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Combined effect of health behaviours and risk of first ever stroke in 20 040 men and women over 11 years' follow-up in Norfolk cohort of European Prospective Investigation of Cancer (EPIC Norfolk): prospective population study

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ABSTRACT

Objective To quantify the potential combined impact of four health behaviours on incidence of stroke in men and women living in the general community.

Design Population based prospective study (EPIC-Norfolk).

Setting Norfolk, United Kingdom.

Participants 20 040 men and women aged 40-79 with no known stroke or myocardial infarction at baseline survey in 1993-7, living in the general community, and followed up to 2007.

Main outcome measure Participants scored one point for each health behaviour: current non-smoking, physically not inactive, moderate alcohol intake (1-14 units a week), and plasma concentration of vitamin C ≥50 μmol/l, indicating fruit and vegetable intake of at least five servings a day, for a total score ranging from 0 to 4.

Results There were 599 incident strokes over 229 993 person years of follow-up; the average follow-up was 11. 5 years. After adjustment for age, sex, body mass index (BMI), systolic blood pressure, cholesterol concentration, history of diabetes and aspirin use, and social class, compared with people with the four health behaviours the relative risks for stroke for men and women were 1.15 (95% confidence interval 0.89 to 1.49) for three health behaviours, 1.58 (1.22 to 2.05) for two, 2.18 (1.63 to 2.92) for one, and 2.31 (1.33 to 4.02) for none (P<0.001 for trend). The relations were consistent in subgroups stratified by sex, age, body mass index, and social class, and after exclusion of deaths within two years.

Conclusion Four health behaviours combined predict more than a twofold difference in incidence of stroke in men and women.

INTRODUCTION

Lifestyle behaviours such as smoking,[1-3] physical activity,[4 5] and diet[6 7] influence the risk of cardiovascular disease, including stroke. These lifestyle behaviours are also related to risk factors for cardiovascular diseases such as hypertension,[8] hypercholesterolaemia,[9] and obesity.[10] The impact of combined health behaviours on risk of stroke independently of these intermediate risk factors in an apparently healthy general population, however, is less well documented.

High intake of fruit and vegetables, as indicated by plasma vitamin C concentrations,[11] and more physical activity at work and during leisure time[12] are associated with a lower incidence of stroke. Previously we looked at the combined impact of four health behaviours—smoking, physical activity, alcohol intake, and fruit and vegetable intake—on total and cause specific mortality in men and women living in the general community.[13] As these health behaviours could beneficially affect the incidence of stroke we examined the potential magnitude of their combined impact on incidence of stroke in men and women aged 40-79.

METHODS

The participants were 20 040 men and women aged 40-79 at baseline, drawn from the Norfolk component of the European Prospective Investigation of Cancer (EPIC-Norfolk). This prospective population study first surveyed participants in 1993-7, 99.5% of whom were white. The detailed recruitment strategy and sample distribution of the whole cohort have been previously described.[14] Briefly, our participants were recruited from age-sex registers of general practices. As nearly all people in the United Kingdom are registered with general practitioners through the National Health Service, the age-sex registers form a population based sampling frame. From the inception of the EPIC-Norfolk cohort, data collection was broadened to enable the examination of a wider range of determinants of chronic diseases, including stroke. The Norfolk cohort was comparable with national population samples with respect to characteristics including anthropometry, blood pressure, and lipids but with a lower prevalence of current smokers.[14]

At the 1993-7 baseline survey, participants completed a detailed health and lifestyle questionnaire. They were asked about medical history with the question "Has a doctor ever told you that you have any of the following?" followed by a list of conditions that included heart attack, stroke, diabetes, and cancer. Smoking history was derived from yes/no responses to the questions "Have you ever smoked as much as one cigarette a day for as long as a year?" and "Do you smoke cigarettes now?" Alcohol consumption was derived from the question "How many alcoholic drinks do you have each week?" with four separate categories of drinks. A unit of alcohol (about 8 g) was defined as a half pint (about 0.2 l) of beer, cider, or lager; a glass of wine; a single unit of spirits (whisky, gin, brandy, or vodka); or a glass of sherry, port, vermouth, or liqueurs. Total alcohol consumption was estimated as the total units of drinks consumed in a week. For these analyses, a moderate drinker was defined as someone who drank one or more units a week (that is, not a non-drinker) but not more than 14 units a week.

Aspirin use was ascertained by a question "Have you taken aspirin continuously for three months or more?" Habitual physical activity was assessed with two questions referring to activity during the past year. The detailed description of this physical activity questionnaire has been previously reported.[12 13] This index was validated against heart rate monitoring with individual calibration in two independent studies.[15 16] For the purposes of the current study, we dichotomised the population into physically inactive (sedentary job and no recreational activity) and physically not inactive (any category with activity levels above the latter).

We classified social class according to the registrar general's occupation based classification scheme into five main categories, with social class I representing professionals, social class II managerial and technical occupations, social class III subdivided into non-manual and manual skilled workers, social class IV partly skilled workers, and social class V unskilled manual workers. For men, social class was coded with their current occupation at the time of survey, except when they were unemployed in which case their partner's social class was used. For women it was based on their partner's occupation unless the partner's social class was unclassified or missing. If they had no partner, it was based on their own occupation. Unemployed men and women without a partner were coded as unclassified and excluded in the current study.

We also re-categorised social class into manual (III manual, IV and V) and non-manual (I, II and III non-manual) social classes.[17]

Trained nurses carried out a health examination at a clinic. They measured height and weight with participants in light clothing without shoes and calculated the body mass index (weight (kg)/(height (m)^2). Blood pressure was measured using an Accutorr sphygmomanometer after each participant had been seated for five minutes. We used the mean of two measurements of blood pressure in analysis. At the baseline clinic visit nurses also took non-fasting blood samples in plain and citrate bottles. After overnight storage in a dark box in a refrigerator at 4-7°C, they were spun at 2100 g for 15 minutes at 4°C, and plasma and serum samples obtained. Serum concentrations of total cholesterol, high density lipoprotein cholesterol, and triglycerides were measured on fresh samples with the RA 1000 (Bayer Diagnostics, Basingstoke).

Six months after the start of the study, when funding became available, we also collected samples to measure vitamin C concentration. Plasma vitamin C was measured from blood drawn into citrate bottles and stabilised in a standardised volume of metaphosphoric acid stored at −70°C. Plasma vitamin C

Table 1 | Distribution of variables in 20 040 men and women aged 40-79 without known stroke and myocardial infarction in EPIC-Norfolk at baseline, 1993-7, and incidence of stroke after follow-up to 2007 (average 11.5 years). Figures are mean (SD) for continuous variables and numbers (percentage) for categorical variables

Variable	Men (n=8967)	Women (n=11 073)	P value
Age (years)	58.6 (9.2)	58.0 (9.2)	<0.001
BMI (kg/m^2)	26.4 (3.2)	26.1 (4.2)	<0.001
BMI category:			
<25	3036 (33.9)	5060 (45.7)	<0.001
25-30	4820 (53.8)	4271 (38.6)	
≥30	1111 (12.4)	1742 (15.7)	
Systolic blood pressure (mm Hg)	137 (17)	133 (19)	<0.001
Cholesterol concentration (mmol/l)	6.0 (1.1)	6.3 (1.2)	<0.001
Diabetes mellitus (yes)	239 (2.7)	149 (1.3)	<0.001
Aspirin user (yes)	776 (8.7)	641 (5.8)	<0.001
Social class:			
I	705 (7.9)	724 (6.5)	<0.001
II	3488 (38.9)	3936 (35.5)	
III non-manual	1106 (12.3)	2223 (20.1)	
III manual	2245 (25.0)	2322 (21.0)	
IV	1167 (13.0)	1457 (13.2)	
V	256 (2.9)	411 (3.7)	
Smoking status:			
Current smoker	1045 (11.7)	1223 (11.0)	<0.001
Ex-smoker	4790 (53.4)	3535 (31.9)	
Never smoked	3132 (34.9)	6315 (57.0)	
Physical activity level:			
Inactive	2615 (29.2)	3150 (28.4)	<0.001
Moderately inactive	2205 (24.6)	3590 (32.4)	
Moderately active	2116 (23.6)	2566 (23.2)	
Active	2031 (22.6)	1767 (16.0)	
Alcohol consumption:			
None	1703 (19.0)	3908 (35.3)	<0.001
1-<7 units	3027 (33.8)	4466 (40.3)	
7-<14 units	2139 (23.9)	1787 (16.1)	
14-<21 units	683 (7.6)	344 (3.1)	
≥21 units	1415 (15.8)	568 (5.1)	
Vitamin C concentration:			
<50 µmol/l	4748 (52.9)	3124 (28.2)	<0.001
≥50 µmol/l	4219 (47.1)	7949 (71.8)	
Health behaviour score:			
0	132 (1.5)	127 (1.1)	<0.001
1	948 (10.6)	814 (7.4)	
2	2671 (29.8)	2520 (22.8)	
3	3495 (39.0)	4327 (39.1)	
4	1721 (19.2)	3285 (29.7)	
Stroke incidence	289 (3.2)	310 (2.8)	0.08

concentration was estimated with a fluorometric assay within a week of sampling.[18] The coefficient of variation was 5.6% at the lower end of the range (mean 33.2 μmol/l) and 4.6% at the upper end (mean 102.3 μmol/l). We have previously reported that high plasma vitamin C concentration is inversely associated with mortality from all causes. Because humans do not manufacture vitamin C and have to rely on exogenous sources, plasma vitamin C is a good biomarker of plant food intake; previous studies have reported that a blood value of 50 mmol/l or more indicates an intake of at least five servings of fruit and vegetables daily.[19 20] We therefore used plasma vitamin C concentrations as an objective biomarker of fruit and vegetable intake.

We constructed a simple pragmatic health behaviour score (box).[13] Participants scored one point for each of the following health behaviours: current non-smoking, physically not inactive, moderate alcohol intake (1-14 units a week), and plasma vitamin C concentration ≥50 μmol/l, indicating an intake of fruit and vegetables of at least five servings a day. Participants could therefore have a total health behaviour score ranging from 0 to 4. We chose these particular health behaviours and their categorisation on the basis of extensive previous evidence on the relation between these lifestyle factors and health end points.

Case ascertainment

We ascertained incident cases of stroke using death certificate data and hospital record linkage. All participants were flagged for death at the UK Office of National Statistics (ONS), and trained nosologists coded death certificates using the international classification of disease (ICD), revisions 9 and 10. Participants are also linked to NHS hospital information systems so that admission anywhere in the UK are notified to EPIC-Norfolk through routine annual record linkage. Stroke death was defined as ICD-9 codes 430-438 or ICD-10 codes 60-69 anywhere on the death certificate. Incident stroke was defined as death from stroke or hospital discharge code ICD-9 codes 430-438 or ICD-10 codes 60-69 for the first ever stroke. The current study is based on follow-up to end March 2007. A separate validation study showed this method for stroke ascertainment had high positive predictive value of 94% (unpublished data). The follow-up period was defined as time interval between the date of the health examination at enrolment to the date of death for those who died, the date of first stroke for those who had a stroke, and the end of follow-up (31 March 2007) for the remaining participants.

Health behaviour score

Smoking habit

Non-smoker=1

Physical activity

Not inactive=1—that is, if a person has a sedentary occupation, at least half an hour of leisure time activity a day, such as cycling or swimming; or else a non-sedentary occupation with or without leisure time activity

Alcohol intake

One or more but <14 units/week=1; 1 unit=about 8 g alcohol—that is, one glass of wine, one small glass of sherry, one single shot of spirits, or one half pint (about 0.2 l) of beer

Fruit and vegetable intake

Five servings or more as indicated by blood concentration of vitamin C ≥50 μmol/l=1

Adapted from: Khaw et al, 2008[13]

Statistical analysis

We used SPSS for Windows version 14.0 (SPSS, IL, USA) for statistical analyses. We excluded participants with a history of stroke and myocardial infarction at baseline (n=913) and those who had any missing values for the variables included in the study (n=9492). The missing values are mainly because out of 30 445 participants who provided the baseline data, only 25 633 attended the health check where we measured cardiovascular disease risk factors and obtained blood samples for measurement of vitamin C concentration. We included only participants with all available data for all the covariates in the models.

We used Cox proportional hazards models to determine the associations between health behaviours, either individually or as their combined score, and the risk of incident stroke during the follow-up. Multivariate Cox regression models were constructed for health behaviour scores (0-4) with the highest score category (4) as the reference category.

We made multivariate adjustments to examine how far the effect of health behaviours might be explained by known cardiovascular risk factors. We adjusted for age (and sex in the combined model) in model A; age (sex), body mass index, systolic blood pressure,

Table 2 | **Independent relative risk (RR) of incident stroke for individual health behaviours adjusted for age, sex, body mass index, systolic blood pressure, cholesterol concentration, aspirin use, history of diabetes mellitus, and social class in men and women aged 40-79 without known stroke and myocardial infarction at the baseline in EPIC-Norfolk 1993-2007, Cox regression model**

	RR (95% CI)	P value
Men and women		
Current smoker *v* non-current smoker	1.69 (1.34 to 2.13)	<0.001
Physically inactive *v* not inactive	1.29 (1.09 to 1.52)	0.003
Alcohol consumption <1 or >14 *v* 1-14 units/week	1.28 (1.09 to 1.50)	0.003
Vitamin C ≥50 *v* <50 μmol/l	1.39 (1.17 to 1.64)	<0.001
Men		
Current smoker *v* non-current smoker	1.50 (1.07 to 2.09)	0.018
Physically inactive *v* not inactive	1.20 (0.94 to 1.52)	0.15
Alcohol consumption <1 or >14 *v* 1-14 units/week	1.20 (0.96 to 1.52)	0.12
Vitamin C ≥50 *v* <50 μmol/l	1.22 (0.95 to 1.55)	0.11
Women		
Current smoker *v* non-current smoker	1.93 (1.40 to 2.67)	<0.001
Physically inactive *v* not inactive	1.37 (1.08 to 1.73)	0.009
Alcohol consumption <1 or >14 *v* 1-14 units/week	1.36 (1.08 to 1.71)	0.008
Vitamin C ≥50 *v* <50 μmol/l	1.56 (1.24 to 1.96)	<0.001

Table 3 | Relative risk (95% confidence interval) of incident stroke by number of health behaviours in various adjusted models in men and women aged 40-79 without known stroke and myocardial infarction in EPIC-Norfolk 1993-2007, Cox regression model

	Health behaviour score					
Model*	4	3	2	1	0	P value
Model A						
All	1.0	1.19 (0.92 to 1.54)	1.67 (1.29 to 2.16)	2.42 (1.81 to 3.23)	2.59 (1.50 to 4.50)	<0.001
Men	1.0	1.12 (0.76 to 1.64)	1.45 (0.99 to 2.12)	2.04 (1.33 to 3.13)	1.77 (0.75 to 4.21)	0.003
Women	1.0	1.20 (0.85 to 1.70)	1.84 (1.30 to 2.60)	2.71 (1.84 to 4.02)	3.51 (1.72 to 7.16)	<0.001
Model B						
All	1.0	1.16 (0.89 to 1.50)	1.61 (1.25 to 2.09)	2.26 (1.69 to 3.02)	2.39 (1.38 to 4.15)	<0.001
Men	1.0	1.05 (0.71 to 1.54)	1.36 (0.93 to 1.99)	1.85 (1.21 to 2.84)	1.50 (0.63 to 3.57)	0.01
Women	1.0	1.21 (0.85 to 1.71)	1.83 (1.29 to 2.59)	2.59 (1.74 to 3.84)	3.50 (1.71 to 7.13)	<0.001
Model C						
All	1.0	1.15 (0.89 to 1.49)	1.58 (1.22 to 2.05)	2.18 (1.63 to 2.92)	2.31 (1.33 to 4.02)	<0.001
Men	1.0	1.04 (0.71 to 1.53)	1.33 (0.91 to 1.96)	1.79 (1.16 to 2.74)	1.45 (0.61 to 3.45)	0.019
Women	1.0	1.20 (0.85 to 1.70)	1.80 (1.27 to 2.56)	2.53 (1.70 to 3.77)	3.40 (1.66 to 6.96)	<0.001
Model D						
All	1.0	1.09 (0.84 to 1.42)	1.53 (1.18 to 1.98)	2.07 (1.54 to 2.79)	2.15 (1.22 to 3.80)	<0.001
Men	1.0	1.00 (0.67 to 1.47)	1.28 (0.87 to 1.89)	1.69 (1.09 to 2.61)	1.46 (0.61 to 3.48)	0.034
Women	1.0	1.13 (0.80 to 1.61)	1.75 (1.23 to 2.49)	2.41 (1.61 to 3.60)	3.00 (1.41 to 6.37)	<0.001

*Model A: adjusted by age and sex; model B additionally adjusted for BMI, systolic blood pressure, cholesterol concentration, aspirin use, and diabetes mellitus; model C additionally adjusted for social class; model D: excluding incident strokes occurring within first 2 years of follow-up.

cholesterol concentration, aspirin use, and history of diabetes mellitus in model B; and as for model B with the addition of social class in model C.

To address the issue of reverse causality—that is, when people with subclinical chronic disease might be likely to change their lifestyle, such as reducing their physical activity—we excluded all those who had stroke within the first two years of follow-up and constructed model D controlling for all of the above mentioned variables. We also performed stratified analyses by sex, age category (<65 and ≥65), body mass index (<25, 25-30, ≥30), and social class (non-manual and manual).

RESULTS

There were a total of 599 strokes during the 229 992 person years of follow-up (average 11.5 years). Of these, 168 (28%) were fatal. The number of participants with missing values for individual variables included in the study were none for age, sex, history of diabetes, stroke, myocardial infarction, and previous aspirin use; one for physical activity; 287 for smoking status; 772 for social class; 4860 for BMI; 4866 for systolic blood pressure; 5592 for alcohol consumption; 6574 for cholesterol concentration; and 7971 for vitamin C concentration. Comparison between those included (20 040) and excluded (10 405) from the study showed no material difference in terms of their mean age (58.2 *v* 60.0, sex (44.7% *v* 45.5% male), BMI 26.5 *v* 26.9 (n=5545), systolic blood pressure 135 mm Hg (n=20 040) *v* 137 mm Hg, and total cholesterol concentration 6.2 mmol/l (n=20 040) *v* 6.3 mmol/l).

Table 1 shows the characteristics of the sample according to sex. Men were older, had higher BMI and higher systolic blood pressure. More men were current or previous smokers, consumed ≥21 units of alcohol a week, and were physically active, and fewer consumed five or more portions of fruit and vegetables. With large numbers, these and other characteristics showed significant differences between men and women. A significantly higher percentage of women scored 4 for combined health behaviours. Incidence of stroke was not significantly different between men and women.

Table 2 shows the independent relative risks and their corresponding 95% confidence intervals for the individual life style behaviours and risk of stroke for men and women combined and separately. People who smoked, were physically inactive, consumed no alcohol or more than 14 units/week, and ate fewer than five portions of fruit and vegetables as indicated by blood vitamin C concentrations <50 µmol/l had a significantly higher risk of stroke than those who were not current smokers, were physically not inactive, consumed alcohol moderately (1-14 units a week), and consumed five or more portions of fruit and vegetables (vitamin C concentration ≥50 µmol/l) at the study baseline.

Table 3 shows the relation between combined health behaviour score and risk of stroke in different multivariate adjusted Cox regression models. The risk of stroke increased in linear fashion with every point decrease in combined health behaviour score. In the fully adjusted model (model C), men and women who scored 0 for health behaviours had about 2.3 times the risk of stroke (relative risk 2.31, 95% confidence interval 1.33 to 4.02) compared with those who scored 4.

Table 4 shows stratified analyses with a model with all covariates (model C) from table 3. The findings were consistent across the sample population regardless of sex, age, BMI, and social class. The absolute risks for incident stroke were 1.7% (84 events/5006), 2.4%

(186/7822), 4.0% (206/5191), 6.1% (108/176), and 5.8% (15/259) for behaviour scores of 4, 3, 2, 1, and 0, respectively (P<0.001).

DISCUSSION

Modifiable lifestyle behaviours including not smoking, physically not inactive, moderate consumption of alcohol (1-14 units/week), and eating at least five portions of fruit and vegetables a day are associated with a substantially lower risk of subsequent stroke. Stroke is one of the leading causes of mortality and morbidity in the UK and beyond. In the UK, the major associated costs come from the long term care of those disabled by their stroke.[21 22] A recent report from the National Audit Office[23] estimated the annual cost of caring for people with stroke at about £7bn a year in the UK alone.

There is little doubt from randomised trials that targeting and controlling risk factors such as hypertension and atrial fibrillation are effective in preventing stroke. A large proportion of strokes, however, occur in people who do not have these risk factors. The large geographical variations and secular trends in incidence of and mortality from stroke suggest that environmental factors have an important role, and a substantial body of evidence indicates that lifestyle factors such as smoking, physical activity, and dietary intake influence risk.

The AHA guidelines identified smoking and lack of physical activity as well documented modifiable risk factors and alcohol abuse as a less well documented but potentially modifiable risk factor.[24] It is interesting that the effect of health behaviours on risk was only slightly attenuated by adjustment for known risk factors such as blood pressure and aspirin use, suggesting that they might relate to risk of stroke through mechanisms other than classic risk factors.

Other studies support the strong relation between lifestyle behaviours and cardiovascular disease. Hardoon et al reported that modest favourable changes in major cardiovascular risk factors contribute to considerable reductions in the incidence of myocardial infarction; the fall in cigarette smoking explained the greatest part of the decline in incidence (23%), highlighting the potential value of population wide measures to reduce exposure to these risk factors in the prevention of coronary heart disease.[25] The fact that the lifestyle behaviours examined in this study are potentially achievable in the general population means that our findings are of relevance to middle aged and older populations worldwide.

There seemed to be some differences in the relation between number of health behaviours between men and women and between older and younger groups. While we could speculate on whether these were real differences relating to differences in health behaviour profiles in men and women or by age, these age and sex differences were not significant (tables 3 and 4).

Our primary aim was to examine the relation between health behaviours and risk of stroke, irrespective of the probable biological mediating factors. Some of these health behaviours, such as high intake of fruit and vegetables or physical activity, might relate to lower levels of blood pressure, a major risk factor for stroke. Nevertheless the relation of health behaviours with risk of stroke was independent of systolic blood pressure.

Study limitations

Naturally, there are limitations in our study. Reverse causality is a potential major issue. People who are already ill might be more likely to be physically inactive and change their diet as a result of prevalent disease. To address this we excluded those with prevalent stroke and myocardial infarction, adjusted for other potential indicators of ill health such as blood pressure, cholesterol concentration, BMI, diabetes mellitus, and aspirin use, and also repeated the analyses

Table 4 | Rates and relative risk of incident stroke by number of health behaviours, adjusted by age, sex, and BMI, systolic blood pressure, cholesterol, diabetes mellitus, social class category (manual and non-manual), and aspirin use stratified by sex, age, body mass index, and social class in men and women aged 40-79 without known stroke and myocardial infarction in EPIC-Norfolk 1993-2007, Cox regression model

Category	Events/No of participants	Health behaviour score: 4	3	2	1	0	P value
By sex							
Male	289/8967	1.0	1.05 (0.71 to 1.54)	1.35 (0.92 to 1.98)	1.84 (1.20 to 2.82)	1.48 (0.62 to 3.53)	0.012
Female	310/11 073	1.0	1.21 (0.85 to 1.71)	1.82 (1.29 to 2.59)	2.58 (1.73 to 3.84)	3.49 (1.71 to 7.12)	<0.001
By age group							
<65 years	194/14 178	1.0	1.27 (0.83 to 1.93)	2.02 (1.32 to 3.08)	1.92 (1.10 to 3.37)	4.48 (2.06 to 9.76)	<0.001
≥65 years	405/5862	1.0	1.06 (0.77 to 1.48)	1.39 (1.01 to 1.93)	2.22 (1.56 to 3.15)	1.48 (0.67 to 3.27)	<0.001
By BMI							
<25	222/8096	1.0	0.83 (0.57 to 1.22)	1.28 (0.87 to 1.88)	1.62 (1.04 to 2.54)	2.76 (1.34 to 5.69)	0.001
25-30	283/9091	1.0	1.41 (0.95 to 2.10)	1.85 (1.24 to 2.76)	2.65 (1.70 to 4.13)	1.29 (0.39 to 4.22)	<0.001
≥30	94/2853	1.0	2.17 (0.84 to 5.65)	2.67 (1.05 to 6.84)	4.12 (1.53 to 11.12)	4.59 (1.08 to 19.53)	0.036
By social class							
Non-manual	351/12 182	1.0	1.12 (0.81 to 1.55)	1.73 (1.25 to 2.39)	2.38 (1.63 to 3.47)	3.23 (1.59 to 6.55)	<0.001
Manual	248/7858	1.0	1.20 (0.78 to 1.84)	1.42 (0.93 to 2.18)	2.02 (1.27 to 3.22)	1.61 (0.66 to 3.89)	0.022

WHAT IS ALREADY KNOWN ON THIS TOPIC

The relation between individual lifestyle behaviours such as smoking and health has been examined

Four health behaviours combined—smoking, physical activity, alcohol intake, and fruit and vegetable intake—have an impact on mortality

WHAT THIS STUDY ADDS

Relatively modest and achievable health behaviours in combination can produce a substantial reduction in risk of stroke

excluding people with stroke within the first two years of follow-up. Secondly, residual confounding with known or unknown factors is always possible. Nevertheless, our results are consistent with the existing evidence, indicating these behavioural factors are associated with lower risk of stroke.

Thirdly, there are potential measurement errors in the assessment of exposures. We used only one measure at one point in time to characterise individuals and did not take into account possible changes in lifestyles over follow-up. Nevertheless, random measurement error would probably attenuate any associations observed, so the estimated differences in risk are likely to be larger than those observed. Fourthly, the proportions of the population with some or all positive health behaviours were relatively high as the definitions for health behaviours were not necessarily optimal—for example, for physical activity, dichotomising behaviours between inactive and not inactive might have obscured the gradient in incidence of stroke between those who were moderately inactive and those who were active. Nevertheless, this shows that the behaviours associated with substantial differences in risk of stroke are entirely feasible and achievable by most of the population. Fifthly, we excluded about 9000 participants who consented to the study but were not able to attend the health check (hence missing values for covariates, for example the blood pressure). Exclusion of these individuals, however, is unlikely to influence the relation between health behaviours in stroke observed in the rest of the cohort unless this association were in the opposite direction in those excluded, which seems implausible. The potential healthy responder bias resulting in truncation of sample distribution would probably only attenuate the findings and be unlikely to change the direction of the study results.

Stroke is a heterogeneous disorder with various underlying pathophysiology. Broadly speaking it is divided into ischaemic and haemorrhagic stroke. Pathophysiological classification of stroke is much more complex. In middle aged and older people, however, the underlying pathophysiology is likely to be vascular in origin and probably shares common risk factors such as age, hypertension, diabetes mellitus, and evidence of ischaemic heart disease, depicted by current aspirin use. We were not able to distinguish between different subtypes of stroke. The most common strokes in this population are probably thrombotic as haemorrhagic strokes are less common in the UK (about 10-15%).

We used death registration data and hospital record linkage system to ascertain incident cases of stroke. We were unable to identify people with mild stroke who were not admitted to hospital, and some strokes might have been included in the "non-stroke" group. In a cohort of this size, however, the effect on estimates of risk would not be substantial. Misclassification of non-stroke cases as stroke cases would attenuate the association between health behaviours and stroke risk. Data from death certificates and hospital record linkage data are routinely used in epidemiological studies. A separate validation study showed this method in EPIC-Norfolk has a high accuracy with positive predictive value of up to 94% (unpublished data). Nevertheless, we observed a relation between four health behaviours and arguably the most clinically important strokes, those that resulted in death or hospital admission, whatever the stroke subtype.

Conclusion

In summary, the combined impact of the four health behaviours, though relatively modest and potentially achievable across all ages, sex, and social classes, was associated with an estimated 2.3-fold difference in risk of stroke. These results provide further incentive and support for the notion that small differences in lifestyle can have a substantial potential impact on risk.

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