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# Lactation and Maternal Cardio-Metabolic Health*

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## Abstract

Researchers hypothesize that pregnancy and lactation are part of a continuum, with lactation meant to "reset" the adverse metabolic profile that develops as a part of normal pregnancy, and that when lactation does not occur, women maintain an elevated risk of cardio-metabolic diseases. Several large prospective and retrospective studies, mostly from the United States and other industrialized countries, have examined the associations between lactation and cardio-metabolic outcomes. Less evidence exists regarding an association of lactation with maternal postpartum weight status and dyslipidemia, whereas more evidence exists for an association with diabetes, hypertension, and subclinical and clinical cardiovascular disease.

### Keywords

breastfeeding; hypertension; diabetes; dyslipidemia; cardiovascular disease; metabolic syndrome

## INTRODUCTION

Cardiovascular diseases are the leading cause of death globally (80). The modification of key risk factors, including obesity, poor diet, physical inactivity, high blood pressure, and dyslipidemia, could prevent many of these deaths (80), and identification of any additional potential risk or protective factors could reduce the high burden of cardiovascular diseases. In 2007, the Agency for Healthcare Research and Quality (AHRQ) published a review examining the effects of lactation on maternal and child health outcomes in developed countries (30). Regarding maternal outcomes, the review found that among parous women, each additional year of lactation was associated with a 4% to 12% reduced risk of type 2 diabetes (from here on referred to as diabetes), whereas there was inconsistent evidence on the association between lactation and postpartum weight retention (30); other maternal



**DISCLOSURE STATEMENT**

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

**DISCLAIMER**

The findings and conclusions in this review are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

cardio-metabolic outcomes were not included. However, since the publication of the AHRQ review, which included studies published through 2005, a number of studies have examined the association between lactation and some of these cardio-metabolic outcomes. The current review summarizes the evidence of the association between lactation and maternal cardio-metabolic health, including weight status, diabetes, dyslipidemia, hypertension, cardiovascular disease, and the metabolic syndrome (MetS).

## METHODS

We conducted literature searches for each outcome separately, recognizing that overlap would likely exist in studies that included multiple metabolic outcomes. We searched Medline, Embase (Excerpta Medica Database), and CINAHL (Cumulative Index to Nursing and Allied Health Literature) for articles published through August 2015, with key words such as breastfeeding, lactation, weight loss, body mass index (BMI), obesity, diabetes, insulin resistance, cardiovascular disease, lipids, hypertension, blood pressure, and MetS. We identified additional studies from the reference lists of the studies identified in our original searches. For weight status and diabetes outcomes, we identified recent systematic reviews (3, 31, 54) that serve as the basis for these sections, with other key or newly published studies also described. We found no systematic reviews describing how lactation is associated with maternal dyslipidemia, hypertension, cardiovascular disease, or MetS. For these outcomes, we reviewed relevant literature to summarize the associations. Descriptive information about several of the key studies referenced throughout the review is presented in Table 1.

## WEIGHT STATUS

### Short Term

Postpartum weight retention, regardless of gestational weight gain, is a predictor of long-term weight retention and higher BMI at least 10 to 15 years after pregnancy (39, 65). This is concerning because a significant proportion of women retain large amounts of weight after pregnancy (18, 27, 43), and excess weight is a strong risk factor for cardiovascular disease. A meta-analysis found that obesity in women, assessed by BMI, was associated with an increased incidence of multiple chronic conditions, including diabetes [relative risk (RR) 12.41, 95% confidence interval (CI) 9.03, 17.06], hypertension (RR 2.42, 95% CI 1.59, 3.67), and coronary artery disease (RR 3.10, 95% CI 2.81, 3.43) (22).

A portion of the body fat stored during pregnancy serves as an energy reserve for lactation (8). Thus breastfeeding, in theory, may contribute to weight loss and mobilization of fat deposits. A recent systematic review found significant methodological challenges in summarizing studies that examined the relationship between breastfeeding and postpartum weight change; 35 prospective and 8 retrospective studies that included breastfeeding women two years or less postpartum were reviewed (54). Most studies, including 21 of 35 (60%) prospective and 6 of 8 (75%) retrospective studies, reported no significant relationship between breastfeeding and weight change. However, many of these studies had limitations, such as relying on self-reported weight, not adjusting for potential confounding factors, small sample sizes ($n < 60$), and short durations of follow-up (22 studies only

assessed weight change through 6 months postpartum). Four of the five prospective studies with more robust methods, including objectively measured postpartum weight change, adjustment for key covariates, and follow-up for ≥12 months, found decreased weight retention among women who breastfed. Fourteen prospective studies examined some combination of breast-feeding intensity and duration, and six prospective studies examined breastfeeding intensity only. Together, these studies suggest that breastfeeding for at least 6 months, and in several studies longer, and exclusive or predominant breastfeeding for 5 to 6 months may be associated with greater postpartum weight loss.

This systematic review also examined the association between breastfeeding and change in body composition (e.g., skinfold thickness, fat-free mass, or fat mass) in 18 prospective studies (54). No significant association between breastfeeding and change in body composition in the first two years postpartum was found among 13 of the studies. Many of these studies, however, were limited by small sample sizes and lack of adjustment for key confounding factors, leading the authors to conclude there was insufficient evidence to assess whether an association existed between breastfeeding and change in body composition.

Two large studies that examined weight status in the short term were not included in the review. Among 17,343 mothers in the prospective Norwegian Mother and Child Cohort Study, lactation was associated with a modest reduction in postpartum weight retention. For each additional month of full breastfeeding (no infant formula, other milks, or solid foods) through 6 months, maternal weight at 36 months postpartum was lower by 0.14 kg/month, adjusting for prepregnancy BMI, gestational weight gain, age, and parity (6). Among a national sample of 10,524 mothers in Ireland, those who breastfed >1 to <6 months and 6 months or more had a lower odds of obesity [odds ratio (OR) 0.80, 95% CI 0.66, 0.97 and OR 0.65, 95% CI 0.52, 0.81, respectively] at 9 months postpartum compared to mothers who did not breastfeed (76). This analysis did account for parity and gestational weight gain, but no data on prepregnancy BMI were available.

### Longer Term

Four large studies have examined how lactation was associated with weight status in later life. Baseline data from the Norwegian Nord-Trøndelag Health Study (HUNT2) of 21,368 parous women indicated that among women ≤50 years of age, the odds of obesity for those who never breastfed was 3.37 times higher (95% CI 2.51, 4.51) compared to women with a lifetime duration of breastfeeding ≥24 months (52). A dose-response relationship was observed, with the odds of obesity decreasing as the months of lifetime lactation increased. However, among women >50 years of age, this association was no longer observed. In an analysis of baseline data from the Million Women Study (United Kingdom), among 740,628 postmenopausal women (mean age 57.5 years), BMI increased with number of births but was lower the longer average duration of breastfeeding per child, at every level of parity. Overall, mean BMI was 0.22 kg/m$^2$ lower for each additional six months of breastfeeding (5). Two other large studies found no association between lactation and later weight status. The Promotion of Breastfeeding Intervention Trial (PROBIT) randomized maternity facilities to a breastfeeding support intervention versus standard of care at 31 hospitals in

Belarus. All women initiated breastfeeding, and rates of breastfeeding duration and exclusivity were greater in the intervention group than in the control; however, overall breastfeeding rates were still generally low (49.8% and 36.1% rates, respectively, for any breastfeeding at six months, and 43.3% and 6.4% rates, respectively, for exclusive breastfeeding at three months) (36). Maternal BMI was assessed among approximately 11,800 mothers from the PROBIT study (mean age 25 years at baseline) at 11.5 years postpartum and was similar in the intervention and control groups (difference −0.06, 95% CI −0.62, 0.48) (58). Findings were similar when the data were analyzed using women's actual breastfeeding duration instead of comparing intervention with control group. In an analysis of enrollment data from more than 139,000 postmenopausal women with at least one live birth participating in the Women's Health Initiative (mean age 63 years), no association existed between lifetime duration of lactation and obesity in fully adjusted models (68). These large studies suggest that although breastfeeding may mitigate the increased risk of weight retention associated with increased parity, this effect may be reduced as a woman ages. A major limitation of these studies is that it is not possible to determine if women who breastfed had a lower BMI before pregnancy.

## Visceral Adiposity

During pregnancy, women develop increased stores of visceral fat (34), which is more strongly associated with cardio-metabolic risk factors than subcutaneous abdominal adipose tissue, which is typically greater in volume (20). Two retrospective studies have examined how lactation is associated with visceral adiposity specifically. One study assessed abdominal adiposity by computed tomography in 89 women who were on average seven years postpartum. Visceral adiposity varied by lactation history, whereas waist circumference did not. Compared to women who breastfed each child for ≥3 months, women who never breastfed or who breastfed any child for <3 months had 36.96 $cm^2$ and 20.38 $cm^2$ greater visceral adiposity, respectively, in models adjusted for parity, current BMI, and other potential confounders (45). In an ancillary study of the US multisite Study of Women's Health Across the Nation (SWAN), SWAN-Heart, that included women aged 45 to 58 years, visceral adiposity was assessed by computed tomography (47). Among premenopausal and early-perimenopausal parous women ($n$ = 170), those who never breastfed had 28% greater visceral adiposity and a 20% greater ratio of visceral to total abdominal fat compared to women who breastfed all children ≥3 months, adjusting for BMI, parity, and various demographic and lifestyle factors. The visceral adiposity of premenopausal and early-perimenopausal women who breastfed all children ≥3 months was similar to that of nulliparous women, which suggests that breastfeeding women had utilized fat deposits acquired during pregnancy. These relationships were not apparent among postmenopausal women ($n$ = 131).

In summary, excess postpartum weight retention is a risk factor for long-term obesity, placing women at increased risk for cardiovascular disease. A portion of body fat stored during pregnancy is used for lactation, but studies that examine the extent to which lactation contributes to post-partum weight loss have shown inconsistent results. A recent systematic review (54) concluded that evidence is insufficient to determine if associations exist between breastfeeding and weight retention and change in body composition in the first two years

postpartum. In addition, comparisons were limited because many studies had methodological limitations and different definitions of breastfeeding history and body composition. Several large studies have shown an inverse association between breastfeeding and obesity (5, 52, 76), with the effect appearing to depend on the duration and intensity of breastfeeding and the mother's age; however, this association has not been consistent across studies (58, 68). Data are limited but suggest that lactation may be associated with lower visceral adiposity among parous women until menopause.

## DIABETES

Both insulin resistance and glucose intolerance increase as part of normal pregnancy physiology, with a 44% increase in insulin resistance in nonobese pregnant women by 36 weeks' gestation (11). This relative hyperinsulinemic state helps support fetal nutrient delivery both by slowing glucose absorption by maternal tissue and by increasing maternal fat reserves (9). It is not surprising that parity has been shown to be a significant risk factor for diabetes, after controlling for BMI and other diabetes risk factors (16, 49, 55). Glucose and other carbohydrate stores are mobilized and expended for lactose production (10), and the diversion of this metabolic fuel for milk production may be the unifying mechanism by which lactation improves glucose regulation.

Several large prospective cohorts have examined the link between lactation and diabetes risk and have sought to establish the extent to which a dose-response relationship may exist. Most of these studies have shown a decrease in diabetes risk among parous women who have lactated compared to those who have not, after adjusting for parity, BMI, and other diabetes risk factors. Specifically, data from the prospective US Nurses' Health Studies (which include women aged 25 to 55 years at baseline) show that among women who had given birth in the previous 15 years, each additional year of lactation decreased diabetes risk by 14% to 15% compared to parous women who had not lactated, after controlling for BMI and other diabetes risk factors (73). A 4.6-year follow-up of a large cohort of Chinese women observed similar results: Benefits were seen with one year of lifetime breastfeeding and included further dose-dependent risk reductions (77).

These results raise the question of the minimum total lactation duration required to reduce diabetes risk. Upon enrollment in the prospective Women's Health Initiative, postmenopausal women with a lifetime lactation history of ≥12 months were less likely to have diabetes than were parous women who never breastfed (OR 0.80, $p < 0.001$), with a dose-response relationship seen as total duration of lactation increased (68). A lower odds of diabetes was seen even in women with the shortest total lifetime lactation duration range of one to six months (OR 0.91, 95% CI 0.84, 0.99). In an observational study of nearly 2,000 parous women aged 40 to 78 years, who were members of a large health maintenance organization in California, women who had breastfed all of their infants for at least one month had an odds of diabetes that was comparable to nulliparous women (OR 1.01, 95% CI 0.56, 1.81) (66). Conversely, women who gave birth yet never breastfed had a diabetes odds that was nearly double that of nulliparous women (OR 1.93, 95% CI 1.14, 3.27) (66). Exclusive breastfeeding for one to three months, as compared to nonexclusive breastfeeding,

was also associated with reduced odds of diabetes. These results suggest there may be a protective effect of breastfeeding, even with relatively short durations.

Although the majority of studies examining the impact of lactation on diabetes have shown a significant inverse association in extended postpartum follow-up, this finding is not entirely consistent across the lactation literature. In Project Viva, women were recruited at their first prenatal visit to clinics in eastern Massachusetts. Prepregnancy metabolic markers were not assessed. No consistent associations were found between lactation and hemoglobin A1c, insulin resistance, or fasting insulin after adjustment for BMI and waist circumference measured at three years postpartum (70). It is unlikely that these conflicting results are due to a waning of lactation's benefits over time because the large cohorts that found an association (66, 77) assessed participants much further postpartum than the three years in Project Viva. Although this cohort was much smaller than many others, and although intermediate end points were studied, these disparate results raise the question of which factors fundamentally mediate the diabetes risk reduction observed in multiple studies with large cohorts.

Two recent meta-analyses of prospective studies examined the association between lactation and maternal diabetes and investigated the extent to which this association was mediated by metabolic and biochemical factors. The first presented data on a new prospective cohort, the European Prospective Investigation into Cancer and Nutrition (EPIC-Potsdam) (31), and a meta-analysis of this study with three previous prospective studies, including the Nurses' Health Studies and the Shanghai Women's Health Study (73, 77). The authors found an inverse association between breastfeeding duration and diabetes risk after adjusting for multiple potential confounders [hazard ratio (HR) 0.89, 95% CI 0.82, 0.97]; the effect size was the same, but the association was no longer statistically significant after controlling for baseline BMI, waist circumference, and other biomarkers such as lipids (HR 0.89, 95% CI 0.69, 1.16). A second meta-analysis of six cohort studies [one of which studied women with prior gestational diabetes mellitus (GDM)] showed a significant dose-dependent (although nonlinear) decrease in diabetes risk with lactation, independent of BMI (3). In this analysis, the risk reduction was steepest with increasing breastfeeding from the shortest duration (approximately one to three months) to durations of approximately six to ten months. The conflicting results regarding the impact of weight in these two systematic reviews demonstrate the uncertainty of the mechanism of lactation's potentially protective effect on diabetes.

Women with prior GDM are at increased diabetes risk compared to parous women without prior GDM, with an overall RR for diabetes between seven (4) and thirteen (19). It is not surprising, therefore, that up to 50% of women will be diagnosed with diabetes within five to eight years after a pregnancy complicated by GDM (4, 33, 41). Although data are limited, evidence indicates that lactation may help reestablish postpartum glucose homeostasis and mitigate future diabetes onset among women with GDM. For example, in women with prior GDM, lactation is an independent predictor of higher insulin sensitivity, higher glucose tolerance, and lower insulin concentrations (14, 35). The benefits of lactation on glucose tolerance have been shown to persist after controlling for BMI (35). Evidence is lacking as to the duration of the benefits of lactation after women with a history of GDM wean, and

some existing data are limited by failure to control for other lifestyle behaviors and/or by assessment of diabetes incidence by self-report (23). Prospective studies that avoid these methodologic pitfalls are necessary to better delineate the mechanism and duration (including beyond the reproductive years) of the beneficial effects of lactation in women with a history of GDM.

One of the challenges to fully describing the mechanism of lactation with diabetes is the issue of directionality. Emerging evidence suggests that insulin resistance interferes with lactogenesis and lactation (56), and therefore successful breastfeeding may be a marker of more favorable glucose tolerance rather than a cause of it. Additionally, both prepregnancy obesity and GDM requiring insulin treatment during pregnancy are associated with delayed lactogenesis (44), and GDM requiring insulin is associated with impaired infant sucking patterns (7). Taken together, these findings raise the question of causation regarding the cardiovascular benefits associated with breastfeeding.

In conclusion, the majority of existing data from large diverse studies demonstrate a significant, dose-dependent inverse association between lactation and diabetes. The association is seen even with short durations of breastfeeding and in women with a history of GDM. Further research is needed to fully understand the issue of directionality and the extent to which the relationship may be mediated by postpartum weight retention or other biomarkers.

## DYSLIPIDEMIA

As pregnancy progresses, women develop an atherogenic lipid profile, including significantly elevated levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides (17, 40). These metabolic changes accommodate the demands of the growing fetus and help to prepare for lactation. One of the most significant changes, maternal hypertriglyceridemia, is beneficial to the fetus and newborn through several mechanisms: Circulating triglycerides aid in the transfer of essential fatty acids to the fetus (28) and can be quickly converted to ketone bodies for use by the fetus during a state of maternal fasting (28, 29).

Lactation serves as a route of physiologic excretion for triglycerides and cholesterol. As the demand for triglycerides increases in the lactating mother, it is met by enhanced catabolism of very-low-density lipoproteins and generation of increased high-density lipoprotein (HDL) components (63), leading to a more rapid decline in triglycerides (10, 17, 32, 63). In addition, large amounts of cholesterol are secreted in milk, thereby reducing maternal serum concentrations, although serum lipid concentrations may return to normal levels after lactation ends (32). Some investigators have hypothesized that lactation serves to reset the abnormal metabolic changes that occur during pregnancy (72), suggesting that if a mother does not lactate, she may have a persistent adverse metabolic profile, leading to an increased risk of cardiovascular disease.

At least two prospective studies have examined this association (25, 70). The multicenter Coronary Artery Risk Development in Young Adults (CARDIA) study did not find

significant differences in change in total cholesterol, LDL, or triglyceride concentrations by lactation duration (<3 months versus ≥3 months) at a three-year follow-up among women with a single live birth during the follow-up period (25). This lack of a statistically significant difference was hypothesized to be due to the small number of women studied (*n* = 109). However, the same study found that the decrease in HDL from preconception to postweaning was smaller among parous women who breastfed for ≥3 months versus <3 months (−1.3 mg/dl versus −7.3 mg/dl, $p < 0.01$). In Project Viva participants, among a subsample of women with a fasting blood sample (*n* = 175), there was no association between breastfeeding duration and total cholesterol, LDL cholesterol, or triglycerides at three years postpartum (70); although breastfeeding data and weight status were collected prospectively, metabolic markers were available only at the follow-up, so change in these biomarkers could not be assessed. The authors did note a higher HDL cholesterol level with 3 to <6 months of breastfeeding but not with longer breastfeeding durations, which was described as a probable chance finding. The authors noted that the women who participated in Project Viva may have been a healthier group in general, and thus the differences in metabolic markers due to lactation may have been too small to detect (70).

Baseline data from the Women's Health Initiative (*n* = 139,681) demonstrated a reduced odds of self-reported hyperlipidemia (defined as the need to use medication to control cholesterol) with increasing breastfeeding duration (OR 0.93, 0.88, 0.81, and 0.80 for breastfeeding durations of 1–6, 7–12, 13–23, and ≥24 months, respectively) compared to parous women who never breastfed (68). Models controlled for numerous potential confounders including BMI, family history of diabetes or cardiovascular disease, physical activity, and dietary intake. However, the outcome may have been misclassified due to self-report of hyperlipidemia; additionally, it is not possible to assess whether women may have had dyslipidemia before becoming pregnant. In the Norwegian HUNT2 study (52), nonfasting serum lipids were assessed among approximately 20,000 parous women aged 20 to 85 years. This study found a significant inverse, dose-response relationship of lifetime duration of lactation with total cholesterol, LDL cholesterol, and triglycerides, and a positive association with HDL for women <50 years, but not among women ≥50 years. In SWAN, 12-hour fasting blood samples were collected at baseline among a diverse group of women aged 42 to 52 years (64). Lactation history was not associated with HDL or triglycerides. No data on total cholesterol or LDL were described, as the focus of the manuscript was MetS, of which low HDL and elevated triglycerides are components.

Several other smaller retrospective studies have also examined how lactation is associated with serum lipids. A study of 212 Finnish women who gave birth 16 to 20 years earlier found that women who had breastfed for a short (<6 months) duration had higher total cholesterol, LDL cholesterol, and triglycerides yet similar HDL cholesterol compared to women who had breastfed for a long (>10 months) duration (79). No differences in total cholesterol or LDL cholesterol were observed when short duration was compared to medium (>6 months to <10 months) duration; however, HDL cholesterol levels were lower among women with short compared to medium duration of breastfeeding. A smaller (*n* = 98) cross-sectional study of parous Norwegian women aged 25 to 35 years also revealed significantly higher concentrations of total cholesterol and triglycerides among women who breastfed <10 months compared to >10 months; HDL cholesterol levels did not differ, and LDL cholesterol

was not measured (75). The US Women and Infant Study of Healthy Hearts studied 607 women 5 to 10 years after giving birth (46). A decreasing trend in total cholesterol and triglycerides was identified among women who never breastfed, those who breastfed <3 months after some births, and those who breastfed ≥ 3 months after all births. A decreasing trend for LDL was suggested, although it was not statistically significant ($p = 0.09$) (46). There was no association between lactation and HDL.

In summary, two prospective studies (25, 70) have found little evidence of an association between lactation and serum lipids. Both had small samples and may not have been adequately powered to find these associations, and one only had data on the metabolic markers at baseline. Retrospective studies (44, 64, 68, 75, 79) have not found consistent evidence of an association between lactation and cholesterol or triglyceride concentrations. Differences in assessment of the outcome (self-report and fasting versus nonfasting serum lipids) and time since lactation may account for some of the inconsistencies in findings. Maternal health behaviors are also important factors to consider when interpreting results of these studies.

## HYPERTENSION

Physiologic changes during pregnancy include increased blood volume and cardiac output and reduced blood pressure (59). Small clinical studies have shown that lower blood pressure lasts up to at least 30 months postpartum (48). Whether parity is associated with blood pressure later in life is less clear, with some studies finding a reduced risk of hypertension with increasing number of pregnancies (53) and others finding no association (37). Whether or not studies accounted for lactation history could explain these inconsistent findings, as key hormones involved in lactation, including oxytocin and prolactin, are also associated with blood pressure regulation.

Three large prospective studies have assessed how lactation is associated with hypertension (38, 58, 74). Among a large ($n = 177,749$) cohort of premenopausal Korean women, lifetime duration of lactation up to 18 months was associated with a small reduced risk of hypertension compared to parous women who never breastfed (RR range 0.90–0.93 for 1–6, 7–12, and 13–18 months, $p < 0.05$), adjusting for age, parity, BMI, and other key covariates (38). However, there was no association with lifetime lactation >18 months (RR 1.00 and 1.06 for 19–24 months and >24 months, respectively). Among 44,198 parous women in the Nurses' Health Study II, women who did not breastfeed their first child, or who breastfed for shorter durations, were at increased risk of developing hypertension compared to mothers who breastfed their first child for ≥12 months [never breastfed HR 1.22, 95% CI 1.13, 1.30; >0–<3 months HR 1.24, 95% CI 1.15, 1.33; >3–<6 months HR 1.13, 95% CI 1.05, 1.22; >6–<9 months HR 1.09, 95% CI 1.01, 1.17; >9–<12 months HR 1.03 (not significant)]. The authors found similar results for women who never breastfed in comparison with those who breastfed each child for an average of ≥12 months (74). Among women assessed at 11.5 years after participation in PROBIT, no significant difference existed between intervention and control groups in either systolic or diastolic blood pressure (−0.23 mm Hg, 95% CI −2.71, 2.25 and −0.74 mm Hg, −2.02, 0.53, respectively) (58). Although PROBIT is a prospective cohort, no information on blood pressure before pregnancy was available, so it is

possible that some women had hypertension before giving birth. The authors argue that randomization of birth hospitals should have balanced this possibility across intervention versus control groups. Additionally, all women participating in PROBIT initiated breastfeeding, so this study is only able to compare longer with shorter durations among breastfeeding women. When the data were analyzed by actual breastfeeding duration, systolic blood pressure was found to be lower among women who breastfed for ≥6 to <9 months (−1.19 mm Hg, 95% CI −2.12, −0.25) compared to women who breastfed for >0 to <3 months); however, there was no association among women who breastfed for ≥9 months.

Several large retrospective studies have also examined the association between lactation and hypertension. At enrollment in the Women's Health Initiative, parous women with a lifetime lactation duration of ≥12 months had a reduced odds of hypertension compared to women who never breastfed (OR 0.88, $p < 0.001$), after adjusting for many confounders including parity, physical activity, dietary intake, smoking, and BMI (68). Among women <50 years at enrollment in the HUNT2 study, compared to women with a lifetime breastfeeding history of ≥24 months, parous women who never breastfed or had a lifetime breastfeeding duration of one to six months had an increased odds of hypertension (OR 1.88, 95% CI 1.41, 2.51 and OR 1.24, 95% CI 1.03, 1.49, respectively) in adjusted analyses (52). There were no significant associations between lactation and hypertension among women ≥50 years. An interaction with age was also found in the Australian 45 and Up Study ($n = 74{,}785$). Among parous women aged 45 to 64 years, lifetime duration of lactation of ≥6 months was associated with a lower odds of hypertension compared to women who never breastfed (42); the effect was stronger with longer durations of breastfeeding, with an OR range of 0.57 to 0.81. There was no association among women ≥64 years. In the SWAN study, each additional year of breastfeeding was associated with a reduced odds of hypertension (OR 0.90, $p < 0.05$). This association was adjusted for smoking, parity, high school BMI, and other potential confounders, but not current BMI (64). Finally, among more than 9,000 Chinese women with one lifetime birth (mean age 54 years), longer breastfeeding duration was associated with lower odds of hypertension compared to women who never breastfed (OR 0.87, 0.83, and 0.79 for duration >0–6, >6–12, and >12 months, respectively, all $p < 0.05$) (81). Breastfeeding rates among this sample of women were relatively low, with 47% who had never breastfed.

In summary, most studies, including several prospective (38, 58, 74) and large well-designed retrospective studies (43, 52, 64, 68, 81), have found breastfeeding to be associated with a lower risk of hypertension. Several studies have shown a dose-response relationship with longer durations of breastfeeding; however, this effect does not appear to persist into older age (42, 64, 81). Age is a strong independent risk factor for hypertension (21), and the protective effect of lactation may not be sufficient to overcome the risk of hypertension due to aging. We did not find any studies that addressed how lactation may be associated with hypertension among women who experienced preeclampsia or gestational hypertension; this is an area for future research.

## CARDIOVASCULAR DISEASE

Vascular changes, such as atherosclerotic plaques, carotid intima-media thickness, and increases in lumen and adventitial diameter, elevate the risk of cardiovascular disease (61). Several studies have examined the association between lactation and these markers of subclinical cardiovascular disease. In CARDIA, among 846 women who were without heart disease or diabetes at baseline and who gave birth during the follow-up period, a graded inverse association was identified between lactation duration and common carotid intima-media thickness at 20 years (26). In the SWAN-Heart study, Schwarz et al. (67) assessed aortic and coronary calcification, carotid adventitial diameter, intima-media thickness, and carotid plaque among 297 women 45 to 58 years old who were free of clinical cardiovascular disease. In analyses adjusted for socioeconomic status, lifestyle, and family history, women who reported no breastfeeding had increased odds of aortic (OR 3.85, 95% CI 1.47, 10.00) and coronary (OR 2.78, 95% CI 1.05, 7.14) calcification compared to women who reported breastfeeding each child for ≥3 months. After further adjustment for BMI and other cardiovascular risk factors (e.g., blood pressure, lipids, and glucose), the association remained significant only for aortic calcification (OR 5.26, 95% CI 1.47, 20.00). No significant associations were found between lactation and carotid plaque, carotid adventitial diameter, or intima-media thickness. In the Women and Infants Study of Healthy Hearts, carotid lumen diameters were 0.13 mm (95% CI 0.04, 0.22) larger and adventitial diameters were 0.12 mm (95% CI 0.02, 0.22) larger among parous women who never breastfed compared to women who reported breastfeeding for ≥3 months after each birth (46). This analysis accounted for a series of maternal, family, and health-related factors, including maternal BMI; C-reactive protein; blood pressure; and levels of lipids, glucose, and insulin.

Three prospective studies have examined the association of lactation with cardiovascular events. In the Nurses' Health Study, among approximately 89,000 parous women, those with a lifetime lactation duration of >23 months had a lower incidence of myocardial infarction compared to women who never breastfed (HR 0.63, 95% CI 0.51, 0.77) (71). This relationship was attenuated slightly after adjustment for multiple cardiovascular and lifestyle risk factors (HR 0.77, 95% CI 0.62, 0.94) but remained significant. In the Women's Health Initiative, among 59,769 postmenopausal parous women with an average of 7.9 years of follow-up, overall there was no association with lifetime duration of lactation and incident cardiovascular disease (including coronary heart disease, stroke, and congestive heart failure); however, there was an interaction with age. Among women who were age 50 to 59 years at baseline, those with a lifetime lactation of 7 to 12 months or ≥24 months were less likely to develop cardiovascular disease (HR 0.80, 95% CI 0.67, 0.95 and 0.68, 95% CI 0.52, 0.89, respectively) compared to women who never breastfed (68). Stratified results were included in the text, but the association among women who breastfed 13 to 23 months was not described, suggesting it may not have been significant. Lactation history was not associated with incident cardiovascular disease among women who were ≥60 years at enrollment.

In the HUNT2 study, among women who had no cardiovascular disease prior to their first pregnancy, mortality from cardiovascular disease was assessed over 15 years of follow-up

from linkage to the death registry (51). Among parous women <65 years, those who never breastfed had an increased risk of cardiovascular mortality (HR 2.86, 95% CI 1.51, 5.39) compared to women who ever breastfed, after adjusting for parity and sociodemographic factors. This association remained significant after additionally adjusting for potential mediators including BMI, blood pressure, antihypertensive medication use, triglycerides, total cholesterol, and diabetes (HR 2.53, 95% CI 1.39, 4.99). No associations were found among women aged ≥65 years. Compared to other countries, Norway has relatively high breastfeeding rates. In the HUNT2 study, only 4% of women had never breastfed, and 20% of women <65 years had a lifetime lactation duration ≥24 months.

In summary, women who breastfeed for longer durations appear to have a lower risk of subclinical and clinical cardiovascular disease and cardiovascular mortality compared to parous women who do not breastfeed. The associations appear to be stronger with longer lifetime durations of breastfeeding but may wane as a woman ages.

## METABOLIC SYNDROME

MetS is a clustering of metabolic abnormalities including central obesity, hypertension, insulin resistance, and dyslipidemia (50). One prospective (24) and three retrospective (13, 15, 64) studies have examined the association of lactation with maternal MetS. Among a sample of women who were followed prospectively for 20 years in the CARDIA study, and who were nulliparous and without MetS at baseline, parous women with longer breastfeeding durations had a lower risk of incident MetS after adjustment for baseline BMI, parity, and numerous other potential confounders (24). This protective effect was stronger among women with a history of GDM (HR range 0.09–0.49 for various categorizations of lactation duration) compared to women without GDM (HR range 0.56–0.71).

Among parous women aged ≥20 years in the US National Health and Nutrition Examination Survey III, breastfeeding for ≥1 month was associated with a reduced odds of MetS (OR 0.78, 95% CI 0.61, 0.99), after adjusting for multiple sociodemographic and behavioral factors, including parity (15). BMI was not included in this final model owing to concerns that BMI and waist circumference, a component of MetS, are often highly correlated. No information was given on the degree of correlation among these variables in this population. However, the authors did explore adding BMI to their model, after which the association between breastfeeding and MetS was no longer significant (OR 1.02, 95% CI 0.78, 1.34). An analysis of 892 postmenopausal women (mean age approximately 63 years) in the Korean National Health and Nutrition Survey appears to include both parous and nulliparous women; however, approximately 90% had lactated, defined as breastfeeding for ≥1 month, and on average women had more than three live births (13). In this cohort, lactation was not associated with MetS in unadjusted or adjusted analyses (adjusted OR 1.20, 95% CI 0.56, 2.20). Among parous women in the SWAN study, ever breastfeeding (OR 0.77, 95% CI 0.62, 0.96) and each additional year of breastfeeding (OR 0.88, 95% CI 0.77, 0.99) were associated with a reduced odds of MetS (64). In an attempt to address whether this association was mediated by body composition, the authors used an outcome without the waist circumference component and entered BMI into the model; the association of lactation with this metabolic clustering, which excluded central adiposity, remained significant. It is

worth noting that when stratifying by parity, a dose-response relationship was seen, with a more protective effect of lactation among women with fewer children; this protective effect was no longer observed among women with four or more children. The authors hypothesized that the increased metabolic risk of pregnancy may outweigh the benefits of lactation after four or more pregnancies (64).

In summary, these data suggest that breastfeeding may be protective against MetS. This relationship appears to be influenced by breastfeeding duration and parity, with longer lifetime duration of breastfeeding associated with a protective effect, and increased parity nullifying the effect. Some data suggest the association may be attenuated by BMI; however, this was not found in the CARDIA study, which has the strongest study design. A history of gestational diabetes is an independent risk factor for MetS, and breastfeeding may have a stronger protective effect against MetS for women with previous GDM compared to those without.

## LIMITATIONS

The gold standard for assessing causal relationships, randomized controlled trials, will not be done to examine how lactation is associated with cardio-metabolic outcomes because it is not ethical to randomize women to not breastfeed. As such, large well-designed studies conducted among different populations that control for numerous potential confounders provide the best evidence likely to be obtained. However, these types of studies will always have limitations. First, breastfeeding status may be misclassified, particularly if breastfeeding duration or exclusivity are recalled from the distant past. Women tend to recall ever breastfeeding accurately, but those with shorter durations may overreport, whereas those with longer durations may underreport (62); such inaccuracies would attenuate the association of lactation with health outcomes. Furthermore, recall of breastfeeding after diagnosis with a condition thought to be associated with breastfeeding may be biased. Second, many of the studies assessed breastfeeding duration, but very few included exclusive breastfeeding or breastfeeding intensity, which may be important in describing these associations. Third, in many countries there is a social patterning of breastfeeding, with women who breastfeed often being older, married, more educated, and of higher socioeconomic status (1, 12). Breastfeeding and the decision to breastfeed may also be associated with other maternal health behaviors that confound the association of lactation and cardiovascular outcomes. Women who breastfeed are typically less likely to smoke (60, 78) and more likely to eat five or more servings of fruit and vegetables daily (60). Although many of the studies described in this review controlled for many of these demographic factors and some of the lifestyle behaviors, there may still be residual confounding that explains the maternal health benefits associated with lactation (69).

It is also important to consider the issue of directionality, particularly for obesity and diabetes outcomes. Obese women are more likely to experience problems breastfeeding and to stop breast-feeding early (2, 57). Recent evidence also suggests that insulin resistance may contribute to low milk supply and poorer breastfeeding outcomes (56). Thus, lack of or early cessation of breastfeeding may be a marker of insulin resistance or obesity, rather than a predictor. Prospective studies that include women without these conditions at baseline will

help to tease out this relationship. The issue of directionality is not as relevant for hypertension or dyslipidemia. We are not aware of a biological mechanism by which these conditions would contribute to poor lactation outcomes.

## CONCLUSION

In conclusion, several large prospective and retrospective studies suggest that lactation is associated with better cardio-metabolic health among parous women, although the effect may not persist as women age. The strength of the evidence differs by cardio-metabolic outcomes. Less evidence exists regarding an association with postpartum weight status and dyslipidemia, whereas more exists for diabetes, hypertension, and both subclinical and clinical cardiovascular disease. More research is needed into the mechanisms underlying these associations to further elucidate both the physiologic basis and duration of the effect. As suggested by the reset hypothesis, lactation may be part of a continuum required to correct the adverse cardio-metabolic profile that develops during pregnancy. Given these data and the well-established health benefits of breastfeeding for infants, all women should receive information about the benefits of breastfeeding and be supported to breastfeed if they choose to do so.

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**Table 1**

Details of key studies included in the present review

| Study; country | Study design | Analytic sample | Lactation status | Cardio-metabolic measures |
|---|---|---|---|---|
| 45 and Up (42); Australia | Retrospective study of baseline data of the 45 and Up cohort. | 74,785 women aged ≥45 years, selected from the Australian Medicare Database. Recruited from 2006–2009. | Total breastfeeding duration was assessed by the question, "For how many months, in total, have you breastfed?" Average breastfeeding duration was calculated as total duration divided by reported number of births. | Blood pressure: self-reported treatment for high blood pressure in the past month. |
| Coronary Artery Risk Development in Young Adults (CARDIA) (24, 25); United States | Prospective cohort with 20-year follow-up.<br>Women were reexamined at 7, 10, 15, and/or 20 years. | 1,399 black and white women from 4 geographic areas of the US. Baseline data were collected in 1985–1986 when participants were aged 18–30 years. | At each exam, women reported births since the previous exam. For each pregnancy, women reported lactation history as none, <6 weeks, 6–11 weeks, 3–6 months, or >6 months. The midpoint of each interval was used, or a value of 210 days for >6 months, to sum total duration of lifetime lactation. | Anthropometry: weight, height, and waist circumference measured by trained technicians.<br>Blood pressure: average of the second and third measures taken by trained technicians.<br>Lipids: fasting measured total cholesterol, HDL, and triglycerides. LDL calculated from Friedwald equation.<br>Glucose: fasting measured glucose and insulin. |
| Korean Women's Cohort (38); South Korea | Prospective cohort study with 6-year follow-up. | 177,749 premenopausal women ≥20 years (mean age 30.1 years) insured by the Korean Medical Insurance Company. Baseline data were collected in 1994. | Lifetime duration of lactation: the sum of reported lactation for each child. Lactation history was asked for each child, up to a maximum of 5 children. | Blood pressure: elevated blood pressure or current use of hypertensive medication. A health-care professional measured blood pressure a single time. |
| Million Women Study (5); United Kingdom | Retrospective study of baseline data of the Million Women Study. | 740,628 postmenopausal women (mean age 57.5 years) invited to the National Health Service Breast Screening Program in England and Scotland between 1996 and 2001. | Lifetime duration of lactation: the sum of reported breastfeeding, in months, for each child. | Anthropometry: self-reported current height and weight. |
| Nord-Trøndelag Health Study (HUNT2) (51, 52); Norway | Prospective cohort study with 15-year follow-up.<br>Additional retrospective analyses using baseline data. | 21,889 women aged 20–85 years living in Nord-Trøndelag, Norway. HUNT2 baseline was 1995–1997. | Lifetime duration of lactation: the sum of responses to the question, "For how many months did you breastfeed?" asked for each live birth. | Anthropometry: measured height, weight, and waist circumference.<br>Blood pressure: mean of the second and third measures taken by trained technicians.<br>Lipids: nonfasting measured total cholesterol, HDL, and triglycerides. LDL calculated from Friedwald equation.<br>Glucose: nonfasting measured glucose.<br>Cardiovascular mortality: assessed prospectively from linked death records. |
| Nurses' Health Study (NHS) and NHS II (71, 73, 74); United States | Prospective cohort studies, with questionnaires sent every 2 years. | 83,585–89,326 * parous women in NHS. Women were from 11 states and aged 30–55 years at enrollment, which began in 1976.<br>44,198–73,418 * parous women in NHS II. Women were from 14 states and aged 25–42 years at baseline (1989). | Lactation history was assessed once in NHS (1986), when the youngest woman was age 40 years. Women reported total duration of lactation for all pregnancies.<br>Lactation history was assessed in NHS II in 1993, 1997, and 2003. In 1993, women were asked about lifetime duration of lactation. In 1997, a more detailed questionnaire asked about lactation history, including timing of introduction of formula and solid foods, for up to 4 children; women with ≥5 children reported total additional months of breastfeeding. Women who gave birth after 1997 completed a similar questionnaire in 2003. | Incident myocardial infarction (MI): women reported nonfatal MI, which was confirmed by medical records. Fatal MIs were assessed from death records or family members (NHS).<br>Blood pressure: self-report of physician's diagnosis of high blood pressure, excluding during pregnancy (NHS II).<br>Glucose: self-reported diabetes diagnosis, if also supported by report of classic symptoms, elevated plasma glucose, or diabetes treatment (NHS and NHS II). |

| Study; country | Study design | Analytic sample | Lactation status | Cardio-metabolic measures |
|---|---|---|---|---|
| Project Viva (70); United States | Prospective cohort study with 3-year follow-up. | 570 women (mean age 36.0–38.8 years across lactation groups) recruited during their first prenatal visit from obstetric practices in eastern Massachusetts. Sample size was smaller for fasting blood samples ($n$ = 175). | At 6- and 12-month follow-up visits, women were asked if they were breastfeeding and if they had introduced formula or solid foods. Timing of stopping breastfeeding and introducing solid foods was reported in months, weeks, or days. These data were used to calculate duration of any and exclusive breastfeeding. | Anthropometry: measured weight, height, waist circumference, and subscapular and triceps skinfolds.<br>Lipids: measured total cholesterol, HDL, LDL, and triglycerides.<br>Glucose: fasting measured glucose and insulin. Hemoglobin $A_{1c}$ was assessed on all samples.<br>Insulin resistance was calculated from a homeostasis model using fasting insulin and glucose. |
| Study of Women's Health Across the Nation (SWAN) (64) and SWAN-Heart (47, 67); United States | Retrospective study of baseline data of the SWAN cohort. SWAN-Heart is an ancillary study. | 2,516 women aged 42–52 years, recruited from 7 clinical sites across the US. Enrollment was 1996–1997. SWAN-Heart (2001–2005) participants were aged 45–58 years ($n$ = 297–351). * | Lactation duration: participants reported lactation duration in months for each live birth. Duration was truncated at one year per pregnancy. | Anthropometry: height, weight, and waist circumference.<br>Blood pressure: measured.<br>Lipids: measured fasting total cholesterol and HDL.<br>Glucose: measured fasting glucose and insulin.<br>Subclinical cardiovascular disease (SWAN-Heart): coronary artery calcification, aortic calcification, common carotid artery intima-media thickness, and adventitial diameters.<br>Anthropometry (SWAN-Heart): visceral adiposity assessed by computed tomography. |
| Women's Health Initiative (68); United States | Prospective cohort study with 7.9-year follow-up. Additional retrospective analyses using baseline data. | 139,681 postmenopausal women aged 50–79 years at enrollment. | Lifetime duration of lactation: assessed from responses to the question, "Did you breastfeed or nurse any children for at least one month?" Those who responded yes were asked, "Thinking about all the children you breastfed, how many months total did you breastfed (your best guess)?" | Anthropometry: measured height and weight.<br>Blood pressure: self-reported history of treatment for hypertension and measured blood pressure.<br>Lipids and glucose: self-reported need to take medication for "cholesterol" or "sugar diabetes." Nurses validated medication use.<br>Prevalent cardiovascular disease: self-reported.<br>Incident cardiovascular disease: confirmed by physician. |

* Sample sizes varied depending on outcomes examined.