Cardiovascular health and stroke in older British men: prospective findings from the British Regional Heart Study

Ayesha Ahmed[1*], MPH; Snehal M Pinto Pereira[2], PhD; Lucy Lennon[1], MSc; Olia Papacosta[1],MSc; Peter Whincup[3], FRCP; Goya Wannamethee[1], PhD

1. Department of Primary Care and Population Health, University College London;

2. Department of Epidemiology and Public Health, University College London;

3. Population Health Research Institute, St George's, University of London

*Corresponding Author: ayesha.ahmed.18@ucl.ac.uk ; +44 020 8016 8021

Research Department of Primary Care and Population Health

Upper Third Floor

UCL Medical School (Royal Free Campus)

Rowland Hill Street

London, NW3 2PF

Cover Title: Cardiovascular health and stroke in older age

Tables: 2, Figures: 2

Key Words: cardiovascular health, life's simple 7, stroke, prevention, middle age, older age

Subject Terms: aging, cardiovascular disease, cerebrovascular disease/stroke, epidemiology, primary prevention, risk factors

Word count: 5993

ABSTRACT

Background and Purpose

Research exploring the utility of cardiovascular health (CVH) and its Life's Simple 7 (LS7) components (body mass index, blood pressure (BP), glucose, cholesterol, physical activity, smoking and diet) for prevention of stroke in older adults is limited. In the British Regional Heart Study we explored (1) prospective associations of LS7 metrics and composite CVH scores with, and their impact on, stroke in middle and older age; and (2) if change in CVH was associated with subsequent stroke.

Methods

Men without cardiovascular disease were followed from baseline recruitment (1978-1980), and again from re-examination 20y later (Q20), for stroke over a median period of 20y and 16y respectively. LS7 were measured at each time-point except baseline diet. Cox models estimated hazard ratios (HRs [95% CI]) of stroke for (i) ideal and intermediate vs poor levels of LS7; (ii) composite CVH scores; and (iii) 4 CVH trajectory groups (Low-Low, Low-High, High-Low, High-High) derived by dichotomising CVH scores from each time point across the median value. Population attributable fractions (PAFs) measured impact of LS7.

Results

At baseline (n=7274, mean age 50y), healthier levels of BP, physical activity and smoking were associated with reduced stroke risk. At Q20 (n=3798, mean age 69y) only BP displayed an association. HRs for intermediate and ideal (vs poor) levels of BP 0.65 [0.52-0.81] and 0.40 [0.24-0.65] at baseline; and 0.84 [0.67-1.05] and 0.57 [0.36-0.90] at Q20. With reference to Low-Low trajectory, the Low-High trajectory was associated with 40% reduced risk, HR 0.60 [0.44-0.83]. Associations of CVH scores weakened, and PAFs of LS7 reduced, from middle to old age; PAF of non-ideal BP from 53% to 39%.

Conclusions

Except for BP, CVH is weakly associated with stroke at older ages. Prevention strategies for older adults should prioritise BP control but also enhance focus beyond traditional risk factors.

Non-standard Abbreviations and Acronyms

AF	atrial fibrillation
BMI	body mass index
BP	blood pressure
BRHS	British Regional Heart Study
CVD	cardiovascular disease
CVH	cardiovascular health
LS7	Life's Simple 7
PA	physical activity
PY	person years
Q20	20-year follow-up

Stroke remains a major global cause of morbidity and mortality[1]. Its incidence rises sharply with age[2]. In the UK more than 25 billion pounds ($30 billion) are spent annually on stroke care and stroke related disability. With more adults surviving to older ages, this burden is expected to increase[3].

Primary prevention is seen as the best approach to reducing the burden of stroke[4]. The European Stroke Organisation and Stroke Alliance For Europe emphasize both risk factor modification and improved stroke risk assessment as means to improve primary prevention in their latest European Stroke Action Plan[5]. A risk factor based model of cardiovascular health (CVH) was developed by the American Heart Association in 2010 for prevention of cardiovascular disease (CVD) and stroke[6]. CVH is measured using 7 traditional health metrics: smoking, body mass index (BMI), physical activity (PA), diet patterns, total cholesterol, blood pressure (BP) and fasting glucose, referred to as Life's Simple 7 (LS7). Population prevalences of ideal, intermediate or poor levels of each metric, and of summary CVH scores based on all seven metrics, have been explored in association with a range of CVD outcomes[7,8] to identify metrics that can be targeted as part of health promotion programs.

Most studies however, have either evaluated stroke as a combined end-point within CVD[9-13]; are constrained by examining CVH at middle age[14,15]; or have limited follow up[13,15,16]. Few have analysed how CVH relates specifically to stroke in older populations[17,18]. Similarly, there is limited clarity on how transitions in CVH over time can influence stroke incidence at an older age[19-21]. These issues are essential to explore because associations between conventional risk factors and CVD weaken with age due to a selection of survivors[22-24]. Secondly, despite some shared risk factors, stroke epidemiology and aetiology is somewhat distinct from broader CVD outcomes[7,25]. Stroke prevention strategies for older adults may hence require a different focus.

To assess the influence of CVH on incidence of stroke in older age, we used data from the British Regional Heart Study (BRHS), which has been following cardiovascular outcomes in a representative cohort of British men for more than 40 years. Our specific aims were to (1) compare associations between LS7 metrics, composite CVH scores, and stroke in middle and older age; (2) explore if change in CVH between middle and older age was associated with subsequent stroke incidence; and (3) determine the impact of LS7 metrics on the burden of stroke across middle and older age.

Methods

Data supporting the findings of this study are available from the study manager (Ms L Lennon; l.lennon@ucl.ac.uk) upon reasonable request.

The BRHS recruited 7,735 men 40-59y, from 24 primary care practices across Britain in 1978-1980[26-28]. Participants contributed sociodemographic, health, medication and lifestyle data through questionnaires; and underwent objective and lab-based examinations, including an ECG, at baseline[29,30] and 20-year follow-up (Q20)[27,28]. This analysis used information on LS7 metrics collected at both time points together with CVD events and deaths to June 2018. All participants provided written informed consent in accordance with the Declaration of Helsinki. Ethical approval was obtained from relevant local research ethics committees.

Assessment of CVH

Life's Simple 7 metrics were measured objectively except for smoking, PA and diet which were self-reported. Diet was measured at Q20 only[31]. Metrics were categorised as poor, intermediate and ideal using American Heart Association definitions except smoking, PA and diet, which were classified using BRHS specific cut-offs[29,31-37] (details in Supplemental Table I).

Composite CVH scores were sum of points (0, 1, 2 respectively) assigned to poor, intermediate and ideal levels of each LS7 metric. CVH scores ranged from 0-12 at baseline (dietary information was not available) and 0-14 at Q20. Lower scores indicated poorer CVH. CVH categories[38] were derived from CVH score as inadequate (0-4 baseline and Q20), average (5-8 baseline, 5-9 Q20) and optimum (9-12 baseline, 10-14 Q20).

For capturing change in CVH from baseline to Q20, CVH trajectories were derived using CVH scores (exclusive of diet, range 0-12) from each time point. .Scores were dichotomised using the median value. A score ≤7 was classed as low and >7 as high CVH; hence each participant belonged to one of 4 CVH trajectory groups: low-low, low-high, high-low and high-high.

Ascertainment of Stroke, Myocardial Infarction and Mortality

Participants were followed up for mortality and non-fatal stroke and myocardial infarction (MI). Deaths were collected through National Health Service Central Registers in Southport (for England and Wales) and Edinburgh (for Scotland), with cause of death coded using the International Classification of Diseases, Ninth Revision. Fatal stroke was coded as 430-438 and fatal MI as 410-414.

Non-fatal events were ascertained from ongoing general practitioner reports and biennial reviews of participants' medical records[27]. Non-fatal MI was defined according to World Health Organization criteria[39] and non-fatal stroke as an event producing a neurological deficit for more than 24h. General practitioners were asked to review records of all surviving participants every 2 years and identify any non-fatal stroke on a standard form. In such cases, they were also asked to provide information on clinical presentation, hospital record summaries and results of specific investigations where available, including brain scans. This

material was reviewed by a BRHS clinical assessor, particularly to exclude any non-stroke diagnoses.

Analyses excluded men with prevalent CVD. Prevalent CVD at baseline (stroke, angina, coronary thrombosis and MI) was determined from self-report of physician diagnosis; and at Q20 if a stroke or MI was noted in record review data prior to Q20.

Covariates

Self–reported social class (manual, non-manual and armed forces; based on longest held occupation) and alcohol intake (none, occasional, light, moderate and heavy) were recorded at both waves[28]. Atrial fibrillation (AF) was recorded using a 12-lead ECG at Q20.

Statistical Analyses

Descriptive statistics compared sociodemographic characteristics, LS7 metrics, composite CVH scores and stroke incidence per 1000 person years (PY) from baseline and Q20; as well as profiles of CVH trajectories. Cox proportional hazards models estimated hazard ratios (HRs) of stroke for individual LS7 metrics, CVH scores and trajectory groups. Time to event was calculated from the baseline/Q20 date of examination to a stroke event or death, whichever came first. For participants with neither event, data was censored at the Q20 date for baseline and 1st June 2018 for Q20 analysis respectively. Adjustments were made for social class at baseline, and age and alcohol intake at the respective time point. Proportional hazards assumptions examined using Schoenfeld residuals were found to hold.

Associations were based on available complete cases. However, in sensitivity analyses we investigated characteristics of men with missing covariates; and robustness of associations by assigning the worst possible LS7 level (poor) to those with missing data on any LS7.

Analyses were conducted using Stata software version 15 (StataCorp LLC, Texas, USA). To explore how useful LS7 metrics were at discriminating between cases and non-cases of stroke we compared Harell's C-statistics of multivariate models at baseline and Q20. We also compared the fraction of incident stroke attributable to individual LS7 metrics-population attributable fraction (PAF) at each time point, using the punafcc[40] package for Stata, evaluating the scenario where all participants had the metric in question at the ideal level.

We examined whether excluding men with prevalent heart failure (n=73, 2%) and those with ECG evidence of AF (n=122, 3%) at Q20 affected results; and further explored associations between LS7 metrics, CVH scores, trajectories and a CVD outcome of stroke and MI combined.

Results

LS7 and Composite CVH scores

There were 7274 men (mean age 50y) without prevalent CVD at baseline. After a median follow-up of 19.8 years, 434 fatal and non-fatal stroke events occurred at a rate of 3.3/1000PY. Among LS7, glucose (65%) was most and BP (9%) least prevalent at ideal levels. Mean composite CVH score was 6.3 (range 0-12), with 71% men in the average and only 12% in the optimal CVH category (Fig1 and Supp.Table II).

At Q20, there were 3798 men (mean age 69y) without prevalent CVD. After a median follow-up of 15.7 years, there were 446 stroke events at a rate of 8.7/1000PY. Among measured LS7, smoking status (84%) was most and BP (7%) least prevalent at ideal levels. Mean composite CVH score was 7.7 (range 0-14; exclusive of diet: mean 6.8, range 0-12), with 76% of men in the average and 18% in the optimal CVH category (Fig1 and Supp.Table II).

Cox regression of individual LS7 metrics (Table 1) revealed that at younger ages, healthier levels of BP, PA and smoking status were associated with reduced risk of stroke. Compared to poor levels, adjusted HRs (95% CI) for intermediate and ideal levels were respectively 0.65 (0.52, 0.81) and 0.40 (0.24, 0.65) for BP; 0.79 (0.58, 1.08) and 0.63 (0.45, 0.88) for PA; and 0.69 (0.56, 0.86) and 0.59 (0.45, 0.78) for smoking. Favourable trends were also seen for better BMI and glucose levels although not statistically significant at a conventional cut-off of p=0.05. A unit increase in composite CVH score was associated with 16% reduced risk of stroke, adjusted HR 0.84 (0.79, 0.89). Better categories of overall CVH were also protective for stroke: compared to the inadequate category, an average to optimal CVH status was associated with between a 40 to 60% reduction in hazard ratios (p for trend <0.0001).

At Q20, BP was the only LS7 metric showing a clear (but attenuated) association with subsequent stroke. Compared to poor BP, adjusted HRs for intermediate and ideal levels were 0.84 (0.67, 1.05) and 0.57 (0.36, 0.90) respectively, p for trend 0.0168 (Table 1). Each unit increase in composite CVH score was associated with 5% reduced risk of stroke (adjusted HR 0.95 (0.90, 1.01)). Associations between CVH score categories and stroke similarly became weaker and non-significant, p for trend 0.1394.

Trajectories of CVH between baseline and Q20

A fifth of men maintained high CVH from baseline to Q20 (n=641), while more than half had persistently low CVH over the same period (n=1740). Five hundred and sixty three men improved their CVH from low to high, while CVH of 425 men deteriorated from high to low (Table 2). Incidence rates (95% CI) of stroke per 1000PY were low-low 9.8 (8.6, 11.2); low-high 6.2 (4.7, 8.2); high-low 7.3 (5.5, 9.8) and high-high 7.9 (6.3, 9.8). In comparison to low-low, all remaining groups showed reduced probabilities of stroke (Figure 2). Low-high in particular had a 40% reduced stroke risk (adjusted HR 0.60 95% CI 0.44, 0.83).

Excluding men with heart failure and AF at Q20 did not materially affect results of the above analyses.

Less than 3% of the men had missing data at baseline. At Q20, a maximum of 18% of the men had missing covariates. These men were slightly older with a higher incidence of stroke but with similar mean blood pressures and smoking habits to those with complete data (Supp.Table III). The men had poorer CVH at baseline. However, associations were robust even in analyses that assumed a poor level for missing LS7 data (Supp.Table IV).

Impact of LS7 across time

In multivariable models containing all LS7 metrics except diet; and adjusted for age, social class and alcohol intake, Harrell's C statistic decreased from 0.7103 at baseline to 0.6548 at Q20. The PAFs of LS7 metrics also decreased over time (Supp.Table V). Notably, the burden of stroke that could be eliminated by control of high BP reduced from 53% in middle age to 39% in older age.

CVH and a combined CVD outcome

All LS7 metrics measured at Q20, except BMI and cholesterol, showed significant associations in expected directions with MI and stroke combined (Supp.Table VI). In analysis comparing trajectories to low-low, all groups had significantly reduced risk of a combined CVD outcome with high-high and low-high groups having a risk reduction of similar magnitude.

Discussion

This prospective analysis assessed the associations and impact of CVH and its component LS7 metrics on stroke burden, during middle and older ages in a general population sample of British men free of CVD.

We noted that BP, PA and smoking at baseline were associated with stroke in middle age, but only BP maintained a clear (albeit weaker) inverse association with stroke in later life. Others looking at older subjects[16,23,41] have established the influence of BP on stroke across the life-course. Our findings reaffirm its value as a key target in stroke prevention strategies. However, we highlight that the burden of stroke which can potentially be eliminated by achieving ideal BP control decreases with increasing age. Our PAF (39%) among older men (vs 53% at baseline), of BP higher than the ideal (of untreated 120/80 mmHg) is similar to that estimated by the Rotterdam study[42] among men of a similar mean age (69y) as BRHS; and to the PAF of hypertension calculated (with a higher cut-off) among European participants of the INTERSTROKE study[43] (which also noted hypertension as a stronger risk factor in those <55y). It is likely that even this (39%) is an overestimate, since in reality all men of older age are unlikely to attain ideal BP as defined by the American Heart Association. It has in fact been observed that among those ≥80y, the PAF for stroke due to hypertension becomes insignificant[44].

Apart from BP, no other LS7 metrics individually influenced stroke in older men. Accordingly, higher (healthier) composite CVH scores at older ages offered weaker protection against stroke. The C statistic for our multivariate Q20 model, similar to that recorded by Dong et al[17] among participants of a comparable age, also reflects the weak ability of these metrics to jointly, correctly classify stroke events from non-events at older age.

These findings underscore the need to optimize the detection and/or management of wider conditions known to increase the risk of stroke in older populations. Research from primary care in the UK indicates that both screening of AF among those >65y[45] and its anticoagulation management among those >85y[46] can be improved. More recently, aging related atrial cardiopathy has been linked to stroke independent of AF[47]. Other risk factors to

direct prevention strategies towards include subclinical cardiac dysfunction[48] and impaired kidney function, which has been recently highlighted to increase in impact with increasing life span[49].

Our analysis using a composite endpoint of MI and stroke observed that among older men, most individual LS7 metrics as well as CVH score categories exhibited clear expected associations with combined CVD. This may reflect greater influence of conventional factors in old age on coronary outcomes as opposed to stroke, and has also been noted among Swedish men[41]. It further suggests that health promotion targeting conventional factors such as LS7 among older adults would be less likely to reduce the burden of stroke in contrast to MI.

Nevertheless, the trajectory analysis indicated that the importance of adopting and maintaining a healthy lifestyle even in later life cannot be undermined. In previous work analyzing associations of change in CVH status with broad CVD outcomes, Enserro et al[21] using data from the Framingham Offspring study concluded that irrespective of whether they improved or not, people starting with low CVH status had higher rates of composite CVD compared to those maintaining high CVH throughout the study period. Analysis of Whitehall II data using a more precise categorization of CVH trajectories (9 groups) failed to show consistent associations with incident CVD[19]. In comparison, older BRHS men who improved CVH from low to high had reduced risk of stroke and MI combined, of a magnitude similar to that offered by maintaining high CVH throughout life. This suggests that later life CVH has a greater bearing on subsequent CVD. We further noted this benefit, although not as large, for stroke alone. Yang et al[50] do identify a similar protective trend against stroke from positive changes in CVH but among a younger Chinese cohort and over a shorter transition period. We must point out however; that we cannot identify the exact time between baseline and Q20 when men may have transitioned in CVH status, or indeed, if there was more than

one transition. Exposure durations may hence be variable and hazards may not accurately reflect this. Moreover, although similar to the creation of trajectory groups by others[21], our binary CVH score cut-off is arbitrarily based on the median for both baseline and Q20.

Our study is novel in its exploration of CVH and its association with stroke as a specific outcome during both middle and older age within the same population; with near complete follow up, over an extended period. Stroke capture has been reliable - the incidence rates of stroke during both middle and older age observed using the study protocol have been comparable with national data[51,52]. Furthermore, we based our analyses on the full range of CVH score (0-12/14) as opposed to only an aggregate of ideal LS7 metrics (0-6/7). This takes into account intermediate levels of a metric and may be more realistic for older ages when drug therapies for diabetes, dyslipidemia and hypertension preclude ideal levels of these metrics. It is worth noting here that less than a fifth of our older men attained an optimal composite CVH score needing ≥5 metrics at the ideal level.

Men participating in the BRHS are of predominantly white ethnicity so generalizability of our findings to women and wider British population groups will be limited; however, findings are still relevant to a large section of the contemporary older population in the UK. Additionally, we lacked a measure of diet at baseline and in deriving CVH trajectories. However, the utility of an overall dietary score may be less consistent with respect to stroke/CVD[14,16,18]. Finally, we were unable to classify stroke into its subtypes and acknowledge that observed associations may not apply equally to ischemic and haemorrhagic stroke.

Conclusion

With the exception of BP, CVH is weakly associated with stroke at older ages. Prevention strategies should prioritise control of BP and energise efforts beyond traditional risk factors

towards better detection and management of wider causes, including AF. Research into stroke prevention in older adults should also consider potential subclinical conditions such as cardiac and kidney dysfunction that can influence stroke burden.

Sources of funding

AA is funded by UK Medical Research Council Doctoral Training Programme (MR/N013867/1). SMPP by UK Medical Research Council Career Development Award (MR/P020372/1). The BRHS is funded by a British Heart Foundation grant (RG/13/16/30528).

Disclosures

None

Supplemental Materials

Expanded Materials and Methods

Online Tables I-VI

References 31-37

References

1. Johnson CO, Nguyen M, Roth GA, Nichols E, Alam T, Abate D, Abd-Allah F, Abdelalim A, Abraha HN, Abu-Rmeileh NM, et al. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2019;18:439-458.
2. Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, Culebras A, DeGraba TJ, Gorelick PB, Guyton JR, et al. Primary Prevention of Ischemic Stroke. *Stroke.* 2006;37:1583-1633.
3. King D, Wittenberg R, Patel A, Quayyum Z, Berdunov V, Knapp M. The future incidence, prevalence and costs of stroke in the UK. *Age Ageing.* 2020;49:277-282.
4. Feigin VL, Norrving B, George MG, Foltz JL, Roth GA, Mensah GA. Prevention of stroke: a strategic global imperative. *Nature Reviews Neurology.* 2016;12:501-512.
5. Norrving B, Barrick J, Davalos A, Dichgans M, Cordonnier C, Guekht A, Kutluk K, Mikulik R, Wardlaw J, Richard E, et al. Action Plan for Stroke in Europe 2018–2030. *European Stroke Journal.* 2018;3:309-336.
6. Lloyd-Jones DM, Hong YL, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, Greenlund K, Daniels S, Nichol G, Tomaselli GF, et al. Defining and Setting National Goals for Cardiovascular Health Promotion and Disease Reduction The American Heart Association's Strategic Impact Goal Through 2020 and Beyond. *Circulation.* 2010;121:586-613.
7. Ramirez-Velez R, Saavedra JM, Lobelo F, Celis-Morales CA, del Pozo-Cruz B, Garcia-Hermoso A. Ideal Cardiovascular Health and Incident Cardiovascular Disease Among Adults: A Systematic Review and Meta-analysis. *Mayo Clin Proc.* 2018;93:1589-1599.

8. Younus A, Aneni EC, Spatz ES, Osondu CU, Roberson L, Ogunmoroti O, Malik R, Ali SS, Aziz M, Feldman T, et al. A Systematic Review of the Prevalence and Outcomes of Ideal Cardiovascular Health in US and Non-US Populations. *Mayo Clin Proc.* 2016;91:649-670.

9. Peng Y, Wang Z. Association of Life's Simple 7 and presence of cardiovascular disease in general Australians. *Open Heart.* 2017;4:e000622.

10. Kim JY, Ko YJ, Rhee CW, Park BJ, Kim DH, Bae JM, Shin MH, Lee MS, Li ZM, Ahn YO. Cardiovascular health metrics and all-cause and cardiovascular disease mortality among middle-aged men in Korea: the Seoul male cohort study. *J Prev Med Public Health.* 2013;46:319-328.

11. Ford ES, Greenlund KJ, Hong Y. Ideal cardiovascular health and mortality from all causes and diseases of the circulatory system among adults in the United States. *Circulation.* 2012;125:987-995.

12. Folsom AR, Yatsuya H, Nettleton JA, Lutsey PL, Cushman M, Rosamond WD. Community prevalence of ideal cardiovascular health, by the American Heart Association definition, and relationship with cardiovascular disease incidence. *J Am Coll Cardiol.* 2011;57:1690-1696.

13. Miao CL, Bao MH, Xing AJ, Chen SH, Wu YT, Cai J, Chen YR, Yang XC. Cardiovascular Health Score and the Risk of Cardiovascular Diseases. *Plos One.* 2015;10.

14. Lachman S, Peters RJ, Lentjes MA, Mulligan AA, Luben RN, Wareham NJ, Khaw KT, Boekholdt SM. Ideal cardiovascular health and risk of cardiovascular events in the EPIC-Norfolk prospective population study. *Eur J Prev Cardiol.* 2016;23:986-994.

15. Zhang Q, Zhou Y, Gao X, Wang CX, Zhang SF, Wang AX, Li N, Bian LH, Wu JW, Jia Q, et al. Ideal Cardiovascular Health Metrics and the Risks of Ischemic and Intracerebral Hemorrhagic Stroke. *Stroke.* 2013;44:2451-2456.

16. Kulshreshtha A, Vaccarino V, Judd SE, Howard VJ, McClellan WM, Muntner P, Hong YL, Safford MM, Goyal A, Cushman M. Life's Simple 7 and Risk of Incident Stroke The Reasons for Geographic and Racial Differences in Stroke Study. *Stroke.* 2013;44:1909-+.

17. Dong CH, Rundek T, Wright CB, Anwar Z, Elkind MSV, Sacco RL. Ideal Cardiovascular Health Predicts Lower Risks of Myocardial Infarction, Stroke, and Vascular Death Across Whites, Blacks, and Hispanics The Northern Manhattan Study. *Circulation.* 2012;125:2975-+.

18. Gaye B, Canonico M, Perier MC, Samieri C, Berr C, Dartigues JF, Tzourio C, Elbaz A, Empana JP. Ideal Cardiovascular Health, Mortality, and Vascular Events in Elderly Subjects: The Three-City Study. *J Am Coll Cardiol.* 2017;69:3015-3026.

19. van Sloten TT, Tafflet M, Perier MC, Dugravot A, Climie RED, Singh-Manoux A, Empana JP. Association of Change in Cardiovascular Risk Factors With Incident Cardiovascular Events. *JAMA.* 2018;320:1793-1804.

20. Wu S, An S, Li W, Lichtenstein AH, Gao J, Kris-Etherton PM, Wu Y, Jin C, Huang S, Hu FB, et al. Association of Trajectory of Cardiovascular Health Score and Incident Cardiovascular Disease. *JAMA Netw Open.* 2019;2:e194758.

21. Enserro DM, Vasan RS, Xanthakis V. Twenty-Year Trends in the American Heart Association Cardiovascular Health Score and Impact on Subclinical and Clinical Cardiovascular Disease: The Framingham Offspring Study. *J Am Heart Assoc.* 2018;7.

22. Lind L, Sundström J, Ärnlöv J, Lampa E. Impact of Aging on the Strength of Cardiovascular Risk Factors: A Longitudinal Study Over 40 Years. *Journal of the American Heart Association.* 2018;7:e007061.

23. Murakami K, Asayama K, Satoh M, Inoue R, Tsubota-Utsugi M, Hosaka M, Matsuda A, Nomura K, Murakami T, Kikuya M, et al. Risk Factors for Stroke among Young-Old and Old-Old Community-Dwelling Adults in Japan: The Ohasama Study. *J Atheroscler Thromb.* 2017;24:290-300.

24. Odden MC, Shlipak MG, Whitson HE, Katz R, Kearney PM, defilippi C, Shastri S, Sarnak MJ, Siscovick DS, Cushman M, et al. Risk factors for cardiovascular disease across the spectrum of older age: the Cardiovascular Health Study. *Atherosclerosis.* 2014;237:336-342.

25. Soler EP, Ruiz VC. Epidemiology and risk factors of cerebral ischemia and ischemic heart diseases: similarities and differences. *Curr Cardiol Rev.* 2010;6:138-149.

26. Lennon LT, Ramsay SE, Papacosta O, Shaper AG, Wannamethee SG, Whincup PH. Cohort Profile Update: The British Regional Heart Study 1978-2014: 35 years follow-up of cardiovascular disease and ageing. *International Journal of Epidemiology.* 2015;44.

27. Walker M, Shaper AG, Lennon L, Whincup PH. Twenty year follow-up of a cohort based in general practices in 24 British towns. *J Public Health Med.* 2000;22:479-485.

28. Walker M, Whincup PH, Shaper AG. The British Regional Heart Study 1975-2004. *Int J Epidemiol.* 2004;33:1185-1192.

29. Shaper AG, Phillips AN, Pocock SJ, Walker M, Macfarlane PW. Risk factors for stroke in middle aged British men. *BMJ.* 1991;302:1111-1115.

30. Shaper AG, Pocock SJ, Walker M, Cohen NM, Wale CJ, Thomson AG. British Regional Heart Study: cardiovascular risk factors in middle-aged men in 24 towns. *Br Med J (Clin Res Ed).* 1981;283:179-186.

31. Atkins JL, Whincup PH, Morris RW, Lennon LT, Papacosta O, Wannamethee SG. High Diet Quality Is Associated with a Lower Risk of Cardiovascular Disease and All-Cause Mortality in Older Men. *J Nutr.* 2014;144:673-680.

32. Aggio D, Papachristou E, Papacosta O, Lennon LT, Ash S, Whincup P, Wannamethee SG, Jefferis BJ. Trajectories of physical activity from midlife to old age and associations with subsequent cardiovascular disease and all-cause mortality. *J Epidemiol Community Health.* 2020;74:130-136.

33. Kourlaba G, Polychronopoulos E, Zampelas A, Lionis C, Panagiotakos DB. Development of a diet index for older adults and its relation to cardiovascular disease risk factors: the Elderly Dietary Index. *J Am Diet Assoc.* 2009;109:1022-1030.

34. Taylor HL, Jacobs DR, Jr., Schucker B, Knudsen J, Leon AS, Debacker G. A questionnaire for the assessment of leisure time physical activities. *J Chronic Dis.* 1978;31:741-755.

35. Wilson PW, Paffenbarger RS, Jr., Morris JN, Havlik RJ. Assessment methods for physical activity and physical fitness in population studies: report of a NHLBI workshop. *Am Heart J.* 1986;111:1177-1192.

36. World Health Organization. The World Health Organization MONICA Project (monitoring trends and determinants in cardiovascular disease): a major international collaboration. WHO MONICA Project Principal Investigators. *J Clin Epidemiol.* 1988;41:105-114.

37. Yarnell JW, Fehily AM, Milbank JE, Sweetnam PM, Walker CL. A short dietary questionnaire for use in an epidemiological survey: comparison with weighed dietary records. *Hum Nutr Appl Nutr.* 1983;37:103-112.

38. Huffman MD, Capewell S, Ning H, Shay CM, Ford ES, Lloyd-Jones DM. Cardiovascular Health Behavior and Health Factor Changes and Projections to 2020. *Circulation.* 2012;125:2595-2602.

39. Rose GA, Blackburn H, Gillum RF, Prineas RJ. *Cradiovascular Survey Methods, 2nd Edition.* Geneva, Switzerland: World Health Organization; 1982.

40. Newson RB. Attributable and Unattributable Risks and Fractions and other Scenario Comparisons. *The Stata Journal.* 2013;13:672-698.

41. Giang KW, Bjorck L, Novak M, Lappas G, Wilhelmsen L, Toren K, Rosengren A. Stroke and coronary heart disease: predictive power of standard risk factors into old age--long-term cumulative risk study among men in Gothenburg, Sweden. *Eur Heart J.* 2013;34:1068-1074.

42. Bos MJ, Koudstaal PJ, Hofman A, Ikram MA. Modifiable Etiological Factors and the Burden of Stroke from the Rotterdam Study: A Population-Based Cohort Study. *PLOS Medicine.* 2014;11:e1001634.

43. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu LS, Zhang HY, Rao-Melacini P, Zhang XH, Pais P, Agapay S, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *Lancet.* 2016;388:761-775.

44. Willey JZ, Moon YP, Kahn E, Rodriguez CJ, Rundek T, Cheung K, Sacco RL, Elkind MS. Population attributable risks of hypertension and diabetes for cardiovascular disease and stroke in the northern Manhattan study. *J Am Heart Assoc.* 2014;3:e001106.

45. Karnad A, Pannelay A, Boshnakova A, Lovell AD, Cook RG. Stroke prevention in Europe: how are 11 European countries progressing toward the European Society of Cardiology (ESC) recommendations? *Risk Manag Healthc Policy.* 2018;11:117-125.

46. Turner GM, Calvert M, Feltham MG, Ryan R, Finnikin S, Marshall T. Clinical and Demographic Characteristics Associated With Suboptimal Primary Stroke and Transient Ischemic Attack Prevention: Retrospective Analysis. *Stroke.* 2018;49:682-687.

47. Boehme AK, Esenwa C, Elkind MS. Stroke Risk Factors, Genetics, and Prevention. *Circ Res.* 2017;120:472-495.

48. Portegies ML, Kavousi M, Leening MJ, Bos MJ, van den Meiracker AH, Hofman A, Franco OH, Koudstaal PJ, Ikram MA. N-terminal pro-B-type natriuretic peptide and the risk of stroke and transient ischaemic attack: the Rotterdam Study. *Eur J Neurol.* 2015;22:695-701.

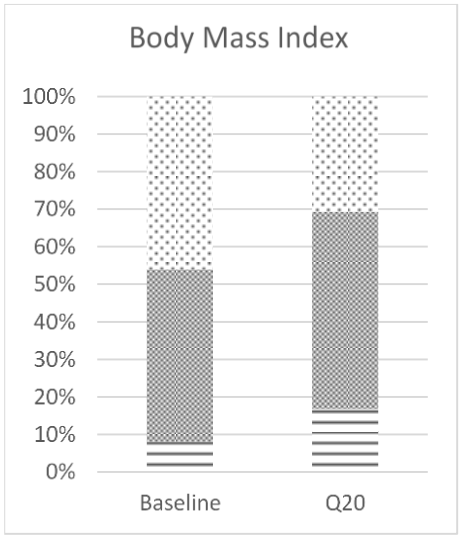
49. Hankey GJ. Population Impact of Potentially Modifiable Risk Factors for Stroke. *Stroke.* 2020;51:719-728.

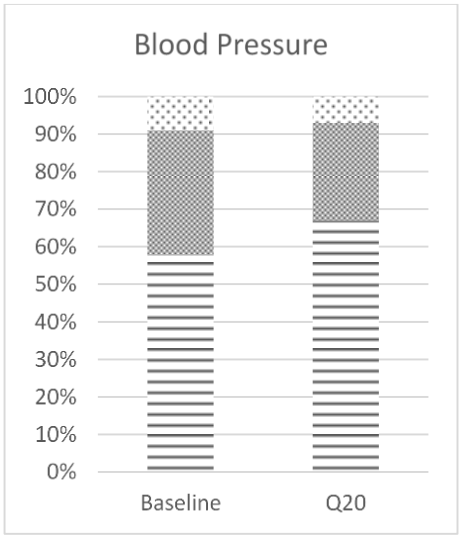
50. Yang X, Wang A, Liu X, An S, Chen S, Wang Y, Wang Y, Wu S. Positive changes in ideal CVH metrics reduce the incidence of stroke. *Sci Rep.* 2016;6:19673.

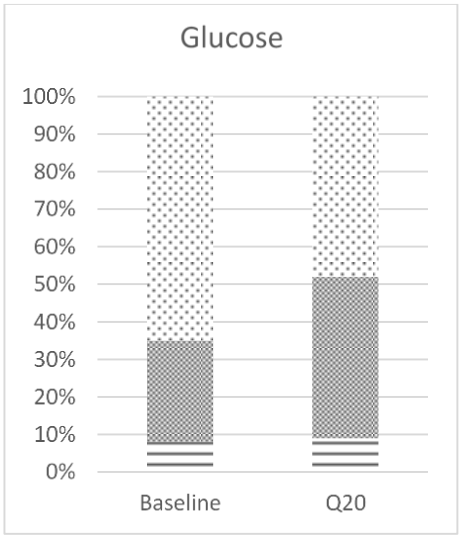
51. Wolfe CD, Rudd AG, Howard R, Coshall C, Stewart J, Lawrence E, Hajat C, Hillen T. Incidence and case fatality rates of stroke subtypes in a multiethnic population: the South London Stroke Register. *J Neurol Neurosurg Psychiatry.* 2002;72:211-216.

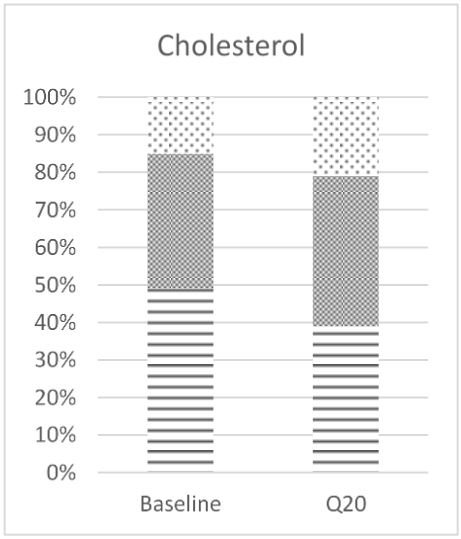
52. Scarborough P, Peto V, Bhatnagar P, Kaur A, Leal J, Luengo-Fernandez R, Gray A, Rayner M, Allender S. *Stroke Statistics* Oxford, England: British Heart Foundation & Stroke Association; 2009.

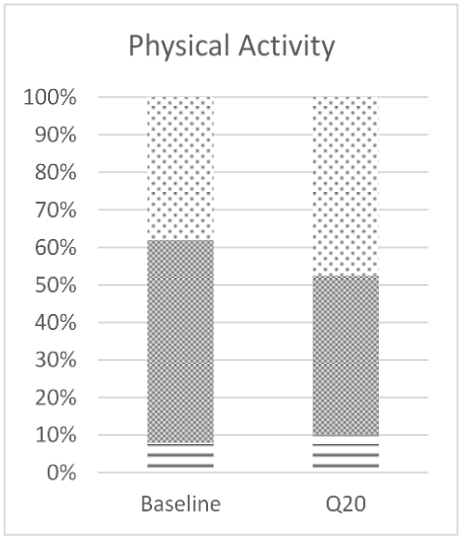
FIGURE 1. Proportions of LS7 metrics at baseline and at 20y follow-up (Q20) among men of the British Regional Heart study free of prevalent CVD

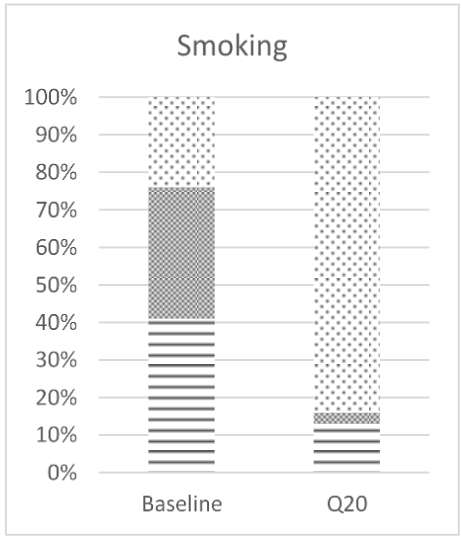

Body Mass Index
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Baseline
Q20


Blood Pressure
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Baseline
Q20


Glucose
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Baseline
Q20


Cholesterol
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Baseline
Q20


Physical Activity
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Baseline
Q20


Smoking
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Baseline
Q20

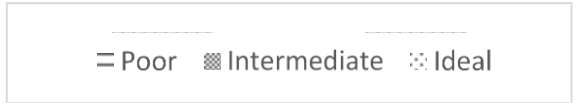

Poor
Intermediate
Ideal

FIGURE 2. Stroke free probability curves in cardiovascular health trajectory groups among men free of prevalent cardiovascular disease at 20y of follow-up; adjusted for age, social class and alcohol intake

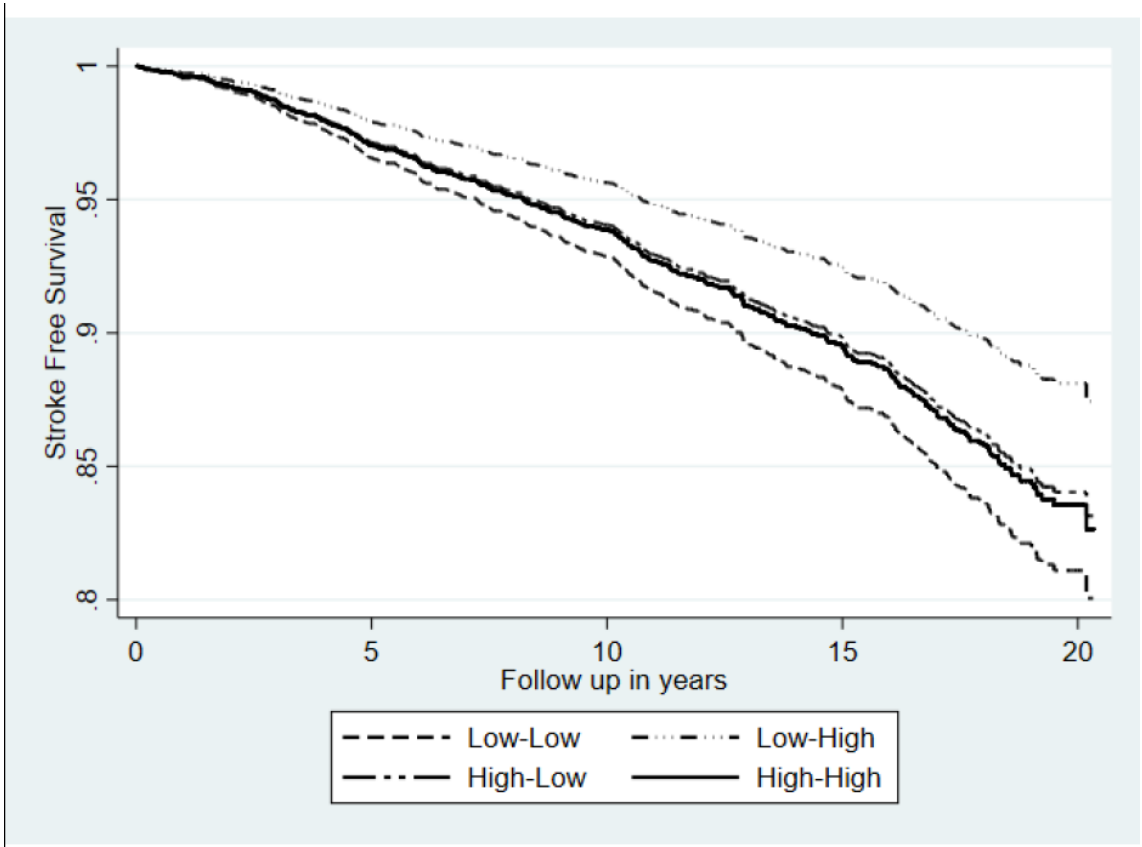


TABLE 1. Hazard ratios [95% CI] for stroke among men in the BRHS, free of prevalent CVD at baseline and at Q20

	Baseline 1978-1980[1]		**Q20 1998-2000[2]**	
	Model 1	Model 2	Model 1	Model 2
BMI	N=7273	N=7256	N=3783	N=3717
Poor	1	1	1	1
Intermediate	0.79 [0.57, 1.10]	0.81 [0.58, 1.13]	1.20 [0.90, 1.60]	1.22 [0.91, 1.62]
Ideal	0.72 [0.52, 1.00]	0.75 [0.54, 1.05]	1.18 [0.87, 1.60]	1.19 [0.87, 1.62]
P for trend	0.0524	0.0950	0.2982	0.2720
BP	N=7267	N=7250	N=3779	N=3713
Poor	1	1	1	1
Intermediate	0.63 [0.51, 0.79]	0.65 [0.52, 0.81]	0.86 [0.69, 1.08]	0.84 [0.67, 1.05]
Ideal	0.38 [0.23, 0.62]	0.40 [0.24, 0.65]	0.57 [0.36, 0.91]	0.57 [0.36, 0.90]
P for trend	0.0001	0.0002	0.0190	0.0168
Glucose	N=7228	N=7211	N=3590	N=3528
Poor	1	1	1	1
Intermediate	0.86 [0.62, 1.20]	0.88 [0.63, 1.23]	0.87 [0.62, 1.22]	0.85 [0.61, 1.20]
Ideal	0.72 [0.53, 0.98]	0.74 [0.54, 1.01]	0.79 [0.56, 1.11]	0.78 [0.55, 1.09]
P for trend	0.0397	0.0617	0.1762	0.1467
Cholesterol	N=7232	N=7215	N=3618	N=3556
Poor	1	1	1	1
Intermediate	1.04 [0.85, 1.27]	1.03 [0.84, 1.26]	0.87 [0.70, 1.08]	0.85 [0.69, 1.06]
Ideal	0.87 [0.65, 1.17]	0.84 [0.63, 1.14]	1.07 [0.84, 1.38]	1.09 [0.85, 1.40]
P for trend	0.3625	0.2659	0.5800	0.4981
Physical Activity	N=7178	N=7163	N=3665	N=3616
Poor	1	1	1	1

Intermediate	0.78 [0.57, 1.06]	0.79 [0.58, 1.08]	1.01 [0.71, 1.44]	1.02 [0.71, 1.45]
Ideal	0.59 [0.42, 0.82]	0.63 [0.45, 0.88]	0.86 [0.60, 1.22]	0.88 [0.62, 1.26]
P for trend	0.0018	0.0066	0.3900	0.4988
Smoking	N=7260	N=7244	N=3792	N=3727
Poor	1	1	1	1
Intermediate	0.66 [0.54, 0.82]	0.69 [0.56, 0.86]	0.57 [0.25, 1.34]	0.57 [0.25, 1.34]
Ideal	0.54 [0.41, 0.71]	0.59 [0.45, 0.78]	0.86 [0.64, 1.14]	0.86 [0.64, 1.16]
P for trend	<0.0001	0.0002	0.2933	0.3266
Elderly Diet Index			N=3512	N=3452
Poor	…	…	1	1
Intermediate	…	…	1.08 [0.86, 1.35]	1.13 [0.89, 1.42]
Ideal	…	…	1.01 [0.78, 1.30]	1.06 [0.82, 1.37]
P for trend	…	…	0.9413	0.6780
	N=7112	N=7097	N=3177	N=3135
Composite CVH Score	0.83 [0.78, 0.87]	0.84 [0.79, 0.89]	0.95 [0.90, 1.00]	0.95 [0.90, 1.01]
CVH score categories[§]				
Inadequate	1	1	1	1
Average	0.56 [0.45, 0.70]	0.59 [0.47, 0.73]	0.71 [0.45, 1.10]	0.73 [0.46, 1.15]
Optimal	0.35 [0.23, 0.54]	0.39 [0.25, 0.61]	0.65 [0.40, 1.07]	0.68 [0.41, 1.13]
P for trend	<0.0001	<0.0001	0.0924	0.1394

Model 1 adjusted for age. Model 2 adjusted additionally for social class and alcohol intake at baseline/Q20.

Abbreviations: BMI, Body Mass Index; BP, Blood Pressure; BRHS, British Regional Heart Study; CVD, cardiovascular disease; CVH, cardiovascular health; Q20, 20y follow-up.

[1]Followed from baseline to Q20; [2]Followed from Q20 to June 2018; [§]Inadequate: 0-4 baseline and Q20, Average: 5-8 baseline/5-9 Q20, Optimal: 9-12 baseline/10-14 Q20.

TABLE 2. Profiles of CVH Trajectories and hazard ratios [95% CI] for stroke among men in the BRHS, free of prevalent CVD at Q20

	CVH Trajectories over 20 years[1]			
	Low-Low (N=1740)	**Low-High (N=563)**	**High-Low (N=425)**	**High-High (N=641)**
Stroke events	217	48	46	78
Incidence Rate per 1000PY (95% CI)	9.8 (8.6, 11.2)	6.2 (4.7, 8.2)	7.3 (5.5, 9.8)	7.9 (6.3, 9.8)
Age (yrs)*	69 (5.4)	69 (5.5)	67 (5.2)	67 (5.4)
Social class				
Non-Manual	711 (41)	258 (46)	238 (56)	379 (59)
Manual	979 (56)	287 (51)	177 (42)	249 (39)
Armed Forces	44 (3)	18 (3)	10 (2)	12 (2)
BMI (kg/m^2)*	27.9 (3.8)	25.6 (3.1)	26.7 (3.0)	24.8 (2.6)
Poor	25	4	13	2
Intermediate	56	50	63	39
Ideal	19	46	23	58
BP (mmHg)				
Sitting Systolic*	156 (23)	144 (23)	152 (21)	138 (24)
Sitting Diastolic*	87 (11)	83 (10)	88 (10)	83 (11)
Poor	79	51	77	44
Intermediate	19	37	21	39
Ideal	2	12	2	17
Glucose (mmol/l)*	6.4 (2.2)	5.5 (0.9)	5.9 (1.0)	5.5 (0.7)
Poor	16	1	6	1
Intermediate	49	30	55	31
Ideal	36	69	40	68

	CVH Trajectories over 20 years[1]			
	Low-Low (N=1740)	**Low-High (N=563)**	**High-Low (N=425)**	**High-High (N=641)**
Cholesterol (mmol/l)*	6.3 (1.1)	5.6 (0.9)	6.2 (1.0)	5.5 (0.9)
Poor	52	15	53	17
Intermediate	36	50	36	43
Ideal	12	35	11	40
Physical Activity				
Poor	15	2	11	3
Intermediate	50	28	49	28
Ideal	35	70	40	70
Smoking				
Poor	20	4	10	3
Intermediate	5	1	1	1
Ideal	75	95	88	97
Composite CVH score*†	5.7 (1.2)	8.5 (0.7)	6.3 (0.9)	8.8 (0.9)
Hazard Ratio (95% CI) ‡	1	0.60 (0.44, 0.83)	0.83 (0.60, 1.15)	0.86 (0.66, 1.12)

Profiles are as at Q20. N varies due to missing data.

Abbreviations: as in Table 1

[1]N=3369, stroke events=389 for men followed from 1998/2000 to June 2018; *mean (sd); †range 0-12 excluding diet; ‡adjusted for social class at baseline, age and alcohol intake at Q20, N=3323.