

REVIEW ARTICLE

Breastfeeding and maternal health outcomes: a systematic review and meta-analysis

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ABSTRACT

Aim: To evaluate the effect of breastfeeding on long-term (breast carcinoma, ovarian carcinoma, osteoporosis and type 2 diabetes mellitus) and short-term (lactational amenorrhoea, postpartum depression, postpartum weight change) maternal health outcomes.

Methods: A systematic literature search was conducted in PubMed, Cochrane Library and CABI databases. Outcome estimates of odds ratios or relative risks or standardised mean differences were pooled. In cases of heterogeneity, subgroup analysis and meta-regression were explored.

Results: Breastfeeding >12 months was associated with reduced risk of breast and ovarian carcinoma by 26% and 37%, respectively. No conclusive evidence of an association between breastfeeding and bone mineral density was found. Breastfeeding was associated with 32% lower risk of type 2 diabetes. Exclusive breastfeeding and predominant breastfeeding were associated with longer duration of amenorrhoea. Shorter duration of breastfeeding was associated with higher risk of postpartum depression. Evidence suggesting an association of breastfeeding with postpartum weight change was lacking.

Conclusion: This review supports the hypothesis that breastfeeding is protective against breast and ovarian carcinoma, and exclusive breastfeeding and predominant breastfeeding increase the duration of lactational amenorrhoea. There is evidence that breastfeeding reduces the risk of type 2 diabetes. However, an association between breastfeeding and bone mineral density or maternal depression or postpartum weight change was not evident.

INTRODUCTION

Breast milk is the natural first food for newborns. It provides all the energy and nutrients that an infant needs for the first six months of life, up to half or more during the second half of infancy and up to one-third during the second year of life (1,2). For mothers, breastfeeding has been reported to confer lower risk of breast and ovarian carcinoma (3,4), greater postpartum weight loss (5) and decreased blood pressure (6) compared with no breastfeeding. The World Health Organization (WHO) recommends exclusive breastfeeding in the first six months and continuation of breastfeeding for 2 years and beyond (1).

The association between breastfeeding and breast carcinoma in mothers has received increased scrutiny in recent years. A number of studies have suggested that breastfeeding, particularly for an extended period of time, may be associated with a decreased risk of breast carcinoma, even after adjustment for potential confounders (7). It is difficult, however, to estimate the magnitude of association between breastfeeding duration and breast carcinoma if any, because of the different methodologies used in breastfeeding his-

Abbreviations

CI, Confidence interval; HIC, High-income country; LMIC, Low- and middle-income country; MeSH, Medical Subject Heading; OR, Odds ratio; PPD, Postpartum depression; RCTs, Randomised controlled trials; RR, Relative risk; SMD, Standardised mean difference; UNICEF, United Nations Children's Fund; WHO, World Health Organization.

Key Notes

- Longer duration of breastfeeding protects against breast and ovarian carcinoma.
- Exclusive breastfeeding and predominant breastfeeding increase the duration of lactational amenorrhoea.
- Evidence on the association between breastfeeding and maternal bone mineral density, maternal depression or postpartum weight change was lacking.

tories. Parity is also a protective factor against breast carcinoma (8), and there may be an interaction between parity and breastfeeding duration interplay in protecting women from breast carcinoma.

Ovarian cancer is one of the most common cancers in female (9,10). Reproductive factors have been identified as markers of risk for ovarian cancer. These reproductive factors mainly include total number of pregnancies, parity, age at menarche and menopause, as well as breastfeeding (11). Evidence from previous analyses indicates an inverse association between breastfeeding and the risk of ovarian carcinoma (4,12).

Calcium metabolism and bone metabolism are substantially altered with increased calcium demands during pregnancy and lactation. Bone densities can decrease by between 3 and 10 per cent in the span of a few months in a healthy mother (13). Confounders commonly considered in the studies of the relationship between fracture risk and breastfeeding are age, hormone replacement therapy, parity and BMI (4).

Available literature suggests that breastfeeding reduces the risk of maternal type 2 diabetes in some cohort studies, but the evidence from published studies has differed with regard to the strength of the association (14,15).

The literature suggests that exclusive breastfeeding protects against pregnancy (16,17). Some studies, however, show that exclusive breastfeeding is not always associated with inhibition of ovulation (18,19).

The incidence of postpartum depression (PPD) is high (10–15%) (20), and depression during pregnancy usually continues into the postpartum period (21). Postpartum depression has an immediate impact on mothers. It carries long-term risks for their mental health (22) and may also have significant negative effects on the cognitive, social and physical development of their children (23). The evidence for an association between breastfeeding and PPD is, however, unclear (23,24).

Postpartum weight retention is a predictor for future overweight and obesity (25) and is associated with obesity-related illnesses, such as type 2 diabetes mellitus and cardiovascular disease (26). Breastfeeding may promote weight loss due to lactation (27), but there is a lack of strong evidence to support this hypothesis (28).

We conducted this review to summarise the literature and explore the relationship of breastfeeding and its duration with long-term (breast carcinoma, ovarian carcinoma, osteoporosis and type 2 diabetes mellitus) and short-term (lactational amenorrhoea, postpartum depression, postpartum weight change) maternal health outcomes. Outcomes for review were selected during an expert meeting at the World Health Organization (October 2014) that was reviewing the impact of breastfeeding on maternal and child health.

METHODS

A search strategy (Box 1) was developed and reviewed by all authors. Medical Subject Heading (29) terms and

Box 1. Search strategy for breastfeeding & maternal health

- 1 Breastfeeding OR Breast Feeding OR Lactation OR Human Milk OR Breast Milk
- 2 Women OR Maternal OR Postpartum OR puerperal OR postnatal OR Birth OR gestation
- 3 Diabetes OR (Breast AND (Carcinoma OR carcinoma OR tumor OR malignancy)) OR (Ovarian OR Ovary AND (Carcinoma OR carcinoma OR tumor OR malignancy)) OR (depression OR Blues OR psychosis) OR (Amenorrhoea OR Contraception) OR (Osteoporosis OR Bone mineral density) OR Weight OR BMI OR body mass index
- 4 (Addresses[ptyp] OR Autobiography[ptyp] OR Bibliography[ptyp] OR Biography[ptyp] OR pubmed books[filter] OR Case Reports[ptyp] OR Congresses[ptyp] OR Consensus Development Conference[ptyp] OR Directory[ptyp] OR Duplicate Publication[ptyp] OR Editorial[ptyp] OR Festschrift[ptyp] OR Guideline[ptyp] OR *In Vitro*[ptyp] OR Interview[ptyp] OR Lectures [ptyp] OR Legal Cases[ptyp] OR News[ptyp] OR Newspaper Article[ptyp] OR Personal Narratives [ptyp] OR Portraits[ptyp] OR Retracted Publication[ptyp] OR Twin Study[ptyp] OR Video-Audio Media[ptyp])
- 5 #1 AND #2 AND #3
- 6 #5 NOT #4

keywords were used in various combinations. We searched published literature from PubMed, Cochrane Library and CABI databases to identify studies examining the effect of type and duration of breastfeeding on maternal health outcomes. We conducted the search in February 2015. No language or date restrictions were employed in the electronic search.

Two review authors (RC and BS) screened the titles and abstracts independently to identify potentially relevant citations. These review authors retrieved the full texts of all potentially relevant articles and independently assessed the eligibility of the studies using predefined inclusion criteria. We extracted data from all articles found to be relevant by both authors. Any disagreements or discrepancies between reviewers were resolved by discussion and if necessary by consulting a third author (JSM). In addition to the electronic search, we searched reference lists of the articles identified. We used Web-based citation index for citing manuscripts of these identified articles.

We identified four recent systematic reviews addressing the following outcomes: ovarian carcinoma (30), type 2 diabetes mellitus (31), postpartum depression (32) and postpartum weight change (33). We planned to update these reviews and provide new quantitative estimates of breastfeeding on these health outcomes. For other maternal health outcomes, that is breast carcinoma, osteoporosis and lactational amenorrhoea, we planned for new reviews.

Inclusion criteria

We selected all observational studies (prospective/retrospective cohort and case-control), randomised controlled trials (RCTs), including cluster randomised trials, and quasi-experimental trials which examined the impact of duration and type of breastfeeding on maternal health outcomes. For articles not written in English, we attempted to get an English abstract. If it was not available, the article was excluded.

Abstraction, summary measure, breastfeeding categories and analysis

We abstracted data using a modified Cochrane data abstraction form. If a study provided separate estimates for hospital- and community-based populations, then the outcome estimates were pooled separately. We used odds ratios (ORs), both adjusted and unadjusted, as our outcome estimate for breast and ovarian carcinoma. Relative risk (RR) was used as the outcome estimate for lactational amenorrhoea. To examine the effect on breast and ovarian carcinoma, breastfeeding was categorised into ever breastfed vs. never breastfed and also by breastfeeding duration, that is breastfed less than six months vs. not breastfed; breastfed 6 to 12 months vs. not breastfed; and breastfed >12 months vs. not breastfed. For lactational amenorrhoea, we used exclusive, predominant, partial, any and no breastfeeding as the categories (Table A1). Standardised mean differences in bone mineral density between highest and lowest breastfeeding duration categories were used for osteoporosis outcome. A narrative approach was used to summarise the studies for postpartum weight change as the studies were very heterogeneous.

We performed meta-analysis with Stata 11.2 software (StataCorp, College Station, TX, USA). We calculated the pooled estimates of the outcome measures from the odds ratios (ORs), relative risks (RRs), standardised mean differences (SMDs) and 95% confidence intervals (CIs) of the individual studies by inverse variance or DerSimonian and Laird method in Stata (34). High heterogeneity was defined by either a low p-value (<0.10) or I^2 value greater than 60%. In cases of high heterogeneity, the random-effects model was used and causes were explored by conducting subgroup analysis and meta-regression. Subgroup analyses were carried out based on breastfeeding categories (ever vs never, less than six months vs never, 6–12 months vs never, >12 months vs never). Among the ever vs never breastfeeding category, subgroup analyses were carried out based on sample size (<500, 500–1499, ≥1500), individual study setting (i.e. high-income country (HIC) or low- and middle-income country (LMIC) (35)), study design (cohort, case-control), mean age of diagnosis (≤49 years, >49 years), adjustment for parity (fine adjustment, i.e. adjustment according to each parity number measured as 0, 1, 2, 3, 4+; crude adjustment, i.e. groupwise adjustment measured as 0, 1–3, 4+ children; and no adjustment), control for confounding (thorough, i.e. controlled for all potential socio-demographic and reproductive factors such as age, income, ethnicity, parity, contraceptive use, family history of carcinoma, menopausal status and smoking; partial, i.e. only partially controlled for

potential socio-demographic and reproductive factors; and none) and quality of study (adequate, i.e. study had none or one among selection bias, measurement bias, attrition (20%) and confounding bias; inadequate) (36). We also evaluated the presence of publication bias in the extracted data for the primary outcome using Begg's test or Egger's test or funnel plots (37).

RESULTS

We screened the 12 071 titles identified. Of these, after reviewing abstracts of 1501 articles, we selected 341 for full-text review. We identified 163 articles for inclusion in our final database (Fig. 1). Among these, 100 studies examined the impact of breastfeeding on breast carcinoma, 40 studies on ovarian carcinoma, 12 studies on lactational amenorrhoea, five studies on postpartum weight change and six studies on osteoporosis. We did fresh meta-analysis for breast carcinoma, ovarian carcinoma, osteoporosis and lactational amenorrhoea and updated the review on postpartum weight change. No new studies subsequent to the existing reviews on type 2 diabetes mellitus and postpartum depression (31,32) were found to be eligible for inclusion.

Effects of breastfeeding on long-term maternal health outcomes

Breast carcinoma

We identified 98 estimates (38–135) of the association between ever breastfeeding and breast carcinoma risk (Tables 1 and A2). Ever breastfeeding was associated with 22% (OR 0.78, 95% CI 0.74–0.82) (Fig. 2) reduction of breast carcinoma risk compared with never breastfeeding. Compared with no breastfeeding, breastfeeding for less

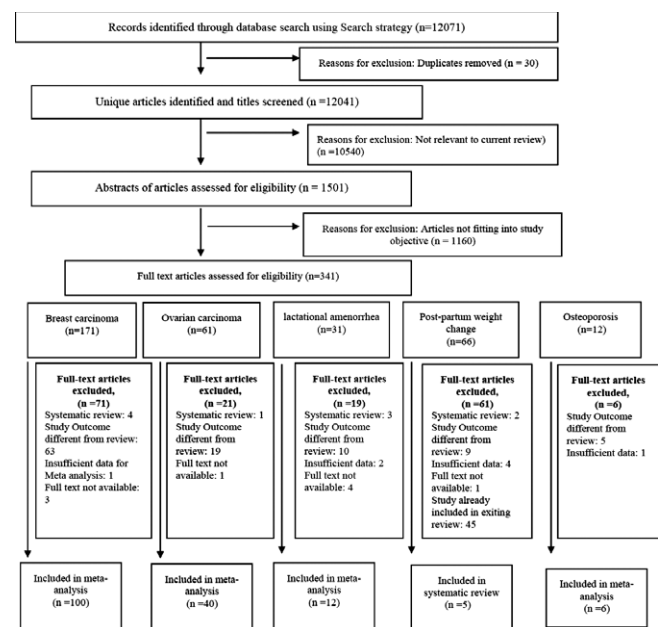


Figure 1 : Prisma Flow chart.

Table 1 Risk of breast carcinoma by breastfeeding duration and by subgroup

	Number of estimates	Pooled odds ratio and 95% confidence interval	p-value	I ² (%)	
Breastfeeding category					
Ever vs. Never	98	0.78 (0.74; 0.82)	<0.001	71.9	
<6 months vs. Never	39	0.93 (0.88; 0.99)	0.05	59.1	
6–12 months vs. Never	36	0.91 (0.87; 0.96)	<0.001	22.5	
>12 months vs. Never	50	0.74 (0.69; 0.79)	<0.001	62.2	
Subgroup analysis (Ever vs. Never)					
	Number of estimates	Pooled odds ratio and 95% confidence interval	p-value	I ² (%)	Meta-regression p-value
Study size					
<500 participants	15	0.50 (0.37; 0.66)	<0.001	59	0.009
500–1499 participants	31	0.74 (0.66; 0.83)	<0.001	66.7	
≥1500 participants	52	0.83 (0.80; 0.88)	<0.001	71.7	
Setting					
High income	72	0.81 (0.77; 0.85)	<0.001	72.5	0.206
Lower mid-income	26	0.66 (0.56; 0.77)	<0.001	68.3	
Study design					
Cohort	12	0.85 (0.83; 0.87)	<0.001	53.5	0.705
Case-control	86	0.77 (0.72; 0.81)	<0.001	73.3	
Mean age					
≤49	28	0.78 (0.71; 0.87)	<0.001	73.5	0.369
>49	28	0.68 (0.60; 0.78)	<0.001	84.8	
Adjusted for parity					
Fine adjustment	19	0.92 (0.88; 0.96)	<0.001	54.8	0.037
Crude adjustment	19	0.86 (0.81; 0.90)	<0.001	23.2	
No adjustment	60	0.73 (0.68; 0.79)	<0.001	77.4	
Control for confounding					
Thorough	40	0.82 (0.77; 0.87)	<0.001	68	0.479
Partial	25	0.77 (0.69; 0.87)	<0.001	71.2	
None	33	0.74 (0.68; 0.81)	<0.001	76.1	
Quality of study					
Adequate	66	0.81 (0.78; 0.85)	<0.001	62.6	0.750
Inadequate	32	0.70 (0.61; 0.80)	<0.001	81.6	

than six months (39 estimates) and breastfeeding for 6–12 months (36 estimates) were associated with 7% (OR 0.93, 95% CI 0.88–0.99) and 9% (OR 0.91, 95% CI 0.87–0.96) risk reduction of breast carcinoma, respectively. We found that mothers who breastfed for >12 months compared with those who did not breastfeed had a 26% lower risk of developing breast carcinoma (50 studies; OR 0.74, 95% CI 0.69–0.79), and when restricted to high-quality studies, only (41 studies) breastfeeding >12 months was associated with 23% lower risk of developing breast carcinoma (OR 0.77, 95% CI 0.72–0.83) (not shown in Table 1). There was, however, an indication of publication bias. Asymmetry was observed in funnel plot when inspected visually. Both Egger's test (p bias <0.001) and Begg's test (p bias <0.001) showed statistically significant findings.

Subgroup analysis of the effects of ever breastfeeding on risk of breast carcinoma among studies conducted in high-income countries, with large sample sizes (>1500), of cohort design, with thorough control of confounding factors and adequate quality showed a smaller breast

carcinoma risk reduction. Studies where fine adjustment for parity was made showed a smaller effect of breastfeeding on breast carcinoma risk reduction (OR 0.92, 95% CI 0.88–0.96) compared with studies where crude adjustment or no adjustment was made. A restricted analysis including parous women in the fine adjustment subgroup showed a risk reduction of 7% for breast carcinoma (OR 0.93, 95% CI 0.89–0.97; 14 estimates) (not shown in Table 1).

Ovarian carcinoma

Pooled results from 41 estimates (65,69,136–173) showed that mothers who ever breastfed their children had a 30% reduction in the risk of ovarian carcinoma, when compared with those who never breastfed (OR 0.70, 95% CI 0.64–0.77) (Tables 2 and A3; Fig. 3). The risk of ovarian carcinoma was 17% lower among women who had breastfed for less than six months when compared with those who did not breastfeed (OR 0.83, 95% CI 0.78–0.89). The risk of ovarian carcinoma among mothers who breastfed for 6–12 months was 28% lower (OR 0.72, 95% CI 0.66–0.78; 19

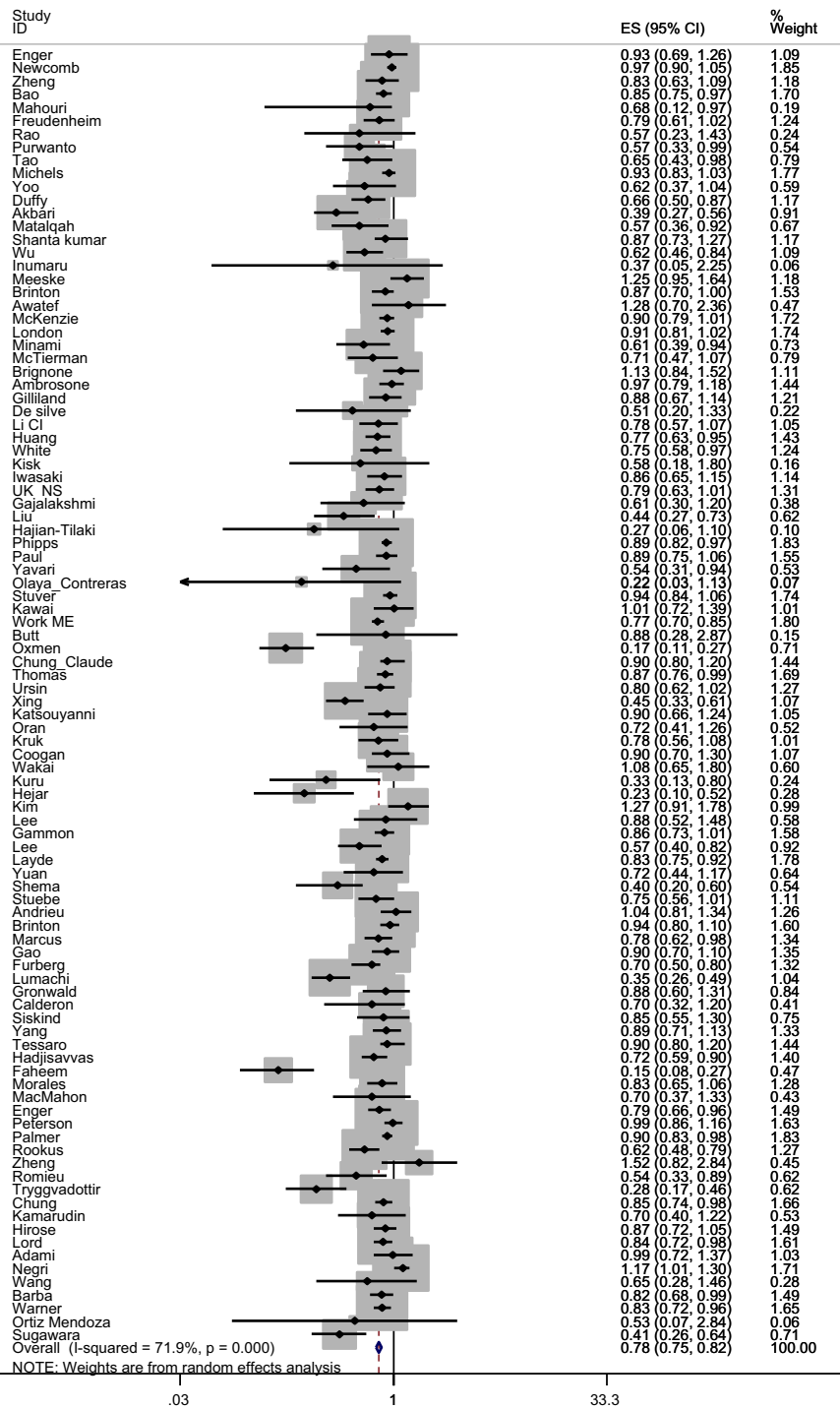


Figure 2 Effect of ever breastfeeding vs. no breastfeeding on risk of breast carcinoma.

estimates) when compared with women who had not breastfed. The highest risk reduction was observed among women who breastfed for more than 12 months, in whom the risk of ovarian carcinoma was 37% lower than among women who had not breastfed (OR 0.63; 95% CI 0.56–0.71; 29 estimates). The effect size was slightly less (OR 0.65, 95%

CI 0.57–0.73), when the analyses were restricted to high-quality studies (29 estimates). There was no evidence of publication bias in Egger’s test or Begg’s test (p bias >0.1) in either of the analyses.

In subgroup analysis, studies with sample sizes of more than 1500 showed a significant protection of 24% from

Table 2 Risk of ovarian carcinoma by breastfeeding duration and by subgroup

	Number of estimates	Pooled odds ratio and 95% confidence interval	p-value	I ² (%)	
Breastfeeding category					
Ever vs. Never	41	0.70 (0.64; 0.77)	<0.001	70.0	
<6 months vs. Never	20	0.83 (0.78; 0.89)	<0.001	3.0	
6–12 months vs. Never	19	0.72 (0.66; 0.78)	<0.001	22.0	
>12 months vs. Never	29	0.63 (0.56; 0.71)	<0.001	51.8	
Subgroup analysis (Ever vs. Never)					
	Number of estimates	Pooled odds ratio and 95% confidence interval	p-value	I ² (%)	Meta-regression p-value
Study size					
<500 participants	7	0.67 (0.53; 0.84)	0.001	2.8	0.241
500–1499 participants	12	0.59 (0.47; 0.74)	<0.001	74.9	
≥1500 participants	22	0.76 (0.69; 0.84)	<0.001	70.9	
Setting					
High income	35	0.74 (0.68; 0.80)	<0.001	64.0	0.007
Lower mid-income	6	0.48 (0.29; 0.77)	<0.001	77.1	
Study design					
Cohort	5	0.87 (0.78; 0.98)	0.02	0.0	0.136
Case-control	36	0.68 (0.61; 0.75)	<0.001	71.6	
Mean age					
≤49	10	0.70 (0.64; 0.77)	<0.001	70	0.744
>49	24	0.71 (0.63; 0.80)	<0.001	77	
Adjusted for parity					
Fine adjustment	16	0.80 (0.75; 0.86)	<0.001	56	0.231
Crude adjustment	4	0.69 (0.59; 0.81)	<0.001	45	
No adjustment	21	0.67 (0.58; 0.77)	<0.001	72	
Control for confounding					
Thorough	14	0.76 (0.67; 0.85)	<0.001	64.9	0.419
Partial	15	0.66 (0.55; 0.81)	<0.001	73	
None	11	0.72 (0.65; 0.78)	<0.001	50.5	
Quality of study					
Adequate	27	0.72 (0.65; 0.80)	<0.001	71	0.505
Inadequate	14	0.63 (0.58; 0.68)	<0.001	54.7	

ovarian carcinoma (OR 0.76, 95% CI 0.69–0.84). This effect size was reduced compared to studies with smaller samples (OR 0.67, 95% CI 0.53–0.84). Studies in HICs also showed a significant but reduced effect (OR 0.74, 95% CI 0.68–0.80) compared with studies in LMICs (OR 0.48, 95% CI 0.29–0.77). Lower quality studies showed a higher risk reduction for ovarian carcinoma (OR 0.63, 95% CI 0.58–0.68) than higher quality studies (OR 0.72, 95% CI 0.65–0.80). Studies where fine adjustment for parity was made showed a modest but still significant (OR 0.80, 95% CI 0.75–0.86) reduction in risk of ovarian carcinoma compared with studies where no or crude adjustment for parity was made. In an analysis restricted to parous women in the fine adjustment subgroup, the effect was further attenuated (OR 0.82, 95% CI 0.75–0.89) (not shown in Table 2).

Osteoporosis

A total of six studies (174–179) were identified (Table 3). Two studies were from LMICs (174,178) and four studies from HICs (175–177,179). Bone mineral density (BMD)

was generally measured at two sites, that is femoral neck and distal radius. For femoral neck, four studies (175,177–179) were identified with small sample size (total 489 women). The pooled effect suggests that breastfeeding had a nonsignificant effect on femoral neck bone mass. With respect to distal radius, four studies (174–177) were identified and the results were heterogeneous. The largest (n = 963) study (176) did not observe any association, whereas Chowdhury et al. (174) (n = 400) reported a negative effect of breastfeeding on bone mineral density. Overall, there was no clear evidence of an effect of breastfeeding on osteoporosis.

Diabetes

A recent systematic review by Aune reported a reduced risk of type 2 diabetes (RR 0.68, 95% CI: 0.57–0.82) with longer duration of lifetime breastfeeding compared with shorter durations. A one-year increase in the total lifetime duration of breastfeeding was associated with 9% protection (RR 0.91, 95% CI: 0.86–0.96) against the presence of type 2 diabetes in the mothers. No new studies were found

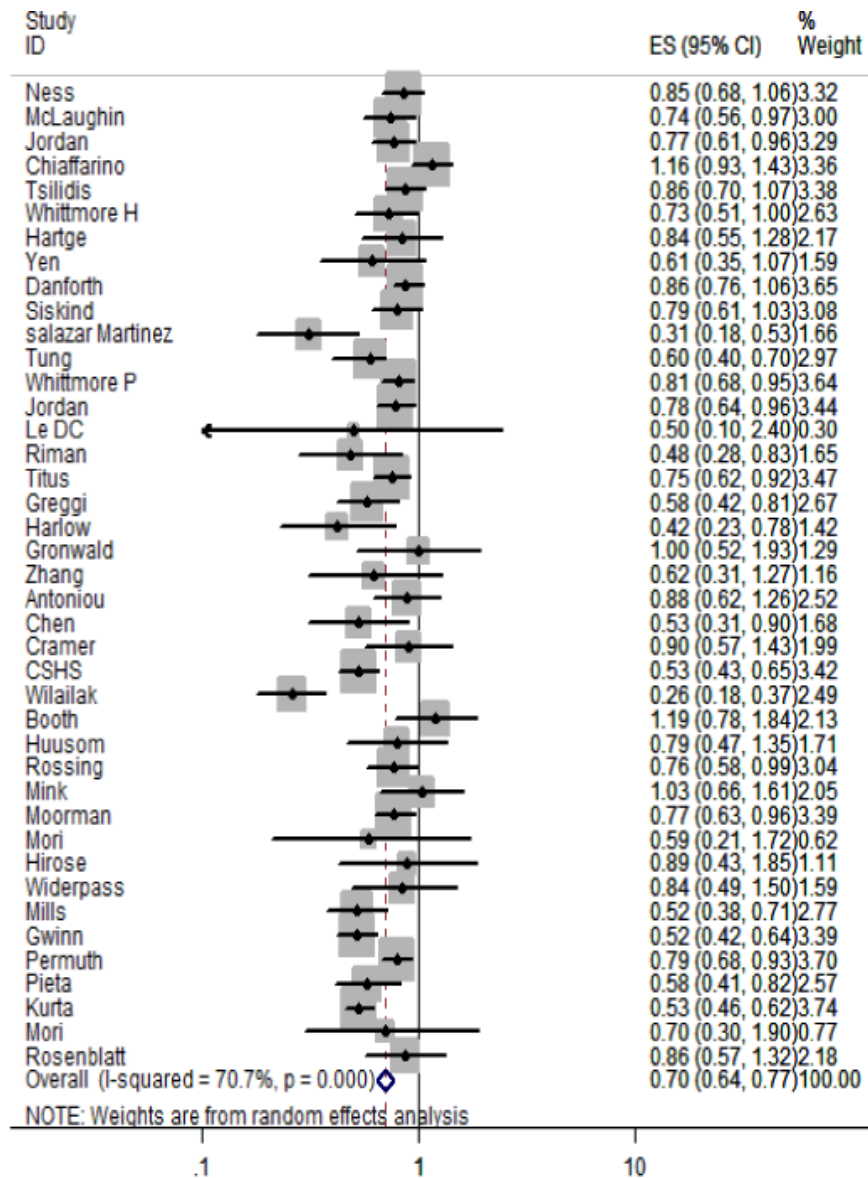


Figure 3 Effect on ever vs. never breastfeeding on risk of ovarian carcinoma.

subsequent to the systemic review by Aune et al. in 2013 (31).

Effects of breastfeeding on short-term maternal health outcomes

Lactational amenorrhoea

We identified 12 studies (173,180–190) that examined the association between breastfeeding and lactational amenorrhoea (Table 4). Four studies (180,182,185,188) did not provide either RR or OR. They reported that exclusive compared to mixed feeding, or longer duration of any breastfeeding, was associated with an increased mean or median duration of lactational amenorrhoea. The remaining studies provided data from which the following estimates were derived: the probability of continued

lactational amenorrhoea at six months postpartum was 23% higher (RR 1.23, 95% CI 1.07–1.41; three studies) for exclusive or predominant breastfeeding compared to no breastfeeding, and 21% higher (RR 1.21, 95% CI 1.01–1.25; five studies) (Table 4) when compared to partial breastfeeding. We found no evidence of publication bias.

Postpartum depression

A recent systematic review conducted by Dias et al. reported that pregnancy depression predicts a shorter breastfeeding duration, but evidence is unclear on whether breastfeeding mediates the association between pregnancy and postpartum depression. No new studies were found subsequent to the systemic review conducted by Dias and Figueiredo in 2015 (32).

Table 3 Association between breastfeeding and bone mineral density

First author name (year)	Mean \pm SD: BMD highest BF group (g/cm ²)	Mean \pm SD: BMD lowest BF group (g/cm ²)	Pooled SMD (95% CI) of BMD
Distal Radius			
Chowdhury (2002) (174)	0.49 \pm 0.11	0.61 \pm 0.08	Fixed effect -0.132 (-0.26 to -0.003)
Hawker (2002) (176)	0.477 \pm 0.05	0.474 \pm 0.03	
Random effect -0.490 (-1.357 to 0.376)			
Henderson (2000) (177)	0.564 \pm 0.06	0.601 \pm 0.05	Random effect -0.490 (-1.357 to 0.376)
Drinkwater (1991) (175)	0.541 \pm 0.07	0.545 \pm 0.05	
Femoral Neck			
Henderson (2000) (177)	0.835 \pm 0.11	0.847 \pm 0.12	Fixed effect -0.142 (-0.426 to 0.142)
Lenora (2009) (178)	0.603 \pm 0.13	0.613 \pm 0.12	
Wiklund (2012) (179)	0.96 \pm 0.11	0.97 \pm 0.11	Fixed effect -0.142 (-0.426 to 0.142)
Drinkwater (1991) (175)	0.95 \pm 0.05	1.01 \pm 0.10	

BMD, bone mineral density; SD, standard deviation; SMD, standardised mean difference.

Table 4 Effect of breastfeeding on probability of lactational amenorrhoea

Breastfeeding category	No. of Estimates	Ref. no	Probability of lactational amenorrhoea RR (95% CI)	p-value (test of heterogeneity)
Exclusive or Predominant BF vs. No BF	03	176,180,185	1.23 (1.07–1.41)	0.34
Exclusive or Predominant BF vs. Partial BF	05	174,178,179,182,184	1.21 (1.01–1.25)	0.08
Any BF (exclusive or predominant or partial BF) vs. No BF	04	181,185,186,190	1.14 (0.92–1.40)	0.01

Postpartum weight change

We updated the systematic review by Neville et al. (33) by including 5 additional studies (Table 5) (191–195). In the review by Neville et al., the majority of identified studies reported little or no association between breastfeeding and weight change. Of those five studies, three studies were performed in low- and middle-income countries, one was performed in high-income country, and one was multicentre study (Brazil, Ghana, India, Norway, Oman, USA). In studies performed in low- and middle-income countries, we have not found any potential differential effect for breastfeeding and postpartum weight loss response as a function of countries being low to middle and high income. Two of the five additionally identified studies (194,195) reported a significant reduction in postpartum weight with breastfeeding. Sarkar and Taylor (191) in a cross-sectional study in Bangladesh revealed that body weight of mothers was negatively correlated with 1–12 and 13–24 months of lactation after controlling for height, education and food consumption. Stuebe et al. (192) showed that women who exclusively breastfed for greater than six months had the lowest BMI at 3 years postpartum as well as the lowest postpartum weight retention at 3 years compared with women who never exclusively breastfed. A multicentre study showed that lactation intensity and duration explained little variation in weight change patterns (193–195). Overall, the role of breastfeeding on postpartum weight change remains unclear.

DISCUSSION

The aim of this review was to systematically examine the effect of breastfeeding on important maternal health outcomes.

The risk of developing breast carcinoma was reduced by 26% among women who cumulatively breastfed for more than 12 months, compared with women who did not breast feed.

Previous reviews suggested that breastfeeding was not strongly related to risk of breast carcinoma (196,197) or found a small but statistically significant protective association (198–200). Our meta-analysis findings are comparable with but suggest a higher level of protection than that found by the Collaborative Group on Hormonal Factors in Breast Carcinoma (201). In this pooled analysis of approximately 50 000 carcinoma cases from 47 studies in 30 countries around the world and after adjustment for confounders including parity and exclusion of nulliparous women, the authors estimated that the risk of invasive breast carcinoma decreased by 4.3% for every 12 months of breastfeeding (201). However, one of the challenges of comparing studies on cumulative breastfeeding duration and determining the effect on breast carcinoma risk is the lack of a standard protocol for grouping the lifetime number of months of breastfeeding for analysis and the adjustment of parity. Lifetime duration of breastfeeding is related to the number of children breastfed, that is parity and the duration of breastfeeding for each child. Our

Table 5 Overview of studies which examined the association between breastfeeding and postpartum weight change

S. No.	Author Name (year)	Location	Age	Association between Breastfeeding and Weight Change			Covariates included in analyses
1	Monteiro et al. 2013 (194)	Brazil	<24 years – 48.2% >24 years – 51.8%	For women within 2-year postpartum period, each breastfeeding score point increases an average postpartum loss of 70 g ($p = 0.002$)			Sanitary condition of household Social programs of income transfer Type of delivery Prepregnancy weight
2	Onyango et al. 2011 (193)	Brazil, Ghana, India, Norway, Oman, USA	Brazil 28.3 (6.3) Ghana 30.8 (3.9) India 29.0 (3.5) Norway 30.8 (4.3) Oman 27.7 (5.0) USA 31.5 (4.5)	Lactation intensity and duration explained little of the variation in weight change patterns			Maternal age BMI at 14 days Parity Delivery mode Infant birthweight Sex
3	Samano et al. 2013 (195)	Mexico	18.8 years	Among both adult and adolescent mothers, those who practised EBF lost more weight than those who did not practise EBF (–2.9 kg, interquartile range, –5.7 to 0.8 kg, vs –1.8 kg, interquartile range –2.8 to 2.2 kg)			Pregestational weight Marital status Education Delivery mode
4	Sarkar et al. 2005 (191)	Bangladesh	18–40 years	Duration of Lactation	Mean Body Weight (kg)	Mean BMI (kg/m ²)	Age Height Education
				Nonlactating	44.3	19.4	
				<12	42.48	18.86	
				12–24	42.96	18.85	
				25–36	43.32	19.11	
				37–48	43.47	19.29	
				49–60	44.11	19.36	
5	Stube et al. 2010 (192)	East Massachusetts, USA	Ghana: 30.8 (3.9)	Months of Lactation	BMI kg/m ² (95% CI)		Prepregnancy BMI Parity Family history of diabetes
				0	26.1 (25.4–26.9)		
				0–3	25.3 (24.6–26.0)		
				3–6	25.5 (24.9–26.2)		
				6–12	25.8 (25.2–26.3)		
				>12	25.4 (24.8–26.0)		
				Months of Lactation	Wt. retention kg mean (95% CI)		
				0	2.5 (0.6–4.3)		
				0–3	0.2 (–1.6–2.0)		
				3–6	0.9 (–0.8–2.6)		
				6–12	1.3 (–0.1–2.8)		
				>12	0.4 (–1.2–1.9)		

results showed that when controlled for parity, breastfeeding independently contributed to a modest but significant risk reduction for breast carcinoma. The risk reduction for breast carcinoma was 8% among ever breastfed mothers when finely adjusted for parity, while it was 22% when all studies were pooled together. Even when our analysis was restricted to only parous women, finely adjusted for parity, ever breastfeeding was associated with a 7% reduction in risk of breast carcinoma compared with never breastfeeding. Longer duration of breastfeeding (>12 months) was associated with more protection of breast carcinoma than shorter duration of breastfeeding (breastfeeding <6 and 6–12 months) when compared to never breastfeeding. Even when our analysis

was restricted to studies with adequate quality, breastfeeding >12 months showed more protection against breast carcinoma. Possible biological mechanisms include that protection may occur through parity-specific changes in levels of circulating hormones such as estradiol, prolactin and growth hormone, as each of these has been associated with breast cancer risk (202), or that the parous mammary gland may contain epithelial cells with a more differentiated and less proliferative character which are less susceptible to transformation (203).

Breastfeeding by women for more than 12 months was also associated with a 35% reduction in ovarian cancer, compared with women who had not breastfed. The protective effect was less in women who had only ever breastfed

(for any duration) ranging from 30% in an unadjusted analysis to 18% when the analysis was restricted to ever breastfeeding parous women (finely adjusted for parity). A number of physiological mechanisms may account for the protective effect of breastfeeding against ovarian cancer through modulating ovarian cycle length (204), and therefore, parity is an important confounder. Longer duration of breastfeeding suppresses ovulation longer and causes suppression of gonadotropins, resulting in depressed production of plasma estradiol, considered to be a potential causal mechanism of ovarian cancer when present at high levels (205). However, breastfeeding must also have an independent effect to explain the estimated reduction in ovarian cancer when parity is adjusted for.

There did not appear to be a significant effect of breastfeeding on the risk of osteoporosis. Calcium metabolism and bone metabolism are substantially altered during pregnancy and lactation, and high calcium demand during lactation makes women more prone to bone resorption and subsequent osteoporosis. There was no evidence of such risk, and it has been suggested that during lactation, oestrogen imposes minor inhibitory effect on periosteal bone formation and permits periosteal expansion which increases bone size after weaning (206).

Available review suggests that longer duration of breastfeeding reduces risk of development of type 2 diabetes mellitus by 32%, and in linear dose–response analyses, there was a 9% reduction in relative risk for each 12-month increase in lifetime duration of breastfeeding. Our review shows that exclusive or predominant breastfeeding during the first six months postpartum was associated with longer periods of amenorrhoea. Less intensive breastfeeding, captured under ‘any or partial breastfeeding’, offers less clear benefit. This finding is biologically plausible. Breastfeeding suppresses the resumption of ovarian activity after childbirth and is thus associated with a period of infertility. Exclusive breastfeeding and predominant breastfeeding are associated with a higher frequency of suckling than other patterns of breastfeeding. Frequent suckling inhibits gonadotropin-releasing hormone and decreases the release of luteinising hormone and follicle-stimulating hormone (207), thus preventing early return of menses.

The association between breastfeeding and postpartum weight change remains uncertain. Factors such as age, gestational weight gain and prepregnancy weight confound such analyses (208,209). As prepregnancy weight and gestational weight gain were found to be strong determinant factors of postpartum weight change, future research should include the preconception period with continued monitoring into the postpartum period to capture the true trajectory of weight change. Even though BF may not lead to postpartum weight loss under ‘natural’ conditions, it remains unknown whether women who wish to lose weight intentionally in the postpartum period are more likely to be successful at doing so if they are vs. if they are not breastfeeding.

Although our original review plans included exploring the associations between breastfeeding and the risk of

maternal postpartum depression and type 2 diabetes, we were unable to identify new studies following the reviews published in 2015 (31) and 2013 (32). The evidence suggests that the relationship between breastfeeding and postpartum depression is lacking.

The range of the maternal outcomes examined and the various categories of breastfeeding exposures that we considered are important strengths of this review. Despite the expanded scope of review, other important maternal health outcomes such as maternal hypertension and cardiovascular disease were not addressed and should be considered in future research and reviews. Also important was the attempt to look for dose–response relationships and the evaluation of heterogeneity and publication biases. However, some limitations should be acknowledged. We have pooled data from many observational studies that are prone to be affected by biases such as in recall or due to selection. Some studies did not control for or collect information on potential confounders that could have affected the association between breastfeeding and the outcome of interest. For postpartum weight change, we were constrained to take a narrative approach to present the outcomes because of the heterogeneous nature of the studies. In cases of significant heterogeneity in study results, we have performed post hoc subgroup analysis and meta-regression and have used the random-effects model. But in some cases even within subgroups, there was significant heterogeneity which suggests some other unidentified factors causing such heterogeneity. Although the meta-regression seemed to explain around 80% of the heterogeneity for breast and ovarian carcinoma, we need to acknowledge the limitation of post hoc subgroup analysis.

CONCLUSION

Our meta-analysis shows that women who had ever breastfed and who breastfed for longer duration have a lower risk of breast and ovarian carcinoma and also type 2 diabetes mellitus. Exclusive or predominant breastfeeding during the first six months postpartum prolongs lactational amenorrhoea. We found no evidence of a clear association between breastfeeding and bone mineral density, maternal depression or postpartum weight change.

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CONFLICT OF INTEREST

The authors have no financial relationships or other conflict of interests to disclose.

DISCLAIMER

The authors alone are responsible for the views expressed in this article and they do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated.

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APPENDIX

Table A1 Breastfeeding exposures (WHO definitions) (210)

Exposure Category	Permitted to Receive
Exclusive breastfeeding	<ul style="list-style-type: none"> Breast milk from mother or wet nurse or expressed breast milk No other liquids or solids except vitamin drops or syrups, mineral supplements, or prescribed medicines
Predominant breastfeeding	<ul style="list-style-type: none"> Breast milk from mother or wet nurse or expressed breast milk Water and water-based drinks No food-based fluid with the exception of fruit juice and sugar water Vitamin drops or syrups, mineral supplements, or prescribed medicines
Partial breastfeeding	<ul style="list-style-type: none"> Breast milk from mother or wet nurse or expressed breast milk Any other liquids or nonliquids, including both milk and nonmilk products
Any breastfeeding	<ul style="list-style-type: none"> Breast milk from mother or wet nurse or expressed breast milk Includes children exclusively, predominantly, fully and partially breastfed
No breastfeeding	<ul style="list-style-type: none"> Formula and/or animal's milk No breast milk

Table A2 Summary of studies included in breast carcinoma

Estimates	Studies	Ref. No.	Design	Country	Quality
Ever vs. Never	98	98	38–135		
			Cohort	12 HIC	72 AQ 66
			Case-control	86 LMIC	26 IQ 32
<6 months vs. Never	39	39	39,40,42,48,51,53,56,57,59,60,62,66,69,71,74,78,80,83,85,88,92,93,95,96,98,99,105,107,110,112,114–116,119–121,135,211,212		
			Cohort	7 HIC	33 AQ 32
			Case-control	32 LMIC	6 IQ 7
6–12 months vs. Never	36	36	39,42,48,51,56,57,59,60,62,63,66,69,71,74,78,80,83,85,88,93,95,96,98,99,105,107,110,112,114–116,119–121,135,211		
			Cohort	7 HIC	31 AQ 31
			Case-control	29 LMIC	5 IQ 5
>12 months vs. Never	50	50	38–40,42,48,51,56,57,59–67,69,71,74,78–80,82,83,85,88,93,95,96,98,99,101,105,107,110,112–116,119–121,125–127,131,135,211		
			Cohort	8 HIC	43 AQ 41
			Case-control	42 LMIC	7 IQ 9

HIC, high-income country; LIC, low-income country; AQ, adequate quality; IQ, inadequate quality.

Table A3 Summary of studies included in ovarian carcinoma

Estimates	Studies	Ref. No.	Design	Country	Quality
Ever vs. Never					
41	40	65,69,136–173	Cohort	HIC	AQ
			Case-control	LMIC	IQ
<6 months vs. Never					
20	19	137,138,142,144,147–150,153,155,158, 161,163,165–168,170,173	Cohort	HIC	AQ
			Case-control	LMIC	IQ
6–12 months vs. Never					
19	18	137,138,142,144,147,148,150,153,155, 158,161,163,165–168,170,173	Cohort	HIC	AQ
			Case-control	LMIC	IQ
>12 months vs. Never					
29	28	65,69,137–140,142–144,146–148,150,152,153, 155,158,161,163–168,170–173	Cohort	HIC	AQ
			Case-control	LMIC	IQ

LIC, low-income country; AQ, adequate quality; IQ, inadequate quality.