 60–64 years, respectively; (f) those who were overweight or obese at some point, but who dropped a category (from obese to overweight or overweight to normal) and did not regain; and (g) those who were overweight or obese at some point and who dropped a category, but subsequently regained.

See Online for appendix

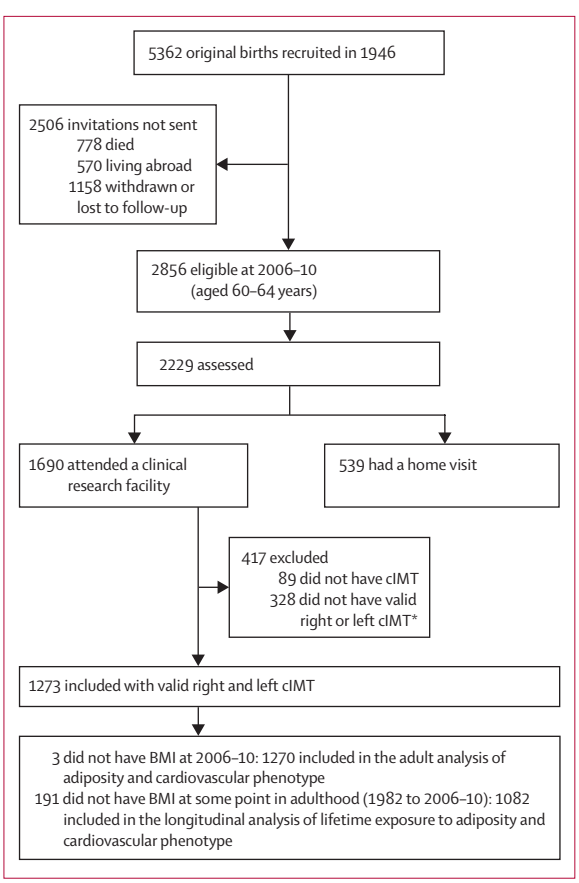


***Figure 1*: Patient flow diagram**
cIMT=carotid intima media thickness. *13 (4%) of 328 people had plaques.

We did a test for trend across the four age-at-first-overweight-or-obesity groups (b–e), with participants in the never overweight or obese group (a) as the baseline, then tested whether the association was modified by physical activity. We then combined the four overweight or obese groups (b–e) and compared mean cIMT in this combined group (in which patients never dropped a BMI category once they reached overweight or obesity) with the two groups who did drop a category (f and g). Analyses were repeated with cardiovascular risk factors and inflammatory markers as outcome measures. We did a complete case analysis for the association between BMI change and cIMT because sensitivity analysis showed that participants with missing BMI (n=191) at some point in adulthood did not have different cIMT or weight compared with those who did not have missing values (appendix).

Analyses of adult onset adiposity were repeated for waist circumference with WHO cutoff points for men and women.[19] Statistical analyses were done with STATA (version 12.1) software.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Figure 1 shows the trial profile. We included 1273 (45%) of 2856 participants eligible in 2006–10 (at age 60–64 years) in this study. In childhood, 926 (73%) individuals were overweight or obese on at least one measurement in childhood. In adulthood, from age 36 years, the prevalence of overweight or obesity increased from 311 (27%) of 1152 patients to 845 (67%) of 1270 patients during 27 years of follow up. Of the 926 children who were either overweight or obese, 621 (67%) remained overweight or obese as adults and 302 (33%) had normal weight at ages 60–64 years.

Whereas 141 (13%) of 1082 people had a reduction in BMI category during 27 years of follow up, with subsequent regain, only 17 (2%) people had a sustained reduction in BMI category in adulthood.

At age 60–64 years, compared with the normal weight group, overweight or obese participants had a higher cIMT (mean difference 0·03 mm, 95% CI 0·015–0·045; p<0·0001; table 1). This association remained after adjustment for cardiovascular risk factors (0·02 mm, 0·005–0·036; p=0·009).

Additionally, overweight or obese individuals had an adverse cardiovascular risk factor profile, with increased concentrations of inflammatory markers, leptin, and

HbA_{1c} (p<0·0001 for all; table 1). Systolic and diastolic blood pressure was also higher in overweight or obese participants than in those with a normal weight (table 1). The odds ratio of type 2 diabetes for the overweight or obese group versus the normal weight group was 2·48 (95% CI 1·37–4·47; p=0·003). Concentrations of total cholesterol were lower in participants in the overweight or obese group than in those in the normal weight group (table 1); however, this difference was greatly reduced with adjustment for lipid-lowering drugs as a binary variable (data not shown).

Childhood overweight or obesity was not associated with cIMT at age 60–64 years and did not change the association between adulthood overweight or obesity and cIMT. Thus, cIMT in participants who were overweight or obese in childhood but normal weight in adulthood was similar to that in those who were normal weight at both periods (table 2). In adulthood, we noted a graded cumulative effect of exposure to adiposity on cIMT at age 60–64 years, so that individuals who were classified as overweight or obese at age 36 years had the highest cIMT, even after adjustment for cardiovascular risk factors (p value for trend <0·0001; figure 2). This association was not changed by physical activity. The association between age at onset of adulthood adiposity and cIMT was similar when analysis was done with waist circumference instead of BMI (appendix). Similar associations were noted for cardiometabolic risk factors: earlier onset of adiposity in adulthood was associated with increased systolic blood pressure (mean difference per decade 2·13 mm Hg, 95% CI 1·39–2·90; p value for trend <0·0001), leptin (mean difference per decade 1·33 ng/mL, 1·29–1·37; p<0·0001), prevalence of diabetes (OR per decade 1·68, 1·34–2·11; p<0·0001) and lower adiponectin (mean reduction per decade 1·46 µg/ml, 1·08–1·84; p<0·0001; appendix).

Participants overweight at 36 years and never dropping a BMI category during adulthood had a higher cIMT than those dropping a BMI category (obese to overweight or overweight to normal) at any time, even if this pattern was not sustained (cIMT lower by an average of 0·03 mm. 95% CI 0·01–0·06; p=0·002), and than those who were always of normal weight (cIMT lower by an average of 0·03 mm, 0·03–0·05; p=0·001). When analysis was done with waist circumference rather than BMI to define adiposity category, the drop in adiposity category, even if not sustained in adult life, was associated with reduced cIMT in women (appendix).

We noted similar associations with cardiometabolic risk factors: individuals who were always overweight or obese in adulthood had higher concentrations of HbA_{1c} (p=0·04) and leptin (p<0·0001), and lower concentrations of adiponectin (p<0·0001) compared with those who lost weight and those who remained lean. However, we recorded no association between patterns of BMI change and LDL cholesterol, smoking, prevalence of type 2 diabetes, or C-reactive protein.

	Normal weight (n=425)	Overweight (n=553)	Obese (n=292)	p value (normal *vs* overweight or obese)
Anthropometric measurements				
Men	165 (38%)	295 (53%)	141 (48%)	<0·0001
Age (years)	63·2 (1·2)	63·1 (1·2)	63·3 (1·1)	0·2
Systolic blood pressure (mmHg)	129·7 (16·6)	137·8 (18·2)	139·2 (19·6)	<0·0001
Diastolic blood pressure (mm Hg)	74·3 (9·3)	78·7 (9·6)	78·9 (9·9)	<0·0001
Pulse pressure (mm Hg)	55·4 (11·8)	59·2 (13·2)	60·3 (15·2)	<0·0001
Heart rate (beats per min)	68 (11·4)	68·3 (10·2)	69·5 (11·1)	0·006
Waist circumference (cm)	84 (7·8)	95·6 (7·6)	108·2 (8·0)	<0·0001
Weight (kg)	65·2 (8·7)	77·9 (9·6)	93·5 (11·9)	<0·0001
Height (m)	1·68 (0·09)	1·69 (0·09)	1·68 (0·09)	0·053
BMI (kg/m^2)	22·9 (1·6)	27·2 (1·4)	33·2 (3·1)	<0·0001
Lipid parameters				
Total cholesterol (mmol/L)	5·9 (1·1)	5·7 (1·1)	5·5 (1·2)	<0·0001
LDL (mmol/L)	3·6 (0·9)	3·6 (1·0)	3·4 (1·1)	<0·0001
HDL (mmol/L)	1·8 (0·4)	1·6 (0·4)	1·4 (0·3)	<0·0001
Triglycerides (mmol/L)	0·9 (0·7–1·2)	1·1 (0·8–1·6)	1·3 (1·0–2·0)	<0·0001†
Inflammatory markers				
Cystatin C (mg/L)	0·8 (0·1)	0·8 (0·1)	0·8 (0·1)	<0·0001
C-reactive protein (mg/L)	2·0 (1·5–3·2)	2·6 (1·8–4·3)	3·2 (2·2–5·1)	<0·0001*
Interleukin-6 (pg/mL)	1·4 (1·0–2·4)	1·8 (1·3–2·7)	2·5 (1·7–3·6)	<0·0001*
Metabolic markers				
Leptin (ng/mL)	7·3 (3·7–12·9)	11·3 (6·4–20·0)	25·4 (12·8–39·7)	<0·00001*
Adiponectin (µg/mL)	16·4 (10·7–25·1)	12·7 (6·8–18·3)	9·7 (6·2–15·8)	<0·0001*
HbA_{1c} (%)	5·7 (0·4)	5·8 (0·6)	6 (0·9)	<0·0001
Diabetes mellitus	14/78 (18%)	28/78 (36%)	36/78 (46%)	<0·0001
Socioeconomic status at age 53 years†				
Professional	40 (10%)	43 (9%)	19 (7%)	0·066
Intermediate	187 (47%)	207 (40%)	120 (43%)	..
Skilled (non-manual)	84 (21%)	139 (27%)	53 (19%)	..
Skilled (manual)	48 (12%)	70 (13%)	44 (16%)	..
Partly skilled	33 (85)	48 (9%)	37 (13%)	..
Unskilled	8 (2%)	15 (3%)	8 (3%)	..
Smoking†				
Never smoked	142 (36%)	159 (30%)	100 (36%)	0·058
Ex-smoker	160 (40%)	213 (41%)	93 (33%)	..
Present smoker	96 (24%)	151 (29%)	89 (32%)	..
Receiving blood-pressure drugs	37 (9%)	123 (22%)	86 (29%)	<0·0001
Receiving lipid-lowering drugs	42 (10%)	104 (19%)	86 (29%)	<0·0001
Physically active since 1982 to 2006–09†				
Inactive	37 (10%)	50 (11%)	40 (15%)	0·021
Active at some point	223 (63%)	323 (70%)	167 (64%)	..
Always active	97 (27%)	90 (19%)	53 (20%)	..
Mean intima media thickness (mm)	0·66 (0·11)	0·69 (0·13)	0·71 (0·12)	<0·0001

Data are n (%), mean (SD), or n/N (%), unless otherwise indicated. *Kruskal-Wallis test. †X_2 test.

***Table 1*: Participant characteristics by BMI category at the age of 60–64 years**

Discussion

Our findings for the oldest British cohort, followed-up for up to 64 years, show that length of exposure to

	N	Regression coefficient	95% CI for cIMT	p value*	p value†
Childhood O/O	926/1273	–0·0005	–0·02 to 0·01	0·49	0·51
Adulthood O/O	845/1270	0·029	0·01 to 0·04	<0·0001	0·009
Adjusted model‡	1270	..	..	..	..
Childhood O/O	..	–0·005	–0·02 to 0·01	0·45	0·48
Adult Obesity O/O	..	0·029	0·02 to 0·04	<0·0001	0·009
Joint effect model§					
NW Child NW Adult	123	Reference			
NW Child O/O Adult	224	0·042	0·015 to 0·069	0·002	0·004
O/O Child NW Adult	302	0·006	–0·019 to 0·031	0·62	0·37
O/O Child O/O Adult	621	0·031	0·007 to 0·054	0·011	0·051

O/O=overweight or obesity. N/W=normal weight. *Adjusted for sex. †Fully adjusted. ‡Adjusted for sex, LDL cholesterol, smoking, heart rate, systolic blood pressure at 60–64 years, and socioeconomic class at 53 years. §Joint effect model between childhood O/O and adulthood O/O (p=0·26).

***Table 2*: Childhood and adulthood overweight or obesity and carotid intima media thickness at age 60–64 years**

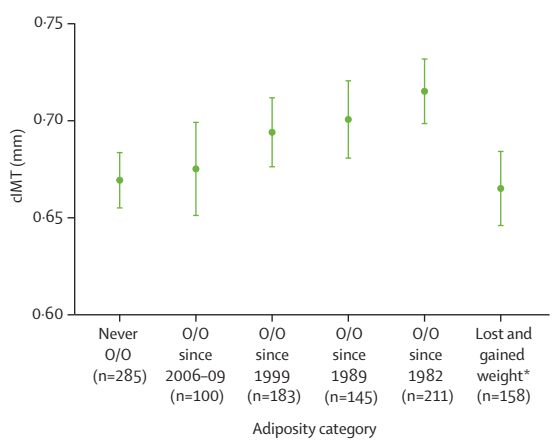


***Figure 2*: Patterns of BMI change in adulthood and cIMT at age 60–64 years**
Data expressed as mean cIMT and 95% CI for each BMI group. Test for trend for O/O since 1982 to O/O since 09: p<0·0001. Pairwise comparison of never O/O versus O/O: p=0·68 since 2009; p=0·033 since 1999; p=0·012 since 1989; p<0·0001 since 1982; and lost and gained, p=0·73. Comparison of never lost weight (composite of O/O since 2009, since 1999, since 1989 and 1982) versus: lost and gained, p=0·002; and never O/O, p=0·001. O/O=overweight or obese. *17 participants lost weight and did not regain it.

adiposity in adulthood had a graded and cumulative adverse effect on development of vascular disease and cardiovascular risk-factor profile in later life. We have also shown, for the first time, that this effect was attenuated by weight loss sufficient to drop a BMI category from obese to overweight, or overweight to normal weight, at any period during adult life. These findings emphasise the potential cardiovascular benefits of clinical and public health strategies that help individuals who are overweight and obese to lose weight at any age (panel).

Overweight and obese individuals have a higher incidence of cardiovascular risk factors (including hypertension, type 2 diabetes, and hyperlipidaemia) and increased cardiovascular mortality compared with participants of a normal weight.[20] Exposure to adiposity from childhood to early adulthood was associated with evidence of early arterial disease in four large cohorts.[21] However, long-term exposure to adiposity in adult life, and its cardiovascular effect at an age when cardiovascular events are likely to take place, have not been previously investigated.

In the 1946 British birth cohort, various measures of BMI from birth were made and vascular phenotyping was undertaken at age 60–64 years with cIMT—a reproducible non-invasive measure that is relevant to both atherosclerosis progression and adverse cardiovascular outcome.[22] This technique provided the unique opportunity to examine the cardiovascular effect of long-term exposure to adiposity, but also to study patterns of BMI change likely to happen during an individual's lifetime. The longer the exposure to adiposity the higher the cIMT and the more unfavorable the cardiovascular risk-factor profile in late adulthood. Systolic blood pressure was raised and the risk of diabetes increased with longer exposure to overweight and obesity in adult life. However, the disturbed cardiometabolic and inflammatory risk profile did not fully account for the link between adiposity and cIMT. These findings extend previous findings for early adulthood and provide important information about the acquisition of adiposity at an age where cardiovascular risk is at its highest.[21,23] Unlike previous reports, in our study physical activity did not change the association between adiposity and cardiovascular phenotype. The use of non-validated activity questionnaires could account for this discrepancy, even though they closely relate to the physical performance of these participants.[18,24]

The independent contribution of childhood adiposity to arterial disease in later life was small in this cohort compared with that reported for adolescence.[25] We used criteria from the International Obesity Taskforce[16] to define adiposity in childhood; therefore, our results are dependent on the cutoff points used. Furthermore, post-war environmental and lifestyle influences differed greatly from the present day, and adiposity levels in childhood were lower than in recent cohorts.[26] Therefore, the relative scarcity of effect of childhood adiposity in the NSHD might not reflect the present risks of childhood obesity.[26]

The prolonged follow-up of participants beyond middle age enabled assessment of patterns of BMI change on vascular phenotype. As little as 5–10% weight loss has previously been associated with improvements in cardiovascular risk-factor profiles and lower cardiovascular mortality in clinical trials of pharmacotherapy or surgery.[27] However, the findings from the LOOK AHEAD trial did not show reduced mortality in patients with diabetes after intensive lifestyle modification, despite initial weight loss of about 9% and improved cardiovascular risk factors.[28] However,

intervention studies only permit short-term assessment, and longer follow up (ie, decades) is necessary to fully capture the vascular effects of weight change. Our study, in which individuals were followed-up over their lifetime for more than 60 years, allowed assessment of the effect of modest, real-life, non-trial-induced, changes in adiposity profile.

We noted an improvement in metabolic profile, with lower concentrations of leptin and HbA_{1c} and higher concentrations of adiponectin, in participants who dropped a BMI category during adulthood, even when this reduction was not sustained. We recorded no effect on the prevalence of type 2 diabetes. However, the association between weight change and development of type 2 diabetes is complex. In a meta-analysis, at- risk individuals had a reduced incidence of diabetes after modest weight loss, even if weight loss was not sustained, although smaller studies suggested that weight cycling is associated with adverse metabolic profile and with increased risk of type 2 diabetes in later life.[29]

The mechanisms by which weight changes affect the arterial wall remain speculative, because most studies to date have focused on intentional weight loss with pharmacological or surgical interventions. Enhanced insulin sensitivity, reduction in inflammatory cytokines and adipokines, mobilisation of fatty acids, hormonal changes, and improvement in cardiovascular risk factors, might have contributed to the cardiovascular benefit we noted with weight loss.[30]

Our study has limitations, because we only had BMI measured at a restricted number of time points up to 10 years apart. We were thus unable to identify the effect of duration of weight loss or weight cycling on cardiovascular health. Although we were able to adjust for various potential confounders, residual confounding by long-term lifestyle patterns and other possible unmeasured variables cannot be excluded. The NSHD study lacks ethnic diversity (mostly white participants) and the cohort had low levels of obesity in childhood and early adulthood compared with other cohorts and hence caution is needed when these findings are generalised to more recent and more ethnically diverse populations. Missing data is unavoidable in long-running studies, such as NSHD, and the sample with cIMT had a lower baseline cardiovascular risk profile than did those who were excluded. Despite this lower risk, we still noted strong associations between patterns of BMI change and cIMT in later life. The fairly small sample size and therefore low statistical power means we cannot yet assess the effect of patterns of change in overweight in adulthood and coronary heart disease and stroke. Our findings suggest that weight reduction or reduced exposure to adiposity might translate to long-term cardiovascular benefit. Findings from a meta-analysis suggest that a 0·1 mm difference in cIMT is associated with a hazard ratio of 1·15 for myocardial infarction and of 1·18 for stroke. Therefore, the mean difference of 0·034 mm in cIMT between participants who lost weight in adulthood compared with those who were always overweight or obese translates to a reduction of roughly 9% in rate for both stroke and myocardial infarction.[22]

In conclusion, our findings suggest that cardiovascular benefit might arise from weight loss in adulthood, irrespective of when this weight loss is achieved, and support public health policies for lifestyle modifications for prevention and management of overweight and obese individuals at all ages.

Panel: Research in context

Systematic review

We searched PubMed for research articles and reviews in English published up to January, 2014. We used the search terms "adiposity", "weight gain", "weight loss", "cardiovascular disease", and "type 2 diabetes". We also retrieved papers from the reference lists of identified articles about the link between exposure to adiposity and weight loss and cardiovascular disease and type 2 diabetes. Consistent evidence exists that longer exposure to adiposity is associated with higher risk of coronary heart disease, whereas for the risk of type 2 diabetes some evidence suggests that recent adiposity status is more important than duration. Inconsistencies exist in the literature regarding the effect of weight cycling. Some epidemiological studies show increases in cardiovascular mortality related to weight cycling, whereas experimental studies contradict these results. The confounding effect of health status has been suggested as the explanation for these discrepancies.

Interpretation

Our findings show that longer exposure to adiposity has a graded and cumulative adverse effect on cIMT and cardiovascular risk factors in later adulthood. Furthermore, we noted that reductions in BMI category, from obese to overweight or overweight to normal weight at any period during adult life even if not sustained, attenuated these adverse effects. These findings suggest that weight loss at any period in adult life could result in long-term cardiovascular benefit.

Contributors

MC did the literature search; designed the study; collected, analysed, and interpreted the data; and wrote the manuscript. TK analysed and interpreted data, designed figures, and wrote and edited the report. WJ analysed and interpreted data and wrote the report. RH designed the study, analysed and interpreted data, and wrote the report. DK interpreted data and wrote and edited the report. NS conceived the study, collected and interpreted data, and wrote the report. PHW collected and interpreted data, and wrote and edited the report. JW collected data and edited the report. NF conceived the study, collected and interpreted data, and wrote and edited the report. JD designed the study, interpreted data, and wrote the report.

Declaration of interests

NF received fees for consultancy from Vivus, Arena, and Janssen, and fees for consultancy, for a speaker's bureau, and for advisory board membership from Novo Nordisk. DK and RH have received grants and personal fees from the Medical Research Council. All other authors declare no competing interests.

Acknowledgments

Our study was funded by grants from the Medical Research Council (number MC_UU12019/02, MC_UU_12019/01, and G1001143) and the British Heart Foundation.

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