# Breastfeeding and Cardiovascular Disease Hospitalization and Mortality in Parous Women: Evidence From a Large Australian Cohort Study

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*Background*—Few studies have investigated the longitudinal association between breastfeeding and maternal cardiovascular disease (CVD) outcomes. This study examined the association between breastfeeding and CVD hospitalization and mortality in a large Australian cohort.

*Methods and Results*—Baseline questionnaire data (2006–2009) from a sample of 100 864 parous women aged ≥45 years from New South Wales, Australia, were linked to hospitalization and death data until June 2014 and December 2013, respectively. Analysis was restricted to women without self-reported medically diagnosed CVD at baseline or without past CVD hospitalization 6 years before study entry. Never versus ever breastfeeding and average breastfeeding duration per child, derived from self-reported lifetime breastfeeding duration and number of children, and categorized as never breastfed, <6, >6 to 12, or >12 months/child, were assessed. Cox proportional hazards models were used to explore the association between breastfeeding and CVD outcomes. Covariates included sociodemographic characteristics, lifestyle risk factors, and medical and reproductive history. There were 3428 (3.4%) first CVD-related hospital admissions and 418 (0.4%) deaths during a mean follow-up time of 6.1 years for CVD hospitalization and 5.7 years for CVD mortality. Ever breastfeeding was associated with lower risk of CVD hospitalization (adjusted hazard ratio [95% CI]: 0.86 [0.78, 0.96]; P=0.005) and CVD mortality (adjusted hazard ratio [95% CI]: 0.66 [0.49, 0.89]; P=0.006) compared with never breastfeeding. Breastfeeding ≤12 months/child was significantly associated with lower risk of CVD hospitalization.

*Conclusions*—Breastfeeding is associated with lower maternal risk of CVD hospitalization and mortality in middle-aged and older Australian women. Breastfeeding may offer long-term maternal cardiovascular health benefits. (*J Am Heart Assoc*. 2019;8: e011056. DOI: 10.1161/JAHA.118.011056.)

*Key Words:* breastfeeding • cardiovascular diseases • lactation • maternal health • prospective studies

Cardiovascular disease (CVD) is the leading cause of death for women worldwide.[1] Preventing CVD through modifying known lifestyle risk factors, such as being

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Accompanying Tables S1 through S5 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.011056

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overweight and an unhealthy diet, is a key public health priority. Whereas changes in established lifestyle risk factors can lead to substantial reduction in risk of developing CVD, prevention approaches should also incorporate emerging knowledge about novel risk factors of CVD, including behaviors that are specific to women. There has been an urgent, global call to conduct more sex-specific research to better inform public health strategies.[2] Sex differences exist in the epidemiology, diagnosis, risk profile, and treatment of CVD. Compared with men, women generally develop CVD at a later age, present with different symptoms and risk factors, are underdiagnosed, and respond differently to various treatments.[2]

Breastfeeding has emerged in recent years as a lifestyle risk factor that may be associated with CVD; however, the evidence is limited by the small number of observational studies, particularly longitudinal studies.[3] Prevalence of early initiation of breastfeeding within 1 hour of birth is ≈30% in high-income countries,[4] and around 79% of newborns in high-income countries are ever breastfed.[5] Globally, prevalence of exclusive

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## Clinical Perspective

### What Is New?

- Findings from this study add to the growing evidence base for the long-term benefits of breastfeeding for maternal cardiovascular health.
- Among parous women aged ≥45 years, ever breastfeeding and average breastfeeding duration per child up to 12 months were associated with substantially lower risk of developing and dying from cardiovascular disease.
- Findings were mostly consistent among women from different socioeconomic backgrounds and with different lifestyle risk.

### What Are the Clinical Implications?

- This study provides evidence that breastfeeding is associated with long-term benefits for maternal cardiovascular health, in addition to its known benefits for infants and mothers.
- Breastfeeding may be promoted as an additional strategy by which parous women can reduce their risk of developing and dying from cardiovascular disease.

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breastfeeding for infants aged <6 months is ≈43%.[5] During pregnancy, profound metabolic changes occur in a mother's body to support fetal growth and prepare for lactation.[6] It has been hypothesized that breastfeeding, which increases metabolic expenditure by an estimated 480 kcal/day, may enable a more rapid reversal of metabolic changes in pregnancy, including improved insulin sensitivity, lipid metabolism, and greater mobilization of accumulated fat stores, thereby "resetting" maternal metabolism after pregnancy and potentially reducing maternal risk of cardiometabolic disease.[7] Multiple studies have reported the short-term benefits of breastfeeding, including lipid homeostasis,[8,9] glucose homeostasis, and insulin sensitivity.[10,11] However, whether these benefits can contribute to long-term maternal health is unclear.

Emerging evidence suggests that breastfeeding may reduce the risk of developing type 2 diabetes mellitus,[12] hypertension,[13] and metabolic syndrome[14] later in life. Although a number of studies have examined the associations between breastfeeding and CVD outcomes, such as incidence of CVD[3,15–18] or death from CVD,[3,19–22] findings from these studies are inconclusive.

An important issue to consider in interpreting these observational studies is confounding.[3] Mothers who have breastfed tend to be older, from a higher socioeconomic background, have achieved higher levels of education, and participate in health-promoting behaviors in comparison with non-breastfeeding mothers.[23,24] Maternal characteristics, such as living in lower socioeconomic areas, have been strongly associated with not breastfeeding over subsequent births,[25] but residual confounding attributed to unmeasured factors may remain an issue. These socioeconomic factors and health-promoting behaviors may also potentially bias the association between breastfeeding and CVD outcomes, and although previous studies have adjusted for their confounding effects,[14–17,20,21] they did not investigate potential effect modification by socioeconomic status and overall lifestyle.

The aims of this article were to examine the association between breastfeeding and CVD hospitalization and mortality in a large cohort of middle-aged and older parous women. Findings from this study can help build the evidence base for breastfeeding as an additional strategy to prevent CVD.

## Methods

The authors declare that all supporting data are available within the article (and its online supplementary files).

## Study Population

The Sax Institute's 45 and Up Study is a large-scale, prospective cohort study of 123 815 men and 143 073 women aged ≥45 years residing in the state of New South Wales (NSW), Australia. From 2006 to 2009, potential participants were randomly sampled from the Department of Human Services enrollment database, the national health insurance provider, and were invited to take part in the study. Individuals joined the study by completing a postal questionnaire and providing informed consent for follow-up, which included linkage of questionnaire data to population health databases. The study methods have been described in detail elsewhere.[26]

We included all women who completed a baseline questionnaire. Women who reported that they had ever been diagnosed with or recently treated for CVD (self-reported heart disease, stroke, or blood clot: n=21 797) or with a hospital admission in the 6 years preceding study entry (with a CVD diagnosis code in any diagnostic field or a CVD-related procedure code in any procedure code field[27]; n=13 323) were excluded from analysis. We further excluded those who were nulliparous (never given birth; n=15 654) or with unknown parity (n=918) at baseline and parous women with unknown breastfeeding duration (n=2187). The final study sample included 100 864 women with reported breastfeeding duration. A participant flow chart for this study is provided in Figure.

The 45 and Up Study received ethics approval from the University of NSW Human Research Ethics Committee. Approval to use data from the 45 and Up Study for this article was obtained from the NSW Population and Health Services Ethics Committee.
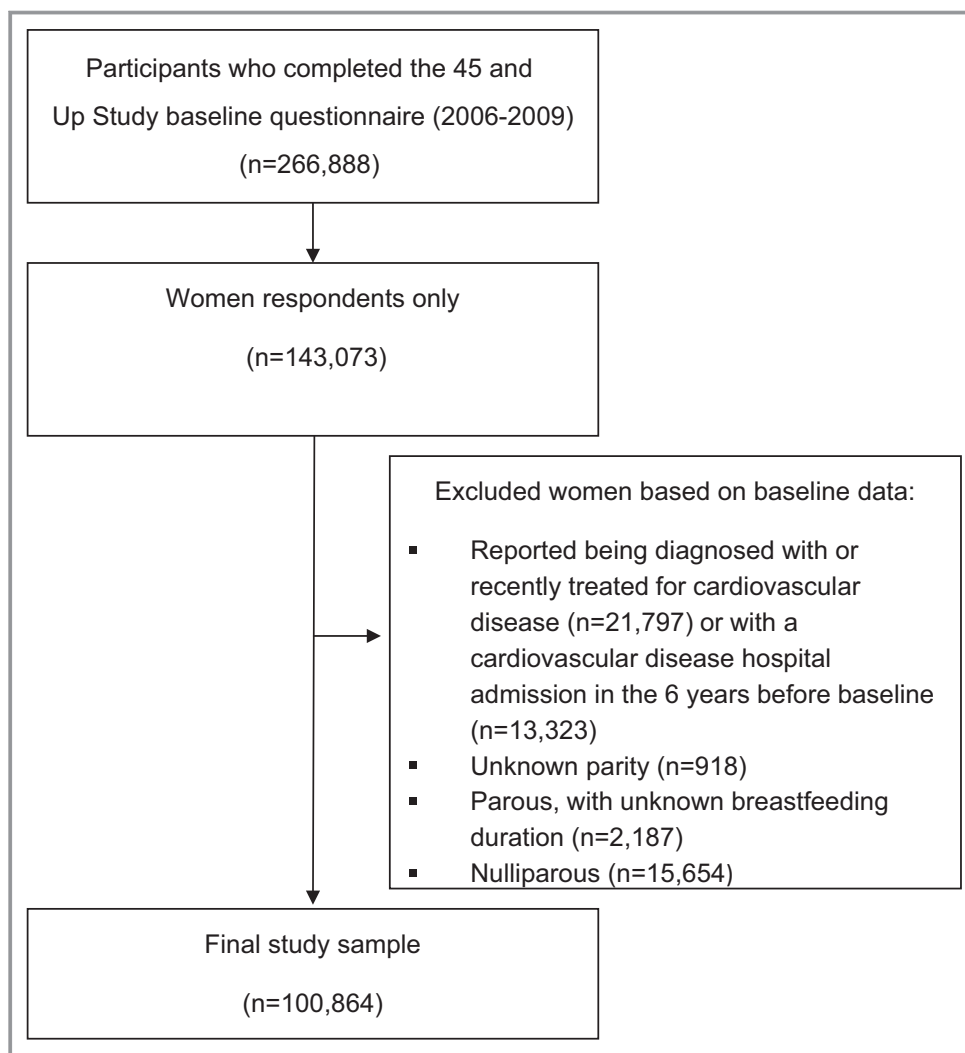
**Figure.** Participant flow chart.

## Measurement

### Exposure

The baseline questionnaire for women (available at http://www.saxinstitute.org.au/our-work/45-up-study/questionnaires/) included self-reported information on sociodemographic and lifestyle factors, height and body weight, and medical and reproductive history. Women were asked to report the number of children they had given birth to and also the cumulative amount of time spent breastfeeding across all pregnancies, based on the question: "For how many months, in total, have you breastfed?" The average breastfeeding duration per child was derived from answers to these questions and categorized as never breastfed, >0 to 6 (<6) months, >6 to 12 months, or >12 months. Breastfeeding was also explored as a binary variable in terms of whether a woman had ever versus never breastfed (also referred to as breastfeeding history).

### Outcomes

Baseline questionnaire data were linked to hospital data from the NSW Admitted Patient Data Collection (APDC; until June 2014), mortality data from the NSW Registry of Births, Deaths, and Marriages (until June 2014), and data on causes of death from the Cause of Death Unit Record File (until December 2013) by the Centre for Health Record Linkage (CHeReL, NSW, Australia) using probabilistic record linkage methods and a commercially available software (ChoiceMaker; ChoiceMaker Technologies Inc., New York, NY). The probabilistic data linkage conducted by CHeReL has been reported to be highly accurate with false-positive and -negative rates below 0.4% (http://www.cherel.org.au/quality-assurance). A recent study has also shown that the accuracy of probabilistic linkage is unlikely to vary by socioeconomic status in older adults.[28]

The APDC is a complete census of all public and private hospital admissions in NSW that includes details of

admissions, such as dates of admission and discharge, and records all related diagnoses for each admission. These are coded using the World Health Organization *International Classification of Diseases, Tenth Revision–Australian Modification* (*ICD-10-AM*) system. The NSW Registrar of Births, Deaths, and Marriages captures all deaths in NSW with causes subsequently coded using the *ICD-10-AM* classification. In both data sources, the first CVD hospitalization or death since baseline was based on a primary diagnosis of CVD of either ischemic heart disease (*ICD-10-AM* codes: I20–I25) or cerebrovascular disease (*ICD-10-AM* codes: I61–I67, I69).[29,30]

## Covariates

Multivariable analyses were adjusted for a range of sociodemographic and lifestyle factors, and medical and reproductive history based on self-reported responses in the baseline survey. Sociodemographic variables included age (45–54, 55–64, or ≥65 years), country of birth (Australia/other), highest educational qualification (≤10 years of schooling, high school/trade apprenticeship/certificate/diploma, or university degree/higher), marital status (married/living with a partner or single/widowed/divorced/separated) and area-level socioeconomic status (population-level quintiles based on the Socio-Economic Indexes For Area—Index of Relative Socio-Economic Disadvantage[31]). Lifestyle factors were based on responses at baseline and used as a marker of health-related behaviors. These included body mass index (kg/m$^2$; calculated as weight divided by height squared), smoking status (never, past, or current), alcohol intake (≤14 or >14 drinks/week[32]), physical activity (assessed using validated questions from the Active Australia Survey[33]; categorized as <150, 150–299, or ≥300 minutes per week), multivitamin use (for most of the last 4 weeks; yes/no), omega 3 or fish oil use (yes/no), use of aspirin (yes/no), and oral contraceptive use (ever/never). Reproductive history was based on number of children given birth to (1, 2, 3, or ≥4), mother's age for first child, and mother's age for last child. Medical history was assessed using family history of CVD (yes/no), family history of hypertension (yes/no), family history of diabetes mellitus (yes/no), self-reported hypertension/recent treatment for hypertension (yes/no), and self-reported diabetes mellitus/recent treatment for diabetes mellitus (yes/no).

## Statistical Analysis

Baseline participant characteristics by breastfeeding history and duration are presented as means (SD) for continuous variables and as percentages for categorical variables. Differences in baseline characteristics were assessed using chi-square tests for categorical variables, Student *t* tests for continuous variables with binary breastfeeding categories, and

F statistics from ANOVA for continuous variables with multiple lactation categories. Crude and adjusted hazard ratios (HRs) with 95% CIs were estimated for associations between either breastfeeding history or average breastfeeding duration per child and CVD outcomes by using Cox proportional hazards models. Separate models were used for CVD hospitalizations and CVD deaths with a time scale in years. In the analyses of incident CVD hospitalization, CVD death before hospitalization was not treated as a competing outcome; instead, participants were censored at death irrespective of cause of death. Eligible women contributed person-years from date of recruitment until admission date, date of death, or end of follow-up (June 18, 2014), whichever was the earliest; end of follow-up was December 31, 2013 for analyses of CVD mortality. Proportionality assumptions were verified based on the methods of Lin et al.[34] The "never breastfed" category was used as the reference category. Left-truncated data were used to adjust for different CVD risk exposure times for each woman before baseline entry into the study.[35] This approach helped to account for differences in the time that some women may have been diagnosed with CVD in the months or years preceding enrollment in the study. For each of the CVD outcomes, 4 sequential models were used: unadjusted models (model 1), models adjusted for parity and sociodemographic characteristics (number of children, age, country of birth, educational level, marital status, and area-level socioeconomic status; model 2), models further adjusted for lifestyle factors (body mass index, smoking status, alcohol intake, and physical activity; model 3), and models further adjusted for medical and reproductive covariates (multivitamin 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 mellitus, self-reported hypertension/recent treatment for hypertension, and self-reported diabetes mellitus/recent treatment for diabetes mellitus; model 4). To account for potential interaction by socioeconomic status and lifestyle risk, multiplicative interaction terms were tested in the model, and analyses were stratified by educational attainment and a healthy lifestyle index, used as a marker for CVD lifestyle risk factors. The healthy lifestyle index has been adapted from a lifestyle risk index previously developed using the 45 and Up Study cohort[36] and the Healthy Heart Score developed by the Harvard School of Public Health.[37] It is based on the following 6 lifestyle risk factors scored individually as healthy (score=1) or not healthy (score=0): body mass index (<25 kg/m$^2$=1, ≥25 kg/m$^2$=0), physical activity level (<150 min/week=1; ≥150 min/week=0), smoking status (past/current smoker=0; never smoker=1), alcohol intake (≤14 drinks/week=1; >14 drinks/week=0), sleep (>7 to <9 h/day=1; <7 h/day or >9 h/day=0), and fruit and vegetable intake (<2 serves of fruit/day or <3 serves of fruit/day=0; ≥2 serves of fruit/day,

and ≥3 serves of vegetables/day=1). For the stratified analyses, the healthy lifestyle index was dichotomized as either healthy (sum of scores=5–6) or not healthy (sum of scores=0–4). Interactions were considered significant if $P<0.05$. Statistical significance was defined as $P<0.05$ and analyses were conducted using SAS software (version 9.3; SAS Institute Inc., Cary, NC).

## Results

### Participant Characteristics

Table 1 shows baseline sociodemographic characteristics and parity of the 100 864 parous women included in our study. Mean age of the sample was 60.2 (SD, 10.2) years. More than three-quarters (76.7%) of women were born in Australia, more than one-third (40%) had ≤10 years of education, three-quarters (75.4%) were married, and nearly two-thirds (61.3%) belonged to the 3 lowest socioeconomic population-level quintiles. Of all parous women, 87.6% had a history of breastfeeding. On average, women had 2.7 (SD, 1.2) children and breastfed for 5.4 (SD, 5.4) months per child. Compared with women who never breastfed, women who ever breastfed were more likely to be younger at baseline, have more children, a higher level of education, be married/living with a partner, and live in an area with higher socioeconomic quintile. Women that had ever breastfed were also less likely to be obese, smoke, and were more likely to engage in higher levels of physical activity and consume omega 3 or fish oil. The 45 to 54 years age group was more likely to have a higher breastfeeding duration per child than the older age groups. Those who breastfed >12 months, on average, per child were more likely to have a university degree. The lifestyle, medical, and reproductive characteristics of women at baseline are presented in Table S1.

### Breastfeeding and CVD Hospitalization/Mortality

Table S2 presents HR and 95% CI for the incidence of CVD hospitalization and mortality by breastfeeding history. During a mean follow-up of 6.1 years for CVD hospitalization, and 5.7 years for CVD mortality, there were 3428 (3.4%) first CVD-related admissions and 418 (0.4%) deaths. Compared with parous women who never breastfed, women who ever breastfed had lower risk of CVD hospitalization (model 4, HR [95% CI]: 0.86 [0.78, 0.96] $P=0.005$) and mortality from CVD (model 4, HR [95% CI]: 0.66 [0.49–0.88] $P=0.006$), in both unadjusted and adjusted models ($P<0.01$).

Table 2 shows HR and 95% CI for the incidence of CVD hospitalization and mortality by average breastfeeding duration per child. In both unadjusted and adjusted models, women who breastfed, on average, for >0 to 6 or >6 to

12 months per child had lower risk of CVD hospitalization (model 4, <6 months, HR [95% CI]: 0.86 (0.78, 0.96); >6–12 months: 0.85 [0.75–0.97]) and mortality (model 4, <6 months: 0.69 (0.51, 0.94); >6–12 months: 0.59 [0.41–0.84]), compared with women who never breastfed.

### Stratified Analyses

Overall, none of the tests for interaction were statistically significant (all $P>0.05$). In the stratified analysis by education, the association between breastfeeding and CVD outcomes were similar across education strata (Table S3), whereas, in the stratified analysis by healthy lifestyle index (Table S4), the association between breastfeeding and CVD hospitalization was nonsignificant in those with lower lifestyle scores ("not healthy") while protective in those with higher lifestyle scores ("healthy"). However, the association with CVD mortality was similarly protective in those with low and high lifestyle scores.

## Discussion

In this large cohort of parous women aged ≥45 years, ever breastfeeding and average breastfeeding duration up to 12 months per child were associated with lower risk of incident CVD hospitalization and CVD mortality. Following adjustment for sociodemographic, lifestyle-related, and reproductive variables, ever breastfeeding was associated with a 14% lower risk of CVD hospitalization and a 34% lower risk of mortality from CVD compared with never breastfeeding. Average breastfeeding duration per child up to 12 months was significantly associated with a ≈15% lower risk of incident CVD and a ≈40% lower risk of CVD mortality compared with never breastfeeding. Findings were mostly consistent among women from different socioeconomic backgrounds and with different lifestyle risk.

This longitudinal study provides further evidence that among childbearing women, breastfeeding may offer long-term cardiovascular health benefits. The protective nature of the association between breastfeeding history and CVD outcomes is generally consistent with findings from the few previous studies that have examined similar associations among parous women from large cohorts (Table S5).[15,16,20] Differences between studies in magnitude of the associations could be attributed to variation in follow-up periods, types of CVD and outcomes examined, covariate adjustment, and cohort characteristics. Compared with previous studies, this study was novel in that it examined associations in an Australian setting, included more sociodemographic and lifestyle covariates, and stratified analyses by socioeconomic status and a healthy lifestyle index.

Whereas previous studies have typically expressed breastfeeding duration in terms of lifetime breastfeeding duration, we

**Table 1.** Baseline Sociodemographic Characteristics and Parity 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 to 6 Months | >6 to 12 Months | >12 Months | P Value[§] |
| No. of subjects, % | 12 517 (12.4) | 88 347 (87.6) | | 56 049 (63.4) | 24 549 (27.8) | 7749 (8.8) | |
| Age group, % | | | | | | | |
| 45 to 54 y | 26.5 | 37.7 | <0.0001 | 29.5 | 47.3 | 66.9 | <0.0001 |
| 55 to 64 y | 42.7 | 34.0 | | 36.5 | 29.7 | 28.9 | |
| ≥65 y | 30.8 | 28.3 | | 34.0 | 23.0 | 4.2 | |
| Mean (SD) age for first child, y | 24.3 (5.15) | 25.1 (4.89) | <0.0001 | 24.3 (4.66) | 26.0 (4.74) | 28.1 (5.29) | <0.0001 |
| Mean (SD) age for last child, y | 28.9 (5.24) | 30.6 (4.96) | <0.0001 | 29.8 (4.93) | 31.6 (4.64) | 33.4 (4.7) | <0.0001 |
| Parity | | | | | | | |
| Mean (SD) parity (no. of births) | 2.4 (1.13) | 2.7 (1.18) | <0.0001 | 2.8 (1.2) | 2.8 (1.15) | 2.6 (1.13) | <0.0001 |
| 1 child, % | 19.0 | 8.7 | <0.0001 | 16.7 | 9.5 | 3.9 | <0.0001 |
| 2 children, % | 43.7 | 39.8 | | 47.7 | 46.4 | 41.5 | |
| 3 children, % | 23.8 | 31.2 | | 24.3 | 29.8 | 35.0 | |
| ≥4 children, % | 13.5 | 20.3 | | 11.3 | 14.3 | 19.6 | |
| Country of birth, % | | | | | | | |
| Australia | 72.0 | 77.3 | <0.0001 | 74.0 | 76.1 | 79.7 | <0.0001 |
| Other | 28.0 | 22.7 | | 26.0 | 23.9 | 20.3 | |
| Highest education, %[‖] | | | | | | | |
| University and higher | 11.1 | 23.8 | <0.0001 | 16.3 | 21.3 | 27.0 | <0.0001 |
| High school/trade apprenticeship/ certificate/diploma | 33.3 | 38.4 | | 37.1 | 37.9 | 39.4 | |
| ≤10 y | 55.6 | 37.8 | | 46.6 | 40.8 | 33.6 | |
| Marital status, %[¶] | | | | | | | |
| Married/living with a partner | 72.7 | 75.8 | <0.0001 | 74.6 | 75.0 | 76.7 | <0.0001 |
| Single/divorced/separated/widowed | 27.3 | 24.2 | | 25.4 | 25.0 | 23.3 | |
| Socioeconomic status (SEIFA-IRSD), %[#] | | | | | | | |
| Quintile 1 (most disadvantaged) | 23.2 | 19.7 | <0.0001 | 21.1 | 19.8 | 18.2 | <0.0001 |
| Quintile 2 | 20.3 | 19.5 | | 20.1 | 18.8 | 19.0 | |
| Quintile 3 | 22.5 | 21.4 | | 21.8 | 21.2 | 20.7 | |
| Quintile 4 | 19.0 | 19.6 | | 19.7 | 19.6 | 20.0 | |
| Quintile 5 (least disadvantaged) | 15.0 | 19.8 | | 17.3 | 20.5 | 22.0 | |

SEIFA-IRSD indicates Socio-Economic Indexes For Area—Index of Relative Socio-Economic Disadvantage.

*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.

[‖]1325 missing.

[¶]268 missing.

[#]66 missing.

chose to present breastfeeding duration as the average duration per child to help standardize findings, better account for parity, and facilitate interpretation of findings. We modeled average breastfeeding duration as a categorical variable because of the nonlinearity of the distribution and chose clinically relevant cut

points based on breastfeeding guidelines. This study showed that an average breastfeeding duration per child up to 12 months was associated with lower risk of incident CVD hospitalization and mortality compared with never breastfeeding. To our knowledge, there have been only 2 previous studies that have examined the

**Table 2.** Hazard Ratios and 95% CIs for the Incidence of CVD Hospitalization and Mortality in Parous Women by Average Breastfeeding Duration Per Child*

| Average Breastfeeding Duration Per Child* | No. of People, 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) |
|---|---|---|---|---|---|---|---|
| CVD hospitalization | | | | | | | |
| Never breastfed | 12 517 | 76 164 | 527 | Reference | Reference | Reference | Reference |
| >0 to 6 months | 56 049 | 342 296 | 2076 | 0.82 (0.74, 0.91) | 0.84 (0.76, 0.93) | 0.86 (0.77, 0.95) | 0.86 (0.78, 0.96) |
| >6 to 12 months | 24 549 | 150 489 | 708 | 0.77 (0.68, 0.87) | 0.79 (0.70, 0.89) | 0.84 (0.74, 0.96) | 0.85 (0.75, 0.97) |
| >12 months | 7749 | 47 911 | 117 | 0.80 (0.65, 0.99) | 0.84 (0.68, 1.04) | 0.89 (0.71, 1.12) | 0.89 (0.71, 1.12) |
| CVD mortality | | | | | | | |
| Never breastfed | 12 517 | 71 730 | 66 | Reference | Reference | Reference | Reference |
| >0 to 6 months | 56 049 | 321 326 | 247 | 0.69 (0.53, 0.92) | 0.74 (0.56, 0.98) | 0.69 (0.51, 0.94) | 0.69 (0.51, 0.94) |
| >6 to 12 months | 25 549 | 140 605 | 96 | 0.53 (0.38, 0.73) | 0.56 (0.40, 0.79) | 0.59 (0.41, 0.85) | 0.59 (0.41, 0.84) |
| ≥12 months | 7749 | 44 453 | 9 | 0.76 (0.36, 1.61) | 0.80 (0.38, 1.69) | 0.70 (0.30, 1.65) | 0.67 (0.28, 1.57) |

CVD indicates cardiovascular disease.

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

[†]Model 1 was unadjusted.

[‡]Model 2 was adjusted for parity (number of children) and sociodemographic characteristics (age, country of birth, educational level, marital status, area-level socioeconomic 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: multivitamin 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 mellitus, self-reported hypertension/recent treatment for hypertension, and self-reported diabetes mellitus/recent treatment for diabetes mellitus.

association between average breastfeeding duration per child and CVD outcomes (Table S5)[15,16] and both have reported inverse associations. In the case-cohort study nested within EPIC (European Prospective Investigation into Cancer and Nutrition), an average breastfeeding duration ≥6 months, the highest breastfeeding duration considered, was associated with a 33% lower risk of incident ischemic heart disease.[15] In the China Kadoorie Biobank study, each additional 6 months of breastfeeding per child was associated with a 4% and 3% lower risk of incident ischemic heart disease and stroke, respectively.[16] However, different breastfeeding measures and study settings may limit the comparability of findings across studies.

In the present study, there was no clear evidence for a dose-response relationship between average lactation duration per child and CVD outcomes. In agreement with findings from our study, there was no solid evidence for a threshold or dose-response effect in the few studies that have examined average breastfeeding duration per child.[15,16] Whereas inconsistent associations have been shown between lifetime breastfeeding duration and CVD mortality, findings from some studies suggest a potential threshold effect[18] or a U-shaped association.[21] However, further longitudinal research is needed.

## Strengths and Limitations

Strengths of this study include a large cohort size and prospective follow-up, which enabled us to examine the asso-

ciation between breastfeeding and long-term cardiovascular outcomes. Compared with previous studies, this study adjusted for a comprehensive range of covariates including relevant sociodemographic, lifestyle and reproductive factors, and sensitivity analyses stratified by socioeconomic status and a healthy lifestyle index were conducted.

Several limitations should be mentioned. As for all observational studies, residual confounding may be an issue. Mothers that have breastfed may generally lead healthier lifestyles and come from higher socioeconomic backgrounds[23,24] that could have contributed to the observed associations. However, adjusting for socioeconomic factors and lifestyle-related covariates did not alter the findings of this study, and associations appeared mostly consistent across different education and lifestyle categories. Some of the findings should nonetheless be interpreted with caution because of small cell-sample sizes in some of the stratified analyses, and particularly in relation to CVD mortality. Our results may also be subject to reverse causation. From the data collected, we could not assess whether women had pre-existing metabolic conditions, such as obesity and type 1 diabetes mellitus, or conditions during pregnancy, such as pre-eclampsia and gestational diabetes mellitus, which could have unfavorably influenced breastfeeding practice.[38–40] Breastfeeding duration was assessed retrospectively many years later and may be prone to recall bias, which can lead to under- or over-reporting of breastfeeding duration.[41] However,

maternal recall of lactation has been shown to be a valid and reliable measure,[41] even many years following weaning.[42] Finally, it was also not possible to assess the exclusivity of breastfeeding (ie, whether other complementary foods were being offered to breastfed children), which is a measure of breastfeeding intensity.

## Implications and Conclusions

With CVD being the leading cause of death in women, it is important to explore a range of strategies by which CVD can be prevented, involving established as well as emerging lifestyle behaviors. This study provides evidence that ever breastfeeding and average breastfeeding duration up to 12 months per child were associated with substantially lower risk of CVD hospitalization and mortality. Although further longitudinal studies are needed to achieve greater consensus, findings from this study add to the growing evidence base for the long-term benefits of breastfeeding for maternal cardiovascular health, promoting added benefits of breastfeeding beyond known benefits for infants and short-term benefits for mothers, and support breastfeeding as an important strategy by which parous women can reduce their risk of developing and dying from CVD.

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## Disclosures

None.

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# 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 | 88,347 | | 56,049 | 24,549 | 7,749 | |
| | (12.4) | (87.6) | | (63.4) | (27.8) | (8.8) | |
| *BMI category[ǁ] (%)* | | | | | | | |
| 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 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 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 |
|---|---|---|---|---|---|---|---|

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/m$^2$=score 1, ≥25 kg/m$^2$=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.

\*\*\* 9 missing.

††† 9 missing.

‡‡‡ 9 missing.

**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) |
|---|---|---|---|---|---|---|---|
| *CVD hospitalisation* | | | | | | | |
| **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 |
| *CVD mortality* | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **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) |
|---|---|---|---|---|---|
| *CVD hospitalisation* | | | | | |
| 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 breastfed** | 6,830 | 41,444 | 320 | Reference |
| | **>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) |
| *CVD mortality* | | | | | |
| University and higher | **Never breastfed** | 1,362 | 7,808 | <5 | Reference |
| | **>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 breastfed** | 4,089 | 23,470 | 20 | Reference |
| | **>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 breastfed** | 6,830 | 39,118 | 41 | Reference |
| | **>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) |
|---|---|---|---|---|---|
| *CVD hospitalisation* | | | | | |
| 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) |
| *CVD mortality* | | | | | |
| 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/m$^2$=score 1, ≥25 kg/m$^2$=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: | | | Education level, BMI, physical activity, smoking status/intensity and duration, menopausal status |
| | | | | Circulatory disease | Never | Reference | |
| | | | | | Ever | 0.80 (0.70, 0.91) | |
| | | | | Cerebrovascular disease | Never | Reference | |
| | | | | | Ever | 0.94 (0.74, 1.21) | |
| | | | | IHD | Never | Reference | |
| | | | | | Ever | 0.69 (0.54, 0.87) | |

| Peters et al. (2016) [2] | 10 European countries, case-cohort study nested within EPIC study | 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 | Reference | Study centre, age, education level, BMI, smoking status, number of live births, high blood pressure, HDL cholesterol, total cholesterol, history of diabetes mellitus |
| | | | | | Ever | 0.71 (0.52, 0.98) | |
| | | | | | Average breastfeeding duration/child | | |
| | | | | | Never | | |
| | | | | | >0-<1 month | 1.00 (0.73, 1.37) | |
| | | | | | ≥1-<3 months | 0.77 (0.63, 0.94) | |
| | | | | | ≥3-<6 months | 0.69 (0.61, 0.78) | |
| | | | | | ≥6 months | 0.67 (0.57, 0.77) | |
| | | | | | | 0.67 (0.56, 0.80) | |

| 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<br>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<br>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<br>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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