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Secular changes in mid-adulthood body mass index, waist circumference, and low HDL cholesterol between 1990, 2003, and 2018 in Great Britain

Trends in waist circumference and HDL-cholesterol

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Abstract

Objective: To investigate the extent to which 1) secular changes in mid-adulthood WC are independent of BMI and 2) secular changes in low HDL-C are dependent on WC in each sex.

Methods: The sample comprised 19,406 adults (aged 43-47 years) from three birth cohort studies with BMI and WC measured in 1990, 2003, or 2018; 13,239 participants additionally had HDL-C measured in 2003 or 2018. Quantile regression was used to model differences between 1990-2003 and 2003-2018 in 1) BMI and WC internal Z-scores and 2) WC in cm before and after adjustment for BMI. Binary logistic regression was used to model differences between 2003-2018 in low HDL-C, before and after adjustment for BMI or WC.

Results: Secular increases in BMI and WC were larger between 1990-2003 than 2003-2018 and at the upper ends of the distributions. At the 85th quantile, effect sizes were larger for WC than BMI Z-scores in females but not males. Adjustment for BMI attenuated estimates of secular increases in WC in cm more in males than females. Odds ratios for low HDL-C in 2018 compared to 2003 were 1.73 (95% CI 1.32, 2.28) in males and 1.34 (1.01, 1.78) in females. Adjustment for WC did not substantially change the estimate in males but attenuated the estimate for females to 1.09 (0.81, 1.47).

Conclusions: In women much more so than in men, secular increases in mid-adulthood WC appear to have occurred independently of BMI and largely explain the observed rise in low HDL-C prevalence between 2003-2018.

41 **Introduction**

42

43 Secular trends in adulthood obesity, defined using body mass index (BMI), have been
44 extensively documented [1, 2]. The BMI is not, however, a measure of adiposity and tells us
45 nothing about body fat distribution [3, 4]. Most of the effects of obesity on increased
46 cardiometabolic disease risk are arguably explained by central adiposity [5], and specifically
47 a high level of visceral fat [6]. This is why waist circumference (WC), a better indicator of
48 visceral fat than BMI [7, 8], is more strongly associated with adverse outcomes than BMI and
49 explains variation in disease risk independently of BMI [9-13].

50

51 The correlation between BMI and WC is approximately 0.9 in adults [14], but this does not
52 mean that one should necessarily expect secular changes in each variable to be of the same
53 magnitude. Previous studies, mainly in the USA, have shown that WC has increased above
54 and beyond what would be anticipated based on secular trends in BMI [15-20]. For example,
55 using NHANES data, Freedman et al estimated that, after adjustment for BMI, the mean
56 increase in WC between 1999-2000 and 2011-2012 was 0.2 cm in men and 2.4 cm in
57 women [18]. Very similar effect sizes have been reported by Albrecht et al using data from
58 the Health Survey for England in 1992-1993 and 2008-2009 [15]. Neither of these papers,
59 however, provided an explanation for the observed sex difference. The consequences for
60 cardiometabolic disease risk, of WC increasing over time independently of BMI, are also not
61 well-understood despite clearly being important. High-density lipoprotein cholesterol (HDL-C)
62 is a key measure to consider because of its causal link to adiposity [21] and possible role in
63 the development of coronary artery disease [22, 23]. WC has a stronger association with
64 HDL-C than does BMI [24, 25], which suggests that possible secular trends toward lower
65 HDL-C [26] might be due to increases over time in WC more so than BMI.

66

In Great Britain, we have documented changes over time in BMI trajectories using data from a series of large nationally-representative birth cohort studies initiated in 1946, 1958, 1970, and 2001 [27]. The first three of these cohorts now have data on BMI, WC, and HDL-C at similar ages in mid-adulthood. The first aim of the present study was to investigate the extent to which between-cohort differences (i.e., secular changes) in WC are comparable to, and independent of, those in BMI. We build on the Albrecht et al [15] study by considering changes over time in the distributions of BMI and WC not just the means and by incorporating much more recent data. The second aim was to document secular changes in HDL-C and investigate the extent to which the expected increase in low HDL-C prevalence might be explained by BMI or WC. Given likely differences between males and females, an a priori decision was made to stratify all analyses by sex.

Subjects and methods

Cohorts: The 1946 Medical Research Council National Survey of Health and Development (NSHD) is based on a sample (N = 5,362) born in one week in March 1946 in England, Scotland, and Wales [28, 29]. The sample comprises all singleton births from women with husbands in non-manual and agricultural employment and a random selection of one in four singleton births to females with husbands in manual employment. The 1958 National Child Development Study (NCDS) is based on 17,638 people born in one week in March 1958 in England, Scotland, and Wales; 920 immigrants born in the same week were incorporated during childhood [30]. A similar strategy was used in the 1970 British Cohort Study (BCS), which is based on 17,287 people born in one week in April 1970, with the addition of 1,814 individuals who were 1) born in Northern Ireland and included only in the birth sweep, 2) an immigrant who was incorporated into the study in childhood, or 3) never took part in any sweep [31].

Ethics: All of the studies have received ethical approval and obtained informed parental and/ or participant consent; this information is available from the study websites and/ or cohort profiles.

Samples: This study focuses on data from sweeps at target ages of 43 years in the NSHD, 44 years in the NCDS, and 46 years in the BCS. The primary sample comprised 19,406 individuals in the NSHD (N = 2971), NCDS (N = 9137), or BCS (N = 7298) with data on BMI and WC, in addition to sex, ethnicity (white or non-white), and decimal age. This N represents over 90% of the individuals still participating in these studies at the above-mentioned sweeps. The secondary sample comprised 13,239 individuals in the NCDS (N = 7413) or BCS (N = 5826) who additionally had data on HDL-C and smoking status. This N represents over 75% of the individuals still participating in these studies at the above-mentioned sweeps.

Data: Weight, height, and WC (midway between the iliac crest and the costal margin) were measured by trained research nurses using comparable methods. In the NCDS and BCS, non-fasting venous blood samples were obtained. HDL-C was assayed via standard enzymatic methods using an Olympus model AU640 autoanalyser (Olympus Corporation; Tokyo, Japan) in the NCDS and using a Roche Cobas c702 analyser (Roche Holding AG; Basel, Switzerland) in the BCS. Smoking status (never, ex, current) was self-reported in both studies.

Statistics: BMI was computed as weight (kg)/ height $(m)^2$ and overweight and obesity were defined using standard cut-offs of 25 and 30 kg/m^2. Adults (N = 135) with a BMI less than 18.5 kg/m^2 (i.e., thinness) were not included in any sample or analysis, because this can often reflect underlying disease possibly introducing bias. Central obesity was classified as a WC greater than 88 cm in females or 102 cm in males [32]. Low HDL-C was defined as

values < 1.03 mmol/L in males and values < 1.29 mmol/L in females [33]. Individuals (N = 235) taking lipid-regulating medication, whose HDL-C was not below these cut-offs, were also classified as having low HDL-C.

Descriptive statistics were produced stratified by sex and cohort.

All models were stratified by sex and adjusted for ethnicity and age. Because the obesity epidemic is due to right-skewing of the BMI distribution over time [27], quantile regression was used to estimate between-cohort differences in BMI and WC at different quantiles (15th, 50th, and 85th) of the outcome distributions [34]. Estimates representing secular change in each of the two adjacent time periods (i.e., NSHD and NCDS [1990-2003] and NCDS and BCS [2003-2018]) were obtained and are presented. In the first set of models, BMI and WC were expressed as internal Z-scores (i.e., Observed Value – Sample Mean) / Sample SD) with mean 0 and SD 1 to enable comparison of effect sizes. In the second set of models, WC was modelled in cm before and after adjustment for BMI in kg/m^2. To account for the WC and BMI relationship being non-linear, BMI was entered into these models as a second-degree fractional polynomial function. Briefly, fractional polynomials provide flexible parametrisation by testing a range of powers with which to transform a continuous independent variable (e.g., BMI) and capture a non-linear association with an outcome (e.g., WC). A second-degree fractional polynomial involves two terms and selects the best function, typically out of 36 options [35].

Binary logistic regression was used to estimate the difference in low HDL-C prevalence between the NCDS and BCS, before and after adjustment for BMI (kg/m^2) or WC (cm). Again, BMI and WC were entered into these models as second-degree fractional polynomial functions. Given knowledge that smoking has a strong effect on HDL-C [36, 37] and that smoking rates have reduced dramatically over the last few decades [38, 39], these logistic

models were re-run with additional adjustment for smoking status. Sensitivity analyses were conducted in which individuals taking lipid-regulating medication were not classified as having low HDL-C.

All procedures were performed in Stata 15 (StataCorp LP, College Station, TX, USA).

Code availability: Available from the first author upon request.

Results

The modal year of assessment was 1990 in the 1946 NHSD, 2003 in the NCDS, and 2018 in the BCS (Table 1). Mid-adulthood median BMI and WC demonstrated clear secular increases, while mean HDL-C declined between 2003 and 2018. The between-cohort differences in central obesity prevalence were generally greater than those for obesity, particularly for females. For example, obesity prevalence increased from 14% to 33% between 1990 and 2018 in females, while central obesity prevalence increased more dramatically from 16% to 50%. Rates of low HDL-C were higher in 2018 than 2003 in both sexes, despite there being fewer current smokers and more ex-smokers in 2018 than 2003.

Table 2 shows estimated differences in BMI and WC Z-scores in the NCDS compared to the NSHD (i.e., change from 1990 to 2003) and in the BCS compared to the NCDS (i.e., change from 2003 to 2018). All estimates in males and females, and for BMI and WC Z-scores, were positive and indicative of larger secular increases between 1990 and 2003 than between 2003 and 2018. Further, all effect sizes (except one) were larger at the 85th quantile than the 50th or 15th quantiles, thereby providing evidence that the secular increases were stronger at higher ends of outcome distributions. In males, the effect sizes at the 85th quantile were very similar for BMI and WC. For example, the estimated secular increase between 1990 and

2003 was 0.65 (95% CI 0.49, 0.81) Z-scores for BMI and 0.66 (0.48, 0.84) Z-scores for WC. Conversely, in females, the effect sizes at the 85th quantile were noticeably larger for WC than BMI. For example, the estimated secular increase between 1990 and 2003 was 0.25 (0.06, 0.43) Z-scores for BMI but 0.61 (0.42, 0.81) Z-scores for WC. Between 2003 and 2018, there was no evidence of a secular increase in BMI at the 50th or 85th quantiles in females, yet there was for WC.

Between-cohort differences in WC in cm are shown in Table 3. Adjustment for BMI attenuated estimates more in males than females. For example, in males, the 85th quantile of WC was 2.8 (0.5, 5.1) cm higher in 2018 than 2003 and adjustment for BMI attenuated this estimate by 71% to 0.8 (0.0, 1.6) cm. Conversely, in females, the 85th quantile of WC was 3.8 (1.3, 6.3) cm higher in 2018 than 2003 but adjustment for BMI only attenuated this estimate by 29% to 2.7 (1.7, 3.6) cm. Secular increases in WC, independent of BMI, were stronger in females than males.

Estimated odd ratios for low HDL-C in the BCS (2018) compared to the NCDS (2003) are shown in Table 4. Initial models were not adjusted for smoking status, BMI, or WC. Males in 2018 had a 1.73 (1.32, 2.28) times higher odds of low HDL-C than males in 2003; this estimate only attenuated very slightly after adjustment for BMI or WC. Females in 2018 had a 1.34 (1.01, 1.78) times higher odds of low HDL-C than females in 2003. Adjustment for BMI attenuated this estimate to 1.24 (0.92, 1.67) but adjustment for WC attenuated it even more dramatically to 1.09 (0.81, 1.47). The same pattern of results, with marginally larger effect sizes, were observed when the models were re-run additionally adjusting for smoking status. Sensitivity analyses, in which individuals taking lipid-regulating medication were not classified as having low HDL-C, produced very similar results (data not shown).

Discussion

This paper provides novel evidence that secular increases in mid-adulthood WC between 1990, 2003, and 2018 in Great Britain have generally been larger than those for BMI and occurred, at least partly, independently of BMI. While this pattern of results was found in both sexes, findings were much stronger for women than men. Even after accounting for BMI, our estimates show that WC in females increased by ~4 cm from 1990 to 2003 and by a further ~2 cm from 2003 to 2018. Consequently, the higher prevalence of low HDL-C in 2018 compared to 2003 in females was found to be largely explained by greater WC. In males, adjustment for BMI or WC did little to attenuate the observed secular increase in low HDL-C prevalence, suggesting that other factors are responsible.

The observed sex differences were stark but are in agreement with other studies showing that WC has increased over time more independently of BMI in women than men [15, 18]. Albrecht et al nicely show this finding in the USA and England, but not in China, in different age groups and at different BMI levels [15]. The reasons for this phenomenon are unknown but it may make sense given known sexual dimorphism in fat patterning. Men typically demonstrate an android pattern of fat distribution, with most fat accumulating around the trunk. Secular increases in overall body fat (proxied by BMI) are, therefore, perhaps likely to largely represent gains in central adiposity (proxied by WC) in men. Women typically demonstrate a gynoid pattern of fat distribution, with most fat accumulating around the breasts, hips, and thighs. A secular increase in WC above that in BMI therefore suggest that the conventional pattern of fat distribution in women is changing over time. In support of this idea, Freedman et al found subscapular skinfold thicknesses (a measure of central adiposity) in NHANES to be increasing between 1988-1994 and 2009-2010 more than triceps skinfold thicknesses (a measure of peripheral adiposity) in women (0.4 vs 0.1 mm per decade), but not in men [40].

229 Average HDL-C concentration was found to be lower in 2018 than 2003 and the prevalence
230 of low HDL-C was found to be higher. Sex-specific mean values of HDL-C reported in the
231 2003 Health Survey for England and the 2003 Scottish Health Survey, for the 45-54 year
232 age group, are essentially identical to those reported here for adults aged 45.2 years (on
233 average) in 2003 [41, 42]. This suggests that our reported levels of HDL-C in 2003 are
234 representative of Great Britain. Data from the 2006 Health Survey for England show a
235 marginal decline in mean HDL-C from 1.52 to 1.49 mmol/L in individuals (sexes combined)
236 aged ≥ 16 years [43], but unfortunately more up-to-date statistics have not been published,
237 to the best of our knowledge. We provide evidence of a secular trend towards more adverse
238 levels of HDL-C, particularly in men, such that there was a doubling in the prevalence of low
239 HDL-C between 2003 and 2018. This is concerning and requires further investigation and
240 replication. It is, however, in agreement with a recent publication by the NCD Risk Factor
241 Collaboration which found age-standardised mean HDL-C in men to decline in North-
242 western Europe from ~1.4 to 1.3 mmol/L between 1980-2018 (Extended Data Figure 3) [44].
243
244 In females, the odds ratio for low HDL-C in 2018 compared to 2003 was attenuated from
245 1.34 to 1.24 upon adjustment for BMI and to 1.09 upon adjustment for WC. Cardiometabolic
246 disease risk factors are less consistently correlated with BMI in women than men [21] and,
247 more specifically, total body fat is less strongly related to an abnormal lipid profile in women
248 than men [45]. Central adiposity in both sexes is, however, a strong determinant of HDL-C
249 levels [46, 47]. These observations may explain why WC, more so than BMI, explained the
250 secular increase in low HDL-C prevalence in women. They do not, however, help
251 understand why adjustment for BMI or WC did not substantially attenuate the secular
252 increase in low HDL-C prevalence in men. It may be that the trend in HDL-C in men is
253 explained more by changes over time in modifiable lifestyle factors (e.g., physical activity
254 and diet), and this requires further investigation using large survey data with relevant data.
255

The main strength of this paper lies in the use of measurements taken following very similar protocols at comparable ages (i.e., 43-47 years) in three large birth cohort studies initiated every 12 years in 1946, 1958, and 1970. In terms of limitations, approximately 50% of each initial cohort was included in the present study and differential selection into our sample may have biased results [48]. The cohorts are largely white British thus limiting investigation into ethnic differences. The lack of body composition data means the extent to which our results (e.g., the secular increases in BMI) are explained by differences in fat mass rather than fat-free mass is uncertain. Finally, it was not possible to investigate other lipid outcomes (e.g., low-density lipoprotein and apolipoprotein A-I). The first measurement of HDL-C in the NSHD was not until age 53 years, nine years later than the 44-year sweep in the NCDS. Thus, we made a pragmatic decision not to use the HDL-C data in the NSHD because this difference in age (compared to the NCDS) was likely to distort any secular change.

In conclusion, over the last three decades in Great Britain, secular increases in mid-adulthood WC have been larger than those for BMI and have occurred, at least in part, independently of BMI. This phenomenon was much stronger in women than men, suggesting that the archetypal gynoid pattern of fat distribution in women may be becoming less evident over time. This apparent change in fat patterning in women appears to have contributed to an increase between 2003-2018 in the prevalence of low HDL-C, which was observed in both sexes. The reasons underlying the trend in men do not include changes in BMI or WC according to our analyses.

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WJ conceptualized the study, carried out the analyses, and drafted the initial manuscript. All authors made substantial contributions to the interpretation of the data, revised the manuscript critically for important intellectual content, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

References

1. NCD Risk Factor Collaboration. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. Lancet. 2016;387(10026):1377-96.
2. NCD Risk Factor Collaboration. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet. 2017;390(10113):2627-42.
3. Romero-Corral A, Somers VK, Sierra-Johnson J, Thomas RJ, Collazo-Clavell ML, Korinek J, et al. Accuracy of body mass index in diagnosing obesity in the adult general population. Int J Obes (Lond). 2008;32(6):959-66.
4. Prentice AM, Jebb SA. Beyond body mass index. Obes Rev. 2001;2(3):141-7.
5. Despres JP, Lemieux I, Bergeron J, Pibarot P, Mathieu P, Larose E, et al. Abdominal obesity and the metabolic syndrome: contribution to global cardiometabolic risk. Arterioscler Thromb Vasc Biol. 2008;28(6):1039-49.
6. Despres JP. Is visceral obesity the cause of the metabolic syndrome? Ann Med. 2006;38(1):52-63.
7. Camhi SM, Bray GA, Bouchard C, Greenway FL, Johnson WD, Newton RL, et al. The relationship of waist circumference and BMI to visceral, subcutaneous, and total body fat: sex and race differences. Obesity (Silver Spring). 2011;19(2):402-8.
8. Janssen I, Heymsfield SB, Allison DB, Kotler DP, Ross R. Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous, and visceral fat. Am J Clin Nutr. 2002;75(4):683-8.
9. Carmienke S, Freitag MH, Pischon T, Schlattmann P, Fankhaenel T, Goebel H, et al. General and abdominal obesity parameters and their combination in relation to mortality: a systematic review and meta-regression analysis. Eur J Clin Nutr. 2013;67(6):573-85.
10. de Hollander EL, Bemelmans WJ, Boshuizen HC, Friedrich N, Wallaschofski H, Guallar-Castillon P, et al. The association between waist circumference and risk of mortality considering

322 body mass index in 65- to 74-year-olds: a meta-analysis of 29 cohorts involving more than 58
323 000 elderly persons. Int J Epidemiol. 2012;41(3):805-17.
324 11. Decoda Study G, Nyamdorj R, Qiao Q, Lam TH, Tuomilehto J, Ho SY, et al. BMI compared with
325 central obesity indicators in relation to diabetes and hypertension in Asians. Obesity (Silver
326 Spring). 2008;16(7):1622-35.
327 12. Hamer M, O'Donovan G, Stensel D, Stamatakis E. Normal-Weight Central Obesity and Risk for
328 Mortality. Ann Intern Med. 2017;166(12):917-8.
329 13. Kodama S, Horikawa C, Fujihara K, Heianza Y, Hirasawa R, Yachi Y, et al. Comparisons of the
330 strength of associations with future type 2 diabetes risk among anthropometric obesity
331 indicators, including waist-to-height ratio: a meta-analysis. Am J Epidemiol. 2012;176(11):959-
332 69.
333 14. Flegal KM, Shepherd JA, Looker AC, Graubard BI, Borrud LG, Ogden CL, et al. Comparisons
334 of percentage body fat, body mass index, waist circumference, and waist-stature ratio in adults.
335 Am J Clin Nutr. 2009;89(2):500-8.
336 15. Albrecht SS, Gordon-Larsen P, Stern D, Popkin BM. Is waist circumference per body mass
337 index rising differentially across the United States, England, China and Mexico? Eur J Clin Nutr.
338 2015;69(12):1306-12.
339 16. Elobeid MA, Desmond RA, Thomas O, Keith SW, Allison DB. Waist circumference values are
340 increasing beyond those expected from BMI increases. Obesity (Silver Spring).
341 2007;15(10):2380-3.
342 17. Ford ES, Mokdad AH, Giles WH. Trends in waist circumference among U.S. adults. Obes Res.
343 2003;11(10):1223-31.
344 18. Freedman DS, Ford ES. Are the recent secular increases in the waist circumference of adults
345 independent of changes in BMI? Am J Clin Nutr. 2015;101(3):425-31.
346 19. Visscher TL, Heitmann BL, Rissanen A, Lahti-Koski M, Lissner L. A break in the obesity
347 epidemic? Explained by biases or misinterpretation of the data? Int J Obes (Lond).
348 2015;39(2):189-98.
349 20. Walls HL, Stevenson CE, Mannan HR, Abdullah A, Reid CM, McNeil JJ, et al. Comparing
350 trends in BMI and waist circumference. Obesity (Silver Spring). 2011;19(1):216-9.

351 21. Rashid S, Genest J. Effect of obesity on high-density lipoprotein metabolism. Obesity (Silver
352 Spring). 2007;15(12):2875-88.
353 22. Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. High density lipoprotein as a
354 protective factor against coronary heart disease. The Framingham Study. Am J Med.
355 1977;62(5):707-14.
356 23. Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. Diabetes, blood lipids, and the
357 role of obesity in coronary heart disease risk for women. The Framingham study. Ann Intern
358 Med. 1977;87(4):393-7.
359 24. Brenner DR, Tepylo K, Eny KM, Cahill LE, El-Sohemy A. Comparison of body mass index and
360 waist circumference as predictors of cardiometabolic health in a population of young Canadian
361 adults. Diabetol Metab Syndr. 2010;2(1):28.
362 25. Shen W, Punyanitya M, Chen J, Gallagher D, Albu J, Pi-Sunyer X, et al. Waist circumference
363 correlates with metabolic syndrome indicators better than percentage fat. Obesity (Silver
364 Spring). 2006;14(4):727-36.
365 26. Schreiner PJ, Jacobs DR, Jr., Wong ND, Kiefe CI. Twenty-Five Year Secular Trends in Lipids
366 and Modifiable Risk Factors in a Population-Based Biracial Cohort: The Coronary Artery Risk
367 Development in Young Adults (CARDIA) Study, 1985-2011. J Am Heart Assoc. 2016;5(7).
368 27. Johnson W, Li L, Kuh D, Hardy R. How Has the Age-Related Process of Overweight or Obesity
369 Development Changed over Time? Co-ordinated Analyses of Individual Participant Data from
370 Five United Kingdom Birth Cohorts. PLoS Med. 2015;12(5):e1001828; discussion e.
371 28. Kuh D, Pierce M, Adams J, Deanfield J, Ekelund U, Friberg P, et al. Cohort profile: updating the
372 cohort profile for the MRC National Survey of Health and Development: a new clinic-based data
373 collection for ageing research. Int J Epidemiol. 2011;40(1):e1-9.
374 29. Wadsworth M, Kuh D, Richards M, Hardy R. Cohort Profile: The 1946 National Birth Cohort
375 (MRC National Survey of Health and Development). Int J Epidemiol. 2006;35(1):49-54.
376 30. Power C, Elliott J. Cohort profile: 1958 British birth cohort (National Child Development Study).
377 Int J Epidemiol. 2006;35(1):34-41.
378 31. Elliott J, Shepherd P. Cohort profile: 1970 British Birth Cohort (BCS70). Int J Epidemiol.
379 2006;35(4):836-43.

380 32. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and
381 management of the metabolic syndrome: an American Heart Association/National Heart, Lung,
382 and Blood Institute Scientific Statement. Circulation. 2005;112(17):2735-52.
383 33. Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults.
384 Executive Summary of The Third Report of The National Cholesterol Education Program
385 (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In
386 Adults (Adult Treatment Panel III). JAMA. 2001;285(19):2486-97.
387 34. Bann D, Fitzsimons E, Johnson W. Determinants of the population health distribution: an
388 illustration examining body mass index. Int J Epidemiol. 2020.
389 35. Royston P, Ambler G, Sauerbrei W. The use of fractional polynomials to model continuous risk
390 variables in epidemiology. Int J Epidemiol. 1999;28(5):964-74.
391 36. Craig WY, Palomaki GE, Haddow JE. Cigarette smoking and serum lipid and lipoprotein
392 concentrations: an analysis of published data. BMJ. 1989;298(6676):784-8.
393 37. Freeman DJ, Griffin BA, Murray E, Lindsay GM, Gaffney D, Packard CJ, et al. Smoking and
394 plasma lipoproteins in man: effects on low density lipoprotein cholesterol levels and high
395 density lipoprotein subfraction distribution. Eur J Clin Invest. 1993;23(10):630-40.
396 38. Giskes K, Kunst AE, Benach J, Borrell C, Costa G, Dahl E, et al. Trends in smoking behaviour
397 between 1985 and 2000 in nine European countries by education. J Epidemiol Community
398 Health. 2005;59(5):395-401.
399 39. Ng M, Freeman MK, Fleming TD, Robinson M, Dwyer-Lindgren L, Thomson B, et al. Smoking
400 prevalence and cigarette consumption in 187 countries, 1980-2012. JAMA. 2014;311(2):183-
401 92.
402 40. Freedman DS, Zemel BS, Ogden CL. Secular trends for skinfolds differ from those for BMI and
403 waist circumference among adults examined in NHANES from 1988-1994 through 2009-2010.
404 Am J Clin Nutr. 2017;105(1):169-76.
405 41. Primatesta P, Poulter NR. Levels of dyslipidaemia and improvement in its management in
406 England: results from the Health Survey for England 2003. Clin Endocrinol (Oxf).
407 2006;64(3):292-8.

408 42. The Scottish Government. The Scottish Health Survey 2003. Edinburgh, Scotland: The Scottish
409 Government, 2003.
410 43. Mindell J, Aresu M, Zaninotto P, Falaschetti E, Poulter N. Improving lipid profiles and increasing
411 use of lipid-lowering therapy in England: results from a national cross-sectional survey - 2006.
412 Clin Endocrinol (Oxf). 2011;75(5):621-7.
413 44. NCD Risk Factor Collaboration. Repositioning of the global epicentre of non-optimal
414 cholesterol. Nature. 2020;582(7810):73-7.
415 45. Kissebah AH, Vydelingum N, Murray R, Evans DJ, Hartz AJ, Kalkhoff RK, et al. Relation of
416 body fat distribution to metabolic complications of obesity. J Clin Endocrinol Metab.
417 1982;54(2):254-60.
418 46. Kissebah AH, Alfarsi S, Adams PW. Integrated regulation of very low density lipoprotein
419 triglyceride and apolipoprotein-B kinetics in man: normolipemic subjects, familial
420 hypertriglyceridemia and familial combined hyperlipidemia. Metabolism. 1981;30(9):856-68.
421 47. Peiris AN, Sothmann MS, Hoffmann RG, Hennes MI, Wilson CR, Gustafson AB, et al.
422 Adiposity, fat distribution, and cardiovascular risk. Ann Intern Med. 1989;110(11):867-72.
423 48. Munafo MR, Tilling K, Taylor AE, Evans DM, Davey Smith G. Collider scope: when selection
424 bias can substantially influence observed associations. Int J Epidemiol. 2018;47(1):226-35.
425

Table 1. Description of the study sample

		Males (N = 9616)			Females (N = 9790)		
		NSHD N = 1508	NCDS N = 4561	BCS N = 3547	NSHD N = 1463	NCDS N = 4576	BCS N = 3751
Non-white ethnicity	N (%)	0	107 (2.4)	153 (4.3)	0	93 (2.0)	162 (4.3)
Age (years)	Mean (SD)	43.5 (0.2)	45.2 (0.4)	47.2 (0.7)	43.5 (0.2)	45.2 (0.4)	47.2 (0.7)
Measurement year	Mode (range)	1990 (1989, 1990)	2003 (2002, 2004)	2018 (2016, 2018)	1990 (1989, 1990)	2003 (2002, 2004)	2018 (2016, 2018)
BMI (kg/m^2)	Median (IQR)	25.4 (23.4, 27.8)	27.3 (25.0, 30.1)	28.1 (25.4, 31.3)	24.1 (22.2, 27.2)	25.7 (23.1, 29.7)	27.0 (23.8, 31.7)
Normal weight	N (%)	663 (44)	1124 (25)	760 (21)	866 (59)	1986 (43)	1313 (35)
Overweight	N (%)	685 (45)	2277 (50)	1587 (45)	389 (27)	1510 (33)	1216 (32)
Obese	N (%)	160 (11)	1160 (25)	1200 (34)	208 (14)	1080 (24)	1222 (33)
WC (cm)	Median (IQR)	91.1 (85.5, 97.7)	97.3 (91.1, 104.4)	99.2 (92.0, 107.2)	75.8 (70.8, 83.5)	83.4 (76.3, 92.8)	88.0 (79.2, 99.0)
Not centrally obese	N (%)	1291 (86)	3084 (68)	2113 (60)	1232 (84)	2891 (63)	1885 (50)
Centrally obese	N (%)	217 (14)	1477 (32)	1434 (40)	231 (16)	1685 (37)	1866 (50)
			N = 3719	N = 2871		N = 3694	N = 2955
HDL-C	Mean (SD)		1.43 (0.33)	1.37 (0.38)		1.69 (0.40)	1.66 (0.44)
Normal	N (%)		3309 (89)	2198 (77)		3208 (87)	2394 (81)
Low	N (%)		410 (11)	673 (23)		486 (13)	561 (19)
Smoking							
Never	N (%)		1671 (45)	1376 (48)		1712 (46)	1461 (49)
Ex	N (%)		1170 (31)	912 (32)		1083 (29)	942 (32)
Current	N (%)		878 (24)	583 (20)		899 (24)	552 (19)

Table 2. Between cohort differences in adulthood BMI and WC Z-scores, estimated using quantile regression

	Male				Female			
	NCDS (referent: NSHD) Change from 1990-2003		BCS (referent: NCDS) Change from 2003-2018		NCDS (referent: NSHD) Change from 1990-2003		BCS (referent: NCDS) Change from 2003-2018	
	B (95% CI)	P	B (95% CI)	P	B (95% CI)	P	B (95% CI)	P
BMI (Z-score)								
15th	0.27 (0.16, 0.39)	<0.001	0.00 (-0.10, 0.11)	0.976	0.15 (0.08, 0.22)	<0.001	0.12 (0.03, 0.21)	0.008
50th	0.37 (0.28, 0.46)	<0.001	0.11 (0.00, 0.22)	0.047	0.17 (0.08, 0.26)	<0.001	0.07 (-0.05, 0.18)	0.264
85th	0.65 (0.49, 0.81)	<0.001	0.31 (0.09, 0.53)	0.006	0.25 (0.06, 0.43)	0.011	0.06 (-0.13, 0.26)	0.529
WC (Z-score)								
15th	0.46 (0.37, 0.56)	<0.001	0.04 (-0.07, 0.15)	0.474	0.34 (0.27, 0.42)	<0.001	0.17 (0.09, 0.25)	<0.001
50th	0.51 (0.40, 0.61)	<0.001	0.13 (0.03, 0.22)	0.009	0.47 (0.38, 0.57)	<0.001	0.22 (0.11, 0.34)	<0.001
85th	0.66 (0.48, 0.84)	<0.001	0.24 (0.05, 0.44)	0.014	0.61 (0.42, 0.81)	<0.001	0.28 (0.10, 0.47)	0.003

All models adjusted for ethnicity and age

Table 3. Between cohort differences in adulthood WC, before and after adjustment for BMI, estimated using quantile regression

		Males						Females					
		NCDS (referent: NSHD) Change from 1990-2003			BCS (referent: NCDS) Change from 2003-2018			NCDS (referent: NSHD) Change from 1990-2003			BCS (referent: NCDS) Change from 2003-2018		
		B (95% CI)	P	%Ch	B (95% CI)	P	%Ch	B (95% CI)	P	%Ch	B (95% CI)	P	%Ch
Unadjusted for BMI	WC (cm)												
	15th	5.3 (4.1, 6.5)	<0.001		0.5 (-0.8, 1.7)	0.459		4.7 (3.7, 5.6)	<0.001		2.3 (1.2, 3.4)	<0.001	
	50th	5.8 (4.6, 6.9)	<0.001		1.5 (0.3, 2.7)	0.015		6.4 (5.3, 7.5)	<0.001		3.0 (1.5, 4.5)	<0.001	
	85th	7.6 (5.4, 9.7)	<0.001		2.8 (0.5, 5.1)	0.019		8.3 (5.7, 10.9)	<0.001		3.8 (1.3, 6.3)	0.003	
Adjusted for BMI[a]	WC (cm)												
	15th	2.1 (1.5, 2.7)	<0.001	-60	0.7 (0.0, 1.4)	0.060	+40	4.2 (3.6, 4.9)	<0.001	-11	2.0 (1.4, 2.7)	<0.001	-13
	50th	1.7 (1.1, 2.3)	<0.001	-71	0.5 (0.0, 1.0)	0.040	-67	3.7 (3.1, 4.3)	<0.001	-42	1.4 (0.7, 2.1)	<0.001	-53
	85th	1.8 (1.0, 2.6)	<0.001	-76	0.8 (0.0, 1.6)	0.058	-71	3.8 (3.0, 4.6)	<0.001	-54	2.7 (1.7, 3.6)	<0.001	-29

%Ch = percentage change in estimate from adjusted to adjusted (for BMI) model

All models adjusted for ethnicity and age

[a]Fractional polynomial terms: BMI^2, BMI^3 for males; BMI^{-2}, BMI^{-1} for females

Table 4. Estimated odd ratios for low HDL-C comparing the BCS to the NCDS, before and after adjustment for BMI or WC

			Males			Females		
Adjustments			NCDS 2003	BCS 2018		NCDS 2003	BCS 2018	
Smoking	BMI	WC		OR (95% CI)	P		OR (95% CI)	P
No	No	No	--	1.73 (1.32, 2.28)	<0.001	--	1.34 (1.01, 1.78)	0.042
No	Yes	No	--	1.68 (1.26, 2.23)	<0.001	--	1.24 (0.92, 1.67)	0.151
No	No	Yes	--	1.64 (1.24, 2.19)	0.001	--	1.09 (0.81, 1.47)	0.576
Yes	No	No	--	1.77 (1.34, 2.33)	<0.001	--	1.44 (1.08, 1.91)	0.012
Yes	Yes	No	--	1.73 (1.30, 2.31)	0.001	--	1.33 (0.99, 1.80)	0.058
Yes	No	Yes	--	1.69 (1.27, 2.25)	0.001	--	1.16 (0.86, 1.57)	0.327

All models adjusted for ethnicity and age

[a]Fractional polynomial terms: BMI, BMI*ln(BMI) for males; $BMI^{-0.5}$, BMI^{3} for females
[b]Fractional polynomial terms: WC^{2}, WC^{3} for males; ln(WC), $WC^{0.5}$ for females