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The safety of intrauterine devices in breastfeeding women: a systematic review ⋆,,⋆⋆,,⋆

Erin N. Berry-Bibee[*], **Naomi K. Tepper**,
Tara C. Jatlaoui,
Maura K. Whiteman,
Denise J. Jamieson,
Kathryn M. Curtis

Division of Reproductive Health, Centers for Disease Control and Prevention, Atlanta, GA, USA

Abstract

Objectives: To investigate levonorgestrel (LNG)-releasing and copper-bearing (Cu) intrauterine device (IUD) safety among breastfeeding women and, for Cu-IUD use, breastfeeding performance and infant health.

Study design: Systematic review.

Methods: We searched PubMed, Embase, Cochrane Library and clinicaltrials.gov for articles through January 2016. We included studies of Cu-IUD or LNG-IUD users comparing IUD-specific (perforation, expulsion) and other contraceptive-related (infection, removal/cessation due to bleeding/pain and other adverse events) outcomes for breastfeeding vs. non-breastfeeding women. We also included studies of breastfeeding women comparing contraceptive-related outcome for IUD-users vs. other contraceptive-method users. Finally, we included studies comparing breastfeeding outcomes among Cu-IUD users to users of other nonhormonal contraceptives or no contraception.

Results: Of 548 articles identified, 23 (16 studies) met the inclusion criteria. Two studies suggested that the risk of IUD perforation was 6–10 times higher among breastfeeding vs. non-breastfeeding women. Seven studies suggested that risks for other adverse events were similar or lower among breastfeeding vs. non-breastfeeding women. Three studies among breastfeeding women found no increased risk of adverse events in IUD users vs. nonusers. Breastfeeding performance and infant growth were similar for Cu-IUD users and users of other nonhormonal methods or no contraception.

Conclusion: Overall, risks for adverse events among IUD users, including expulsion, pain and removals, were similar or lower for breastfeeding women vs. non-breastfeeding women. Uterine

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[*]Corresponding author. fax: +1 770 488 6391. wnw4@cdc.gov, eberryb@emory.edu (E.N. Berry-Bibee).

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perforation with IUDs, while rare, appeared more frequent among breastfeeding women. No evidence indicated that Cu-IUD use in breastfeeding women influences breastfeeding performance or infant growth.

Keywords

IUD; Intrauterine device; breastfeeding; uterine perforation

1. Introduction

The American Academy of Pediatrics and the Institute of Medicine recommend breastfeeding through the first 12 months of life, and the World Health Organization (WHO) recommends breastfeeding for up to 2 years, or beyond [1-3]. The Lactational Amenorrhea Method (LAM) is an effective form of contraception for 6 months postpartum among exclusively or nearly exclusively breastfeeding women. However, many women who are breastfeeding may want to use additional forms of contraception, may not choose LAM or may not qualify for LAM [4]. Intrauterine devices (IUDs), including nonhormonal copper IUDs (Cu-IUDs) and levonorgestrel-releasing IUDs (LNG-IUDs), are highly effective and convenient methods of contraception often used by breastfeeding women [5,6]. Women who are in the postpartum period, as compared to those who are not, may have different risk associated with IUD use, such as higher risk of IUD expulsion [7]. The hormonal changes experienced in the postpartum period and during breastfeeding, including low estrogen and elevated oxytocin have been associated with changes to the uterus and endometrium that may impact the performance of an IUD [8,9]. Prior systematic reviews have examined the safety of IUD insertion in the postpartum period but have not looked specifically at the safety of IUD insertion or use among breastfeeding women compared with non-breastfeeding women [10,11].

Our primary objective in this systematic review was to examine the published evidence for the safety of IUD use in breastfeeding women with respect to IUD-related complications (e.g., perforation, expulsion or infection). Another recent systematic review from the WHO examined the safety of progestin-only contraception (including the LNG-IUD) among breastfeeding women with regard to breastfeeding and infant health outcomes; however, that review did not address the Cu-IUD [12]. Thus, our secondary objective was to examine the safety of Cu-IUD use among breastfeeding women with respect to breastfeeding performance and infant health.

We conducted this systematic review in preparation for a meeting held at the Centers for Disease Control and Prevention in August 2015 with the purpose of updating the *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010* [13].

2. Methods

2.1. Search strategy

We conducted a systematic review according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [14]. We searched PubMed, Embase,

Cochrane Library and clinicaltrials.gov databases from database inception through February 10, 2016. The search terms used for each database were generated with assistance from a reference librarian (Appendix 1).

2.2. Selection criteria

We sought studies that examined any of the following three research questions: (1) among IUD users, do women who breastfeed as compared with those who do not have an increased risk of adverse events (perforation, expulsion, infection, pain or other adverse events)? (2) Among breastfeeding women, does IUD use, as compared with use of other contraceptive methods, increase the risk of adverse events (bleeding, infection, pain or other adverse events)? and (3) Among breastfeeding women, does Cu-IUD use, as compared with use of other nonhormonal methods or no method, increase the risk of adverse breastfeeding or infant outcomes (breastfeeding continuation and exclusivity, use of supplementation, infant growth or infant health)? We included randomized controlled trials (RCTs), prospective or retrospective cohort studies and case–control studies published in any language and excluded unpublished data, conference abstracts, dissertations, case reports and case series. For research questions #1 and #2, we included articles that studied Cu-IUDs that are or have been available in the US (Cu 7, TCu200 and TCu380A) and LNG-IUDs currently available in the US. However, for articles that contained multiple IUD types, we included articles if at least 25% of the IUDs in the study met the above criteria (Cu 7, TCu200, TCu380A or LNG-IUDs). If studies included one or more of the qualifying IUDs plus other (excluded) IUD types, then we included the study only if it reported outcomes by IUD type. For breastfeeding assessment, we included articles that reported on women fully or partially breastfeeding by self-report at the time of IUD insertion. We use the term “immediate insertion” for IUD insertion within 10 min after delivery of the placenta, “early postpartum” for insertion greater than 10 min after the placenta but less than 4 weeks postpartum, and “interval insertion” for insertion at least 4 weeks postpartum. For women with immediate postpartum insertion, we included articles that examined outcomes by women who then went on to breastfeed after IUD insertion compared to women who did not breastfeed.

Several included articles used the term lactation infertility to describe the contraceptive method chosen by a study participant who chose no method other than the decreased fertility associated with lactation. In this review, the term lactational infertility is defined as women who were exclusively breastfeeding and amenorrheic. Some or all articles may have been referring to what is now know as LAM, but as they did not provide specific details, we did not use the term LAM.

We included articles that defined outcomes of interest in the following ways: bleeding — removals for bleeding or comparative hemoglobin/hematocrit measures; expulsion — patient report, provider diagnosis or chart review, either complete or partial expulsion; infection — endometritis or pelvic inflammatory disease, with diagnosis criteria reported; pain — removals for pain or pain (visual analog scale scores) at insertion; and perforation — patient report, provider diagnosis by imaging or surgery or chart review. We included studies with at least 4 weeks of follow-up for all outcomes except pain at insertion.

2.3. Study selection, data synthesis and quality rating

One author (E.B.B.) performed the search and reviewed the titles and abstracts of each article to determine the papers requiring full-text review. Two authors (E.B.B. and N.T.) identified the included articles by reviewing the full text and applying the inclusion and exclusion criteria. For articles reporting on the same study containing duplicate results, we only included the article that was most complete.

We analyzed and summarized the data using standard abstraction tables. For each study, two authors (E.B.B. and N.T., T.J. or M.W.) independently used the US Preventative Services Task Force rating system to assess methodological features and assign a quality rating [15].

3. Results

The search strategy yielded 586 articles. We screened the titles and abstracts of all entries and identified 75 articles that required full-text review. A total of 23 articles (16 studies) met the inclusion criteria.

3.1. IUD use among breastfeeding compared with non-breastfeeding women

Nine studies (14 articles) addressed our first research question and compared IUD complications among breastfeeding women compared with non-breastfeeding women. Four studies (five articles) reported on perforations [5,9,16-18], five reported on expulsions [19-23], four studies (eight articles) reported on removals for bleeding or pain [19,20,22-27] and two studies (three articles) reported IUD insertion-related adverse events (pain, cervical lacerations and syncope) [18,23,24] (Table 1). One article reported on IUD insertions immediately postpartum [21], three articles included IUD insertions at mixed or unspecified time points [5,9,17], one article reported on both immediate postpartum and interval insertions [19] and eight articles reported on interval IUD insertions [18,20,22-27].

3.1.1. Perforation—Four studies examined risk for uterine perforation in breastfeeding and non-breastfeeding IUD users. Two of the larger, more recent studies reported increased relative risk (RR) of perforation among breastfeeding women compared with non-breastfeeding women [5,9], while two older studies with fewer perforations found no differences [16-18].

In a large prospective cohort study, 61,448 women who underwent IUD insertions across six European countries were followed for 12 months for incidence of uterine perforations [5]. Over 70% of the IUDs studied were LNG-IUDs and nearly 30% were Cu-IUDs. Among all women, a total of 81 perforations were identified for a proportion of 1.4 perforations per 1000 insertions [95% confidence interval (CI): 1.1–1.8] for LNG-IUDs and 1.1 per 1000 insertions (95% CI 0.7–1.7) for Cu IUDs. The RR of uterine perforation for breastfeeding vs. non-breastfeeding women was 6.1 (95% CI 3.9–9.6). When reported by IUD type, the RR of perforation for breastfeeding compared with non-breastfeeding women was 6.3 (95% CI 3.8–10.5) among LNG-IUD users and was 7.8 (95% CI 2.8–21.4) among Cu-IUD users. Although the time since last delivery was noted, the results were not presented according to traditional clinical timeframes (immediate postpartum or interval placements), but were compared for insertions done at >36 or ≤36 weeks. Both breastfeeding and non-

breastfeeding women had increased risk for perforation with IUD insertion ≤36 weeks postpartum compared with >36 weeks postpartum, although the association was only significant for non-breastfeeding women [RR 3.4 (95% CI 0.5–24.8) for breastfeeding women and RR 2.3 (95% CI: 1.1–4.7) for non-breastfeeding women]. When comparing breastfeeding women and non-breastfeeding women within each insertion time period, breastfeeding women had an increased risk for perforation compared with non-breastfeeding women with IUD insertion ≤36 weeks postpartum (RR 3.3, 95% CI 1.6–6.7). For insertion >36 weeks postpartum, the association was attenuated and no longer significant [RR 2.2 (95% CI 0.3–16.3) for breastfeeding women compared with non-breastfeeding women). No serious complications (bowel or bladder injury, septicemia or peritonitis) were reported with any of the perforations in this study [5].

A multicenter case–control study identified women with uterine perforations admitted to nine hospital centers throughout the United States for IUD removal over a 20-month period (*n*=32) [9]. Controls were IUD users admitted to the hospitals for acute self-limiting conditions (*n*=497). The timing of IUD insertion was not specified, but women who were 6 weeks postpartum or less were excluded. All IUD types were included, but outcomes were not reported by IUD type. Among women with at least one prior live birth, the RR of uterine perforation for women who were breastfeeding at the time of IUD insertion compared with non-breastfeeding women was 10.1 (95% CI 4.9–20.6). The authors did not adjust or stratify this analysis according to time postpartum (although all women within 6 weeks postpartum were excluded). They compared the risks of uterine perforation among non-breastfeeding women for those who were >6 weeks and ≤2 months postpartum at the time of IUD insertion with those >2 months postpartum and did not find a significant difference (RR 1.2, 95% CI 0.4–3.4) [9]. The authors therefore concluded that breastfeeding, not postpartum status ≤ 2 months, was the factor associated with an increased risk of perforation [9].

Two articles reported results for a case–control analysis of a large international IUD dataset [16,17]. Women who underwent IUD insertion (13 different IUD types included) from March 1976 to December 1981 were included in this analysis (*n*=21,610), with the majority (85%) of IUD insertions performed within 48 h after delivery of the placenta. Forty-one cases of uterine perforation were identified and matched by IUD type, provider, center and date with 41 women who did not have a uterine perforation. The authors stated that no statistical differences in risk factors for perforation, including breastfeeding at insertion, were observed [17]. Breastfeeding status was known in 19 of the 41 cases of perforation, and of those 19, 3 (15.8%) were breastfeeding; 31 of the 41 women in the comparison group had known breastfeeding status, and of those 31, 1 (3.2%) was breastfeeding [16].

A retrospective analysis of another international database reported on IUD insertions from 1977–1986 at five different sites among parous women who were at least 42 days postpartum following a term live vaginal birth [18]. Multiple IUD types were included (53.1% were Cu-IUD types of interest to this review). Breastfeeding women (*n*=3043) were compared with non-breastfeeding women (*n*=3450) for insertion-related outcomes. Among women using Cu-IUDs, the rate of perforation detected at the time of insertion was similar between breastfeeding (0.06%) and non-breastfeeding (0.06%) women [18].

Three articles included in this review were designed to look at more common IUD-related outcomes, such as expulsions, and were thus not designed (nor powered) to look at perforation. However, many of these articles noted that no perforations occurred in the study with sample sizes of 559–2293 and follow-up ranges from 6 to 12 months [22-24].

3.1.2. Expulsion—Five studies in seven different articles reported on IUD expulsion outcomes among breastfeeding compared with non-breastfeeding women [19-24,27]. All included Cu-IUDs with follow-up ranging from 6 to 24 months (Table 1). All the studies found either no differences in expulsion rates or lower expulsion rates among breastfeeding women.

Xu and colleagues [21] examined a prospective cohort of women who received a CuT 380A IUD immediately after placental delivery. The authors examined 6-month expulsion rates for breastfeeding women (n=834) compared with non-breastfeeding women (n=76) and found significantly lower expulsion rates for breastfeeding women after insertion compared with non-breastfeeding women (11.9% vs. 22.4%, respectively; p<.05).

A pooled analysis from several multicenter clinical trials that were originally designed to evaluate the safety and effectiveness of several types of IUDs examined women who received IUDs (Cu-T, Lippes loop, Delta T or Delta Loop) from May 1976 to May 1981, either immediately postpartum (n=1839) or interval (n=432) [19]. Six months after IUD insertion, no significant differences were seen in expulsion rates for breastfeeding compared with non-breastfeeding women by either timing of insertion (immediate or interval) or by IUD type (numerical values or p values not reported) [19].

An RCT conducted at six centers in Indonesia randomized 2845 healthy women of reproductive age who were at least 40 days postpartum to one of three IUD types (Lippes Loop, CuT 380A or multiload Cu 375 (MLCu 375) [20]. Life table analysis demonstrated at 12 and 24 months that there were no significant differences, either within or across various IUD types, in expulsion rates among breastfeeding women compared with women not breastfeeding at the time of IUD insertion (no p values reported and significance level not specified) [20].

A cohort study in China followed healthy women undergoing CuT 380A insertion for 12 months [22]. Outcomes were examined for women who underwent IUD insertion at three distinct time periods: (1) Early lactation — breastfeeding women with an IUD inserted 6–12 weeks postpartum, (n=451); (2) late lactation — breastfeeding women with an IUD inserted 4–12 months post-partum (n=399); and (3) interval insertion — at least 6 weeks postpartum in non-breastfeeding women (n=2293). Expulsion rates (per 100 woman years) did not differ between the three groups (early lactation 2.11 vs. late lactation 0.51 vs. interval 1.11; p values>.05) [22].

Five articles reported outcomes from a randomized multicenter clinical trial conducted in 1985–1988 in 14 different countries [23-27]. In this trial, healthy women aged 18–40 years who were at least 42 days postpartum from a term, vaginal, live birth and desiring an IUD were randomized to either a CuT 380A or another common IUD type (model

varied by study site). The study noted breastfeeding status at the time of IUD insertion and at every follow-up visit for 12 months. Three of the five identified articles reported on expulsion rates. In one report, all women who received the CuT 380A from 1985 to 1986 from five sites were evaluated at the 6-month follow-up visit [23]. Expulsion rates at 6 months were similar for breastfeeding women (2.5±0.7 per 100 women) compared with non-breastfeeding women (2.8±0.7 per 100 women; no p value reported) [23]. In a second article from the same study, the authors reported 12-month outcomes for all women who underwent CuT 380A from 1985 to 1988, at all 25 sites [24]. No significant differences were seen in expulsion rates among breastfeeding women compared with non-breastfeeding women (Table 1, p>.05) [24]. Rivera et al. [27] reported on all CuT 380A users, across the entire time frame, at all sites with 12-month follow-up data. This report included 1582 breastfeeding and 1161 non-breastfeeding women at the time of IUD insertion. Gross-cumulative life table rates for expulsions were calculated. Expulsion rates were not statistically different for breastfeeding compared with non-breastfeeding women (p=.23) [27] (Table 1).

3.1.3. Removals for bleeding or pain—Four studies reported in eight articles generally found no differences in rates of IUD removal for bleeding or pain among breastfeeding compared with non-breastfeeding women [19,20,22-27]. All included Cu-IUDs and reported rates of removals for bleeding or pain between 6 and 24 months (Table 1).

In the pooled analysis described above, no significant differences were seen for IUD removals for bleeding or pain at 6 months among breastfeeding compared with non-breastfeeding women by either timing of insertion (immediate or interval) or by IUD type (p<.05) [19]. In the Indonesian RCT described above, no significant differences were seen, either within or across various IUD types, in removals for bleeding or pain among breastfeeding compared with non-breastfeeding women (no p values reported) [20]. In the cohort study out of China described above, the rates of removal for bleeding or pain also did not differ between groups (Table 1; p values >.05) [22].

All five articles from the randomized multicenter international trial included in this review reported on removals for bleeding or pain. The three articles previously discussed all reported decreased rates of removal for bleeding or pain at either 6 or 12 months among breastfeeding women compared with non-breastfeeding women (Table 1) [23,24,27]. In a fourth article, the authors performed a nested case–control analysis of the women randomized to the Cu-T devices from 1985 to 1986 across 13 sites with 12 months of follow-up [25]. Cases included 143 women who underwent removal of their IUDs due to bleeding and/or pain, and controls included the 2023 women who had their IUD in place at the last visit. After adjustment for center, age, parity, level of training of inserter, menstrual status and length from the external os to the fundus, breastfeeding women had a decreased odds of removal for bleeding and/or pain compared with non-breastfeeding women [odds ratio (OR) 0.75, 95% CI 0.59–0.97) [25]. Finally, the fifth article reported on a slightly different subgroup of participants and included all women who underwent insertion of CuT 380A IUDs or multiload 250 IUDs from 1985 to 1986, at 18 sites with 12-month follow-up [26]. They compared 89 women who underwent removals for bleeding and/or pain within 1

year with 2536 women who had the IUD in place at 1 year. Non-breastfeeding women had an increased odds of removal for bleeding/pain compared with breastfeeding women (OR 2.8, 95% CI 1.5–5.2) [26].

3.1.4. IUD insertion-related adverse events—Three articles reported on IUD insertion-related adverse events (other than perforations) [18,23,24]. All three articles reported decreased pain at IUD insertion among breastfeeding women compared with non-breastfeeding women [RR 0.47, 95% CI 0.37–0.59 [18]; 0.9% vs. 2.7%, respectively (p=.026) [23]; 17.1% vs. 25.2% (p=.001) [24]; Table 1). One article calculated a composite score and reported a decreased rate of any insertion-related adverse event (except perforation) (RR 0.46, 95% CI 0.38–0.56) [18]. Two of the three articles reported on cervical laceration and both found no significant difference in either the RR (0.72; 95% CI 0.35–1.47) [18] or rate (4.0% vs. 2.8%; p=.156) [24] of cervical laceration at the time of IUD insertion between breastfeeding and non-breastfeeding women (Table 1).

3.2. Outcomes among breastfeeding IUD users compared with breastfeeding users of other contraceptive methods

We identified three prospective cohort studies that examined adverse events among breastfeeding women using CuT 380A IUDs compared with breastfeeding women using other contraceptive methods [28-30]. In the first study, breastfeeding women self-selected either CuT 380A IUD (*n*=97) or the progesterone vaginal ring (PVR) (*n*=100) between 24 and 64 days postpartum [29]. Gross cumulative rates of removal for bleeding at 12 months were significantly higher for PVR users compared with IUD users (p=.048) [29]. Two studies enrolled breastfeeding women and placed the desired self-selected contraceptive method (either CuT 380A or progestin releasing subdermal implant) approximately 2 month postpartum. In both studies, no differences were seen in removals for bleeding or pain among CuT 380A users compared with implant users after 11–24 months (p>.05) (Table 2) [28,30]. In addition, two of the three studies examined serious adverse events, and neither reported any serious adverse events [28,29].

3.3. Breastfeeding and infant outcomes among women using Cu-IUD compared with women using nonhormonal or no contraceptives

We identified four studies described in six articles that examined breastfeeding outcomes for Cu-IUD users compared with nonhormonal method users or no contraception users (Table 3) [31-35]. All studies were originally designed to look at a hormonal contraceptive method and included Cu-IUD users and non-contraceptive or nonhormonal users as two separate comparison groups. Two studies reported on mean duration of lactation [31,32], one study (in two articles) reported on continuation of breastfeeding at 6 and 12 months [33,34] and one study reported on use of supplementation [35]. Three studies reported on infant growth [32-35]. The studies generally found no differences in these outcomes between groups.

3.3.1. Breastfeeding outcomes—One retrospective cohort study examined the duration of lactation for breastfeeding women (other inclusion criteria were not specified) who were using a Cu-IUD (*n*=68; type not specified) compared with women using lactational infertility alone (or in combination with other nonhormonal methods) (*n*=1972)

[31]. Mean duration of lactation was similar in both groups (IUD 21±10.8 months vs. no contraception 20±9.6 months; no statistical testing done) [31].

In a prospective cohort study, healthy postpartum, amenorrheic women who wanted to fully breastfeed as long as possible self-selected a contraceptive method [33,34]. On postpartum day 30 women who chose to rely on lactational infertility alone for contraception were given an injectable placebo (they were told it would support lactational infertility) and women who chose an IUD had a CuT 200 inserted. No significant differences were seen in the percentage of women continuing to breastfeed at 3, 6 or 9 months; however, at 12 months, IUD users were significantly more likely to be breastfeeding compared with placebo (no p values reported and level of significance not stated) (Table 3) [33].

In a prospective cohort study of 100 women in Egypt, breastfeeding women who had normal vaginal deliveries of term singleton infants chose either CuT 380A IUD (n=50) or barrier methods of contraception (n=50; this group included women who intended to use barrier methods or no method of contraception) [35]. Contraception was initiated at 30–42 days postpartum. The number of women who supplemented while breastfeeding in each group was similar at 2 months (IUD n=5; barrier n=5) and 6 months (IUD n=48; barrier n=47); no p values were reported [35].

In a second prospective cohort from Chile, on postpartum day 57±3, healthy, fully breastfeeding, amenorrheic women selected a CuT 380A IUD or no contraception (other than lactational infertility) [32]. The mean duration of breastfeeding and of exclusive breastfeeding were similar in both groups with 12 months of follow-up, although no p values were reported (Table 3) [32].

3.3.2. Infant growth outcomes—In the cohort study from Chile described above, no significant differences were seen in mean infant growth at 6 months [33] or total infant weight at 12 months among exclusively breastfeeding infants whose mothers used Cu IUDs compared with exclusively breastfeeding infants whose mothers relied on lactational infertility for contraception and were given an injectable placebo to “support” lactational infertility (Table 3) [34]. In the prospective cohort study from Egypt described above, mean daily infant weight gains were similar between IUD users and barrier users at 2 and 6 months (no p values reported; Table 3) [35]. In the second study from Chile, mean infant growth was not statistically different between IUD users compared with the lactational infertility alone over 12 months (no p values reported; Table 3) [32].

4. Discussion

Evidence identified in this systematic review generally suggested that IUD-related adverse events, except uterine perforation, are similar between breastfeeding and non-breastfeeding women and, for the Cu-IUD, suggested no negative effects on breastfeeding performance or infant growth. Uterine perforation remains rare (1.1–1.4 per 1000 insertions) among IUD users but the only two studies that were designed and powered to detect differences in perforations demonstrated a 6- to 10-fold higher risk of perforation among breastfeeding compared with non-breastfeeding women [5,9]. The largest study was a prospective cohort

study of good quality that demonstrated a significantly increased risk of perforation among breastfeeding women when IUD insertion occurred within 36 weeks postpartum but not thereafter [5]. All other studies had either no perforations in either group [22-24] or extremely few perforations (n=2) [18] and were not large enough to have appropriate power to detect differences for this rare event among breastfeeding compared with non-breastfeeding women. One poor-quality case–control analysis of a large FHI data set (n=21,610 IUD insertions) identified 41 perforations, but the breastfeeding status was only known for less than half of the cases and too few women were known to be breastfeeding (cases n=3 and controls n=1) for adequate statistical comparison [16,17].

Evidence suggested that breastfeeding women do not have an increased risk for other adverse events including expulsion [19,20,22-24,27] or cervical laceration [18,24] compared with non-breastfeeding women. Breastfeeding was associated with significant decreases in pain at IUD insertion [18,23,24] and overall risk for any insertion-related adverse event other than perforation [18]. Five of eight articles reported significantly lower rates of removal for bleeding and/or pain [23-27], and the other three demonstrated no significant differences [19,20,22] among breastfeeding women compared with non-breastfeeding women.

We identified very few articles that examined breastfeeding women and compared adverse events for IUD users compared with those using other contraceptive methods. The three articles included in this review did not find any clinically meaningful differences in adverse events among breastfeeding women who were IUD users compared with breastfeeding implant or PVR users [28-30].

In the four studies that examined breastfeeding-related outcomes among breastfeeding women who were using a Cu-IUD compared with nonhormonal or non-contraception users, we did not identify any negative effects on breastfeeding duration, breastfeeding continuation, use of supplementation or infant growth among Cu-IUD users [31-35]. Although statistical testing was not performed for the majority of comparisons of interest, results between the groups of interest were either similar or without clinically meaningful differences.

Evidence in this review on the risk of uterine perforation is of good quality and includes a large prospective comparative cohort study, but is limited to only two studies [5,9]. Additionally, these studies were not able to fully examine the often co-existing states of breastfeeding and the traditional clinical postpartum time points (e.g., immediate post-placental IUD insertion, 4–6 weeks postpartum), both of which may contribute to IUD safety and performance. The other articles in this review are largely from fair to poor quality observational studies, most of which were not specifically designed to address the questions in this review. All of the studies measured breastfeeding status by self-report, which may have led to misclassification of breastfeeding as either the exposure or the outcome. Many studies had incompletely defined or measured outcomes. The majority of the studies were on multiple IUD types or the CuT 380A, and only 1 article included information on LNG IUDs [5]. The article that included LNG-IUDs only reported on the outcome of perforation; therefore, the body of evidence for the other outcomes in this review (e.g., expulsions, IUD removals or other insertion-related adverse events) consists only of

studies with nonhormonal IUDs. Thus, although findings for the majority of our outcomes do follow a clear pattern indicating that IUDs are safe to use among breastfeeding women, the ability to draw firm conclusions is limited by quality of the evidence.

The benefits of breastfeeding are numerous and breastfeeding is encouraged for at least 1 year; however, during that time, breastfeeding women are often in need of highly effective forms of contraception [2,3]. The safety of IUDs among breastfeeding women is thus of great clinical importance. Overall, risks for IUD-related events including expulsion, pain, infection and removals were similar or lower for breastfeeding women compared with non-breastfeeding women. Uterine perforation with IUD insertion was rare but appeared to be more frequent among breastfeeding women. Evidence reviewed did not indicate that Cu-IUD use in breastfeeding women influences breastfeeding performance or infant growth. Therefore, IUDs are potentially well suited for many breastfeeding women as they provide safe, highly effective, convenient and reversible methods of contraception that have high rates of continuation and satisfaction [6,36].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Articles identified, divided by time of insertion for research question #1: Among IUD users, do women who breastfeed have an increased risk of adverse events (perforation, expulsion, infection, pain, or other adverse events) compared with women who do not breastfeed?

Author, location and funding source	Study design	Study population	IUD type	Outcomes, follow-up duration	Results	Strengths	Weaknesses	Quality
Immediate PPIUD insertion								
Xu et al. [21], China, FHI and USAID	Cohort study (within RCT)	Women age 20–40 y, willing to receive immediate PP IUD Exposed: BF women (*n*=834) Unexposed: non-BF women (*n*=76)	CuT 380A	Expulsion	**BF** / **Expulsion rate at 6 mos; n (%)** / Yes / 99 (11.9) / p<0.05 No / 17 (22.4) /	Low attrition Adequate follow-up Outcome well defined		II-2, fair
Mixed immediate PP/interval IUD insertion or unspecified timing								
Cole et al. [19]; 35 countries from Asia, Latin America, Middle East and Africa; IFRP, USAID	Cohort (pooled analysis from a series of multicentered trials)	Immediate PP insertion: Exposed: BF women receiving IUD (*n*=1022) Unexposed: non-BF women receiving IUD (*n*=817) Interval insertion: Exposed: BF women receiving IUD (*n*=282) Unexposed: non-BF women receiving IUD (*n*=150)	Cu-T	Expulsion Removal for bleeding or pain Follow-up 3 and 6 months	Immediate PP: **BF** / **Expulsion rate at 3 mos** / **Removal bldg./pain at 3 mos** Yes / 10.9 / 2.3 No / 7.3 / 0.7 Interval: **BF** / **Expulsion rate at 3 mos** / **Removal bldg./pain at 3 mos** Yes / 2.1 / 0.0 No / 2.6 / 4.3	Exposure well defined Large sample size for outcomes Adequate follow-up	No information about attrition Outcomes not defined Values not shown for 6-month time frame	II-2, fair

<table>
<tr><th>Author, location and funding source</th><th>Study design</th><th>Study population</th><th>IUD type</th><th>Outcomes, follow-up duration</th><th>Results</th><th>Strengths</th><th>Weaknesses</th><th>Quality</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>No p values reported for 6-month time point; however, text says “no statistical differences” between any outcome at either time period for BF women compared to non-BF women.</td><td></td><td></td><td></td></tr>
<tr><td>Heartwell, 1983 [9]

United States

NICHD</td><td>Multicenter case control</td><td>Cases (n=32): women with IUD perforation admitted to hospital for removal

Controls (n=497): women with IUD in place admitted for acute self-limiting condition

Exclusions: women <6 weeks PP</td><td>Many</td><td>Perforation

Difficult removal (not further defined)</td><td><table><tr><th>BF at time of IUD insertion*</th><th>Perforation RR (95% CI)</th><th>Difficult removal RR (95% CI)</th></tr><tr><td>Yes</td><td>10.1 (4.9-20.6)</td><td>2.3 (1.1-4.4)</td></tr><tr><td>No</td><td>Ref</td><td>Ref</td></tr></table>*Analysis limited to women with at least 1 prior live birth</td><td>Multiple hospitals</td><td>Results not reported by IUD type

Unclear how BF status measured (recall)

Perforation status not ascertained from controls

Analysis not adjusted for potential confounders</td><td>II-2, poor</td></tr>
<tr><td>Chi and Kelly [16] andChietal. [17], 31 countries, FHI and USAID</td><td>Case–control analysis of large FHI international dataset

March 1976–December 1981</td><td>Cases (n=41): women with IUD perforation

Controls (n=41): women with no perforation matched by IUD type, inserter, center and date</td><td>Many</td><td>Perforation</td><td><table><tr><th>Perforations in women in which BF status was known</th><th>BF women N (%)*</th></tr><tr><td>Cases (n=19)</td><td>3 (15.8)</td></tr><tr><td>Controls (n=31)</td><td>1 (3.2)</td></tr></table>*No p value reported but authors stated “no significant difference” in risk of perforation for women breastfeeding at time of insertion compared to non-breastfeeding</td><td>Clearly defined outcomes and measurement clear</td><td>Small sample size

Results not reported separately by IUD type

No information about attrition

Unclear how BF status measured</td><td>II-2, poor</td></tr>
<tr><td>Heinemann et al. [5], 6 European countries, Center for Epidemiology and Health Research,</td><td>Prospective cohort</td><td>Women, at least 18 years, with a newly inserted IUD (n=61,448)

Exposed: BF</td><td>Cu-IUD (many types) and LNG IUD

LNG-IUD n= 43,078</td><td>Incidence of uterine perforation (self-reported, validated by physicians)</td><td>Cu-IUD:</td><td>Large sample size

Very low attrition (2%)

Adequate</td><td>More than 30 types of Cu-IUDs were included.</td><td>II-2,good</td></tr>
</table>

Author, location and funding source	Study design	Study population	IUD type	Outcomes, follow-up duration	Results	Strengths	Weaknesses	Quality
Germany, and Bayer		women (*n*=6645) *Cu-IUD (n=2682) LNG IUD (n=3963)* Unexposed: Non-BF women (*n*=54,803) *Cu-IUD (n=15,688) LNGIUD (n=39,115)*	*(70.1%)* *Cu-IUD n=18,370 (29.9%)*	Follow-up 12-months Noninferiority of LNG vs. Cu-IUD		follow-up Well defined exposure and outcome Results separated by IUD type		

BF	Perforation incidence per 1000 women (95% CI)	Perforation RR (95% CI)
Yes	3.7 (1.8-6.8)	**7.8 (2.8-21.4)**
No	0.5 (0.2-1.0)	Ref
All women	1.1 (0.7-1.7)	--

LNG-IUD:

BF	Perforation incidence per 1000 women (95% CI)	Perforation RR (95% CI)
Yes	6.3 (4.1-9.3)	**6.3 (3.8-10.5)**
No	1.0 (0.7-1.4)	Ref
All women	1.4 (1.1-1.8)	--

Combined Cu-IUD and LNG-IUD:

BF	Perforation RR (95% CI)
Yes	**6.1 (3.9-9.6)**
No	Ref

Author, location and funding source	Study design	Study population	IUD type	Outcomes, follow-up duration	Results	Strengths	Weaknesses	Quality
					<table><tr><th>BF</th><th>Perforation incidence (≤36 wks PP at the time of IUD insertion)</th><th>Perforation incidence (>36 wks PP at the time of IUD insertion)</th><th>RR (95% CI)</th></tr><tr><td>Yes</td><td>5.6 (3.9-7.9)</td><td>1.6 (0.0-9.1)</td><td>3.4 (0.5-24.8)</td></tr><tr><td>No</td><td>1.7 (0.8-3.1)</td><td>0.7 (0.5-1.1)</td><td>2.3 (1.1-4.7)</td></tr><tr><td>RR 95% CI</td><td>3.3 (1.6-6.7)</td><td>2.2 (0.3-16.3)</td><td></td></tr></table>			
Interval IUD insertions								
Chi et al. [18] (insertional pain); 18centersinAsia, Latin America and the Middle East; FHI and USAID	Retrospective cohort (analysis oflarge FHI international IUD database) 1977–1986	Parous women at least 42 days PP whose last delivery was term, live, vaginal birth Exposed: BF women (*n*=3043) Unexposed: non-BF women (*n*=3450)	Many (Loops, Cu-Ts and multiloads: 55.7% Cu-IUD types that met inclusion criteria)	Mod/severe insertional pain Perforation Cervical laceration Syncope Any insertion-related adverse event	Cu-Ts: <table><tr><th>BF</th><th>Syncope n (%)*</th><th>Immediate perforation n(%)*</th></tr><tr><td>Full</td><td>2 (0.12)</td><td>1 (0.06)</td></tr><tr><td>No</td><td>0 (0.0)</td><td>1 (0.06)</td></tr></table>* p Values>.05 Results not separated by IUD type: <table><tr><th>BF</th><th>Mod/severe pain at insertion RR (95% CI)</th><th>Cervical laceration RR (95% CI)</th><th>Any insertion related adverse event **</th></tr><tr><td>Full</td><td>0.47 (0.37-0.59)</td><td>0.72 (0.35-1.47)</td><td>0.46 (0.38-0.56)</td></tr></table>	Large sample size Adequate exposure and outcome definition Adequate follow-up	Multiple IUD types No information on attrition Some results not reported separately by IUD type	II-2, poor

Author, location and funding source	Study design	Study population	IUD type	Outcomes, follow-up duration	Results	Strengths	Weaknesses	Quality
					BF | **Mod/severe pain at insertion RR (95% CI)** | **Cervical laceration RR (95% CI)** | **Any insertion related adverse event **** No | ref | ref | ** Except perforation			
Sastrawinata et al. [20], Indonesia, National Family Planning Coordinating Board of Indonesia USAID	Prospective cohort study (within an RCT)	Healthy women ages 18–40 aged years; ≥40 days PP Exposed: BF women (*n*=2237) Unexposed: non-BF women (*n*=608)	CuT 380A	Expulsion Removals for bleeding/pain Follow-up 24 months	**BF** | **Expulsion at 24 mos (Rate/100 women + SE)** | **Removal for bleeding/pain at 24 mos (Rate/100 women + SE)** Yes | 6.0 ±0.9 | 1.6 ±0.5 No | 6.9±1.7 | 4.1±1.4 (no p values reported, stated no statistically significant differences)	Long follow-up Low attrition Adequate definition and measurement of outcomes	Poor description of definition ofBF or how BF status may have changed over 24-month study time	II-2, fair
Wu [22], China	Prospective cohort	Healthy women with IUD Exposed: BF women (*n*=850) “early” 6–12 weeks PP (*n*=451) “late” 4–12 months PP (*n*=399) Unexposed: non-BF women; >6 weeks PP (*n*=2293)	CuT 380A	Perforation Infection Expulsion Removals for bleeding/pain Follow-up 12 month	No perforations No PID **BF** | **Expulsion at 12 mos (Rate/100 women)*** | **Removal for bleeding/pain at 12 mos (Rate/100 women)*** Yes; early | 0.51 | 1.42 Yes; late | 2.11 | 1.33 No | 1.11 | 1.94 * p>.05 for all comparisons	Long follow-up Large sample size	Outcome assessment not well defined	II-2, fair

Studies from FHI’s randomized, multicenter clinical trial from May 1985 to September 1988. Women (N42 days PP) were randomized to either CuT 380A or another common IUD type used at multiple centers across 14 countries. Follow-up time occurred at 1, 3, 6 and 12 months.

<table>
<tr><th>Author, location and funding source</th><th>Study design</th><th>Study population</th><th>IUD type</th><th>Outcomes, follow-up duration</th><th>Results</th><th>Strengths</th><th>Weaknesses</th><th>Quality</th></tr>
<tr><td>Chi et al. [23] (performance ofCu)</td><td>Prospective cohort study (within larger RCT)

Data from 1985 to 1986; CuT T380A users; 5 sites</td><td>Healthy women aged 18–40 years at least 42 days PP

Exposed: BF women (n=559)

Unexposed: non-BF women (n=590)</td><td>CuT 380A</td><td>Mod/severe pain at insertion

Perforation

Cervical laceration

Expulsion

Removal for bleeding/pain

Follow-up: 6 months</td><td>
<table>
<tr><th>BF</th><th>Pain at insertion n(%)</th><th>Perforation n(%)</th><th>Cervical laceration n(%)</th></tr>
<tr><td>Yes</td><td>5 (0.9)</td><td>0 (0.0)</td><td>5 (0.9)</td></tr>
<tr><td>No</td><td>16 (2.7)</td><td>0 (0.0)</td><td>8 (1.4)</td></tr>
<tr><td>p-value</td><td>0.026</td><td>--</td><td>0.581</td></tr>
</table>
<table>
<tr><th>BF</th><th>Expulsion at 6 mos (Rate*/100 women + SE)</th><th>Removal for bleeding/pain at 6 mos (Rate*/100 women + SE)**</th></tr>
<tr><td>Yes</td><td>2.5 ±0.7</td><td>0.4 ±0.4</td></tr>
<tr><td>No</td><td>2.8 ±0.7</td><td>3.2 ±0.8</td></tr>
</table>
*Adjusted for age.

**p<.05.</td><td>Large sample size

Adequate follow-up Adequate exposure and outcome definition

Single IUD type</td><td>Outcome assessment not well defined</td><td>II-2, good</td></tr>
<tr><td>Farr and Rivera [24]</td><td>Prospective cohort study (within larger RCT)

Data from May 1985 to Sept. 1988; 25 sites; CuT 380A users</td><td>Healthy women aged 18–40 years at least 42 days PP

Exposed: BF women (n=1032)

Unexposed: non-BF women (n=1243)</td><td>CuT 380A</td><td>Pain at insertion

Perforation

Cervical laceration

Expulsion

Removal for bleeding/pain

Follow-up: 12 months</td><td>
<table>
<tr><th>BF</th><th>Pain at insertion (%)</th><th>Perforation (%)</th><th>Cervical laceration (%)</th></tr>
<tr><td>Yes</td><td>17.1</td><td>0</td><td>4.0</td></tr>
<tr><td>No</td><td>25.2</td><td>0</td><td>2.8</td></tr>
<tr><td>p-value</td><td>0.001</td><td>--</td><td>0.156</td></tr>
</table></td><td>Large sample size

Long follow-up

Low attrition Single IUD type

Adequate definition of BF status</td><td></td><td>II-2, good</td></tr>
</table>

Author, location and funding source	Study design	Study population	IUD type	Outcomes, follow-up duration	Results	Strengths	Weaknesses	Quality
					<table><tr><th>BF</th><th>Expulsion at 12 mos (Rate/100 women + SE)*</th><th>Removal for bleeding/pain at 12 mos (Rate/100 women + SE)**</th></tr><tr><td>Yes</td><td>3.9 ±0.7</td><td>2.9 ±0.6</td></tr><tr><td>No</td><td>2.8 ±0.5</td><td>5.1 ±0.7</td></tr></table> *Not significant. **p=.05.			
Zhang [25]; FHI, USAID	Nested case–control Data from 1985 to 1986; 13 sites	Healthy women aged 18–40 years at least 42 days PP Cases (n=143): women with IUD removal for bleeding/ pain Controls (*n*=2023): women with IUD in place at last visit	TCu-200, TCu-220C or CuT 380A	Removal for bleeding/pain Follow-up: 12 months	<table><tr><th>BF</th><th>Removal for bleeding/pain at 12 mos hazard ratio (95% CI)*</th></tr><tr><td>Yes</td><td>0.75 (0.59-0.97</td></tr><tr><td>No</td><td>Ref</td></tr></table> *Adjusted for center, age, parity, level of training of inserter, menstrual status and length from the external os to the fundus	Adequate sample size Long follow-up Adequate definition of BF status and outcome	Results not reported separately by IUD type No information on attrition for this subset	II-2, fair
Stanback and Grimes [26], USAID	Case–control analysis of multicenter FHI RCT. Data from1985 to 1986; 18 sites	Healthy women aged 18–40 years at least 42 days PP Cases (n=89): women with IUD removal for bleeding/ pain Controls (*n*=20,536):	CuT 380A or Multiload 250	Removal for bleeding/pain Follow-up: 12 months	<table><tr><th>BF</th><th>Removal for bleeding/pain at 12 mos OR (95% CI)</th></tr><tr><td>Yes</td><td>Ref</td></tr><tr><td>No</td><td>2.8 (1.5-5.2)</td></tr></table>	Long follow-up Large sample size Adequately defined exposure and outcome	Results not reported separately by IUD type No mention of attrition rates for this subpopulation	II-2, poor

Author, location and funding source	Study design	Study population	IUD type	Outcomes, follow-up duration	Results	Strengths	Weaknesses	Quality
		women with IUD at 1 year						
Rivera et al. [27]; FHI, USAID	Secondary cohort analysis of multicenter RCT Data from 1985 to 1989; number of sites not specified	Healthy women aged 18–40 years at least 42 days PP Exposed: BF women (*n*=1582) Unexposed: non-BF women (*n*=1161)	CuT 380A	Expulsion Removals for bleeding/pain Follow-up: 12 months	**BF** / **Expulsion rate at 12 mos Rate (95% CI)** / **Rate of removal for bleeding/pain at 12 mos (95% CI** Yes / 3.6 (2.4-4.7) / 3.2 (2.1-4.4) No / 2.8 (1.9-3.7 / 5.5 (4.2-6.7) p-value / 0.23 / 0.01	Long follow-up Large sample size Adequately defined exposure and outcome	Attrition rates not reported	II-2, good

BF, breastfeeding; FHI, Family health International; PID, pelvic inflammatory disease; PP, postpartum; SE, standard error; USAID, United States Agency of International Development.

Table 2

Articles identified for research question #2: Among breastfeeding women, does IUD use, as compared with use of other contraceptive methods, increase the risk of adverse events (bleeding, infection, pain, or other adverse events)?

Author, location and funding source	Study design	Study population	Contraceptive methods	Outcomes, follow-up duration	Results	Strengths	Weaknesses	Quality
Chen et al. [29], China, Population Council	Prospective cohort	Healthy, fully breastfeeding, age 18–35 years, women desiring contraception Exposed: IUD users (*n*=97) Unexposed: PVR users (*n*=100)	CuT 380A PVR Initiated 29–64 days PP	Removals for bleeding complications Follow-up: 12 months	No insertion failures, perforations or PID among IUD users at 1 year Removals for bleeding: IUD *n*=0 PVR *n*=3 (p=.048)	Adequate follow-up duration Adequately defined outcome for bleeding and exposures	No information about attrition or possible changes in BF status across study period Groups differed at baseline; no assessment of prior bleeding history or hemoglobin at baseline	II-2; poor
Abdel-Aleem et al. [30], Egypt, South-to-South Cooperation in Reproductive Health	Prospective cohort	Healthy exclusive breastfeeding women desiring contraception Exposed: IUD users (*n*=120) Unexposed: Nomegestrol implant users (*n*=120)	CuT 380A Nomesgestrol implant Initiated during 2nd PP month	Removals for bleeding at 11 months	Removals for bleeding: Implant *n*=2 IUD *n*=2 (no p values reported)	Low attrition Adequate follow-up duration Baseline hemoglobin levels similar between groups	Groups differed at baseline Small sample size	II-2; poor
Massai et al. [28], Chile, International Committee for Contraception Research of the Population Council, New York	Prospective cohort	Healthy PP (term, NSVD) women willing to breastfeed for at least 6 months PP desiring contraception, fully nursing and amenorrheic Exposed: IUD users (*n*=100) Unexposed: NES implant users (*n*=100)	CuT 380A NES implant Initiated 55–60 days PP	Adverse events Removals for bleeding/pain 2-year follow-up	No serious adverse events Removal for bleeding at 24 months: (no significant difference, no p value reported) NES *n*=4 IUD *n*=1	Groups similar at baseline regarding age, parity, height, weight and hemoglobin Long follow-up duration Low attrition Adequately defined exposure and outcome	Small sample size with uncommon events to compare	II-2; fair

NES, Nestrone; PP, postpartum.

Table 3

Among breastfeeding women, does Cu-IUD use, as compared with non-use of an IUD and non-use of a hormonal contraceptive, increase the risk of breastfeeding-related adverse events (breastfeeding continuation and exclusivity, use of supplementation, infant growth, or infant health)?

Author, location and funding source	Study design	Study population	Contraceptive methods	Outcomes, follow-up duration	Results	Strengths	Weaknesses	Quality
Prema [31], India, National Institute of Nutrition, Indian Council of Medical Research	Retrospective cohort	BF women. (otherwise unclear) Exposed: Cu IUD users (*n*=68) Unexposed: nonusers of contraception (*n*=1917)	Cu-IUD (type not stated)	Duration of lactation and duration of amenorrhea, collected prospectively for Cu-IUD users and retrospectively for nonusers of contraception	Duration of lactation (months): (no p value) IUD: 21±10.8 No contraception: 20±9.6 Duration of amenorrhea (months): (no p value) IUD: 11±5.6 No contraception: 11±5.0		No report on attrition Standard follow-up not reported No statistical comparisons Small sample size Poorly defined exposure and outcome	II-2; poor
(a) Croxatto et al. [33] (b) Croaxatto et al. [34] Chile The Population Council, International Research Centre of Canada, WHO, Instituto Biomedico and Laboratorio Berlimed	Prospective cohort	Healthy PP (term, NSVD) women, age 18–35 years, parity 1–3 desiring contraception, fully nursing and amenorrheic (a) Exposed: CuT 200IUD users (*n*=125) Unexposed: placebo users (*n*=130) (b) Exposed: CuT 200IUD users (*n*=118) Unexposed: placebo users (*n*=109)	CuT 200 Lactational infertility (given an injectable placebo on PP day 30)	(a) BF continuation, infant weight gain at 6 months (b) BF discontinuation, infant weight through 12 months	(a) BF Continuation: no significant differences at 3,6 and 9 months. At 12 months, IUD users have significantly more women fully BF and lowest % of BF discontinuers vs. placebo. (no p values reported) Infant growth at 6 months: no sig differences (no p values reported) IUD: 4801±817 g; placebo: 4633±529 g (b) *IUD* vs. *placebo* % of women discontinued BF: 2 months: 0% vs. 0% (no p values) 6 months: 4.7% vs. 9% 12 months: 34.7% vs. 40.7% Mean weight of BF infants only (grams): 2 months: 5211±504 vs. 5366±554 6 months: 8102±766 vs. 8333±717 12 months: 10,208±819 vs. 10,746±721	Adequate follow-up Adequate sample size Adequate definition of outcomes	No information on attrition No statistical comparison While use of a placebo that women were told would support lactational infertility may be unethical we felt this would be unlikely to affect the results pertaining to this research question.	II-2, fair
Shaaban et al. [35], Egypt, Rockefeller Foundation	Prospective cohort	Healthy, PP, BF women, normal singleton delivery Exposed: CuT 380A users (*n*=50) Unexposed: barrier/no	CuT 380A initiated 30–42 days PP Barrier/non method included	Supplementation Infant growth Maternal assessment of breast milk quantity Follow-up monthly to 6 months PP	*IUD* vs. *Barrier/no contraception* Number of women supplementing: 2 months: 5 vs. 5 (no p value) 6 months 48 vs. 47 (no p value) Mean daily weight gain (grams): 2 months: 33.4±2.3 vs. 33.3±2.5 (no p value) 6 months 19.7±1.4 vs. 19.5±2.3 (no p value)	Adequate follow-up Low attrition	Small sample size No statistical comparisons	II-2; poor

Author, location and funding source	Study design	Study population	Contraceptive methods	Outcomes, follow-up duration	Results	Strengths	Weaknesses	Quality
		contraception users (*n*=50)			Mean daily length gain (cm): 2 months: 0.12± 0.03 vs.0.11±0.03 (no p value) 6months0.07±0.01 vs. 0.08±0.02 (no p value) No one indicated a decline in quantity of breast milk up to 6 months PP			
Diaz et al. [32]; Chile; WHO, CON-RAD, Eastern Virginia Medical School, The Population Council	Prospective cohort	Healthy PP (vaginal delivery of a single, term, healthy infant of normal weight) women, age 18–35 years, parity 1–3 desiring contraception, fully nursing and amenorrheic Exposed: CuT 380A users (*n*=122) Unexposed: historical control using lactational infertility (*n*=236)	Cu T380A initiated 57±3 days PP. Lactational infertility	Duration of lactation Duration of full BF Infant growth Follow-up at 15, 30 days after contraceptive initiation, every 2 months thereafter to 12 months	*(Mean days±SE)* Total duration of lactation: T380A: 342±9 Untreated: 344±9 Duration of full BF: T380A: 245±9 Untreated: 234±8 Infant growth (birth to 6 months) T380A: 4606±74 g Untreated: 4800± 62 g No significant differences for all comparisons, but no p values reported	Adequate follow-up Adequate sample size Adequate definition of outcomes	No report of on attrition No control for differences in baseline characteristics	II-2, fair

BF, breastfeeding; PP, postpartum; SE, standard error.