

SUPPLEMENTAL MATERIAL

Table S1. Baseline lifestyle, medical and reproductive characteristics of parous women (n=100,864) in the 45 and Up Study by breastfeeding history and average breastfeeding duration per child.*

Variables	Breastfeeding history			Average breastfeeding duration per child [†]			
	Never breastfed	Ever breastfed	P-value [‡]	>0-6 months	>6-12 months	>12 months	P-value [§]
Number of subjects (%)	12,517 (12.4)	88,347 (87.6)		56,049 (63.4)	24,549 (27.8)	7,749 (8.8)	
<i>BMI category (%)</i>							
Underweight/healthy weight (≤18.5 to <25.0 kg/m ²)	38.8	45.2	<0.0001	42.6	48.8	52.7	<0.0001
Overweight (25.0 to <30.0 kg/m ²)	33.0	33.4		23.2	18.5	17.5	
Obese (≥30.0 kg/m ²)	28.2	21.4		24.2	21.2	19.6	
Mean (SD) physical activity time (minutes/week)	599 (711)	602 (650)	0.68	601 (662)	601 (629)	606 (627)	0.90

Physical activity category[¶] (%)

<150 minutes/week	26.8	21.2	<0.0001	22.8	19.0	16.5	<0.0001
150 to 299 minutes/week	14.8	16.0		15.6	16.4	18.1	
≥300 minutes/week	58.4	62.8		61.6	64.6	65.4	

*Smoking status^{**} (%)*

Never smoker	60.5	65.5	<0.0001	63.9	69.0	65.6	<0.0001
Past regular smoker	28.8	28.0		28.7	26.1	29.1	
Current smoker	10.6	6.5		7.4	4.9	5.3	

Current alcohol intake

(drinks/week)^{††} (%)

≤14 drinks/week	90.5	89.7	<0.0001	89.3	90.3	91.1	<0.0001
>14 drinks/week	9.5	10.3		10.7	9.7	8.9	

Healthy lifestyle index^{‡‡}

Healthy	72.7	63.5	<0.0001	66.6	59.1	56.5	<0.0001
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Not healthy	27.3	36.5		33.4	40.9	43.5	
Current use of multivitamins (%)	25.5	30.1	<0.0001	29.2	30.6	34.6	<0.0001
Current use of omega 3 or fish oil (%) ^{§§}	34.2	37.0	<0.0001	38.0	35.5	34.8	<0.0001
Current use of aspirin (%)	14.7	13.3	<0.0001	14.8	11.5	7.6	<0.0001
History of oral contraceptive use ^{¶¶} (%)	80.1	83.6	<0.0001	83.0	83.4	89.3	<0.0001
Family history of cardiovascular disease ^{***} (%)	58.1	57.9	0.78	59.0	55.9	56.3	<0.0001
Family history of hypertension ^{†††} (%)	54.7	56.1	0.004	55.4	56.4	60.0	<0.0001
Family history of diabetes ^{†††} (%)	27.0	24.0	<0.0001	24.5	23.1	24.2	<0.0001
Self-reported hypertension/ recent treatment for hypertension (%)	24.9	20.5	<0.0001	23.2	17.6	10.6	<0.0001

Self-reported diabetes/ recent treatment for diabetes (%)	9.8	5.6	<0.0001	6.4	4.6	3.5	<0.0001
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BMI= body mass index; SD=standard deviation.

* Data are presented as means (SD) or percentages.

† Average breastfeeding duration per child was calculated as self-reported lifetime breastfeeding duration divided by the reported number of children.

‡ Based on chi-square test for categorical variables and student t-test for continuous variables.

§ Based on chi-square test for categorical variables and F statistics from ANOVA for continuous variables.

|| 8,273 missing.

¶ 1,370 missing.

** 5 missing.

†† 2,091 missing.

‡‡ 15,623 missing. Based on six lifestyle risk factors scored individually as either healthy (score=1) or not healthy (score=0), as follows: body mass index (<25 kg/m²=score 1, ≥25 kg/m²=score 0), physical activity level (<150 min/week=score 0; ≥150 min/week=score 1), smoking status (past/current smoker=score 0; never smoker=score 1), alcohol intake (≤14 drinks/week=score 0; >14 drinks/week=score 1), sleep (>7-<9 hours/day=score 0; <7 hours/day or >9 hours/day=score 1), fruit and vegetable intake (<2 serves of fruit/day and <3 serves of fruit/day=score 0; ≥2 serves of fruit/day and ≥3 serves of vegetables/day=score 1). Based on the

sum of these scores, the healthy lifestyle index was dichotomised as either healthy (sum of scores=5-6) or not healthy (sum of scores=0-4).

§§ 1 missing.

||| 6 missing.

¶¶ 1,571 missing.

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Table S2. Hazard ratios and 95% confidence intervals for the incidence of CVD hospitalisation and mortality in parous women, by breastfeeding history.

Breastfeeding history	No. of persons, n	Person-years from baseline	No. of incident cases/deaths	Model 1* (95% CI)	Model 2† (95% CI)	Model 3‡ (95% CI)	Model 4§ (95% CI)
<i>CVD hospitalisation</i>							
Parous, Never breastfed	12,517	76,164	527	Reference	Reference	Reference	Reference
Parous, Ever breastfed	88,347	540 696	2,901	0.81 (0.73,0.89)	0.83 (0.75,0.91)	0.85 (0.77,0.95)	0.86 (0.78,0.96)
P-value				<0.001	<0.001	0.003	0.005
<i>CVD mortality</i>							

Parous, Never breastfed	12,517	71 730	66	Reference	Reference	Reference	Reference
Parous, Ever breastfed	88,347	506,383	352	0.65 (0.49,0.85)	0.69 (0.52,0.91)	0.66 (0.50,0.89)	0.66 (0.49,0.89)
P-value				0.002	0.008	0.006	0.006

CI= confidence interval, CVD=cardiovascular disease.

* Model 1 was unadjusted.

† Model 2 was adjusted for parity (number of children) and socio-demographic characteristics (age, country of birth, educational level, marital status, area-level socio-economic status).

‡ Model 3 was further adjusted for lifestyle factors: body mass index, smoking status, alcohol intake, physical activity.

§ Model 4 was additionally adjusted for medical and reproductive covariates: multi-vitamin use, omega 3 or fish oil use, use of aspirin, oral contraceptive use, mother's age for first child, mother's age for last child, family history of CVD, family history of hypertension, family history of diabetes, self-reported hypertension/recent treatment for hypertension, and self-reported diabetes/recent treatment for diabetes.

|| From Type 3 Wald chi-square test.

Table S3. Adjusted hazard ratios and 95% confidence intervals for associations between average breastfeeding duration per child and the incidence of CVD hospitalisation and mortality in parous women, stratified by highest educational level.

Highest educational level	Average breastfeeding duration per child	No. of persons, n	Person-years from baseline (from birth of first child)	No. of incident cases/deaths	Multivariate-adjusted* (95% CI)
<i>CVD hospitalisation</i>					
University and higher	Never breastfed	1,362	8,364	38	Reference
	>0-6 months	9,915	61,035	239	0.90 (0.62, 1.30)
	>6-12 months	7,462	46,238	111	0.81 (0.55, 1.20)
	>12 months	3,383	21,027	39	0.92 (0.57, 1.48)
High school/trade apprenticeship/ certificate/diploma	Never breastfed	4,089	24,986	152	Reference
	>0-6 months	20,696	126,795	680	0.89 (0.74, 1.08)

	>6-12 months	9,730	59,834	238	0.83 (0.66, 1.03)
	>12 months	3,101	19,141	49	0.94 (0.66, 1.33)
≤10 years	Never	6,830	41,444	320	Reference
	breastfed				
	>0-6 months	24,669	149,919	1,113	0.85 (0.74, 0.97)
	>6-12 months	7,098	42,878	348	0.90 (0.76, 1.07)
	>12 months	1,204	7,374	25	0.75 (0.48, 1.18)
<i>CVD mortality</i>					
University and higher	Never	1,362	7,808	<5	Reference
	breastfed				
	>0-6 months	9,915	56,884	20	0.66 (0.19, 2.26)
	>6-12 months	7,462	42,910	<5	0.28 (0.06, 1.27)
	>12 months	3,383	19,477	0	-

High school/trade apprenticeship/ certificate/diploma	Never	4,089	23,470	20	Reference
	breastfed				
	>0-6 months	20,696	118,767	63	0.51 (0.30, 0.87)
	>6-12 months	9,730	55,765	32	0.65 (0.36, 1.17)
	>12 months	3,101	17,769	<5	0.26 (0.03, 1.94)
≤10 years	Never	6,830	39,118	41	Reference
	breastfed				
	>0-6 months	24,669	141,360	154	0.77 (0.53, 1.13)
	>6-12 months	7,098	40,484	51	0.52 (0.33, 0.84)
	>12 months	1,204	6,860	6	1.06 (0.37, 3.02)

CI= confidence interval, CVD=cardiovascular disease.

* Adjusted for age, country of birth, educational level, marital status, area-level socio-economic status, body mass index, smoking status, alcohol intake, physical activity, multi-vitamin use, omega 3 or fish oil use, use of aspirin, oral contraceptive use, number of children, mother's age for first child, mother's age for last child, family history of CVD, family history of hypertension, family history of diabetes, self-reported hypertension/recent treatment for hypertension, and self-reported diabetes/recent treatment for diabetes.

Table S4. Adjusted hazard ratios and 95% confidence intervals for associations between average breastfeeding duration per child and the incidence of CVD hospitalisation and mortality in parous women, stratified by the healthy lifestyle index.

Healthy lifestyle index*	Average breastfeeding duration per child†	No. of persons, n	Person-years from baseline (from birth of first child)	No. of incident cases/deaths	Multivariate-adjusted‡ (95% CI)
<i>CVD hospitalisation</i>					
Healthy	Never breastfed	2,812	17,354	77	Reference
	>0-6 months	15,724	96,582	490	1.11 (0.87, 1.42)
	>6-12 months	8,652	53,261	197	1.01 (0.77, 1.32)
	>12 months	2,948	18,230	37	1.15 (0.77, 1.72)
Not healthy	Never breastfed	7,487	45,413	345	Reference
	>0-6 months	31,297	191,309	1,157	0.79 (0.70, 0.90)

	>6-12 months	12,485	76,576	371	0.80 (0.68, 0.93)
	>12 months	3,836	23,718	61	0.82 (0.62, 1.09)
<i>CVD mortality</i>					
Healthy	Never breastfed	2,812	16,201	10	Reference
	>0-6 months	15,724	90,369	43	0.68 (0.34, 1.36)
	>6-12 months	8,652	49,616	15	0.40 (0.18, 0.90)
	>12 months	2,948	16,894	<5	0.93 (0.20, 4.31)
Not healthy	Never breastfed	7,487	42,853	39	Reference
	>0-6 months	31,297	179,631	130	0.68 (0.47, 0.99)
	>6-12 months	12,485	71,602	48	0.59 (0.38, 0.92)
	>12 months	3,836	22,019	<5	0.57 (0.18, 1.88)

CI= confidence interval, CVD=cardiovascular disease.

* Based on six lifestyle risk factors scored individually as either healthy (score=1) or not healthy (score=0): body mass index (<25 kg/m²=score 1, ≥25 kg/m²=score 0), physical activity level (<150 min/week=score 0; ≥150 min/week=score 1), smoking status (past/current smoker=score 0; never smoker=score 1), alcohol intake (≤14 drinks/week=score 0; >14 drinks/week=score 1), sleep (>7-<9 hours/day=score 0; <7 hours/day or >9 hours/day=score 1), fruit and vegetable intake (<2 serves of fruit/day and <3 serves of fruit/day=score 0; ≥2 serves of fruit/day and ≥3 serves of vegetables/day=score 1). Based on the sum of these scores, the healthy lifestyle index was dichotomised as either healthy (sum of scores=5-6) or not healthy (sum of scores=0-4).

† Average breastfeeding duration per child was calculated as self-reported lifetime breastfeeding duration divided by the reported number of children.

‡ Adjusted for age, country of birth, educational level, marital status, area-level socio-economic status, multi-vitamin use, omega 3 or fish oil use, use of aspirin, oral contraceptive use, number of children, mother's age for first child, mother's age for last child, family history of CVD, family history of hypertension, family history of diabetes, self-reported hypertension/recent treatment for hypertension, and self-reported diabetes/recent treatment for diabetes.

Table S5. Summary of recent prospective/case-cohort studies that have examined the association between breastfeeding history/duration and CVD outcomes.

First author (year)	Country and cohort designation	Participants	Mean follow- up (years)	Outcome assessment	Breastfeeding comparison categories	Adjusted HR (95% CI) by breastfeeding history/ duration	Covariates
Merritt et al. (2015) [1]	10 European countries, EPIC study	322,972 parous women without a history of MI/heart attack, angina, stroke or cancer; 25-70 years	12.9	Mortality from: Circulatory disease Cerebrovascular disease IHD	Never Ever Never Ever	Reference 0.80 (0.70, 0.91) Reference 0.94 (0.74, 1.21) Reference 0.69 (0.54, 0.87)	Education level, BMI, physical activity, smoking status/intensity and duration, menopausal status

Peters et al. (2016) [2]	10	Parous women without a history of IHD or stroke; mean age=52.7 (SD: 9.1) years; n=8,044 for analyses comparing never vs. ever breastfeeding and n=8,012 for analyses involving breastfeeding duration	11	Incidence of first-time non-fatal/fatal IHD event	Never Ever Average breastfeeding duration/child Never >0-<1 month ≥1-<3 months ≥3-<6 months ≥6 months	Reference 0.71 (0.52, 0.98) 1.00 (0.73, 1.37) 0.77 (0.63, 0.94) 0.69 (0.61, 0.78) 0.67 (0.57, 0.77) 0.67 (0.56, 0.80)	Study centre, age, education level, BMI, smoking status, number of live births, high blood pressure, HDL cholesterol, total cholesterol, history of diabetes mellitus
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Peters et al. (2017) [3]	10 diverse regions in China, China Kadoorie Biobank	289,573 without a history of IHD or stroke; 30-79 years	8.1 (median)	Incidence of:			Education level, household income, BMI, physical activity, smoking status, alcohol intake, systolic blood pressure, history of hypertension, history of diabetes mellitus
				All CVD	Never	1.00 (0.95, 1.05)	
					Ever	0.96 (0.95, 0.97)	
					Each additional 6 months/child*	0.98 (0.97, 0.99)	
				Major CVD	Never	1.00 (0.92, 1.09)	
					Ever	0.88 (0.87, 0.90)	
					Each additional 6 months/child*	0.97 (0.96, 0.99)	
				Fatal CVD	Never	1.00 (0.77, 1.29)	

	Ever	0.90 (0.87, 0.94)
	Each additional 6 months/child*	0.98 (0.95, 1.01)
Stroke	Never	1.00 (0.93, 1.08)
	Ever	0.92 (0.90, 0.93)
	Each additional 6 months/child*	0.97 (0.96, 0.98)
Haemorrhagic stroke	Never	1.00 (0.77, 1.31)
	Ever	0.84 (0.81, 0.88)

	Each additional 6 months/child*	0.99 (0.96, 1.03)
Ischemic stroke	Never	1.00 (0.91, 1.09)
	Ever	0.88 (0.86, 0.90)
	Each additional 6 months/child*	0.97 (0.95, 0.98)
IHD	Never	1.00 (0.92, 1.09)
	Ever	0.91 (0.89, 0.93)
	Each additional 6 months/child*	0.96 (0.95, 0.98)

BMI=body mass index, CVD=cardiovascular disease, EPIC=European Investigation into Cancer and Nutrition prospective cohort study, HDL=high-density lipoprotein, HR=hazard ratio, IHD=ischaemic heart disease, MI=myocardial infarction, SD=standard deviation.

* Among parous women that had ever breastfed.

Supplemental References:

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