Stroke

ORIGINAL CONTRIBUTION

Physical Activity, Mental Activity and Risk of Incident Stroke: A Prospective Cohort Study

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BACKGROUND: Cumulative evidence suggests a correlation between physical or mental activity and the risk of stroke. However, the combined impact of these activities on stroke onset remains unexplored. This study identified physical and mental activity patterns using principal component analysis and investigated their associations with risk of incident stroke in the general population.

METHODS: Our study was sourced from the UK Biobank cohort between 2006 and 2010. Information on physical and mental-related activities were obtained through a touch-screen questionnaire. The incident stroke was diagnosed by physicians and subsequently verified through linkage to Hospital Episode Statistics. Principal component analysis was used to identify potential physical and mental activity patterns. Cox proportional hazard regression models were performed to calculate hazard ratios (HRs) and 95% CIs of incident stroke, adjusting for potential confounders.

RESULTS: The initial UK Biobank cohort originally consisted of 502 411 individuals, of whom a total of 386 902 participants (aged 38–79 years) without any history of stroke at baseline were included in our study. During a median follow-up of 7.7 years, 6983 (1.8%) cases of stroke were documented. The mean age of the included participants was 55.9 years, and the proportion of women was 55.1%. We found that multiple individual items related to physical and mental activity showed significant associations with risk of stroke. We identified 4 patterns of physical activity and 3 patterns of mental activity using principal component analysis. The adherence to activity patterns of vigorous exercise, housework, and walking predominant patterns were associated with a lower risk of stroke by 17% (HR, 0.83 [95% CI, 0.78–0.89]; 20% (HR, 0.80 [95% CI, 0.75–0.85]; and 20% (HR, 0.80 [95% CI, 0.75–0.86), respectively. Additionally, the transportation predominant pattern (HR, 1.36 [95% CI, 1.28–1.45) and watching TV pattern (HR, 1.43 [95% CI, 1.33–1.53) were found to be significantly associated with a higher risk of stroke. These associations remained consistent across all subtypes of stroke.

CONCLUSIONS: Activity patterns mainly related to frequent vigorous exercise, housework, and walking were associated with lower risks of stroke and all its subtypes. Our findings provide new insights for promoting suitable patterns of physical and mental activity for primary prevention of stroke.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: mental activity pattern ■ physical activity pattern ■ stroke ■ UK Biobank

Stroke is a leading cause of morbidity and mortality worldwide, with increasing incidence rates of various subtypes in low- and middle-income countries.[1] A prospective cohort study conducted in India revealed an incidence rate 140 per 100 000 person-years (95% CI, 133–147).[2] Another separate investigation conducted in the United Kingdom has documented an incidence rate of stroke at 149.5 per 100 000 person-years (95% CI, 139.4–160.1).[3] Due to its adverse prognosis, the early detection of risk factors and prevention of stroke becomes an urgent issue.[4] Several systematic reviews and meta-analyses have suggested that physical activity of varying intensity and duration plays a protective role in preventing stroke and other cardiovascular diseases

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Nonstandard Abbreviations and Acronyms

BDNF	brain-derived neurotrophic factor
CVD	cardiovascular disease
HR	hazard ratio
PC	principal component
PCA	principal component analysis

(CVDs).[5–7] In addition to physical activity, mental activity constitutes a significant aspect of an individual's daily behavior and exerts a profound impact on health outcomes.[8] There are various physical and mental activities in an individual's daily life, each with different effects on stroke and other CVD outcomes. Furthermore, multiple activities may exert mutual influence. However, few present studies have examined the combined impact of multiple mental and physical activities on stroke. This study aims to identify physical and mental activity patterns using principal component (PC) analysis (PCA) and investigated their associations with risks of incident stroke and stroke subtypes.

METHODS

Study Participants

Participants with accessible data were sourced from the UK Biobank (https://biobank.ctsu.ox.ac.uk/) in this study. The UK Biobank cohort recruited >500 000 participants aged between middle and old age across the United Kingdom from 2006 to 2010.[9] Participants provided information on sociodemographic characteristics, lifestyle, medical and family history, health status, and attendance at physical measurements in the assessment centers at baseline. UK Biobank was approved by the Northwest Multicenter Research Ethics Committee as a research tissue bank (reference: 11/NW/03820). All participants provided written informed consent. This study identified physical and mental activity patterns using PCA and investigated their associations with the risk of incident stroke in the general population. It should also be noted that the UK Biobank, despite its large sample size, may not fully represent the general population.[10]

The present study included a total of 502 411 participants from the UK Biobank who were enrolled from 2006 to 2010. After removing those with incomplete data or those diagnosed with cardiovascular-related diseases, as well as cancer at baseline, and further excluding those with strokes occurring within 1 year of follow-up, 386 902 participants were included in further analyses and divided into 3 distinct cohort groups based on specific objectives (Figure 1). The analysis 1 cohort excluded participants with any missing data on specific items, resulting in a sample size of 319 938 participants for investigating the associations between 21 physical/mental activity items and stroke. The analysis 2 and 3 cohorts were derived to analyze 2 distinct patterns related to mental and physical activity patterns. Participants with missing values on specific patterns were excluded from the analyses of pertaining to those particular patterns. Meanwhile, we provided a detailed description of the exclusion criteria for the censored population in Supplemental Methods S1.

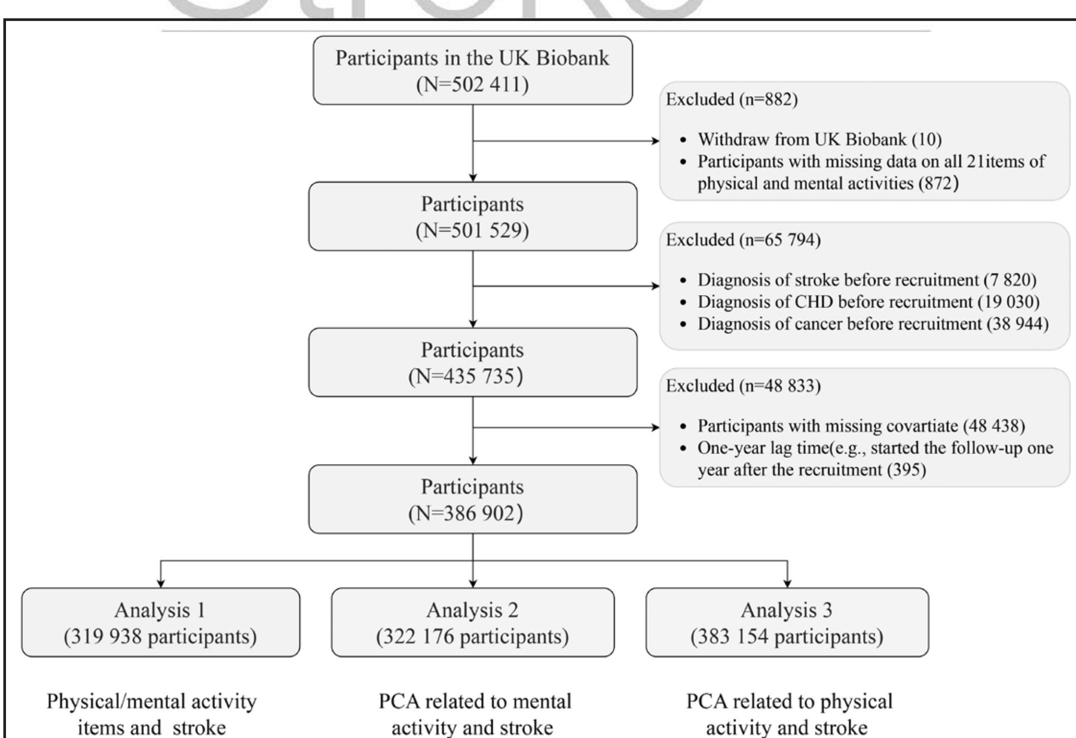

Figure 1. Study flowchart.
CHD indicates coronary heart disease; and PCA, principal component analysis.

Measurements of Physical and Mental Activity Items

Information on physical activity items were collected with utilization of the well-validated short International Physical Activity Questionnaire.[11–13] There are 4 major categories of physical activity included in this study, as defined by the International Physical Activity Questionnaire: leisure-time activities (eg, walking for pleasure, exercise), job-related activities (eg, employment status), household activities (eg, pruning, watering), and transportation-related activities (eg, walking, cycling, or by car). Besides, sleep duration was considering to be a factor affecting stroke occurrence, so it was included as one of the items in our study.[14]

Mental activity-related items were defined as behaviors associated with intelligence (eg, obtaining qualifications, attending adult education classes), social support (eg, visiting family and friends or participating in the pub), and the use of electronic devices (eg, watching television, using computers). These items were collected via touch-screen questionnaire at baseline centers, which was consistent with previous research.[15,16] For each physical and mental item, participants reported their attendance (yes or no), frequency (days per week), and duration (minutes per day).

Ascertainment of Outcomes

The primary outcome in the current study was the incidence of stroke, and the secondary outcomes included the incidence of ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage. Record linkage containing admissions and diagnoses information was linked to the Hospital Episode Statistics, Scottish Morbidity Record data, and the Patient Episode Database. Stroke events during the follow-up were ascertained from hospital inpatient records according to the *International Classification of Diseases*, *Tenth Revision* (codes: I60–I64).[17] Each eligible individual was followed from when they met our eligibility criteria described above and ended at diagnosis of stroke, death, loss to follow-up, or until November 30, 2021, whichever occurred first. The total follow-up time of our research accounted to 15 years.

Assessment of Covariates

We compiled data on age, sex (women and men), ethnicity (White, Asian, Black, mixed, and other), body mass index, education attainment (college/university degree and other), lifestyle factors (alcohol drinking status and smoking status), Townsend deprivation index, the history of hypertension, and CVD at recruitment. Townsend deprivation index represents area-based deprivation levels, which is a target of the socioeconomic circumstances of the population.[18] The diet scores were constructed to reflect the diet pattern including the frequency of consumption of fruits, vegetables, fish, processed meat, unprocessed red meat, whole grains, and refined grains.[19,20] History of cancer or CVD was determined by hospital inpatient records, and the history of hypertension was obtained by questionnaire. We provided the detailed explanations for each adjusted variable, see Supplemental Methods S2. We also constructed a Directed Acyclic Graph to visually depict and elucidate the impact of exposure and outcome (Figure S1).

Statistical Analysis

We used the mean and SD to describe continuous variables, and numbers (percentages) to describe categorical variables. Baseline characteristics were compared according to the presence or absence of stroke.

Due to the complexity and interaction of physical and mental activity, we employed PCA to identify activity patterns according to physical and mental items. In brief, PCA was a data-driven method that extracts PC from variables with high information content to identify distinct subjective behavior patterns in low-dimensional data.[21] The PCs in this study assigned weights to various activity items in participants' daily lives, resulting in a diverse range of activity patterns as defined by the present study. We retained PCs with eigenvalues >1.0 and a cumulative variance exceeding 50%.[15] Each participant was assigned an individual PCs, which was categorized into terciles based on the distribution of scores in the sample. The categories were ordered as low (<first tercile), moderate (first-second tercile), and high groups (>second tercile).

Cox proportional hazards regression models were employed to assess the associations between individual physical and mental activity items, as well as physical and mental activity patterns, and risks of stroke subtypes, represented as hazard ratios (HRs) with 95% CIs. All models were adjusted for age, sex, ethnicity, Townsend deprivation index, qualification, smoking status, alcohol status, diet pattern, body mass index, history of hypertension, history of CVD, and family history of stroke. The proportional hazards assumptions were verified for all Cox proportional hazards regression models by using Schoenfeld residual test, and no violations were observed. Missing values for covariates with a missing rate of <1% (such as smoking status and body mass index) were completely excluded, whereas missing covariates with a missing rate >1% (such as education) were coded as an additional category for categorical variables or the mean of continuous variables.

We performed several sensitivity analyses to evaluate the robustness of the main results. First, to reduce the interrelation between physical and mental activity, we conducted additional pattern analyses of physical activity while controlling for all meaningful PCs of mental activity, and vice versa. Second, we adjusted for different covariates in each of the 3 Cox proportional hazards models to explore whether adjusting these confounders could bias the associations between physical or mental activity patterns and stroke. Third, we calculated the E value to assess the effect of unmeasured confounding, which is defined as the minimum strength of association that an unmeasured confounder must have with both the exposure and outcome.[22,23] Fourth, we prolonged the duration of follow-up to 3 or 5 years after recruitment to further ensure the effect of reverse causality on our findings. Fifth, we conducted several subgroup analyses by age group (≤65 and >65 years), sex (men and women), and family history of stroke (yes and no) to access the potential modifying effects.

The analyses were conducted using Stata 15 statistical software (Stata Corp LLP) and R software (R 4.0.2). We used *P* value to verify compatibility between the data and the correct statistical model predictions.

Table 1. Characteristics of the Study Participants Categorized by the Incidence of Stroke

Characteristics	Stroke free	Stroke
N	379 919	6983
Age, y	55.8 (8.04)	60.8 (6.88)
Follow-up time, y; mean (SD)	12.59 (11.48)	7.68 (3.58)
Sex (%)		
Women	210 231 (55.3)	3063 (43.9)
Men	169 688 (44.7)	3920 (56.1)
Ethnicity		
Asian	8224 (2.16)	123 (1.76)
Black	5417 (1.43)	104 (1.49)
Mixed	1944 (0.51)	21 (0.30)
White	361 012 (95.0)	6695 (95.9)
Unknown	3322 (0.87)	40 (0.57)
Townsend deprivation index	−1.44 (3.01)	−1.16 (3.17)
Smoking status		
Never	215 729 (56.8)	3348 (47.9)
Previous	126 564 (33.3)	2595 (37.2)
Current	37 626 (9.90)	1040 (14.9)
BMI, kg/m^2		
<18 5	1963 (0.52)	39 (0.56)
18 5–24.9	128 535 (33.8)	1876 (26.9)
25–29.9	161 370 (42.5)	3095 (44.3)
≥30	88 051 (23.2)	1973 (28.3)
Education attainment		
College/University degree	131 768 (34.7)	1864 (26.7)
Other	248 151 (65.3)	5119 (73.3)
Family history of stroke		
Yes	39 824 (10.5)	1031 (14.8)
No	340 095 (89.5)	5952 (85.2)
Alcohol status		
>7 times/wk	27 723 (7.30)	688 (9.85)
3–4 times/wk	41 367 (10.9)	882 (12.6)
1–2 times/wk	42 585 (11.2)	648 (9.28)
1–3 times/mo	99 169 (26.1)	1677 (24.0)
<1 times/mo	90 804 (23.9)	1471 (21.1)
Never	78 271 (20.6)	1617 (23.2)
History of hypertension		
Yes	90 436 (23.8)	2829 (40.5)
No	289 483 (76.2)	4154 (59.5)
History of cardiovascular diseases		
Yes	4838 (1.27)	390 (5.58)
No	375 081 (98.7)	6593 (94.4)
Diet pattern*		
Healthy	195 617 (51.5)	3327 (47.6)
Unhealthy	184 302 (48.5)	3656 (52.4)

Values are numbers (percentages) unless stated otherwise. BMI indicates body mass index.

*Healthy diet pattern was summarized by using the following food categories: ≥4.5 servings total fruit and vegetable intake consumption per wk, ≥2 fish intake per wk, ≤2× intake of processed meat per wk, and ≤5× red meat intake per wk. A healthy diet pattern was defined as a diet score of 2 or more.

RESULTS

Baseline Characteristics of Participants

The baseline characteristics of the 386 902 participants are presented in Table 1. Table S1 compares the baseline characteristics between the sample and the total UK Biobank participants, and Table S2 compares the baseline characteristics of the included participants with those who were excluded. Table S3 presents the baseline characteristics of different stroke subtypes in the included participants. Over the median follow-up of 7.7 years, 6983 cases of stroke with initial diagnosis were identified, and 5426 cases of ischemic stroke, 1157 intracerebral hemorrhage, and 738 subarachnoid hemorrhage were recorded. The average age of participants included was 55.9 years, and the proportion of women was 55.1%. They displayed a higher proportion of female participants, nonsmokers, and individuals with higher socioeconomic status and educational attainment. Additionally, there was a lower prevalence of hypertension, CVD or familial stroke among the included population along with fewer Black individuals.

Associations Between Items Related to Physical/Mental Activity and Stroke Risk

Among physical activity items, we found that adherence to the longest sleep duration (HR, 1.17 [95% CI, 1.06–1.29) and multiple types of job-related activities including voluntary work (1.82, 1.14–2.90), other types of commuting (1.63, 1.53–1.74), were associated with a higher risk of stroke, while a higher level of walking duration and strenuous exercise were associated with an 11% (95% CI, 0.84%–0.95%) and 27% (95% CI, 0.62%–0.86%) lower risk of stroke, respectively (Figures S2 and S3; Table 2).

Among mental activity items, we observed a higher risk of stroke in relation to a greater adherence to watching TV (1.15, 1.09–1.22) and participating in pub or social club activities (1.25, 1.16–1.36). In contrast, using computers (0.83, 0.69–1.00) and mobile phones (0.91, 0.83–0.99) were associated with lower risks of stroke.

Associations Between Physical and Mental Activity Patterns and Stroke

We identified 4 distinct patterns of physical activity, which together account for 52.5% of the total variance and can be used to generalize most types of physical activity which were categorized as vigorous exercise predominant pattern, transport- and job-related pattern, housework predominant pattern, and walking predominant pattern. Similarly, we identified 3 PCs of mental activity that collectively accounted for 51.5% of the total variance and categorized as watching TV pattern, computer using pattern, family and social club visit pattern. We

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Table 2. The Association Between Specific Physical and Mental Activity Items and the Risk of Stroke

Physical activity Items	HR (95% CI)	*P* value	Physical activity Items	HR (95% CI)	*P* value
Duration of light DIY			Frequency of heavy DIY		
<0.5 h	Reference		<1/wk	Reference	
0.5–1 h	0.97 (0.89–1.05)	0.444	1–3/wk	1.14 (1.00–1.30)	0.056
>1.5 h	0.94 (0.84–1.05)	0.276	>4/wk	1.12 (0.90–1.38)	0.311
Sleep duration			Walking duration		
3–8 h	Reference		<0.5 h	Reference	
9–10 h	1.11 (0.98–1.26)	0.093	0.5–1 h	0.90 (0.83–0.97)	0.005
>10 h	1.43 (0.86–2.37)	0.171	>1.5 h	0.92 (0.83–1.02)	0.130
Frequency of light DIY			Duration of strenuous sports		
<1/wk	Reference		<0.5 h	Reference	
1–3/wk	1.03 (0.93–1.14)	0.551	0.5–1 h	0.68 (0.58–0.80)	<0.001
>4/wk	1.09 (0.95–1.23)	0.213	>1.5 h	0.94 (0.74–1.20)	0.618
Duration of other exercise			Frequency of other exercise		
<0.5 h	Reference		<1/wk	Reference	
0.5–1 h	0.84 (0.78–0.92)	<0.001	1–3/wk	0.86 (0.78–0.95)	0.002
>1.5 h	0.95 (0.84–1.09)	0.498	>4/wk	0.86 (0.76–0.98)	0.028
Duration of heavy DIY			Employment status		
<0.5 h	Reference		In paid employment or self-employed	Reference	
0.5–1 h	0.96 (0.87–1.05)	0.377	Looking after home and family	0.92 (0.69–1.23)	0.567
>1.5 h	0.92 (0.83–1.03)	0.149	Unable to work because of sickness	1.83 (1.51–2.23)	<0.001
Frequency of walking			Doing unpaid or voluntary work	1.82 (1.14, 2.90)	0.012
<1/wk	Reference		Unemployed	1.24 (0.93–1.66)	0.150
1–3/wk	0.95 (0.87–1.05)	0.339	Full or part-time student	0.55 (0.18–1.70)	0.295
>4/wk	0.98 (0.89– 1.08)	0.733	Retired	1.80 (1.66–1.96)	<0.001
Frequency of strenuous sports			Other	1.44 (0.89–2.32)	0.135
<1/wk	Reference		Physical type		
1–3/wk	0.68 (0.58–0.80)	<0.001	Walk	Reference	
>4/wk	0.94 (0.74–1.20)	0.618	Cycle	1.04 (0.94–1.16)	0.475
Transport types			Strenuous sports	0.80 (0.52–1.25)	0.329
Car	Reference		Light DIY	1.28 (1.13–1.45)	<0.001
Walk	0.73 (0.58–0.91)	0.006	Heavy DIY	1.29 (1.07–1.56)	0.007
Public transport	1.05 (0.87–1.27)	0.600	Sleep	1.37 (1.11–1.61)	0.012
Cycle	0.74 (0.48–1.16)	0.193	Other	1.44 (1.25–1.64)	<0.001
Mental activity items	**HR (95% CI)**	***P* value**	**Mental activity items**	**HR (95% CI)**	***P* value**
Watching TV			Qualification		
0–2 h	Reference		College	Reference	
3–4 h	1.15 (1.06–1.24)	<0.001	Noncollege	1.13 (1.03–1.23)	0.006
5–6 h	1.29 (1.16–1.44)	<0.001	Other	1.39 (1.26–1.53)	<0.001
>6 h	1.42 (1.13–1.79)	0.003	Family visits frequency		
Mobile phone			<1/wk	Reference	
<0.5 h	Reference		1–3/wk	0.78 (0.68–0.89)	<0.001
0.5–1 h	0.93 (0.84–1.02)	0.118	>4/wk	0.82 (0.69–0.97)	0.021
1–3 h	0.87 (0.78–0.97)	0.011	Computer duration		
4–6 h	0.79 (0.65–0.96)	0.019	0–2 h	Reference	
>6 h	0.73 (0.60–0.90)	0.003	3–4 h	1.07 (0.94–1.22)	0.276
Leisure activity			5–6 h	0.84 (0.67–1.06)	0.154
Sports club or gum	Reference		>6 h	0.73 (0.48–1.10)	0.133
Pub or social club	1.24 (1.12–1.37)	<0.001	Computer games		
Religious group	1.34 (1.18–1.52)	<0.001	Never	Reference	
Adult education class	1.23 (0.99–1.52)	0.059	Sometimes	1.05 (0.96–1.14)	0.312
Other group activity	1.27 (1.11–1.44)	<0.001	Often	1.08 (0.90–1.29)	0.434

*HRs (95%CIs) were derived from Cox proportional hazards regression models, adjusted for age, sex, ethnicity, Townsend deprivation index, education, body mass index, smoking status, alcohol status, family history of stroke, history of hypertension, history of cardiovascular diseases, and diet pattern.

have added Table S4 to show each physical and mental activity item, along with their respective grouping in relation to the PCs. In addition, we showed the coefficient of variance of each activity item on PCs of physical or mental activity patterns (Figures S4 and S5). With the lowest PC tercile as a reference, for physical activity patterns, we explored that of the 4 identified groups of PCs, the multivariable adjusted HR (95% CI) for the highest PC was 0.83 (0.78–0.89) in relation to vigorous exercise predominant pattern, 0.80 (0.75–0.85) for housework predominant pattern, and 0.80 (0.75–0.86) for walking predominant pattern (Figure 2). However, transport- and job-related pattern was associated with higher risk of stroke (HR, 1.36 [95% CI, 1.28–1.45]). Propinquity effects were identified in both ischemic stroke and intracerebral hemorrhage subtypes, except subarachnoid hemorrhage, which was not statistically significant. We observed that watching TV pattern was associated with 43% (95% CI, 1.33–1.53) higher risk of stroke in terms of mental activity patterns, while none of the other mental activity PCs exhibited a statistically significant association with stroke risk (*P*>0.05; Figure 3).

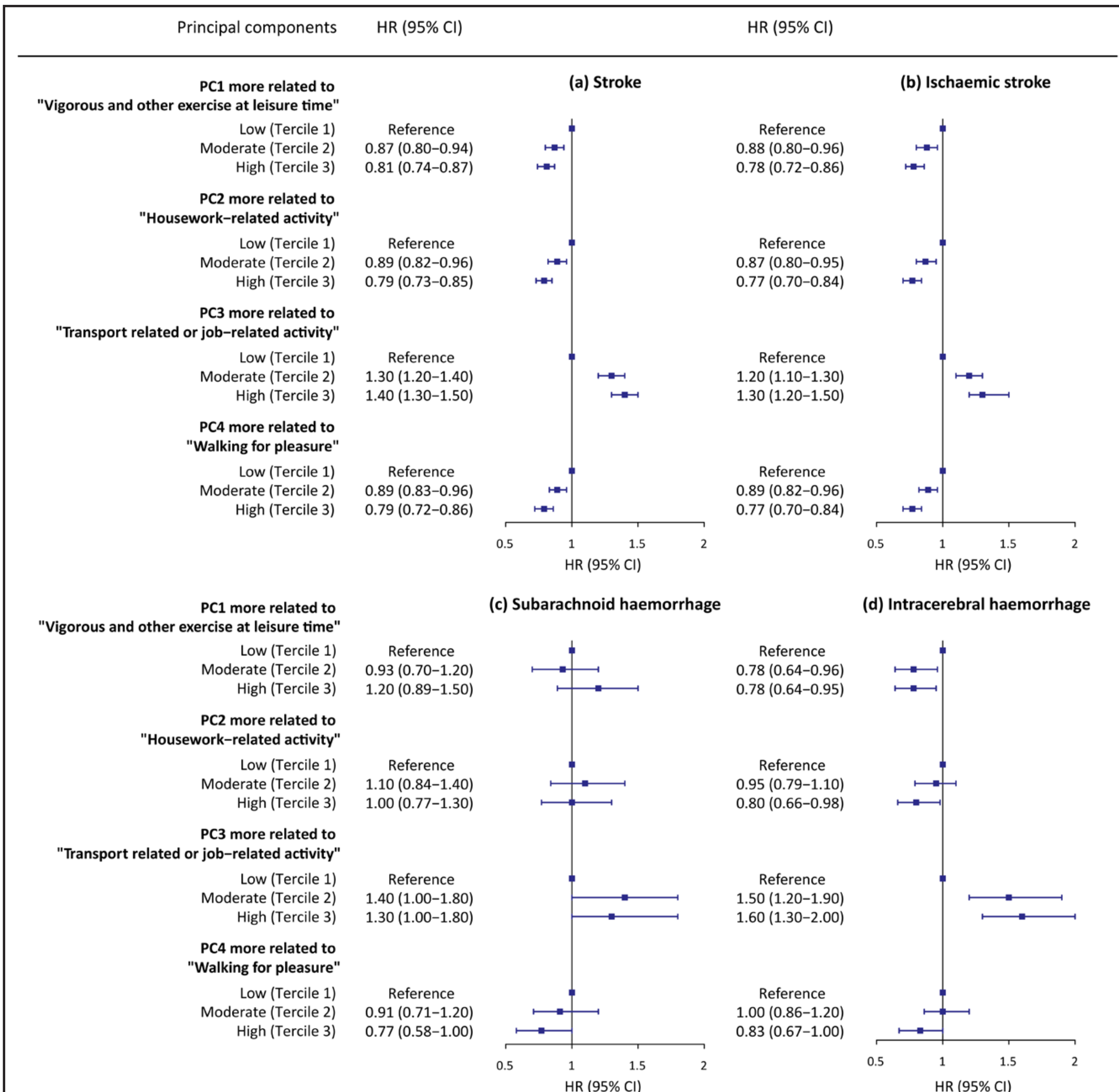

Figure 2. Associations between physical activity patterns and various subtypes of stroke.
Data were presented as hazard ratios (HRs) and 95% CI. The 4 principal component (PC) patterns were calculated by PC analysis (PCA) from physical activities. The first tercile is the reference tercile. HRs (95% CIs) were derived from Cox proportional hazards regression models, adjusted for age, sex, ethnicity, Townsend deprivation index, education, body mass index, smoking status, alcohol status, family history of stroke, history of hypertension, history of cardiovascular, and diet pattern. Ref indicates reference.

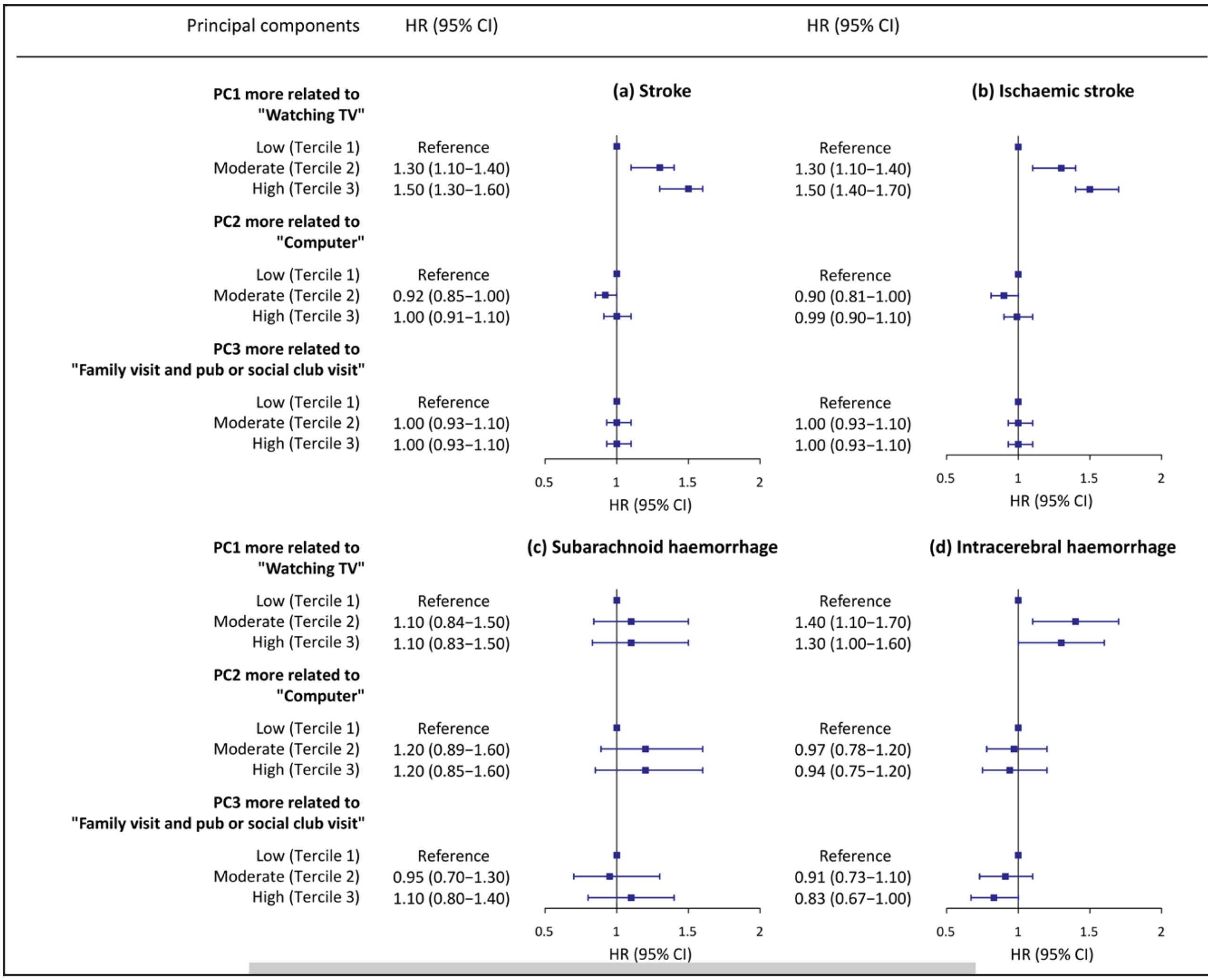

Figure 3. Associations between mental activity patterns and various subtypes of stroke.
Data were presented as hazard ratio (HRs) and 95% CI. The 4 principal component (PC) patterns were calculated by PC analysis (PCA) from mental activities. The first tercile is the reference tercile. HRs (95% CIs) were derived from Cox proportional hazards regression models, adjusted for age, sex, ethnicity, Townsend deprivation index, education, body mass index, smoking status, alcohol status, family history of stroke, history of hypertension, history of cardiovascular, and diet pattern. Ref indicates reference.

Sensitivity Analyses

The associations of physical and mental activity patterns with the risk of stroke, after adjusting for all relevant confounding factors in the respective domains, revealed a HR of 0.86 (95% CI, 0.80–0.93) for vigorous exercise predominant pattern, 0.85 (95% CI, 0.79–0.91) for housework predominant pattern, and 0.85 (95% CI, 0.79–0.92) for walking predominant pattern (Table S5). The observed estimates for stroke remained consistent when adjusting for different covariates in 3 separate Cox proportional hazards models (Table S6). The E values analysis showed that the estimate was 1.70 for vigorous exercise predominant pattern, and 2.21 for watching TV predominant pattern, respectively (Table S7). The E-value for the upper confidence bond was 1.29 for vigorous exercise predominant pattern, and the lower confidence bond was 2.00 for watching TV predominant pattern. The application of a 3-year lag time of follow-up had identified specific activity patterns, including those related to vigorous exercise predominant pattern, housework predominant pattern, and walking predominant pattern, with HR (95% CI) of 0.84 (0.79 to 0.90), 0.81, (0.76 to 0.86), and 0.80, (0.75 to 0.86), respectively (Table S8). These findings were consistent with the primary results, and the extension of follow-up by 5 years yielded comparable results. The subgroup analyses, stratified by age, sex, and family history of stroke, revealed consistent findings (Tables S9 through S11). Specifically, among female participants under the age of 65 years without a family history of stroke, a stronger association and adherence to these patterns were observed.

DISCUSSION

In this large population-based cohort, we have identified several physical and mental activity patterns through

PCA. Our findings suggested that engaging in vigorous exercise, housework and walking predominant patterns were associated with lower risks of incident stroke and stroke subtypes. However, transport- and job- related pattern, as well as prolonged TV watching were found to be associated with a higher risk of stroke.

Prior studies have examined the relationship between activity items and incident stroke. In accordance with our findings, previous studies showed that adherence to high-level specific physical activity was associated with a lower risk of each subtype of stroke, except subarachnoid hemorrhage. For example, in a meta-analysis of 13 670 573 person-years, individuals who maintained high-intensity physical activity (total physical activity ≥8000 metabolic equivalent [MET] minutes/week) were found to have a lower risk of ischemic stroke compared with participants with lower levels of adherence (<600 MET minutes/week)[24] The limited sample size may have led to less precise and generalizable findings. Additionally, previous investigations mainly focused on singular activity items or general physical activity, potentially impacting result reliability. It is important to note that adherence to high-intensity physical activity for lower risk of stroke is not entirely accurate. Accordingly, it is crucial to define diverse types of physical activities in stroke outcome results. Our study utilized PCA to identify physical activity patterns and assess HRs of stroke across patterns.

Several previous biological studies may explain the results of our present study. Physical activity is believed to enhance neuronal activity and synaptic sensitivity, to promote cerebral blood flow and reduce the occurrence of brain diseases.[25] In particularly, aerobic exercise has been shown to increase BDNF (brain-derived neurotrophic factor), which is a serum that stimulates cell growth and maintains neurons.[26] Besides, physical activities could relieve the hardening of blood vessels and increase cerebral blood flow to reduce the burden of cardiovascular risk factors to improve brain health and prevent stroke.[27] Additionally, the influence of mental activity on stroke may be related to dietary habits, with frequent TV watchers potentially consuming unhealthy diets from snacks and soft drinks during watching TV.[28]

Strengths and Limitations

This study has several notable strengths. Firstly, we applied PCA for dimensionality reduction of multiactivity data to identify key activity patterns, simplifying complex interactions. Additionally, the large sample size of the UK Biobank and the prospective study design enabled thorough evaluation of physical activity and mental activity's association with stroke risk. The UK Biobank database contains extensive population phenotypic characteristics, and consistent follow-up ensured data reliability. Therefore, the clinical diagnosis data of stroke in the UK Biobank is highly reliable. Furthermore, we conducted sensitivity analyses to ensure the stability of our findings. Overall, these strengths add to the robustness and validity of our investigation.

However, some limitations remained to be considered. First, self-reported physical and mental activity questionnaires at baseline could introduce information bias. Future studies should employ more accurate measures for data reliability. Second, the classification of stroke subtypes is not always clear.[29] ≈13% of stroke cases in our data were diagnosed as having multiple subtypes. However, previous researchers have developed methods to automate stroke disease subtypes in the UK Biobank.[30] Third, the UK Biobank cohort may not fully represent the general population due to the low response rates (5.5%) of and the healthy volunteer effect, which may affect the representation of the middle-aged and older UK population,[10] and limit the generalizability of the current findings. Meanwhile, low response rates and poor representation may have distorted the association between physical and mental activity patterns and risk of stroke.[31] Fourth, missing covariates were imputed by removing missing samples or mean imputation, which may reduce the variation of the data to some extent, making the covariate values more centralized. Finally, this study was an observational study to explore the associations between physical/mental activities and incident stroke, which inevitably lacked the ability to draw conclusions on causal inference. In our study, we defined Time 0 as the initiation of follow-up (from 2006 to 2010). Despite implementing a 1-year lag in the primary analysis to address temporal asynchrony and reverse causality, it was not feasible to synchronize the commencement of follow-up with intervention assignment due to data constraints from the observational study. Meanwhile, we have chosen an end date for follow-up instead of a 10-year follow-up time, potentially resulting in inconsistent follow-up times within the sample, although this may not have an impact on our HR estimates. Similar to any other observational study, reverse causality or unmeasured confounders couldn't be entirely ruled out. The utilization of PCA, a unique technique for reducing dimensionality, constrained our exposure PCs, thereby precluding us from employing the parametric g formula or inverse probability of censoring weighting (IPCW) methods to replicate the target trial.[32,33]

Conclusions

In summary, our study found that adherence to physical and mental activity patterns related to vigorous exercise, housework, walking predominant patterns, and minimizing TV viewing and transportation commutes were associated with a lower risk of stroke. Our findings support the recommendation that adherence to vigorous exercise, housework, walking, and minimizing

TV viewing and transportation commutes could be a healthy lifestyle to lowering the risk of stroke in the general population.

ARTICLE INFORMATION

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Disclosures

None.

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REFERENCES

1. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the global burden of disease study 2013. *Lancet*. 2015;385:117–171. doi: 10.1016/S0140-6736(14)61682-2
2. Pandian JD, Singh G, Kaur P, Bansal R, Paul BS, Singla M, Singh S, Samuel CJ, Verma SJ, Moodbidri P, et al. Incidence, short-term outcome, and spatial distribution of stroke patients in Ludhiana, India. *Neurology*. 2016;86:425–433. doi: 10.1212/WNL.0000000000002335
3. Wang Y, Rudd AG, Wolfe CDA. Age and ethnic disparities in incidence of stroke over time: the south London stroke register. *Stroke*. 2013;44:3298–3304. doi: 10.1161/STROKEAHA.113.002604
4. Kim J, Thayabaranathan T, Donnan GA, Howard G, Howard VJ, Rothwell PM, Feigin V, Norrving B, Owolabi M, Pandian J, et al. Global stroke statistics 2019. *Int J Stroke*. 2020;15:819–838. doi: 10.1177/1747493020909545
5. Belfiore P, Miele A, Gallè F, Liguori G. Adapted physical activity and stroke: a systematic review. *J Sports Med Phys Fitness*. 2018;58:1867–1875. doi: 10.23736/S0022-4707.17.07749-0
6. Hooker SP, Diaz KM, Blair SN, Colabianchi N, Hutto B, McDonnell MN, Vena JE, Howard VJ. Association of accelerometer-measured sedentary time and physical activity with risk of stroke among us adults. *JAMA Netw Open*. 2022;5:e2215385. doi: 10.1001/jamanetworkopen.2022.15385
7. Kramer SF, Hung SH, Brodtmann A. The impact of physical activity before and after stroke on stroke risk and recovery: a narrative review. *Curr Neurol Neurosci Rep*. 2019;19:28. doi: 10.1007/s11910-019-0949-4
8. Shiue I. Duration of daily TV/screen watching with cardiovascular, respiratory, mental and psychiatric health: Scottish Health Survey, 2012-2013. *Int J Cardiol*. 2015;186:241–246. doi: 10.1016/j.ijcard.2015.03.259
9. Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, Downey P, Elliott P, Green J, Landray M, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med*. 2015;12:e1001779. doi: 10.1371/journal.pmed.1001779
10. Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, Collins R, Allen NE. Comparison of sociodemographic and health-related characteristics of UK biobank participants with those of the general population. *Am J Epidemiol*. 2017;186:1026–1034. doi: 10.1093/aje/kwx246
11. Zhu J, Chen W, Hu Y, Qu Y, Yang H, Zeng Y, Hou C, Ge F, Zhou Z, Song H. Physical activity patterns, genetic susceptibility, and risk of hip/knee osteoarthritis: a prospective cohort study based on the UK biobank. *Osteoarthritis Cartilage*. 2022;30:1079–1090. doi: 10.1016/j.joca.2022.04.004
12. Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the international physical activity questionnaire short form (IPAQ-SF): a systematic review. *Int J Behav Nutr Phys Act*. 2011;8:115. doi: 10.1186/1479-5868-8-115
13. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*. 2003;35:1381–1395. doi: 10.1249/01.MSS.0000078924.61453.FB
14. McDermott M, Brown DL, Chervin RD. Sleep disorders and the risk of stroke. *Expert Rev Neurother*. 2018;18:523–531. doi: 10.1080/14737175.2018.1489239
15. Zhu J, Ge F, Zeng Y, Qu Y, Chen W, Yang H, Yang L, Fang F, Song H. Physical and mental activity, disease susceptibility, and risk of dementia. *A Prospective Cohort Study Based on UK Biobank*. 2022;99:e799–e813. doi: 10.1212/WNL.0000000000200701
16. Sommerlad A, Sabia S, Singh-Manoux A, Lewis G, Livingston G. Association of social contact with dementia and cognition: 28-year follow-up of the whitehall ii cohort study. *PLoS Med*. 2019;16:e1002862. doi: 10.1371/journal.pmed.1002862
17. World Health Organization. ICD-10 Version: 2019. Geneva. https://icd.who.int/browse10/2019/en
18. Blane DPT, Phillimore P, *Alastair Beattie. Health and deprivation: inequality and the north*. Routledge. 1988
19. Mozaffarian D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: a comprehensive review. *Circulation*. 2016;133:187–225. doi: 10.1161/CIRCULATIONAHA.115.018585
20. Morris MC, Tangney CC, Wang Y, Sacks FM, Bennett DA, Aggarwal NT. Mind diet associated with reduced incidence of Alzheimer's disease. *Alzheimers Dement*. 2015;11:1007–1014. doi: 10.1016/j.jalz.2014.11.009
21. Jannasch F, Riordan F, Andersen LF, Schulze MB. Exploratory dietary patterns: a systematic review of methods applied in pan-European studies and of validation studies. *Br J Nutr*. 2018;120:601–611. doi: 10.1017/S0007114518001800
22. Haneuse S, VanderWeele TJ, Arterburn D. Using the e-value to assess the potential effect of unmeasured confounding in observational studies. *JAMA*. 2019;321:602–603. doi: 10.1001/jama.2018.21554
23. VanderWeele TJ, Ding P. Sensitivity analysis in observational research: Introducing the e-value. *Ann Intern Med*. 2017;167:268–274. doi: 10.7326/M16-2607
24. Kyu HH, Bachman VF, Alexander LT, Mumford JE, Afshin A, Estep K, Veerman JL, Delwiche K, Iannarone ML, Moyer ML, et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the global burden of disease study 2013. *BMJ*. 2016;354:i3857. doi: 10.1136/bmj.i3857
25. Boecker H. On the emerging role of neuroimaging in determining functional and structural brain integrity induced by physical exercise: impact for predictive, preventive, and personalized medicine. *EPMA J*. 2011;2:277–285. doi: 10.1007/s13167-011-0093-y
26. Håkansson K, Ledreux A, Daffner K, Terjestam Y, Bergman P, Carlsson R, Kivipelto M, Winblad B, Granholm AC, Mohammed AKH. BDNF responses in healthy older persons to 35 minutes of physical exercise, cognitive training, and mindfulness: associations with working memory function. *J Alzheimers Dis*. 2017;55:645–657. doi: 10.3233/JAD-160593
27. Bagi Z, Broskova Z, Feher A. Obesity and coronary microvascular disease - implications for adipose tissue-mediated remote inflammatory response. *Curr Vasc Pharmacol*. 2014;12:453–461. doi: 10.2174/1570161112666140423221843

28. Frydenlund G, Jørgensen T, Toft U, Pisinger C, Aadahl M. Sedentary leisure time behavior, snacking habits and cardiovascular biomarkers: the inter99 study. *Eur J Prev Cardiol*. 2012;19:1111–1119. doi: 10.1177/1741826711419999
29. Rannikmäe K, Ngoh K, Bush K, Al-Shahi Salman R, Doubal F, Flaig R, Henshall DE, Hutchison A, Nolan J, Osborne S, et al. Accuracy of identifying incident stroke cases from linked health care data in UK biobank. *Neurology*. 2020;95:e697–e707. doi: 10.1212/WNL.0000000000009924
30. Rannikmäe K, Wu H, Tominey S, Whiteley W, Allen N, Sudlow C; UK Biobank. Developing automated methods for disease subtyping in UK biobank: an exemplar study on stroke. *BMC Med Inform Decis Mak*. 2021;21:191. doi: 10.1186/s12911-021-01556-0
31. Stamatakis E, Owen KB, Shepherd L, Drayton B, Hamer M, Bauman AE. Is cohort representativeness passé? Poststratified associations of lifestyle risk factors with mortality in the UK biobank. *Epidemiology*. 2021;32:179–188. doi: 10.1097/EDE.0000000000001316
32. Hernán MA, Wang W, Leaf DE. Target trial emulation: a framework for causal inference from observational data. *JAMA*. 2022;328:2446–2447. doi: 10.1001/jama.2022.21383
33. Hernán MA, Robins JM. Using big data to emulate a target trial when a randomized trial is not available. *Am J Epidemiol*. 2016;183:758–764. doi: 10.1093/aje/kwv254
34. Tsao CW, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL, Baker-Smith CM, Beaton AZ, Boehme AK, Buxton AE, et al; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2023 update: a report from the American Heart Association. *Circulation*. 2023;147:e93–e621. doi: 10.1161/CIR.0000000000001123
35. Zhang Y, Yang H, Li S, Li W-D, Wang Y. Consumption of coffee and tea and risk of developing stroke, dementia, and poststroke dementia: a cohort study in the UK biobank. *PLoS Med*. 2021;18:e1003830. doi: 10.1371/journal.pmed.1003830
36. Fan M, Sun D, Zhou T, Heianza Y, Lv J, Li L, Qi L. Sleep patterns, genetic susceptibility, and incident cardiovascular disease: a prospective study of 385 292 UK biobank participants. *Eur Heart J*. 2020;41:1182–1189. doi: 10.1093/eurheartj/ehz849
37. Inoue-Choi M, Ramirez Y, Cornelis MC, Berrington de González A, Freedman ND, Loftfield E. Tea consumption and all-cause and cause-specific mortality in the UK biobank: a prospective cohort study. *Ann Intern Med*. 2022;175:1201–1211. doi: 10.7326/M22-0041
38. Larsson SC, Burgess S, Michaëlsson K. Smoking and stroke: a Mendelian randomization study. *Ann Neurol*. 2019;86:468–471. doi: 10.1002/ana.25534
39. Mukamal KJ, Chung H, Jenny NS, Kuller LH, Longstreth WT Jr, Mittleman MA, Burke GL, Cushman M, Beauchamp NJ Jr, Siscovick DS. Alcohol use and risk of ischemic stroke among older adults: the cardiovascular health study. *Stroke*. 2005;36:1830–1834. doi: 10.1161/01.STR.0000177587.76846.89
40. Fishman B, Bardugo A, Zloof Y, Bendor CD, Libruder C, Zucker I, Lutski M, Ram A, Hershkovitz Y, Orr O, et al. Adolescent hypertension is associated with stroke in young adulthood: a nationwide cohort of 1.9 million adolescents. *Stroke*. 2023;54:1531–1537. doi: 10.1161/STROKEAHA.122.042100