

## Supplementary Appendix

### eTables and figures with legends

#### **eTable 1. Strengthening the reporting of observational studies in epidemiology (STROBE) Statement**

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

#### **eTable 2. Baseline characteristics by quartiles of RLS**

Notes: Values are presented as number (N) with percent (%) or medians (M) with interquartile ranges (IQRs). *P* values represent statistical measurement of comparing different quartiles. BMI, body mass index; WC, waist circumference; MET, metabolic equivalents of task; OCP, oral contraceptive pill; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

#### **eTable 3. Baseline characteristics by quartiles of EEE**

Notes: Values are presented as number (N) with percent (%) or medians (M) with interquartile ranges (IQRs). *P* values represent statistical measurement of comparing different quartiles. BMI, body mass index; WC, waist circumference; MET, metabolic equivalents of task; OCP, oral contraceptive pill; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

#### **eTable 4. Baseline characteristics by quartiles of TEE**

Notes: Values are presented as number (N) with percent (%) or medians (M) with interquartile ranges (IQRs). *P* values represent statistical measurement of comparing different quartiles. BMI, body mass index; WC, waist circumference; MET, metabolic equivalents of task; OCP, oral contraceptive pill; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

#### **eTable 5. Incidence rate of stroke and its subtypes among postmenopausal participants**

Note: Incidence rate was expressed in 100000 person-years, RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

#### **eTable 6. Association between indicators of lifetime cumulative exposure due to reproductive factors and risk of incident stroke: multivariable Cox regression**

Notes: \**P*<0.05; HR and 95% CI in blue indicate a significant protective effect, whereas HR and 95% CI in red indicate a significant hazard effect. HR, hazard ratio; CI, confidence interval; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage. Model 1 was adjusted for age at baseline. Model 2 was adjusted for age at baseline, marital status, residential status, education, occupation, household income, body mass index, waist circumference, tobacco smoking, second hand smoking, alcohol consumption, physical activity in metabolic equivalent-hours/day, anticoagulation therapy, hypolipidemic therapy, diabetes, hypertension. *P* for trend was test based on variable containing median value for each quintile.

#### **eTable 7. Association between each reproductive factor and risk of incident stroke: multivariable Cox regression**

Note: \* $P < 0.05$ ; HR and 95% CI in blue indicate a significant protective effect, whereas HR and 95% CI in red indicate a significant hazard effect. HR, hazard ratio; CI, confidence interval; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; OCP, oral contraceptive pill. HR was adjusted for age at baseline, marital status, residential status, education level, occupation, household income, body mass index, waist circumference, tobacco smoking, second hand smoking, alcohol consumption, physical activity in metabolic equivalent-hours/day, anticoagulation therapy, hypolipidemic therapy, diabetes, hypertension.

**eTable 8. Sensitivity analysis**

Notes: \* $P < 0.05$ ; HR and 95% CI in blue indicate a significant protective effect, whereas HR and 95% CI in red indicate a significant hazard effect. HR, hazard ratio; CI, confidence interval; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

#HR was adjusted for age at baseline, marital status, residential status, education, occupation, household income, body mass index, waist circumference, tobacco smoking, second hand smoking, alcohol consumption, physical activity in metabolic equivalent-hours/day, anticoagulation therapy, hypolipidemic therapy, diabetes, hypertension. ##HR was adjusted for age at baseline, marital status, residential status, education level, occupation, household income, body mass index, waist circumference, tobacco smoking, second hand smoking, alcohol consumption, physical activity in metabolic equivalent-hours/day.

Related drugs included angiotensin-converting enzyme inhibitors (ACEI), aspirin, beta-blocker, calcium antagonist, diuretics, statins. Related diseases included cancer, chronic heart disease, hysterectomy, psychic disorders, rheumatic heart disease, kidney disease.

**eTable 9. Association between indicators of lifetime cumulative exposure due to reproductive factors and risk of incident stroke: age-stratified multivariable Cox regression**

Notes: \* $P < 0.05$ ; HR and 95% CI in blue indicate a significant protective effect, whereas HR and 95% CI in red indicate a significant hazard effect. HR, hazard ratio; CI, confidence interval; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage. #HR was adjusted for age at baseline, marital status, residential status, education, occupation, household income, body mass index, waist circumference, tobacco smoking, second-hand smoking, alcohol consumption, physical activity in metabolic equivalent-hours/day, anticoagulation therapy, hypolipidemic therapy, diabetes, hypertension.

**eFigure 1. Incidence rate of stroke and its subtypes**

Notes: RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

**eTable 1. Strengthening the reporting of observational studies in epidemiology (STROBE) Statement**

	<b>Item No</b>	<b>Recommendation</b>
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses

<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (e.g., average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
<b>Other information</b>		

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Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
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\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

**eTable 2. Baseline characteristics by quartiles of RLS**

Variables	Total (N=122,939)	Q1(<31.0 years) (N=28,956)	Q2(31.0-32.9 years) (N=21,375)	Q3(33.0-35.9 years) (N=38,075)	Q4(≥36.0 years) (N=34,533)	P value
Age at baseline (years)						<0.001
M (IQR)	58.3 (54.0–65.1)	59.2 (53.6–66.3)	57.8 (53.0–64.7)	57.5 (53.5–64.4)	58.8 (55.1–64.9)	
Age of menarche (years)						<0.001
M (IQR)	16.0 (14.0–17.0)	17.0 (15.0–18.0)	16.0 (15.0–17.0)	16.0 (15.0–17.0)	15.0 (13.0–16.0)	
Age of menopause (years)						<0.001
M (IQR)	49.0 (47.0–51.0)	45.0 (43.0–46.0)	48.0 (47.0–49.0)	50.0 (48.0–51.0)	52.0 (51.0–54.0)	
Marital status						<0.001
Never married or separated or widowed or divorced	21,002 (17.1)	5,543 (19.1)	3,525 (16.5)	6,058 (15.9)	5,876 (17.0)	
Married	101,937 (82.9)	23,413 (80.9)	17,850 (83.5)	32,017 (84.1)	28,657 (83.0)	
Residential area						<0.001
Rural	66,599 (54.2)	17,518 (60.5)	12,353 (57.8)	20,391 (53.6)	16,337 (47.3)	
Urban	56,340 (45.8)	11,438 (39.5)	9,022 (42.2)	17,684 (46.4)	18,196 (52.7)	
Education						<0.001
Lower than primary school	89,238 (72.6)	22,682 (78.3)	16,220 (75.9)	27,463 (72.1)	22,873 (66.2)	
Middle school	20,276 (16.5)	4,033 (13.9)	3,172 (14.8)	6,476 (17.0)	6,595 (19.1)	
High school	10,088 (8.2)	1,805 (6.3)	1,566 (7.3)	3,194 (8.4)	3,523 (10.2)	
College or higher	3,337 (2.7)	436 (1.5)	417 (2.0)	942 (2.5)	1,542 (4.5)	
Occupation						<0.001
Agriculture or factory worker	49,487 (40.3)	13,316 (46.0)	9,430 (44.1)	15,275 (40.1)	11,466 (33.2)	
Administrator or manager or professional or technical	1,619 (1.3)	240 (0.8)	236 (1.1)	536 (1.4)	607 (1.8)	
Sales and service workers or self- employed	4,068 (3.3)	860 (3.0)	752 (3.5)	1,328 (3.5)	1,128 (3.3)	
Retired or housewife or house husband or unemployed	65,904 (53.6)	14,033 (48.5)	10,630 (49.8)	20,372 (53.5)	20,869 (60.4)	
Other or not stated	1,861 (1.5)	507 (1.7)	327 (1.5)	564 (1.5)	463 (1.3)	
Household income (¥/year)						<0.001
<10,000	39,899 (32.5)	11,345 (39.2)	7,202 (33.7)	11,677 (30.7)	9,675 (28.0)	
10,000-19,999	35,439 (28.8)	8,441 (29.1)	6,246 (29.2)	10,988 (28.9)	9,764 (28.3)	
20,000-34,999	28,009 (22.8)	5,586 (19.3)	4,713 (22.1)	9,156 (24.0)	8,554 (24.8)	

Variables	Total (N=122,939)	Q1(<31.0 years) (N=28,956)	Q2(31.0-32.9 years) (N=21,375)	Q3(33.0-35.9 years) (N=38,075)	Q4(≥36.0 years) (N=34,533)	P value
≥35,000	19,592 (15.9)	3,584 (12.4)	3,214 (15.0)	6,254 (16.4)	6,540 (18.9)	
BMI (kg/m <sup>2</sup> )						<0.001
<18.5	6,374 (5.2)	2,024 (7.0)	1,208 (5.7)	1,908 (5.0)	1,234 (3.6)	
18.5-23.9	56,400 (45.9)	14,315 (49.4)	10,420 (48.7)	17,384 (45.7)	14,281 (41.4)	
24.0-27.9	43,163 (35.1)	9,187 (31.7)	7,133 (33.4)	13,609 (35.7)	13,234 (38.3)	
≥28	17,002 (13.8)	3,430 (11.9)	2,614 (12.2)	5,174 (13.6)	5,784 (16.7)	
WC (cm)						<0.001
M (IQR)	80.2 (73.5–87.1)	79.3 (72.3–86.3)	79.6 (73.0–86.5)	80.3 (73.5–87.0)	81.5 (75.0–88.1)	
Smoking status						<0.001
Never or occasional or former	118,408 (96.3)	27,579 (95.2)	20,573 (96.2)	36,792 (96.6)	33,464 (96.9)	
Current	4,531 (3.7)	1,377 (4.8)	802 (3.8)	1,283 (3.4)	1,069 (3.1)	
Second-hand smoking						<0.001
Occasionally	56,434 (45.9)	12,628 (43.6)	9,445 (44.2)	17,591 (46.2)	16,770 (48.6)	
Most days	66,505 (54.1)	16,328 (56.4)	11,930 (55.8)	20,484 (53.8)	17,763 (51.4)	
Drinking status						0.041
Never or occasional or former	118,083 (96.1)	27,741 (95.8)	20,511 (96.0)	36,629 (96.2)	33,202 (96.1)	
Current	4,856 (3.9)	1,215 (4.2)	864 (4.0)	1,446 (3.8)	1,331 (3.9)	
Physical activity in MET (hours/day)						<0.001
M (IQR)	13.5 (8.9–21.8)	13.8 (8.8–22.8)	14.0 (8.9–22.9)	13.6 (8.9–22.0)	12.7 (8.6–20.0)	
History of anticoagulation therapy						0.001
No	121,338 (98.7)	28,637 (98.9)	21,097 (98.7)	37,576 (98.7)	34,028 (98.5)	
Yes	1,601 (1.3)	319 (1.1)	278 (1.3)	499 (1.3)	505 (1.5)	
History of hypolipidemic therapy						0.005
No	122,532 (99.7)	28,874 (99.7)	21,317 (99.7)	37,953 (99.7)	34,388 (99.6)	
Yes	407 (0.3)	82 (0.3)	58 (0.3)	122 (0.3)	145 (0.4)	
History of diabetes						<0.001
No	111,607 (90.8)	26,616 (91.9)	19,676 (92.1)	34,656 (91.0)	30,659 (88.8)	
Yes	11,332 (9.2)	2,340 (8.1)	1,699 (7.9)	3,419 (9.0)	3,874 (11.2)	
History of hypertension						<0.001
No	67,355 (54.8)	16,642 (57.5)	12,139 (56.8)	21,057 (55.3)	17,517 (50.7)	
Yes	55,584 (45.2)	12,314 (42.5)	9,236 (43.2)	17,018 (44.7)	17,016 (49.3)	
Number of pregnancies						<0.001

Variables	Total (N=122,939)	Q1(<31.0 years) (N=28,956)	Q2(31.0-32.9 years) (N=21,375)	Q3(33.0-35.9 years) (N=38,075)	Q4(≥36.0 years) (N=34,533)	P value
M (IQR)	4.0 (3.0–5.0)	4.0 (3.0–5.0)	4.0 (3.0–5.0)	4.0 (3.0–5.0)	4.0 (3.0–5.0)	
Number of live births						<0.001
M (IQR)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	3.0 (2.0–3.0)	3.0 (2.0–4.0)	
Number of stillbirths						<0.001
M (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
Number of miscarriages or terminations						<0.001
M (IQR)	1.0 (0.0–2.0)	1.0 (0.0–1.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	
Lifetime lactation duration (years)						<0.001
M (IQR)	3.0 (2.0–5.0)	3.4 (2.0–5.8)	3.0 (2.0–5.0)	3.0 (1.9–5.0)	3.0 (1.8–4.9)	
History of OCP use						<0.001
No	110,364 (89.8)	26,643 (92.0)	19,284 (90.2)	33,999 (89.3)	30,438 (88.1)	
Yes	12,575 (10.2)	2,313 (8.0)	2,091 (9.8)	4,076 (10.7)	4,095 (11.9)	
OCP use duration (years)						<0.001
M (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
EEE (years)						<0.001
M (IQR)	27.3 (23.5–30.7)	22.0 (18.8–24.6)	25.8 (23.1–27.8)	28.5 (25.8–30.4)	32.0 (29.3–34.2)	
TEE (years)						<0.001
M (IQR)	32.5 (29.3–35.3)	27.3 (24.8–29.3)	30.8 (29.3–31.8)	33.3 (31.8–34.5)	36.8 (35.3–38.6)	
Total stroke						<0.001
Non-stroke	107,800 (87.7)	25,312 (87.4)	18,880 (88.3)	33,633 (88.3)	29,975 (86.8)	
Total stroke	15,139 (12.3)	3,644 (12.6)	2,495 (11.7)	4,442 (11.7)	4,558 (13.2)	
IS						<0.001
Non-IS	110,086 (89.5)	25,919 (89.5)	19,267 (90.1)	34,324 (90.1)	30,576 (88.5)	
IS	12,853 (10.5)	3,037 (10.5)	2,108 (9.9)	3,751 (9.9)	3,957 (11.5)	
ICH						<0.001
Non-ICH	120,359 (97.9)	28,255 (97.6)	20,934 (97.9)	37,303 (98.0)	33,867 (98.1)	
ICH	2,580 (2.1)	701 (2.4)	441 (2.1)	772 (2.0)	666 (1.9)	
SAH						0.205
Non-SAH	122,670 (99.8)	28,900 (99.8)	21,336 (99.8)	37,990 (99.8)	34,444 (99.7)	
SAH	269 (0.2)	56 (0.2)	39 (0.2)	85 (0.2)	89 (0.3)	



Notes: Values are presented as number (N) with percent (%) or medians (M) with interquartile ranges (IQRs). *P* values represent statistical measurement of comparing different quartiles. BMI, body mass index; WC, waist circumference; MET, metabolic equivalents of task; OCP, oral contraceptive pill; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

**eTable 3. Baseline characteristics by quartiles of EEE**

Variables	Total (N=122,939)	Q1(<23.5 years) (N=30,125)	Q2(23.5-27.2 years) (N=29,936)	Q3(27.3-30.6 years) (N=31,990)	Q4( $\geq$ 30.7 years) (N=30,888)	P value
Age at baseline (years)						<0.001
M (IQR)	58.3 (54.0–65.1)	63.3 (57.0–69.2)	58.9 (54.0–65.4)	56.8 (53.1–62.4)	56.3 (53.6–61.0)	
Age of menarche (years)						<0.001
M (IQR)	16.0 (14.0–17.0)	16.0 (15.0–17.0)	16.0 (15.0–17.0)	16.0 (15.0–17.0)	15.0 (13.0–16.0)	
Age of menopause (years)						<0.001
M (IQR)	49.0 (47.0–51.0)	46.0 (43.0–48.0)	48.0 (46.0–50.0)	50.0 (48.0–51.0)	52.0 (50.0–53.0)	
Marital status						<0.001
Never married or separated or widowed or divorced	21,002 (17.1)	7,396 (24.6)	5,146 (17.2)	4,453 (13.9)	4,007 (13.0)	
Married	101,937 (82.9)	22,729 (75.4)	24,790 (82.8)	27,537 (86.1)	26,881 (87.0)	
Residential area						<0.001
Rural	66,599 (54.2)	21,338 (70.8)	17,934 (59.9)	16,541 (51.7)	10,786 (34.9)	
Urban	56,340 (45.8)	8,787 (29.2)	12,002 (40.1)	15,449 (48.3)	20,102 (65.1)	
Education						<0.001
Lower than primary school	89,238 (72.6)	26,701 (88.6)	23,747 (79.3)	22,583 (70.6)	16,207 (52.5)	
Middle school	20,276 (16.5)	2,492 (8.3)	4,056 (13.6)	5,753 (18.0)	7,975 (25.8)	
High school	10,088 (8.2)	791 (2.6)	1,739 (5.8)	2,844 (8.9)	4,714 (15.3)	
College or higher	3,337 (2.7)	141 (0.5)	394 (1.3)	810 (2.5)	1,992 (6.4)	
Occupation						<0.001
Agriculture or factory worker	49,487 (40.3)	14,500 (48.1)	13,803 (46.1)	12,974 (40.5)	8,210 (26.6)	
Administrator or manager or professional or technical	1,619 (1.3)	51 (0.2)	188 (0.6)	404 (1.3)	976 (3.1)	
Sales and service workers or self-employed	4,068 (3.3)	429 (1.4)	849 (2.9)	1,280 (4.0)	1,510 (4.9)	
Retired or housewife or house husband or unemployed	65,904 (53.6)	14,755 (49.0)	14,613 (48.8)	16,797 (52.5)	19,739 (63.9)	
Other or not stated	1,861 (1.5)	390 (1.3)	483 (1.6)	535 (1.7)	453 (1.5)	
Household income (¥/year)						<0.001
<10,000	39,899 (32.5)	15,517 (51.5)	10,396 (34.7)	8,504 (26.6)	5,482 (17.7)	
10,000-19,999	35,439 (28.8)	8,316 (27.6)	9,079 (30.3)	9,281 (29.0)	8,763 (28.4)	
20,000-34,999	28,009 (22.8)	4,030 (13.4)	6,453 (21.6)	8,271 (25.9)	9,255 (30.0)	
$\geq$ 35,000	19,592 (15.9)	2,262 (7.5)	4,008 (13.4)	5,934 (18.5)	7,388 (23.9)	

Variables	Total (N=122,939)	Q1(<23.5 years) (N=30,125)	Q2(23.5-27.2 years) (N=29,936)	Q3(27.3-30.6 years) (N=31,990)	Q4(≥30.7 years) (N=30,888)	P value
BMI (kg/m <sup>2</sup> )						<0.001
<18.5	6,374 (5.2)	2,244 (7.4)	1,727 (5.8)	1,437 (4.5)	966 (3.1)	
18.5-23.9	56,400 (45.9)	14,670 (48.7)	14,093 (47.1)	14,824 (46.3)	12,813 (41.5)	
24.0-27.9	43,163 (35.1)	9,517 (31.6)	10,178 (34.0)	11,345 (35.5)	12,123 (39.3)	
≥28	17,002 (13.8)	3,694 (12.3)	3,938 (13.1)	4,384 (13.7)	4,986 (16.1)	
WC (cm)						<0.001
M (IQR)	80.2 (73.5–87.1)	80.0 (73.0–87.2)	80.1 (73.1–87.2)	80.0 (73.4–87.0)	81.0 (74.5–87.3)	
Smoking status						<0.001
Never or occasional or former	118,408 (96.3)	28,535 (94.7)	28,789 (96.2)	30,974 (96.8)	30,110 (97.5)	
Current	4,531 (3.7)	1,590 (5.3)	1,147 (3.8)	1,016 (3.2)	778 (2.5)	
Second-hand smoking						<0.001
Occasionally	56,434 (45.9)	13,286 (44.1)	13,176 (44.0)	14,664 (45.8)	15,308 (49.6)	
Most days	66,505 (54.1)	16,839 (55.9)	16,760 (56.0)	17,326 (54.2)	15,580 (50.4)	
Drinking status						0.126
Never or occasional or former	118,083 (96.1)	28,890 (95.9)	28,805 (96.2)	30,754 (96.1)	29,634 (95.9)	
Current	4,856 (3.9)	1,235 (4.1)	1,131 (3.8)	1,236 (3.9)	1,254 (4.1)	
Physical activity in MET (hours/day)						<0.001
M (IQR)	13.5 (8.9–21.8)	12.4 (8.4–21.3)	13.9 (8.9–22.5)	14.0 (9.3–22.7)	13.1 (8.9–20.2)	
History of anticoagulation therapy						<0.001
No	121,338 (98.7)	29,674 (98.5)	29,528 (98.6)	31,638 (98.9)	30,498 (98.7)	
Yes	1,601 (1.3)	451 (1.5)	408 (1.4)	352 (1.1)	390 (1.3)	
History of hypolipidemic therapy						0.054
No	122,532 (99.7)	30,003 (99.6)	29,850 (99.7)	31,894 (99.7)	30,785 (99.7)	
Yes	407 (0.3)	122 (0.4)	86 (0.3)	96 (0.3)	103 (0.3)	
History of diabetes						<0.001
No	111,607 (90.8)	27,440 (91.1)	27,358 (91.4)	29,103 (91.0)	27,706 (89.7)	
Yes	11,332 (9.2)	2,685 (8.9)	2,578 (8.6)	2,887 (9.0)	3,182 (10.3)	
History of hypertension						<0.001
No	67,355 (54.8)	15,128 (50.2)	16,337 (54.6)	18,318 (57.3)	17,572 (56.9)	
Yes	55,584 (45.2)	14,997 (49.8)	13,599 (45.4)	13,672 (42.7)	13,316 (43.1)	
Number of pregnancies						<0.001
M (IQR)	4.0 (3.0–5.0)	5.0 (4.0–6.0)	4.0 (3.0–5.0)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	
Number of live births						<0.001

Variables	Total (N=122,939)	Q1(<23.5 years) (N=30,125)	Q2(23.5-27.2 years) (N=29,936)	Q3(27.3-30.6 years) (N=31,990)	Q4( $\geq$ 30.7 years) (N=30,888)	P value
M (IQR)	3.0 (2.0–4.0)	4.0 (3.0–5.0)	3.0 (2.0–4.0)	2.0 (2.0–3.0)	2.0 (1.0–2.0)	
Number of stillbirths						<0.001
M (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
Number of miscarriages or terminations						<0.001
M (IQR)	1.0 (0.0–2.0)	0.0 (0.0–1.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	
Lifetime lactation duration(years)						<0.001
M (IQR)	3.0 (2.0–5.0)	6.0 (4.0–8.3)	3.7 (2.3–5.0)	2.6 (1.8–4.0)	1.9 (1.0–2.7)	
History of OCP use						<0.001
No	110,364 (89.8)	27,262 (90.5)	26,451 (88.4)	28,396 (88.8)	28,255 (91.5)	
Yes	12,575 (10.2)	2,863 (9.5)	3,485 (11.6)	3,594 (11.2)	2,633 (8.5)	
OCP use duration (years)						<0.001
M (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
RLS (years)						<0.001
M (IQR)	33.0 (31.0–36.0)	30.0 (27.0–32.0)	32.0 (30.0–34.0)	34.0 (32.0–35.0)	37.0 (35.0–39.0)	
TEE (years)						<0.001
M (IQR)	32.5 (29.3–35.3)	26.8 (24.5–29.0)	30.8 (29.3–32.3)	33.3 (32.0–34.8)	36.8 (35.3–38.5)	
Total stroke						<0.001
Non-stroke	107,800 (87.7)	25,500 (84.6)	26,285 (87.8)	28,587 (89.4)	27,428 (88.8)	
Total stroke	15,139 (12.3)	4,625 (15.4)	3,651 (12.2)	3,403 (10.6)	3,460 (11.2)	
IS						<0.001
Non-IS	110,086 (89.5)	26,407 (87.7)	26,851 (89.7)	29,042 (90.8)	27,786 (90.0)	
IS	12,853 (10.5)	3,718 (12.3)	3,085 (10.3)	2,948 (9.2)	3,102 (10.0)	
ICH						<0.001
Non-ICH	120,359 (97.9)	29,079 (96.5)	29,282 (97.8)	31,475 (98.4)	30,523 (98.8)	
ICH	2,580 (2.1)	1,046 (3.5)	654 (2.2)	515 (1.6)	365 (1.2)	
SAH						0.497
Non-SAH	122,670 (99.8)	30,057 (99.8)	29,877 (99.8)	31,925 (99.8)	30,811 (99.8)	
SAH	269 (0.2)	68 (0.2)	59 (0.2)	65 (0.2)	77 (0.2)	

Notes: Values are presented as number (N) with percent (%) or medians (M) with interquartile ranges (IQRs). *P* values represent statistical measurement of comparing different quartiles. BMI, body mass index; WC, waist circumference; MET, metabolic equivalents of task; OCP, oral contraceptive pill; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

**eTable 4. Baseline characteristics by quartiles of TEE**

Variables	Total (N=122,939)	Q1(<29.3 years) (N=29,760)	Q2(29.3-32.4 years) (N=31,647)	Q3(32.5-35.2 years) (N=29,218)	Q4(≥35.3 years) (N=32,314)	P value
Age at baseline (years)						<0.001
M (IQR)	58.3 (54.0–65.1)	60.4 (54.6–67.3)	58.1 (53.3–64.9)	57.2 (53.4–63.6)	58.1 (54.6–64.1)	
Age of menarche (years)						<0.001
M (IQR)	16.0 (14.0–17.0)	17.0 (15.0–17.0)	16.0 (15.0–17.0)	16.0 (14.0–17.0)	15.0 (13.0–16.0)	
Age of menopause (years)						<0.001
M (IQR)	49.0 (47.0–51.0)	45.0 (43.0–47.0)	48.0 (47.0–50.0)	50.0 (48.0–51.0)	52.0 (50.0–54.0)	
Marital status						<0.001
Never married or separated or widowed or divorced	21,002 (17.1)	6,201 (20.8)	5,300 (16.7)	4,436 (15.2)	5,065 (15.7)	
Married	101,937 (82.9)	23,559 (79.2)	26,347 (83.3)	24,782 (84.8)	27,249 (84.3)	
Residential area						<0.001
Rural	66,599 (54.2)	20,961 (70.4)	18,230 (57.6)	14,661 (50.2)	12,747 (39.4)	
Urban	56,340 (45.8)	8,799 (29.6)	13,417 (42.4)	14,557 (49.8)	19,567 (60.6)	
Education						<0.001
Lower than primary school	89,238 (72.6)	25,282 (85.0)	24,381 (77.0)	20,432 (69.9)	19,143 (59.2)	
Middle school	20,276 (16.5)	3,046 (10.2)	4,634 (14.6)	5,326 (18.2)	7,270 (22.5)	
High school	10,088 (8.2)	1,200 (4.0)	2,071 (6.6)	2,645 (9.1)	4,172 (12.9)	
College or higher	3,337 (2.7)	232 (0.8)	561 (1.8)	815 (2.8)	1,729 (5.4)	
Occupation						<0.001
Agriculture or factory worker	49,487 (40.3)	15,584 (52.4)	14,052 (44.4)	11,078 (37.9)	8,773 (27.1)	
Administrator or manager or professional or technical	1,619 (1.3)	128 (0.4)	298 (1.0)	457 (1.6)	736 (2.3)	
Sales and service workers or self-employed	4,068 (3.3)	596 (2.0)	1,052 (3.3)	1,132 (3.9)	1,288 (4.0)	
Retired or housewife or house husband or unemployed	65,904 (53.6)	12,977 (43.6)	15,739 (49.7)	16,116 (55.1)	21,072 (65.2)	
Other or not stated	1,861 (1.5)	475 (1.6)	506 (1.6)	435 (1.5)	445 (1.4)	

Variables	Total (N=122,939)	Q1(<29.3 years) (N=29,760)	Q2(29.3-32.4 years) (N=31,647)	Q3(32.5-35.2 years) (N=29,218)	Q4(≥35.3 years) (N=32,314)	P value
Household income (¥/year)						<0.001
<10,000	39,899 (32.5)	14,517 (48.8)	10,891 (34.4)	7,880 (27.0)	6,611 (20.4)	
10,000-19,999	35,439 (28.8)	8,484 (28.5)	9,358 (29.6)	8,431 (28.8)	9,166 (28.4)	
20,000-34,999	28,009 (22.8)	4,227 (14.2)	6,886 (21.8)	7,630 (26.1)	9,266 (28.7)	
≥35,000	19,592 (15.9)	2,532 (8.5)	4,512 (14.2)	5,277 (18.1)	7,271 (22.5)	
BMI (kg/m <sup>2</sup> )						<0.001
<18.5	6,374 (5.2)	2,035 (6.8)	1,809 (5.7)	1,368 (4.7)	1,162 (3.6)	
18.5-23.9	56,400 (45.9)	14,627 (49.2)	15,036 (47.5)	13,254 (45.3)	13,483 (41.7)	
24.0-27.9	43,163 (35.1)	9,470 (31.8)	10,659 (33.7)	10,540 (36.1)	12,494 (38.7)	
≥28	17,002 (13.8)	3628 (12.2)	4,143 (13.1)	4,056 (13.9)	5,175 (16.0)	
WC (cm)						<0.001
M (IQR)	80.2 (73.5–87.1)	79.8 (72.7–86.9)	80.0 (73.0–87.0)	80.3 (73.6–87.0)	81.0 (74.6–87.5)	
Smoking status						<0.001
Never or occasional or former	118,408 (96.3)	28,271 (95.0)	30,433 (96.2)	28,277 (96.8)	31,427 (97.3)	
Current	4,531 (3.7)	1,489 (5.0)	1,214 (3.8)	941 (3.2)	887 (2.7)	
Second-hand smoking						<0.001
Occasionally	56,434 (45.9)	12,614 (42.4)	13,880 (43.9)	13,648 (46.7)	16,292 (50.4)	
Most days	66,505 (54.1)	17,146 (57.6)	17,767 (56.1)	15,570 (53.3)	16,022 (49.6)	
Drinking status						0.775
Never or occasional or former	118,083 (96.1)	28,560 (96.0)	30,388 (96.0)	28,084 (96.1)	31,051 (96.1)	
Current	4,856 (3.9)	1,200 (4.0)	1,259 (4.0)	1,134 (3.9)	1,263 (3.9)	
Physical activity in MET (hours/day)						<0.001
M (IQR)	13.5 (8.9–21.8)	13.8 (8.7–23.2)	14.0 (8.9–22.7)	13.6 (8.9–21.7)	12.6 (8.6–19.6)	
History of anticoagulation therapy						0.094
No	121,338 (98.7)	29,351 (98.6)	31,246 (98.7)	28,873 (98.8)	31,868 (98.6)	
Yes	1,601 (1.3)	409 (1.4)	401 (1.3)	345 (1.2)	446 (1.4)	
History of hypolipidemic therapy						0.514
No	122,532 (99.7)	29,663 (99.7)	31,553 (99.7)	29,120 (99.7)	32,196 (99.6)	

Variables	Total (N=122,939)	Q1(<29.3 years) (N=29,760)	Q2(29.3-32.4 years) (N=31,647)	Q3(32.5-35.2 years) (N=29,218)	Q4(≥35.3 years) (N=32,314)	P value
Yes	407 (0.3)	97 (0.3)	94 (0.3)	98 (0.3)	118 (0.4)	
History of diabetes						<0.001
No	111,607 (90.8)	27,390 (92.0)	29,017 (91.7)	26,474 (90.6)	28,726 (88.9)	
Yes	11,332 (9.2)	2,370 (8.0)	2,630 (8.3)	2,744 (9.4)	3,588 (11.1)	
History of hypertension						<0.001
No	67,355 (54.8)	16,063 (54.0)	17,919 (56.6)	16,299 (55.8)	17,074 (52.8)	
Yes	55,584 (45.2)	13,697 (46.0)	13,728 (43.4)	12,919 (44.2)	15,240 (47.2)	
Number of pregnancies						<0.001
M (IQR)	4.0 (3.0–5.0)	4.0 (3.0–5.0)	4.0 (3.0–5.0)	3.0 (2.0–5.0)	4.0 (3.0–5.0)	
Number of live births						<0.001
M (IQR)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	2.0 (2.0–3.0)	2.0 (2.0–3.0)	
Number of stillbirths						<0.001
M (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
Number of miscarriages or terminations						<0.001
M (IQR)	1.0 (0.0–2.0)	0.0 (0.0–1.0)	1.0 (0.0–1.0)	1.0 (0.0–2.0)	1.0 (0.0–2.0)	
Lifetime lactation duration (years)						<0.001
M (IQR)	3.0 (2.0–5.0)	5.5 (3.0–8.0)	3.1 (2.0–5.0)	2.8 (1.7–4.0)	2.0 (1.3–3.2)	
History of OCP use						<0.001
No	110,364 (89.8)	28,821 (96.8)	29,705 (93.9)	26,316 (90.1)	25,522 (79.0)	
Yes	12,575 (10.2)	939 (3.2)	1,942 (6.1)	2,902 (9.9)	6,792 (21.0)	
OCP use duration (years)						<0.001
M (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
RLS (years)						<0.001
M (IQR)	33.0 (31.0–36.0)	29.0 (27.0–31.0)	32.0 (31.0–33.0)	34.0 (33.0–35.0)	37.0 (36.0–39.0)	
EEE (years)						<0.001
M (IQR)	27.3 (23.5–30.7)	21.0 (18.0–23.2)	26.3 (24.5–27.8)	29.3 (27.5–30.7)	32.5 (30.3–34.3)	
Total stroke						<0.001
Non-stroke	107,800 (87.7)	25,671 (86.3)	27,873 (88.1)	25,937 (88.8)	28,319 (87.6)	
Total stroke	15,139 (12.3)	4,089 (13.7)	3,774 (11.9)	3,281 (11.2)	3,995 (12.4)	
IS						<0.001
Non-IS	110,086 (89.5)	26,423 (88.8)	28,458 (89.9)	26,407 (90.4)	28,798 (89.1)	

Variables	Total (N=122,939)	Q1(<29.3 years) (N=29,760)	Q2(29.3-32.4 years) (N=31,647)	Q3(32.5-35.2 years) (N=29,218)	Q4(≥35.3 years) (N=32,314)	P value
IS	12,853 (10.5)	3,337 (11.2)	3,189 (10.1)	2,811 (9.6)	3,516 (10.9)	<0.001
ICH						
Non-ICH	120,359 (97.9)	28,881 (97.0)	30,984 (97.9)	28,697 (98.2)	31,797 (98.4)	0.345
ICH	2,580 (2.1)	879 (3.0)	663 (2.1)	521 (1.8)	517 (1.6)	
SAH						
Non-SAH	122,670 (99.8)	29,698 (99.8)	31,588 (99.8)	29,151 (99.8)	32,233 (99.7)	
SAH	269 (0.2)	62 (0.2)	59 (0.2)	67 (0.2)	81 (0.3)	

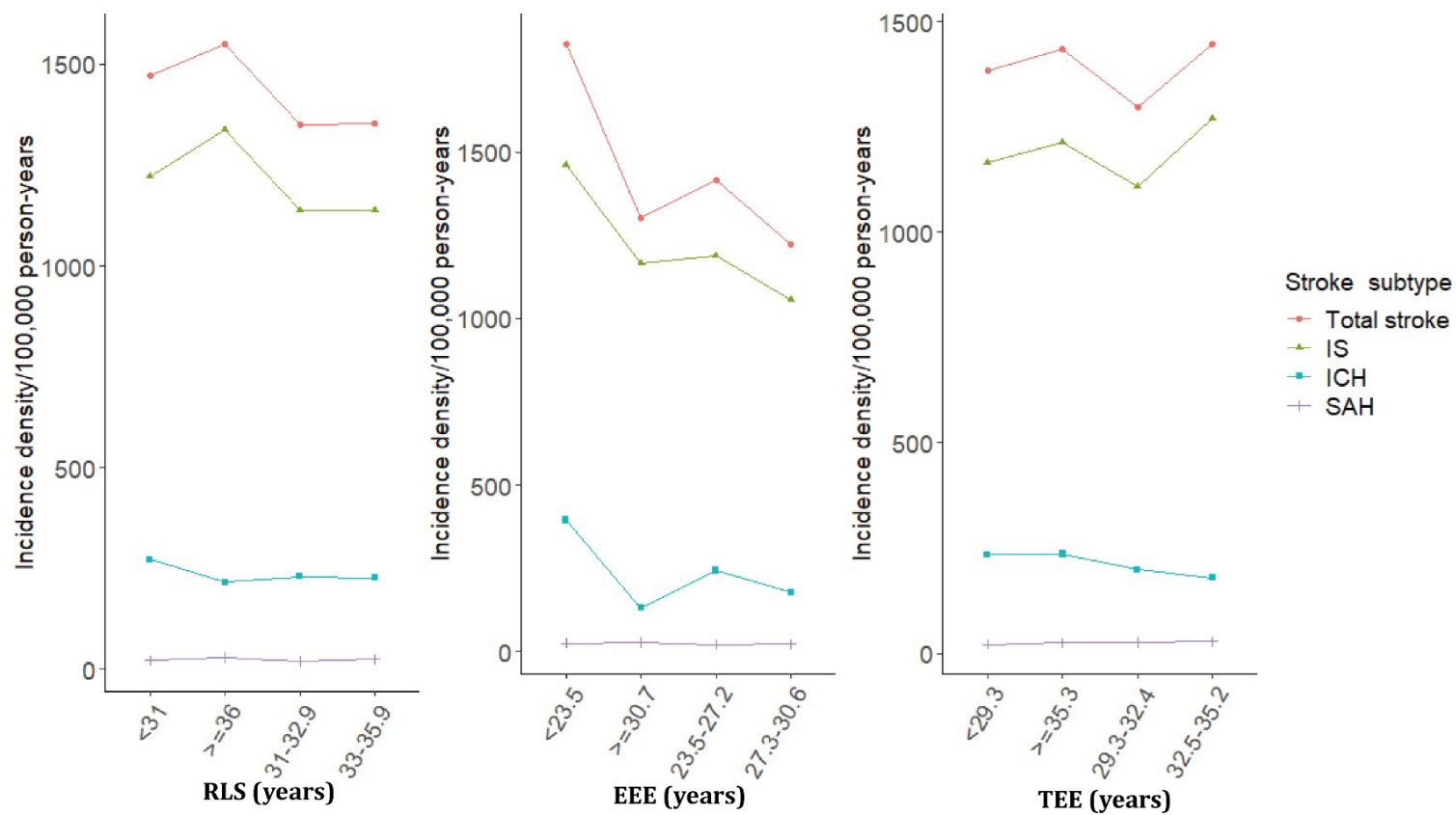
Notes: Values are presented as number (N) with percent (%) or medians (M) with interquartile ranges (IQRs). *P* values represent statistical measurement of comparing different quartiles. BMI, body mass index; WC, waist circumference; MET, metabolic equivalents of task; OCP, oral contraceptive pill; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.



**eTable 5. Incidence rate of stroke and its subtypes among postmenopausal participants**

		Total stroke			IS			ICH			SAH		
		Cases	Person-years	Incidence rate	Cases	Person-years	Incidence rate	Cases	Person-years	Incidence rate	Cases	Person-years	Incidence rate
<b>RLS</b>	Q1 (<31.0 years)	3,644	247,834.8	1,470.3	3,037	24,8782.0	1,220.7	701	257,665.7	272.1	56	258,500.4	21.7
	Q2 (31.0-32.9 years)	2,495	184,663.8	1,351.1	2,108	185,404.0	1,137.0	441	191,816.8	229.9	39	192,458.0	20.3
	Q3 (33.0-35.9 years)	4,442	328,310.9	1,353.0	3,751	329,584.0	1,138.1	772	341,249.4	226.2	85	342,327.9	24.8
	Q4 (≥36.0 years)	4,558	294,247.5	1,549.0	3,957	295,531.5	1,338.9	666	308,249.9	216.1	89	309,314.6	28.8
<b>EEE</b>	Q1 (<23.5 years)	4,625	253,381.2	1,825.3	3,718	254,547.9	1,460.6	1,046	265,006.2	394.7	68	266,065.0	25.6
	Q2 (23.5-27.2 years)	3,651	258,034.5	1,414.9	3,085	259,193.7	1,190.2	654	268,567.3	243.5	59	269,678.1	21.9
	Q3 (27.3-30.6 years)	3,403	278,165.3	1,223.4	2,948	279,202.1	1,055.9	515	288,627.6	178.4	65	289,468.7	22.5
	Q4 (≥30.7 years)	3,460	265,475.9	1,303.3	3,102	266,357.8	1,164.6	365	276,780.7	131.9	77	277,389.1	27.8
<b>TEE</b>	Q1 (<29.3 years)	4,089	253,815.0	1,611.0	3,337	254,838.0	1,309.5	879	264,267.1	332.6	62	265,215.9	23.4
	Q2 (29.3-32.4 years)	3,774	272,691.6	1,384.0	3,189	273,863.2	1,164.5	663	283,394.1	233.9	59	284,468.1	20.7
	Q3 (32.5-35.2 years)	3,281	252,654.1	1,298.6	2,811	253,626.5	1,108.3	521	262,558.5	198.4	67	263,295.2	25.4
	Q4 (≥35.3 years)	3,995	275,896.2	1,448.0	3,516	276,973.8	1,269.4	517	288,762.2	179.0	81	289,621.7	28.0
Total		15,139	1,055,056.9	1,434.9	12,853	1,059,301.5	1,213.3	2,580	1,098,981.9	234.8	269	1,102,600.9	24.4

Note: Incidence rate was expressed in 100,000 person-years, RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.



**eFigure S1. Incidence rate of stroke and its subtypes**

Notes: RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

**eTable 6. Association between indicators of lifetime cumulative exposure due to reproductive factors and risk of incident stroke: multivariable Cox regression**

		Total stroke (HR 95%CI)		IS (HR 95%CI)		ICH (HR 95%CI)		SAH (HR 95%CI)	
		Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
RLS	Q1 (<31.0 years)	1.00 (0.97~1.03)	1.00 (0.97~1.03)	1.00 (0.96~1.04)	1.00 (0.96~1.04)	1.00 (0.93~1.08)	1.00 (0.93~1.08)	1.00 (0.77~1.30)	1.00 (0.77~1.31)
	Q2 (31.0-32.9 years)	0.98 (0.94~1.01)	0.96 (0.92~1.00)*	0.99 (0.94~1.03)	0.96 (0.92~1.00)	0.91 (0.82~0.99)	0.93 (0.85~1.03)	0.94 (0.69~1.29)	0.94 (0.69~1.29)
	Q3 (33.0-35.9 years)	0.98 (0.95~1.01)	0.94 (0.91~0.96)	0.99 (0.96~1.02)	0.93 (0.90~0.96)	0.90 (0.84~0.97)	0.96 (0.89~1.03)	1.16 (0.94~1.43)	1.15 (0.93~1.42)
	Q4 (≥36.0 years)	1.06 (1.03~1.09)	0.95 (0.92~0.98)	1.10 (1.06~1.13)	0.95 (0.92~0.98)	0.81 (0.75~0.87)	0.87 (0.81~0.94)	1.30 (1.06~1.61)	1.27 (1.03~1.58)
	10-year increase	1.00 (1.00~1.01)*	1.00 (1.00~1.00)	1.01 (1.01~1.02)*	1.00 (1.00~1.00)	0.98 (0.97~0.99)	0.99 (0.98~1.00)	1.01 (0.98~1.05)	1.01 (0.98~1.04)
	<i>P</i> for trend	0.010	0.020	<0.001	0.030	<0.001	0.020	0.080	0.110
EEE	Q1 (<23.5 years)	1.00 (0.97~1.03)	1.00 (0.97~1.03)	1.00 (0.97~1.03)	1.00 (0.96~1.04)	1.00 (0.94~1.07)	1.00 (0.93~1.07)	1.00 (0.78~1.29)	1.00 (0.77~1.3)
	Q2 (23.5-27.2 years)	0.95 (0.92~0.98)	0.91 (0.88~0.94)	1.00 (0.96~1.03)	0.92 (0.89~0.95)	0.75 (0.70~0.81)	0.90 (0.84~0.97)	0.94 (0.73~1.22)	0.97 (0.75~1.24)
	Q3 (27.3-30.6 years)	0.93 (0.90~0.96)	0.86 (0.83~0.89)	1.00 (0.96~1.03)	0.87 (0.84~0.90)	0.62 (0.57~0.67)	0.82 (0.75~0.89)	1.02 (0.80~1.30)	1.06 (0.83~1.35)
	Q4 (≥30.7 years)	1.03 (0.99~1.06)	0.85 (0.82~0.89)	1.14 (1.10~1.19)	0.86 (0.83~0.90)	0.47 (0.43~0.53)	0.73 (0.65~0.81)	1.28 (1.02~1.61)	1.34 (1.04~1.71)
	10-year increase	1.00 (1.00~1.00)	0.99 (0.99~0.99)*	1.01 (1.01~1.01)*	0.99 (0.99~0.99)*	0.95 (0.94~0.96)	0.98 (0.97~0.99)	1.01 (0.99~1.04)	1.01 (0.99~1.04)
	<i>P</i> for trend	0.840	<0.001	<0.001	<0.001	<0.001	<0.001	0.160	0.130
TEE	Q1 (<29.3 years)	1.00 (0.97~1.03)	1.00 (0.97~1.03)	1.00 (0.97~1.04)	1.00 (0.96~1.04)	1.00 (0.93~1.07)	1.00 (0.93~1.07)	1.00 (0.78~1.29)	1.00 (0.77~1.3)
	Q2 (29.3-32.4 years)	0.96 (0.93~0.99)	0.92 (0.89~0.95)	0.99 (0.95~1.02)	0.92 (0.89~0.95)	0.79 (0.74~0.86)	0.92 (0.86~1.00)*	0.92 (0.71~1.18)	0.93 (0.72~1.20)
	Q3 (32.5-35.2 years)	0.93 (0.90~0.97)	0.87 (0.84~0.90)	0.98 (0.94~1.01)	0.86 (0.83~0.89)	0.71 (0.65~0.77)	0.88 (0.81~0.96)	1.14 (0.90~1.45)	1.16 (0.91~1.47)
	Q4 (≥35.3 years)	1.00 (0.97~1.03)	0.87 (0.84~0.90)	1.07 (1.04~1.11)	0.86 (0.83~0.89)	0.61 (0.56~0.67)	0.83 (0.76~0.91)	1.23 (0.99~1.53)	1.25 (0.99~1.57)
	10-year increase	1.00 (1.00~1.00)	0.99 (0.99~0.99)*	1.01 (1.00~1.01)*	0.99 (0.99~0.99)*	0.96 (0.95~0.97)	0.99 (0.98~0.99)*	1.02 (0.99~1.04)	1.02 (0.99~1.05)
	<i>P</i> for trend	0.820	<0.001	0.008	<0.001	<0.001	0.001	0.140	0.140

Notes: \* $P < 0.05$ ; HR and 95% CI in blue indicate a significant protective effect, whereas HR and 95% CI in red indicate a significant hazard effect. HR, hazard ratio; CI, confidence interval; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage. Model 1 was adjusted for age at baseline. Model 2 was adjusted for age at baseline, marital status, residential status, education, occupation, household income, body mass index, waist circumference, tobacco smoking, second hand smoking, alcohol consumption, physical activity in metabolic equivalent-hours/day, anticoagulation therapy, hypolipidemic therapy, diabetes, hypertension. *P* for trend was test based on variable containing median value for each quintile.

**eTable 7. Association between each reproductive factor and risk of incident stroke: multivariable Cox regression**

		Total stroke		IS		ICH		SAH	
		N (%)	HR (95%CI)	N (%)	HR (95%CI)	N (%)	HR (95%CI)	N (%)	HR (95%CI)
Age of menarche	Q1 (9.0-13.9 years)	1911 (12.6)	Reference	1669 (13.0)	Reference	283 (11.0)	Reference	39 (14.5)	Reference
	Q2 (14-15.9 years)	5107 (33.7)	1.03 (0.98~1.09)	4340 (33.8)	1.02 (0.97~1.08)	871 (33.8)	1.05 (0.92~1.2)	73 (27.1)	0.72 (0.49~1.06)
	Q3 (16-16.9 years)	3275 (21.6)	0.99 (0.94~1.05)	2757 (21.5)	0.98 (0.92~1.04)	569 (22.1)	1.00 (0.86~1.15)	57 (21.2)	0.83 (0.55~1.26)
	Q4 (17-18 years)	4846 (32.0)	0.97 (0.92~1.02)	4087 (31.8)	0.96 (0.91~1.02)	857 (33.2)	0.97 (0.85~1.12)	100 (37.2)	0.95 (0.65~1.39)
	1-year increase	15139 (100)	<b>0.99 (0.98~1.00)*</b>	12853 (100)	<b>0.99 (0.98~1.00)*</b>	2580 (100)	0.99 (0.97~1.02)	269 (100)	1.02 (0.95~1.10)
Age of menopause	Q1 (40-46.9 years)	3584 (23.7)	Reference	2996 (23.3)	Reference	671 (26.0)	Reference	49 (18.2)	Reference
	Q2 (47-48.9 years)	2989 (19.7)	0.97 (0.92~1.02)	2507 (19.5)	0.96 (0.91~1.01)	550 (21.3)	1.01 (0.90~1.13)	52 (19.3)	1.18 (0.80~1.74)
	Q3 (49-50.9 years)	3773 (24.9)	<b>0.93 (0.89~0.98)</b>	3215 (25.0)	<b>0.93 (0.89~0.98)</b>	652 (25.3)	0.96 (0.86~1.07)	79 (29.4)	1.41 (0.98~2.02)
	Q4 (>=51 years)	4793 (31.7)	<b>0.93 (0.89~0.97)</b>	4135 (32.2)	<b>0.93 (0.89~0.98)</b>	707 (27.4)	<b>0.85 (0.76~0.95)</b>	89 (33.1)	1.32 (0.92~1.88)
	1-year increase	15139 (100)	<b>1.00 (0.99~1.00)*</b>	12853 (100)	<b>1.00 (0.99~1.00)*</b>	2580 (100)	<b>1.00 (0.98~1.00)*</b>	269 (100)	1.02 (0.99~1.06)
Number of pregnancies	1	466 (3.1)	Reference	414 (3.2)	Reference	60 (2.3)	Reference	9 (3.4)	Reference
	2	1735 (11.5)	0.96 (0.86~1.06)	1527 (11.9)	0.97 (0.87~1.08)	216 (8.4)	0.79 (0.59~1.05)	40 (14.9)	1.12 (0.54~2.32)
	3	3174 (21.0)	1.03 (0.94~1.14)	2748 (21.4)	1.04 (0.94~1.15)	469 (18.2)	0.91 (0.70~1.20)	60 (22.3)	1.05 (0.52~2.14)
	4	3372 (22.3)	1.09 (0.98~1.20)	2901 (22.6)	1.10 (0.99~1.22)	523 (20.3)	0.95 (0.72~1.25)	52 (19.3)	0.96 (0.47~1.99)
	5 or above	6392 (42.2)	<b>1.17 (1.06~1.29)</b>	5263 (41.0)	<b>1.16 (1.04~1.29)</b>	1312 (50.9)	1.16 (0.89~1.51)	108 (40.2)	1.27 (0.63~2.59)
	Each number	15139 (100)	<b>1.04 (1.03~1.05)</b>	12853 (100)	<b>1.03 (1.02~1.04)</b>	2580 (100)	<b>1.08 (1.06~1.11)</b>	269 (100)	1.05 (0.97~1.12)
Number of live births	0	53 (0.4)	Reference	47 (0.4)	Reference	9 (0.4)	Reference	2 (0.7)	Reference
	1	1577 (10.4)	<b>0.65 (0.50~0.86)</b>	1410 (11.0)	<b>0.61 (0.45~0.81)</b>	169 (6.6)	0.70 (0.36~1.38)	37 (13.8)	0.42 (0.10~1.8)
	2	3722 (24.6)	<b>0.72 (0.55~0.95)</b>	3278 (25.5)	<b>0.68 (0.51~0.91)</b>	460 (17.8)	0.65 (0.34~1.27)	77 (28.6)	0.41 (0.10~1.67)
	3	4110 (27.2)	0.80 (0.61~1.05)	3571 (27.8)	0.77 (0.58~1.03)	637 (24.7)	0.76 (0.39~1.46)	70 (26.0)	0.38 (0.09~1.54)
	4 or above	5677 (37.5)	0.85 (0.65~1.11)	4547 (35.4)	0.79 (0.59~1.05)	1305 (50.6)	0.92 (0.48~1.78)	83 (30.9)	0.36 (0.09~1.48)
Number of stillbirths	Each number	15139 (100)	<b>1.06 (1.04~1.07)</b>	12853 (100)	<b>1.04 (1.02~1.05)</b>	2580 (100)	<b>1.12 (1.09~1.15)</b>	269 (100)	0.97 (0.87~1.09)
	0	13578 (89.7)	Reference	11602 (90.3)	Reference	2211 (85.7)	Reference	234 (87.0)	Reference
	1 or more	1561 (10.3)	<b>1.08 (1.02~1.14)</b>	1251 (9.7)	<b>1.07 (1.01~1.13)</b>	369 (14.3)	<b>1.17 (1.05~1.31)</b>	35 (13.0)	<b>1.47 (1.02~2.13)</b>
Number of miscarriages or terminations	Each number	15139 (100)	<b>1.03 (1.00~1.07)*</b>	12853 (100)	1.01 (0.98~1.05)	2580 (100)	<b>1.11 (1.05~1.17)</b>	269 (100)	1.11 (0.89~1.39)
	0	6628 (43.8)	Reference	5417 (42.2)	Reference	1355 (52.5)	Reference	107 (39.8)	Reference
	1	4434 (29.3)	1.01 (0.97~1.05)	3854 (30.0)	1.03 (0.98~1.07)	693 (26.9)	1.01 (0.92~1.11)	82 (30.5)	1.19 (0.89~1.59)
	2 or more	4077 (26.9)	<b>1.04 (1.00~1.08)*</b>	3582 (27.9)	<b>1.04 (1.00~1.09)*</b>	532 (20.6)	1.01 (0.91~1.12)	80 (29.7)	1.33 (0.98~1.80)
Lactation	Each number	15139 (100)	<b>1.02 (1.00~1.03)*</b>	12853 (100)	<b>1.02 (1.00~1.03)*</b>	2580 (100)	1.02 (0.98~1.05)	269 (100)	1.10 (0.99~1.21)
	No lactation	463 (3.1)	Reference	424 (3.3)	Reference	50 (1.9)	Reference	9 (3.4)	Reference
	History of lactation	14676 (96.9)	<b>0.75 (0.68~0.83)</b>	12429 (96.7)	<b>0.73 (0.66~0.81)</b>	2530 (98.1)	0.82 (0.62~1.08)	260 (96.7)	0.66 (0.34~1.30)

		Total stroke		IS		ICH		SAH	
		N (%)	HR (95%CI)	N (%)	HR (95%CI)	N (%)	HR (95%CI)	N (%)	HR (95%CI)
OCP	Lifetime lactation duration (years)	15139 (100)	1.07 (1.01~1.13)	12853 (100)	1.07 (1.00~1.14)*	2580 (100)	1.07 (0.92~1.23)	269 (100)	1.00 (0.99~1.00)
	No OCP use	13983 (92.4)	Reference	11842 (92.1)	Reference	2441 (94.6)	Reference	240 (89.2)	Reference
	History of OCP use	1156 (7.6)	0.77 (0.73~0.82)	1011 (7.9)	0.77 (0.72~0.82)	139 (5.4)	0.73 (0.62~0.87)	29 (10.8)	1.12 (0.76~1.66)
	OCP use duration (years)	15139 (100)	0.94 (0.92~0.96)	12853 (100)	0.94 (0.92~0.96)	2580 (100)	0.88 (0.82~0.94)	269 (100)	1.01 (0.89~1.16)

Note: \* $P < 0.05$ ; HR and 95% CI in blue indicate a significant protective effect, whereas HR and 95% CI in red indicate a significant hazard effect. HR, hazard ratio; CI, confidence interval; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; OCP, oral contraceptive pill. HR was adjusted for age at baseline, marital status, residential status, education level, occupation, household income, body mass index, waist circumference, tobacco smoking, second hand smoking, alcohol consumption, physical activity in metabolic equivalent-hours/day, anticoagulation therapy, hypolipidemic therapy, diabetes, hypertension.

eTable 8. Sensitivity analysis

		Total stroke	IS	ICH	SAH
		HR (95%CI)			
<b>Excluding participants diagnosed stroke within the first 2 years of follow-up<sup>#</sup> (N=120,094)</b>					
RLS	Q1 (<31.0 years)	1.00 (0.97~1.04)	1.00 (0.96~1.04)	1.00 (0.92~1.09)	1.00 (0.75~1.33)
	Q2 (31.0-32.9 years)	0.96 (0.92~1.00)	0.96 (0.92~1.01)	0.94 (0.85~1.04)	1.01 (0.73~1.40)
	Q3 (33.0-35.9 years)	0.92 (0.90~0.95)	0.92 (0.89~0.95)	0.95 (0.88~1.02)	1.08 (0.85~1.36)
	Q4 (≥36.0 years)	0.93 (0.90~0.96)	0.93 (0.90~0.97)	0.84 (0.77~0.92)	1.14 (0.90~1.46)
EEE	Q1 (<23.5 years)	1.00 (0.97~1.04)	1.00 (0.96~1.04)	1.00 (0.93~1.08)	1.00 (0.75~1.33)
	Q2 (23.5-27.2 years)	0.9 (0.87~0.94)	0.91 (0.88~0.95)	0.91 (0.84~0.99)	0.93 (0.70~1.23)
	Q3 (27.3-30.6 years)	0.83 (0.80~0.86)	0.84 (0.81~0.88)	0.80 (0.73~0.88)	1.01 (0.78~1.32)
	Q4 (≥30.7 years)	0.83 (0.80~0.87)	0.84 (0.81~0.88)	0.71 (0.63~0.80)	1.21 (0.91~1.59)
TEE	Q1 (<29.3 years)	1.00 (0.97~1.04)	1.00 (0.96~1.04)	1.00 (0.93~1.08)	1.00 (0.75~1.33)
	Q2 (29.3-32.4 years)	0.91 (0.88~0.94)	0.91 (0.87~0.94)	0.92 (0.84~1.00)*	0.96 (0.73~1.26)
	Q3 (32.5-35.2 years)	0.85 (0.82~0.88)	0.84 (0.81~0.87)	0.88 (0.80~0.96)	1.15 (0.89~1.49)
	Q4 (≥35.3 years)	0.84 (0.81~0.87)	0.84 (0.81~0.87)	0.80 (0.73~0.89)	1.15 (0.88~1.49)
<b>Excluding participants with more than one subtype of stroke during follow-up<sup>#</sup> (N=122,157)</b>					
RLS	Q1 (<31.0 years)	1.00 (0.97~1.03)	1.00 (0.96~1.04)	1.00 (0.91~1.09)	1.00 (0.69~1.45)
	Q2 (31.0-32.9 years)	0.96 (0.92~1.00)	0.97 (0.92~1.01)	0.94 (0.84~1.05)	1.05 (0.70~1.58)
	Q3 (33.0-35.9 years)	0.94 (0.91~0.97)	0.93 (0.90~0.96)	0.97 (0.89~1.05)	1.25 (0.95~1.65)
	Q4 (≥36.0 years)	0.95 (0.92~0.98)	0.96 (0.93~0.99)	0.87 (0.79~0.95)	1.36 (1.02~1.82)
EEE	Q1 (<23.5 years)	1.00 (0.97~1.03)	1.00 (0.96~1.04)	1.00 (0.92~1.08)	1.00 (0.69~1.45)
	Q2 (23.5-27.2 years)	0.91 (0.88~0.94)	0.92 (0.89~0.95)	0.87 (0.80~0.95)	0.94 (0.66~1.33)
	Q3 (27.3-30.6 years)	0.86 (0.83~0.89)	0.87 (0.84~0.90)	0.80 (0.72~0.88)	1.04 (0.75~1.44)
	Q4 (≥30.7 years)	0.86 (0.83~0.89)	0.87 (0.84~0.91)	0.74 (0.65~0.85)	1.46 (1.06~2.00)
TEE	Q1 (<29.3 years)	1.00 (0.97~1.03)	1.00 (0.96~1.04)	1.00 (0.92~1.09)	1.00 (0.69~1.44)
	Q2 (29.3-32.4 years)	0.92 (0.89~0.95)	0.92 (0.89~0.95)	0.92 (0.84~1.00)	0.93 (0.66~1.32)
	Q3 (32.5-35.2 years)	0.86 (0.83~0.89)	0.86 (0.82~0.89)	0.88 (0.79~0.97)	1.13 (0.81~1.56)
	Q4 (≥35.3 years)	0.87 (0.84~0.90)	0.87 (0.84~0.90)	0.85 (0.76~0.95)	1.41 (1.05~1.89)
<b>Excluding participants taking related drugs<sup>##</sup> (N=113,474)</b>					
RLS	Q1 (<31.0 years)	1.00 (0.97~1.04)	1.00 (0.96~1.04)	1.00 (0.92~1.08)	1.00 (0.76~1.32)
	Q2 (31.0-32.9 years)	0.97 (0.93~1.01)	0.97 (0.93~1.02)	0.96 (0.87~1.06)	0.96 (0.69~1.33)
	Q3 (33.0-35.9 years)	0.94 (0.91~0.97)	0.93 (0.90~0.97)	0.96 (0.89~1.04)	1.05 (0.83~1.33)
	Q4 (≥36.0 years)	0.96 (0.93~0.99)	0.96 (0.93~0.99)	0.92 (0.84~1.00)*	1.22 (0.96~1.55)
EEE	Q1 (<23.5 years)	1.00 (0.97~1.04)	1.00 (0.96~1.04)	1.00 (0.93~1.08)	1.00 (0.76~1.32)

		Total stroke	IS	ICH	SAH
		HR (95%CI)			
TEE	Q2 (23.5-27.2 years)	0.91 (0.88~0.95)	0.92 (0.89~0.96)	0.89 (0.82~0.96)	0.93 (0.71~1.22)
	Q3 (27.3-30.5 years)	0.86 (0.83~0.89)	0.87 (0.84~0.90)	0.83 (0.75~0.91)	0.96 (0.73~1.25)
	Q4 (≥30.6 years)	0.86 (0.83~0.90)	0.87 (0.84~0.91)	0.75 (0.67~0.85)	1.23 (0.94~1.62)
	Q1 (<29.3 years)	1.00 (0.97~1.04)	1.00 (0.96~1.04)	1.00 (0.93~1.08)	1.00 (0.76~1.32)
	Q2 (29.3-32.2 years)	0.92 (0.88~0.95)	0.91 (0.87~0.94)	0.94 (0.86~1.02)	0.92 (0.70~1.22)
	Q3 (32.3-35.2 years)	0.87 (0.84~0.91)	0.87 (0.83~0.90)	0.88 (0.81~0.97)	1.12 (0.88~1.44)
	Q4 (≥35.3 years)	0.87 (0.84~0.90)	0.86 (0.83~0.89)	0.87 (0.79~0.96)	1.20 (0.93~1.55)
	Excluding participants with related diseases <sup>##</sup> (N=113,752)				
RLS	Q1 (<31.0 years)	1.00 (0.97~1.04)	1.00 (0.96~1.04)	1.00 (0.92~1.08)	1.00 (0.76~1.31)
	Q2 (31.0-32.9 years)	0.96 (0.92~1.00)*	0.95 (0.91~1.00)*	0.95 (0.87~1.05)	0.95 (0.69~1.32)
	Q3 (33.0-35.9 years)	0.95 (0.92~0.98)	0.94 (0.91~0.97)	0.98 (0.91~1.06)	1.13 (0.91~1.41)
	Q4 (≥36.0 years)	0.97 (0.94~1.00)	0.97 (0.93~1.00)	0.90 (0.83~0.98)	1.25 (1.00~1.57)
EEE	Q1 (<23.5 years)	1.00 (0.97~1.04)	1.00 (0.96~1.04)	1.00 (0.93~1.08)	1.00 (0.76~1.31)
	Q2 (23.5-27.2 years)	0.91 (0.88~0.95)	0.92 (0.89~0.95)	0.91 (0.84~0.98)	0.84 (0.64~1.10)
	Q3 (27.3-30.5 years)	0.86 (0.83~0.89)	0.87 (0.83~0.90)	0.84 (0.76~0.92)	1.02 (0.79~1.31)
	Q4 (≥30.6 years)	0.85 (0.82~0.89)	0.85 (0.82~0.89)	0.75 (0.66~0.84)	1.27 (0.98~1.65)
TEE	Q1 (<29.3 years)	1.00 (0.97~1.04)	1.00 (0.96~1.04)	1.00 (0.93~1.08)	1.00 (0.76~1.31)
	Q2 (29.3-32.3 years)	0.93 (0.89~0.96)	0.92 (0.88~0.95)	0.93 (0.86~1.01)	0.97 (0.74~1.26)
	Q3 (32.4-35.2 years)	0.88 (0.85~0.91)	0.87 (0.83~0.90)	0.90 (0.82~0.99)	1.13 (0.88~1.46)
	Q4 (≥35.3 years)	0.88 (0.85~0.92)	0.87 (0.84~0.91)	0.85 (0.77~0.93)	1.36 (1.07~1.72)

Notes: \* $P < 0.05$ ; HR and 95% CI in blue indicate a significant protective effect, whereas HR and 95% CI in red indicate a significant hazard effect. HR, hazard ratio; CI, confidence interval; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

<sup>#</sup>HR was adjusted for age at baseline, marital status, residential status, education, occupation, household income, body mass index, waist circumference, tobacco smoking, second hand smoking, alcohol consumption, physical activity in metabolic equivalent-hours/day, anticoagulation therapy, hypolipidemic therapy, diabetes, hypertension. <sup>##</sup>HR was adjusted for age at baseline, marital status, residential status, education level, occupation, household income, body mass index, waist circumference, tobacco smoking, second hand smoking, alcohol consumption, physical activity in metabolic equivalent-hours/day.

Related drugs included angiotensin converting enzyme inhibitors (ACEI), aspirin, beta-blocker, calcium antagonist, diuretics, statins. Related diseases included cancer, chronic heart disease, psychic disorders, rheumatic heart disease, kidney disease.

**eTable 9. Association between indicators of lifetime cumulative exposure due to reproductive factors and risk of incident stroke: age-stratified multivariable Cox regression**

		Total stroke	IS	ICH	SAH
		HR (95%CI) <sup>#</sup>			
<b>RLS</b>					
40≤age<50 (n=7,216)	Q1 (<29.0 years)	1.00 (0.78~1.28)	1.00 (0.76~1.31)	1.00 (0.49~2.04)	1.00 (1.00~1.00)
	Q2 (29.0-30.9 years)	1.26 (1.04~1.51)	1.21 (0.99~1.48)	1.79 (1.12~2.87)	1.55 (0.32~7.41)
	Q3 (31.0-32.9 years)	1.04 (0.86~1.26)	0.91 (0.73~1.12)	2.13 (1.39~3.26)	2.58 (0.72~9.23)
	Q4 (≥33.0 years)	1.03 (0.84~1.25)	0.96 (0.77~1.19)	1.27 (0.71~2.26)	2.03 (0.52~7.95)
50≤age<60 (n=63,673)	Q1 (<31.0 years)	1.00 (0.94~1.06)	1.00 (0.93~1.07)	1.00 (0.86~1.16)	1.00 (0.66~1.51)
	Q2 (31.0-33.9 years)	0.99 (0.94~1.04)	0.98 (0.92~1.03)	1.10 (0.97~1.24)	0.98 (0.69~1.38)
	Q3 (34.0-35.9 years)	<b>0.94 (0.89~0.99)</b>	<b>0.93 (0.87~0.99)</b>	1.00 (0.87~1.16)	0.91 (0.62~1.35)
	Q4 (≥36.0 years)	0.96 (0.91~1.01)	0.95 (0.91~1.01)	0.93 (0.82~1.06)	1.03 (0.74~1.43)
60≤age<70 (n=39,007)	Q1 (<30.0 years)	1.00 (0.94~1.07)	1.00 (0.93~1.07)	1.00 (0.87~1.15)	1.00 (0.58~1.73)
	Q2 (30.0-32.9 years)	0.97 (0.92~1.02)	0.99 (0.94~1.04)	<b>0.88 (0.78~0.99)</b>	0.72 (0.44~1.18)
	Q3 (33.0-35.9 years)	<b>0.94 (0.90~0.98)</b>	<b>0.94 (0.89~0.99)</b>	0.90 (0.81~1.01)	1.47 (1.06~2.03)
	Q4 (≥36.0 years)	<b>0.95 (0.91~0.99)</b>	0.96 (0.92~1.01)	<b>0.84 (0.75~0.94)</b>	1.60 (1.18~2.18)
age≥70 (n=13,043)	Q1 (<30.0 years)	1.00 (0.92~1.09)	1.00 (0.91~1.10)	1.00 (0.84~1.20)	1.00 (0.45~2.24)
	Q2 (30.0-32.9 years)	0.99 (0.92~1.06)	0.99 (0.92~1.07)	0.91 (0.77~1.06)	1.04 (0.56~1.94)
	Q3 (33.0-35.9 years)	0.99 (0.92~1.05)	0.98 (0.91~1.06)	0.97 (0.84~1.14)	0.93 (0.48~1.79)
	Q4 (≥36.0 years)	1.00 (0.93~1.08)	1.02 (0.94~1.10)	0.87 (0.73~1.03)	0.95 (0.49~1.83)
<b>EEE</b>					
40≤age<50 (n=7,216)	Q1 (<23.9 years)	1.00 (0.81~1.24)	1.00 (0.79~1.27)	1.00 (0.60~1.66)	1.00 (1.00~1.00)
	Q2 (23.9-26.7 years)	0.95 (0.78~1.15)	0.96 (0.78~1.19)	0.95 (0.57~1.57)	1.00 (1.00~1.00)
	Q3 (26.8-29.2 years)	0.87 (0.72~1.05)	<b>0.80 (0.65~0.98)</b>	1.14 (0.71~1.84)	1.53 (0.42~5.62)
	Q4 (≥29.3 years)	<b>0.67 (0.54~0.85)</b>	<b>0.62 (0.49~0.79)</b>	0.69 (0.35~1.37)	2.04 (0.56~7.50)
50≤age<60 (n=63,673)	Q1 (<25.5 years)	1.00 (0.95~1.06)	1.00 (0.94~1.06)	1.00 (0.89~1.12)	1.00 (0.70~1.43)
	Q2 (25.5-28.7 years)	<b>0.86 (0.81~0.91)</b>	<b>0.84 (0.79~0.89)</b>	0.96 (0.85~1.09)	0.83 (0.58~1.19)
	Q3 (28.8-31.5 years)	<b>0.79 (0.75~0.83)</b>	<b>0.80 (0.76~0.85)</b>	<b>0.65 (0.56~0.77)</b>	0.74 (0.51~1.09)
	Q4 (≥31.6 years)	<b>0.79 (0.74~0.84)</b>	<b>0.80 (0.75~0.85)</b>	<b>0.74 (0.62~0.88)</b>	0.79 (0.53~1.18)
60≤age<70 (n=39,007)	Q1 (<22.1 years)	1.00 (0.95~1.05)	1.00 (0.94~1.06)	1.00 (0.90~1.12)	1.00 (0.64~1.57)
	Q2 (22.1-25.9 years)	<b>0.91 (0.86~0.95)</b>	<b>0.90 (0.85~0.95)</b>	0.96 (0.86~1.08)	1.13 (0.75~1.71)
	Q3 (26-29.4 years)	<b>0.87 (0.83~0.92)</b>	<b>0.89 (0.84~0.94)</b>	<b>0.77 (0.67~0.89)</b>	1.25 (0.84~1.85)
	Q4 (≥29.5 years)	<b>0.89 (0.84~0.93)</b>	<b>0.88 (0.83~0.93)</b>	0.87 (0.76~1.01)	1.97 (1.40~2.77)



		Total stroke	IS	ICH	SAH
		HR (95%CI) <sup>#</sup>			
age $\geq$ 70 (n=13,043)	Q1 (<19.4 years)	1.00 (0.93~1.08)	1.00 (0.92~1.09)	1.00 (0.86~1.16)	1.00 (0.51~1.94)
	Q2 (19.4-23.5 years)	0.90 (0.83~0.96)	0.94 (0.86~1.01)	0.79 (0.67~0.93)	0.47 (0.21~1.03)
	Q3 (23.6-27.4 years)	0.88 (0.82~0.95)	0.93 (0.86~1.01)	0.73 (0.61~0.88)	0.53 (0.25~1.10)
	Q4 ( $\geq$ 27.5 years)	0.86 (0.80~0.93)	0.90 (0.83~0.97)	0.73 (0.60~0.90)	0.64 (0.32~1.29)
<b>TEE</b>					
40 $\leq$ age<50 (n=7,216)	Q1 (<28.0 years)	1.00 (0.81~1.24)	1.00 (0.79~1.26)	1.00 (0.58~1.71)	1.00 (1.00~1.00)
	Q2 (28.0-30.3 years)	0.98 (0.81~1.19)	0.94 (0.76~1.16)	1.30 (0.83~2.04)	0.38 (0.05~3.01)
	Q3 (30.4-32.5 years)	0.88 (0.73~1.07)	0.82 (0.66~1.01)	1.27 (0.79~2.05)	1.94 (0.55~6.86)
	Q4 ( $\geq$ 32.6 years)	0.71 (0.57~0.89)	0.70 (0.55~0.88)	0.69 (0.35~1.39)	0.86 (0.18~4.12)
50 $\leq$ age<60 (n=63,673)	Q1 (<30.2 years)	1.00 (0.95~1.06)	1.00 (0.94~1.06)	1.00 (0.89~1.13)	1.00 (0.69~1.44)
	Q2 (30.2-33.0 years)	0.88 (0.83~0.93)	0.86 (0.81~0.91)	0.96 (0.85~1.09)	0.85 (0.59~1.24)
	Q3 (33.1-35.7 years)	0.84 (0.80~0.89)	0.84 (0.79~0.89)	0.77 (0.66~0.89)	0.90 (0.62~1.31)
	Q4 ( $\geq$ 35.8 years)	0.78 (0.74~0.83)	0.78 (0.73~0.83)	0.77 (0.65~0.91)	0.95 (0.65~1.38)
60 $\leq$ age<70 (n=39,007)	Q1 (<28.8 years)	1.00 (0.95~1.05)	1.00 (0.94~1.06)	1.00 (0.89~1.12)	1.00 (0.63~1.58)
	Q2 (28.8-32.0 years)	0.93 (0.89~0.98)	0.94 (0.89~0.99)	0.91 (0.81~1.02)	0.87 (0.55~1.38)
	Q3 (32.1-35.2 years)	0.89 (0.85~0.94)	0.89 (0.84~0.94)	0.88 (0.78~1.01)	1.85 (1.34~2.56)
	Q4 ( $\geq$ 35.3 years)	0.91 (0.86~0.95)	0.91 (0.86~0.95)	0.86 (0.75~0.98)	1.55 (1.09~2.21)
age $\geq$ 70 (n=13,043)	Q1 (<27.8 years)	1.00 (0.93~1.08)	1.00 (0.92~1.09)	1.00 (0.86~1.16)	1.00 (0.49~2.06)
	Q2 (27.8-31.0 years)	0.93 (0.87~1.01)	0.93 (0.86~1.01)	0.88 (0.74~1.03)	1.16 (0.63~2.14)
	Q3 (31.1-34.4 years)	0.97 (0.90~1.04)	0.99 (0.92~1.07)	0.79 (0.66~0.95)	0.91 (0.45~1.82)
	Q4 ( $\geq$ 34.5 years)	0.91 (0.85~0.99)	0.91 (0.84~0.99)	0.88 (0.73~1.05)	0.83 (0.40~1.72)

Notes: \* $P$ <0.05; HR and 95% CI in blue indicate a significant protective effect, whereas HR and 95% CI in red indicate a significant hazard effect. HR, hazard ratio; CI, confidence interval; RLS, reproductive lifespan; EEE, endogenous estrogen exposure; TEE, total estrogen exposure; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage. <sup>#</sup>HR was adjusted for marital status, residential status, education, occupation, household income, body mass index, waist circumference, tobacco smoking, second-hand smoking, alcohol consumption, physical activity in metabolic equivalent-hours/day, anticoagulation therapy, hypolipidemic therapy, diabetes, hypertension.