

SUPPLEMENTAL MATERIAL

Table S1. Relative risk and 95% confidence intervals of ischemic and hemorrhagic stroke according to reproductive lifespan in the Nurses' Health Study

	Reproductive lifespan (years)					p-trend
	<30	30-33	34-37	38-41	≥42	
Ischemic stroke						
<i>Cases/person-years</i>	<i>124/144040</i>	<i>144/192701</i>	<i>388/455685</i>	<i>446/513373</i>	<i>135/164763</i>	
Age adjusted	1.33 (1.04-1.71)	1.05 (0.83-1.33)	1.11 (0.91-1.35)	1.06 (0.88-1.29)	1	0.04
Multivariate-adjusted*	1.21 (0.93-1.59)	1.01 (0.79-1.29)	1.09 (0.89-1.33)	1.08 (0.89-1.30)	1	0.32
Hemorrhagic stroke						
<i>Cases/person-years</i>	<i>28/144127</i>	<i>37/192808</i>	<i>61/456004</i>	<i>65/513740</i>	<i>22/164864</i>	
Age adjusted	1.56 (1.88-2.75)	1.43 (0.84-2.44)	0.96 (0.59-1.58)	0.92 (0.56-1.49)	1	0.01
Multivariate-adjusted*	1.37 (0.73-2.56)	1.27 (0.73-2.21)	0.88 (0.53-1.45)	0.88 (0.54-1.43)	1	0.09

* additionally adjusted for ethnicity (European descent, Asian, Hispanic, African American), hormone therapy use (never, current, past), oral contraceptive use (never, ever), parity (nulliparous, 1-2, ≥3), family history of stroke, smoking (never, past, current 1-14, 15-24, or ≥25 cigarettes/d), moderate to vigorous exercise (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, ≥6 h/wk), Alternate Healthy Eating Index score (<45, 45-<60, ≥60), Aspirin use (yes, no), alcohol intake (0, 0.1-4.9, 5.0-14.9, ≥15.0 g/d), BMI (<18.5, 18.5-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, ≥35.0 kg/m²), BMI at age 18 years (<18.5, 18.5-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, ≥35.0 kg/m²), menopause type (natural, surgical), a history of diabetes, hypertension, hypercholesterolemia

Table S2. Relative risk and 95% confidence intervals of total CVD according to reproductive lifespan in the Nurses' Health Study stratified by menopause type

	Reproductive lifespan (years)					p-trend
	<30	30-33	34-37	38-41	≥42	
Natural menopause						
<i>Cases/person-years</i>	<i>186/38977</i>	<i>473/118277</i>	<i>1388/375762</i>	<i>1697/466701</i>	<i>558/154726</i>	
Age adjusted	1.42 (1.20-1.68)	1.21 (1.07-1.37)	1.06 (0.96-1.17)	1.00 (0.91-1.10)	1	<0.0001
Multivariate-adjusted*	1.33 (1.13-1.58)	1.16 (1.02-1.31)	1.05 (0.95-1.16)	1.01 (0.92-1.11)	1	0.0001
Surgical menopause						
<i>Cases/person-years</i>	<i>383/104779</i>	<i>252/74047</i>	<i>272/79125</i>	<i>165/45833</i>	<i>30/9761</i>	
Age adjusted	1.61 (1.11-2.34)	1.31 (0.90-1.91)	1.22 (0.84-1.78)	1.21 (0.82-1.79)	1	<0.0001
Multivariate-adjusted*	1.38 (0.95-2.01)	1.18 (0.81-2.01)	1.15 (0.78-1.68)	1.16 (0.78-1.71)	1	0.001

* additionally adjusted for ethnicity (European descent, Asian, Hispanic, African American), hormone therapy use (never, current, past), oral contraceptive use (never, ever), parity (nulliparous, 1-2, ≥3), family history of MI, family history of stroke, [smoking (never, past, current 1-14, 15-24, or ≥25 cigarettes/d)], moderate to vigorous exercise (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, ≥6 h/wk), Alternate Healthy Eating Index score (<45, 45-<60, ≥60), Aspirin use (yes, no), alcohol intake (0, 0.1-4.9, 5.0-14.9, ≥15.0 g/d), BMI (<18.5, 18.5-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, ≥35.0 kg/m²), BMI at age 18 years (<18.5, 18.5-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, ≥35.0 kg/m²), [menopause type (natural, surgical)], a history of diabetes, hypertension, hypercholesterolemia
p for interaction is >0.05 between menopause type and reproductive lifespan or between smoking and reproductive lifespan.

Table S3. Sensitivity analysis of relative risk and 95% confidence intervals of total CVD according to reproductive lifespan in the Nurses' Health Study participants who were in postmenopausal status in 1980

	Reproductive lifespan (years)					p-trend
	<30	30-33	34-37	38-41	≥42	
<i>Cases/person-years</i>	<i>598/13188</i>	<i>624/127811</i>	<i>1275/240172</i>	<i>1169/206681</i>	<i>202/34592</i>	
Age adjusted	1.33 (1.13-1.68)	1.15 (0.98-1.36)	1.11 (0.95-1.29)	1.06 (0.91-1.23)	1	<0.0001
Multivariate-adjusted*	1.33 (1.12-1.59)	1.17 (0.99-1.38)	1.13 (0.97-1.32)	1.08 (0.93-1.26)	1	0.0003

* additionally adjusted for ethnicity (European descent, Asian, Hispanic, African American), hormone therapy use (never, current, past), oral contraceptive use (never, ever), parity (nulliparous, 1-2, ≥3), family history of MI, family history of stroke, [smoking (never, past, current 1-14, 15-24, or ≥25 cigarettes/d)], moderate to vigorous exercise (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, ≥6 h/wk), Alternate Healthy Eating Index score (<45, 45-<60, ≥60), Aspirin use (yes, no), alcohol intake (0, 0.1-4.9, 5.0-14.9, ≥15.0 g/d), BMI (<18.5, 18.5-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, ≥35.0 kg/m²), BMI at age 18 years (<18.5, 18.5-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, ≥35.0 kg/m²), menopause type (natural, surgical), a history of diabetes, hypertension, hypercholesterolemia

Table S4. Sensitivity analysis of relative risk and 95% confidence intervals of total CVD according to age at menopause in the Nurses' Health Study participants who were in premenopausal in 1980

	Age at menopause (years)					
	<40	40-44	45-49	50-54	≥55	p-trend
<i>Cases/person-years</i>	8/5902	75/41089	465/212575	1022/410844	288/91190	
Age adjusted	1.71 (0.84-3.50)	1.40 (1.09-1.79)	1.13 (1.00-1.27)	1	1.01 (0.88-1.17)	0.004
Multivariate-adjusted*	1.67 (0.81-3.44)	1.28 (0.99-1.65)	1.06 (0.94-1.19)	1	1.05 (0.91-1.21)	0.12

*adjusted for ethnicity (European descent, Asian, Hispanic, African American), hormone therapy use (never, current, past), oral contraceptive use (never, ever), parity (nulliparous, 1-2, ≥3), family history of MI (excluded in stroke outcome analysis), family history of stroke (excluded in CHD outcome analysis), smoking (never, past, current 1-14, 15-24, or ≥25 cigarettes/d), moderate to vigorous exercise (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, ≥6 h/wk), Alternate Healthy Eating Index score (<45, 45-<60, ≥60), Aspirin use (yes, no), alcohol intake (0, 0.1-4.9, 5.0-14.9, ≥15.0 g/d), BMI (<18.5, 18.5-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, ≥35.0 kg/m²), BMI at age 18 years (<18.5, 18.5-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, ≥35.0 kg/m²), menopause type (natural, surgical), a history of diabetes, hypertension, hypercholesterolemia