Supplemental Appendix

Breastfeeding duration and subsequent risk of mortality among US women: a prospective cohort study

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Appendix Table 1. The baseline demographic characteristics and prepregnancy lifestyle factors between included women and those excluded due to missing data on breastfeeding duration.

Characteristics ^{a,b}	Included	Excluded
The Nurses' Health Study (1986)		
Number of women	85,964	16,009
Age (year), mean (SD)	52.2 (7.1)	51.9 (7.4)
Non-Hispanic White, %	83,834 (97.5)	15,027 (93.8)
Woman's own birth weight less than 2.5kg, %	6306 (7.3)	441 (2.8)
Oral contraceptive use during puberty, %	5358 (6.2)	946 (6.1)
Parity, mean (SD)	3.2 (1.5)	3.1 (1.6)
Age at first birth (year), mean (SD)	25.2 (3.7)	25.4 (5.1)
Prepregnancy cigarette smoking, %	19,044 (22.1)	5505 (34.6)
Pre-pregnancy BMI (kg/m²), mean (SD)	25.3 (4.8)	24.5 (4.7)
Pre-pregnancy diet quality (alternate healthy eating index), mean (SD)	50.2 (12.3)	37.6 (12.4)
Pre-pregnancy alcohol intake (g/d), mean (SD)	6.1 (10.6)	6.5 (11.1)
Pre-pregnancy moderate to vigorous intensity exercise (h/wk), mean (SD)	2.1 (3.3)	3.0 (2.4)
The Nurses' Health Study II (1989)		
Number of women	80,744	10,677
Age (year), mean (SD)	34.3 (4.7)	34.6 (4.6)
Non-Hispanic White, %	75,792 (93.9)	9116 (85.4)
Woman's own birth weight less than 2.5kg, %	5181 (6.4)	503 (4.7)
Oral contraceptive use during puberty, %	17,751 (22.0)	2445 (23.3)
Parity, mean (SD)	1.8 (1.1)	2 (0.9)
Age at first birth (year), mean (SD)	26.6 (4.8)	24.9 (4.2)
Prepregnancy cigarette smoking, %	5622 (7.0)	1385 (12.9)
Pre-pregnancy BMI (kg/m²), mean (SD)	23.9 (4.7)	24.6 (5.2)
Pre-pregnancy diet quality (alternate healthy eating index), mean (SD)	47.4 (10.6)	46.5 (10.4)
Pre-pregnancy alcohol intake (g/d), mean (SD)	2.9 (5.7)	2.6 (5.3)
Pre-pregnancy moderate to vigorous intensity exercise (h/wk), mean (SD)	2.8 (4.8)	2.8 (5.0)

^aValues are means (SD) or N (percentages); means (SD) and percentages of all variables except for age are age-standardised. ^bIn NHS, a total of 176 (0.2%), 16951 (16.6%), and 12195 (12.0%) women had missing data on baseline BMI, diet (including alcohol intake), and physical activity, respectively; in NHS II, a total of 5360 (5.9%), 19866 (21.7%), 6762 (7.4%), and 1245 (1.4%) women had missing data on baseline BMI, diet (including alcohol intake), physical activity, and age at first birth, respectively.

Appendix Table 2. Categories of causes of death and number of reported cases per cause [NHS (1986-2016) and NHS II (1989-2019)].

Causes of death	ICD-8 or 9 code	N of death	
		NHS	NHS II
Cancer	140-207	8753	1127
Breast cancer	174	1226	375
Malignant neoplasm of digestive organs and peritoneum	150-159	1913	183
Malignant neoplasm of genito-urinary organs	180-189	1278	166
Malignant neoplasm of respiratory system	160-163	2135	138
Neoplasms of lymphatic and haematopoietic tissue	200-207	977	95
Malignant neoplasm of bone, connective tissue, and skin	170-174	196	51
Malignant neoplasm of buccal cavity and pharynx	140-149	93	8
Malignant neoplasm of other and unspecified sites	190-199	935	111
Cardiovascular disease	390-459, 795	7517	192
Other causes	460-999	17,452	1593
External causes (accidents, injury, and poisoning)	800-950, 959-999	1131	149
Senility and ill-defined diseases	790-794, 796	2389	107
Suicide	950-959	82	61
Respiratory disease	460-519	2795	59
Diseases of gastro-intestinal system	520-577	843	57
Diseases of the nervous system and sense organs	320-389	886	52
Infectious and parasitic diseases	000-136	689	43
Endocrine, nutritional and metabolic diseases or immunity disorders	240-279	393	30
Mental disorders	290-315	4654	30
Diseases of the musculoskeletal system and connective tissue	710-738	227	19
Benign neoplasm	208-239	122	6
Diseases of genito-urinary system	580-629	531	11
Diseases of the blood and blood-forming organs	280-289	77	5
Complications of pregnancy, childbirth, and the puerperium	630-676, 760-779	1	4
Diseases of the skin and subcutaneous tissue	680-709	7	0
Congenital anomalies	740-759	11	9
Symptoms referable to systems or organs	780-789	14	1
Uncertain	-	2600	950

ICD: International Classification of Diseases.

Appendix Table 3. Pooled hazard ratios (HR) (95% confidence intervals (CI)) for the risk of cause-specific cancer and non-CVD/cancer mortality, according to lifetime total breastfeeding duration among 166,708 women from the NHS (1986-2016) and NHS II (1989-2019).

Cause-specific mortality	Lifetime total brea	Р	
	≤3 months	>3 months	
Cancer			
Breast cancer			
Events, No.	870	731	
HR (95% CI) ^a	1.00 [Reference]	0.95 (0.85, 1.05)	0.32
Malignant neoplasm of digestive organs and peritoneum		0.4.0	
Events, No.	1277	819	0.45
HR (95% CI) ^a	1.00 [Reference]	0.94 (0.86, 1.02)	0.15
Malignant neoplasm of genito-urinary organs Events, No.	860	584	
HR (95% CI) ^a	1.00 [Reference]	0.93 (0.83, 1.04)	0.18
Malignant neoplasm of respiratory system	1.00 [Kelelelice]	0.93 (0.83, 1.04)	0.18
Events, No.	1491	782	
HR (95% CI) ^a	1.00 [Reference]	0.91 (0.84, 1.00)	0.044
Neoplasms of lymphatic and haematopoietic tissue	1.00 [Neterence]	0.51 (0.04, 1.00)	0.044
Events, No.	638	434	
HR (95% CI) ^a	1.00 [Reference]	0.99 (0.87, 1.12)	0.88
Malignant neoplasm of bone, connective tissue, and skin		, ,	
Events, No.	140	107	
HR (95% CI) ^a	1.00 [Reference]	0.90 (0.69, 1.17)	0.44
Malignant neoplasm of other and unspecified sites			
Events, No.	605	441	
HR (95% CI) ^a	1.00 [Reference]	1.05 (0.93, 1.20)	0.42
Non-CVD/Non-cancer death			
External causes (accidents, injury, and poisoning)			
Events, No.	779	501	
HR (95% CI) ^a	1.00 [Reference]	0.92 (0.82, 1.03)	0.15
Senility and ill-defined diseases			
Events, No.	1575	921	
HR (95% CI) ^a	1.00 [Reference]	0.94 (0.87, 1.02)	0.15
Suicide Franta Na	CO	02	
Events, No. HR (95% CI) ^a	60 1.00 [Reference]	83 1.43 (1.00, 2.04)	0.049
Respiratory disease	1.00 [Reference]	1.43 (1.00, 2.04)	0.049
Events, No.	1890	964	
HR (95% CI) ^a	1.00 [Reference]	0.93 (0.86, 1.01)	0.087
Diseases of gastrointestinal system	1.00 [Neterence]	0.55 (0.66, 1.61)	0.007
Events, No.	FOE	204	
HR (95% CI) ^a	596 1.00 [Reference]	304 0.81 (0.70, 0.93)	0.0037
	1.00 [Neterence]	0.01 (0.70, 0.33)	0.0037
Diseases of the nervous system and sense organs	5.40	205	
Events, No.	543	395	0.44
HR (95% CI) ^a	1.00 [Reference]	1.11 (0.97, 1.27)	0.11
Infectious and parasitic diseases			
Events, No.	462	270	
HR (95% CI) ^a	1.00 [Reference]	0.91 (0.78, 1.06)	0.21

Endocrine, nutritional and metabolic diseases or immunity			
disorders			
Events, No.	290	133	
HR (95% CI) ^a	1.00 [Reference]	0.70 (0.56, 0.86)	0.0010
Mental disorders			
Events, No.	2935	1749	
HR (95% CI) ^a	1.00 [Reference]	0.99 (0.93, 1.05)	0.76

 a Cox proportional hazards regression models were stratified jointly by participants' own age in years at the start of follow-up and calendar years of the current questionnaire cycle, with adjustment for race/ethnicity (non-Hispanic White; yes or no), age at first birth (<20, 20-24, 25-29, ≥30 years), woman's own birth weight (<5.5, 5.5-6.9, 7.0-8.4, 8.5-9.9, ≥10 lbs), oral contraceptive use during puberty (yes or no), infertility history (yes or no), woman's parents worked as professionals, managers, or executives during infancy (yes or no), woman's parents owned home during infancy (yes or no), maternal history of cancer (yes or no), parental history of CVD before age 60 years (yes or no), and time-varying pre-pregnancy smoking status (never smoker, former smoker: 1-14, ≥15 cigarettes/d, and current smoker: 1-14, 15-24, ≥25 cigarettes/d), alcohol drinking (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/d), exercise at moderate-to-high intensity (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, or ≥6 h/week), and alternate healthy eating index (five categories), and body mass index (<21, 21-24.9, 25-29.9, 30-31.9, or ≥32 kg/m²).

Appendix Table 4. Pooled hazard ratios (HR) (95% confidence intervals (CI)) of all-cause mortality according to the average duration of total breastfeeding (per parity) among 166,708 women from the NHS (1986-2016) and NHS II (1989-2019).

		Crude	HRs (95% CIs)		
Average duration of total breastfeeding (per parity)	Death cases	incidence per 1000 person- years	Age-adjusted models ^a	Multivariable model 1 ^b	Multivariable model 2 ^c
<1	21324	17.12	1.00 [Reference]	1.00 [Reference]	1.00 [Reference]
1-3	8560	14.89	0.91 (0.88, 0.93)	0.92 (0.89, 0.94)	0.95 (0.93, 0.98)
4-6	3296	12.54	0.84 (0.81, 0.87)	0.85 (0.82, 0.89)	0.92 (0.89, 0.96)
≥7	3454	10.81	0.85 (0.82, 0.88)	0.87 (0.84, 0.90)	0.97 (0.93, 1.00)
p for linear trend			< 0.0001	<0.0001	0.0005

 $^{\circ}$ Cox proportional hazard regression models were stratified jointly by participants' own age in years at the start of follow-up and calendar years of the current questionnaire cycle. $^{\text{b}}$ Multivariable Cox model 1 was further adjusted for race/ethnicity (non-Hispanic White; yes or no), age at first birth (<20, 20-24, 25-29, ≥30 years), woman's own birth weight (<5.5, 5.5-6.9, 7.0-8.4, 8.5-9.9, ≥10 lbs), oral contraceptive use during puberty (yes or no), infertility history (yes or no), woman's parents worked as professionals, managers, or executives during infancy (yes or no), woman's parents owned home during infancy (yes or no), maternal history of cancer (yes or no), and parental history of CVD before age 60 years (yes or no). $^{\text{c}}$ Multivariable Cox model 2 was further adjusted for time-varying pre-pregnancy smoking status (never smoker, former smoker: 1-14, ≥15 cigarettes/d, and current smoker: 1-14, 15-24, ≥25 cigarettes/d), alcohol drinking (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/d), exercise at moderate-to-high intensity (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, or ≥6 h/week), and alternate healthy eating index (five categories), and body mass index (<21, 21-24.9, 25-29.9, 30-31.9, or ≥32 kg/m²). Tests for linear trends were evaluated using the Wald test on the continuous breastfeeding duration representing the median values of each category.

Appendix Table 5. Sensitivity analysis of the pooled hazard ratios (HR) (95% confidence intervals (CI)) of cause-specific mortality according to lifetime total breastfeeding duration among 166,708 women from the NHS (1986-2016) and NHS II (1989-2019), with additional adjustment for time-varying parity.

Lifetime total breastfeeding duration	Death cases	Crude incidence per	HRs (95% CIs) ^a
Energine total of castreeaning daration	Death cases	1000 person-years	
≤3	5936	449	1.00 [Reference]
4-6	1137	394	0.95 (0.92, 0.98)
7-11	936	361	0.95 (0.92, 0.98)
12-23	1146	344	0.94 (0.91, 0.97)
≥24	725	345	0.95 (0.91, 1.00)
p for linear trend			0.0007

 $^{\circ}$ Cox proportional hazards regression models were stratified jointly by participants' own age in years at the start of follow-up and calendar years of the current questionnaire cycle, with adjustment for race/ethnicity (non-Hispanic White; yes or no), age at first birth (<20, 20-24, 25-29, ≥30 years), woman's own birth weight (<5.5, 5.5-6.9, 7.0-8.4, 8.5-9.9, ≥10 lbs), oral contraceptive use during puberty (yes or no), infertility history (yes or no), woman's parents worked as professionals, managers, or executives during infancy (yes or no), woman's parents owned home during infancy (yes or no), maternal history of cancer (yes or no), parental history of CVD before age 60 years (yes or no), as well as time-varying parity (continuous) and prepregnancy smoking status (never smoker, former smoker: 1-14, ≥15 cigarettes/d, and current smoker: 1-14, 15-24, ≥25 cigarettes/d), alcohol drinking (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/d), exercise at moderate-to-high intensity (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, or ≥6 h/week), and alternate healthy eating index (five categories), and body mass index (<21, 21-24.9, 25-29.9, 30-31.9, or ≥32 kg/m²). Tests for linear trends were evaluated using the Wald test on the continuous breastfeeding duration representing the median values of each category.

Appendix Table 6. Sensitivity analysis of the pooled hazard ratios (HR) (95% confidence intervals (CI)) of cause-specific mortality according to lifetime total breastfeeding duration among 166,708 women from the NHS (1986-2016) and NHS II (1989-2019), with additional adjustment for the state of birth.

Lifetime total breastfeeding duration	Death cases	Crude incidence per 1000 person-years	HRs (95% CIs) ^a
≤3	5936	449	1.00 [Reference]
4-6	1137	394	0.94 (0.91, 0.97)
7-11	936	361	0.94 (0.90, 0.97)
12-23	1146	344	0.92 (0.89, 0.96)
≥24	725	345	0.92 (0.88, 0.96)
p for linear trend			<0.0001

 $^{\circ}$ Cox proportional hazards regression models were stratified jointly by participants' own age in years at the start of follow-up and calendar years of the current questionnaire cycle, with adjustment for race/ethnicity (non-Hispanic White; yes or no), age at first birth (<20, 20-24, 25-29, ≥30 years), woman's own birth weight (<5.5, 5.5-6.9, 7.0-8.4, 8.5-9.9, ≥10 lbs), oral contraceptive use during puberty (yes or no), infertility history (yes or no), woman's parents worked as professionals, managers, or executives during infancy (yes or no), woman's parents owned home during infancy (yes or no), maternal history of cancer (yes or no), parental history of CVD before age 60 years (yes or no), tier of birth (North, Middle, South, outside of US), and timevarying pre-pregnancy smoking status (never smoker, former smoker: 1-14, ≥15 cigarettes/d, and current smoker: 1-14, 15-24, ≥25 cigarettes/d), alcohol drinking (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/d), exercise at moderate-to-high intensity (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, or ≥6 h/week), and alternate healthy eating index (five categories), and body mass index (<21, 21-24.9, 25-29.9, 30-31.9, or ≥32 kg/m²). Tests for linear trends were evaluated using the Wald test on the continuous breastfeeding duration representing the median values of each category.

Appendix Table 7. Sensitivity analysis of the pooled hazard ratios (HR) (95% confidence intervals (CI)) of cause-specific mortality according to lifetime total breastfeeding duration among 166,708 women from the NHS (1986-2016) and NHS II (1989-2019), by stratifying the analyses jointly by calendar years and participants' own age in months or broader age groups.^a

Lifetime total breastfeeding duration	Death cases	Crude incidence per 1000 person-years	HRs (95% CIs)
The analyses were stratified jointly by participants' own age			
in months at the start of follow-up and calendar years of the			
current questionnaire cycle			
≤3	5936	449	1.00 [Reference]
4-6	1137	394	0.95 (0.92, 0.98)
7-11	936	361	0.94 (0.91, 0.98)
12-23	1146	344	0.93 (0.90, 0.96)
≥24	725	345	0.92 (0.88, 0.97)
p for linear trend			<0.0001
The analyses were stratified jointly by participants' own age			
in years (5 years per category) at the start of follow-up and			
calendar years of the current questionnaire cycle			
≤3	5936	449	1.00 [Reference]
4-6	1137	394	0.93 (0.91, 0.97)
7-11	936	361	0.89 (0.86, 0.92)
12-23	1146	344	0.86 (0.83, 0.89)
≥24	725	345	0.84 (0.81, 0.88)
p for linear trend			<0.0001

 $^{\circ}$ Cox proportional hazards regression models were stratified jointly by participants' own age (in years or months) at the start of follow-up and calendar years of the current questionnaire cycle, with adjustment for race/ethnicity (non-Hispanic White; yes or no), age at first birth (<20, 20-24, 25-29, ≥30 years), woman's own birth weight (<5.5, 5.5-6.9, 7.0-8.4, 8.5-9.9, ≥10 lbs), oral contraceptive use during puberty (yes or no), infertility history (yes or no), woman's parents worked as professionals, managers, or executives during infancy (yes or no), woman's parents owned home during infancy (yes or no), maternal history of cancer (yes or no), parental history of CVD before age 60 years (yes or no), gestational diabetes and hypertensive disorders of pregnancy (yes or no), and time-varying pre-pregnancy smoking status (never smoker, former smoker: 1-14, ≥15 cigarettes/d, and current smoker: 1-14, 15-24, ≥25 cigarettes/d), alcohol drinking (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/d), exercise at moderate-to-high intensity (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, or ≥6 h/week), and alternate healthy eating index (five categories), and body mass index (<21, 21-24.9, 25-29.9, 30-31.9, or ≥32 kg/m²). Tests for linear trends were evaluated using the Wald test on the continuous breastfeeding duration representing the median values of each category.

Appendix Table 8. Sensitivity analysis of the association between lifetime total breastfeeding duration and average duration of total breastfeeding (per child) and all-cause mortality among 80,744 women from the NHS II (1989-2019), with additional adjustment for gestational diabetes and hypertensive disorders of pregnancy.^a

Lifetime total breastfeeding duration	Death cases	Crude incidence per 1000 person-years	HRs (95% CIs)
≤3	969	1.60	1.00 [Reference]
4-6	373	1.43	1.05 (0.93, 1.19)
7-11	478	1.24	0.98 (0.88, 1.10)
12-23	582	1.06	0.87 (0.78, 0.96)
≥24	510	1.03	0.87 (0.78, 0.97)
p for linear trend			0.0013

 $^{\circ}$ Cox proportional hazards regression models were stratified jointly by participants' own age in years at the start of follow-up and calendar years of the current questionnaire cycle, with adjustment for race/ethnicity (non-Hispanic White; yes or no), age at first birth (<20, 20-24, 25-29, ≥30 years), woman's own birth weight (<5.5, 5.5-6.9, 7.0-8.4, 8.5-9.9, ≥10 lbs), oral contraceptive use during puberty (yes or no), infertility history (yes or no), woman's parents worked as professionals, managers, or executives during infancy (yes or no), woman's parents owned home during infancy (yes or no), maternal history of cancer (yes or no), parental history of CVD before age 60 years (yes or no), gestational diabetes (yes or no), hypertensive disorders of pregnancy (yes or no), and time-varying pre-pregnancy smoking status (never smoker, former smoker: 1-14, ≥15 cigarettes/d, and current smoker: 1-14, 15-24, ≥25 cigarettes/d), alcohol drinking (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/d), exercise at moderate-to-high intensity (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, or ≥6 h/week), and alternate healthy eating index (five categories), and body mass index (<21, 21-24.9, 25-29.9, 30-31.9, or ≥32 kg/m²). Tests for linear trends were evaluated using the Wald test on the continuous breastfeeding duration representing the median values of each category.

Appendix Table 9. Hazard ratios (HR) (95% confidence intervals (CI)) of all-cause mortality according to lifetime total exclusive breastfeeding duration among 75,221 women from the NHS II (1989-2019).

		Crude	HRs (95% CIs)		
Average duration of total breastfeeding (per parity)	Death cases	incidence per 1000 person- years	Age-adjusted models ^a	Multivariable model 1 ^b	Multivariable model 2 ^c
0	1300	1.41	1.00 [Reference]	1.00 [Reference]	1.00 [Reference]
0.1-3	265	2.65	0.90 (0.79, 1.02)	0.93 (0.81, 1.06)	0.97 (0.85, 1.11)
4-6	351	1.03	0.78 (0.69, 0.87)	0.82 (0.73, 0.92)	0.91 (0.80, 1.02)
≥7	654	0.99	0.74 (0.67, 0.81)	0.80 (0.73, 0.88)	0.92 (0.83, 1.01)
p for linear trend			< 0.0001	<0.0001	0.060

^aIn age-adjusted Cox proportional hazard regression models, the analyses were stratified jointly by participants' own age in years at the start of follow-up and calendar years of the current questionnaire cycle. ^bMultivariable Cox model 1 was further adjusted for race/ethnicity (non-Hispanic White; yes or no), age at first birth (<20, 20-24, 25-29, ≥30 years), woman's own birth weight (<5.5, 5.5-6.9, 7.0-8.4, 8.5-9.9, ≥10 lbs), oral contraceptive use during puberty (yes or no), infertility history (yes or no), woman's parents worked as professionals, managers, or executives during infancy (yes or no), woman's parents owned home during infancy (yes or no), maternal history of cancer (yes or no), and parental history of CVD before age 60 years (yes or no). ^cMultivariable Cox model 2 was further adjusted for time-varying pre-pregnancy smoking status (never smoker, former smoker: 1-14, ≥15 cigarettes/d, and current smoker: 1-14, 15-24, ≥25 cigarettes/d), alcohol drinking (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/d), exercise at moderate-to-high intensity (0, 0.01-1.0, 1.1-3.4, 3.5-5.9, or ≥6 h/week), and alternate healthy eating index (five categories), and body mass index (<21, 21-24.9, 25-29.9, 30-31.9, or ≥32 kg/m²). Tests for linear trends were evaluated using the Wald test on the continuous breastfeeding duration representing the median values of each category.