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Research Article

# A Meta-Analysis of Postpartum Copper IUD Continuation Rates in Low- and Middle-Income Countries

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## Abstract

**Background:** Long-acting reversible contraception (LARC) initiated immediately postpartum can reduce unintended or mistimed pregnancies, and contribute to proper pregnancy spacing. Data on use and continuation of postpartum LARC in low- and middle-income countries (LMIC) is limited.

**Methods:** We searched PubMed, OVID, Embase, Google Scholar, Cochrane, POPLINE, Global Health (CABI), and LILACS databases for relevant terms. Studies of any design, published in English, were screened for relevance based on six-month continuation rates of postpartum LARC, location of study, and LARC insertion within 48 hours after vaginal or cesarean birth. We found no relevant studies of implant or hormonal intrauterine device (IUD). Therefore, analysis was limited to studies of the copper IUD only. Two authors used the Cochrane Public Health Group Data Extraction and Assessment Template to guide data extraction to estimate pooled six-month continuation rates, and the Cochrane Risk of Bias Tool for Randomized Controlled Trials and the National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies to rate the quality of the studies. A random-effects meta-analysis of proportions was performed.

**Results:** Immediate-postpartum copper IUDs have a six-month continuation rate of 87% (95% CI 80-92%) in LMIC. The pooled estimated rates of six-month adverse outcomes were 6% (95% CI 5-9%) for expulsion, 5%

(95% CI 4-7%) for removal, and 0.2% (95% CI 0.0-0.9%) for infection.

**Conclusions:** High six-month continuation rates and a low rate of adverse outcomes suggest immediate postpartum copper IUD insertion is a feasible and acceptable postpartum contraceptive option for women living in LMIC.

**Keywords:** Postpartum

## 1. Background

Use of effective postpartum contraception can lengthen interpregnancy intervals and reduced unintended pregnancy [1]. The World Health Organization (WHO) recommends an interpregnancy interval of at least 24 months in order to minimize maternal and neonatal risks associated with shorter intervals [2]. Short inter-pregnancy intervals are associated with increased risks of preterm birth, maternal morbidities such as anemia, as well as neonatal risks of low birth weight and perinatal death [2]. In a study of Demographic Health Surveys in 21 countries, 61% of postpartum women in LMIC were identified as having an unmet need for family planning, and at least 50% of non-first births occurred in short interpregnancy intervals in nine countries [3].

Initiation of long-acting reversible contraception (LARC), which includes the subdermal implant, and intrauterine devices (IUDs), in the immediate postpartum period, defined as within 48 hours of birth [4], can reduce unintended and/or short-interval pregnancies in a high-income country setting [1]. LARC methods are more effective than short-acting forms of contraception, such as oral contraceptive pills [5]. When LARC methods are offered in an extended postpartum period (up to six weeks after birth) in LMIC, women find it to be an acceptable and appropriate option [6].

In a high-income country setting, twelve-month continuation rates were higher for long-acting methods (86%), including the copper intrauterine device (IUD, 84%), than oral contraceptive pills (55%) and other short-acting methods of contraception [7]. Among women using postpartum family planning in LMIC, 51 to 96% use short-acting methods [3]. This highlights a possible need for increased access to postpartum LARC in LMIC. Given the burden of unintended and short-interval pregnancies in LMIC, and the adverse outcomes associated with these pregnancies, use of postpartum contraception is important [2]. However, there is limited evidence on continuation rates of postpartum LARC methods in LMIC. Continuation rates of contraceptive methods are a proxy indicator of satisfaction [7], and therefore are an important metric to assess when evaluating postpartum LARC initiatives in LMIC. The Family Planning 2020 (FP2020) initiative [8] is a worldwide partnership hosted by the United Nations Foundation that assists 69 committed low-income countries in improving access to contraceptives and helps women achieve their reproductive goals [8]. This initiative has also works to improve data collection and availability in these countries. A stated goal of FP2020 is to "work toward increasing the availability, visibility, quality, and use of family planning data."

Therefore, the objective of this systematic review and meta-analysis was to determine six-month continuation rates of LARCs inserted within 48 hours of birth in countries involved in the FP2020 initiative [8]. As we found zero relevant studies on other LARC methods, we ultimately focused on the copper IUD that is currently available, the CuT380A. We hypothesized that the six-month continuation rate would be comparable to those in high-income countries, which is over 80% [7]. Secondary aims included determining six-month IUD removal, expulsion, pain, bleeding, infection, pregnancy, and missing string rates.

## 2. Methods

### 2.1 Search strategy

In August 2017, we searched PubMed, OVID, Embase, Google Scholar, Cochrane, POPLINE, Global Health (CABI), and LILACS for search terms and MESH terms (PubMed) developed by the senior author (MSH) and a clinical librarian. We did not use any specialized search software. The search terms included all synonyms and related terms to the following key concepts: (1) "postpartum," (2) "LMIC," (3) FP2020 countries, (4) "LARC," and individual LARC types and (5) "continuation rate." Search formatting was adjusted to fit the interface requirements of each database. No hand searching was performed. See Appendix A for full search strategy.

### 2.2 Inclusion criteria

Studies of any design published in English were considered. The first author (ALM) and MSH screened abstracts for relevance based on publication of six-month continuation rates, location of the study in one of the FP2020 countries [8] (see Appendix B) and insertion of the LARC method either "post-placentally" (within 10 minutes of expulsion of placenta) or "immediately postpartum" (within 48 hours) after vaginal or cesarean deliveries. We focused on this time-period because this is how FP2020 and the WHO define care provided in the "pre-discharge" stage of perinatal care [4]. Included countries were limited to those in the FP2020 initiative to improve the relevance of results, given that these countries are committed to postpartum contraceptive initiatives [8]. After all relevant abstracts were identified, inclusion criteria were then refined to include only copper IUDs when scant to no evidence for other LARC methods (implant or other types of IUDs) was identified. When a citation yielded only an abstract, we attempted to contact a corresponding author electronically to inquire whether a subsequent article had been published based on the abstract data, or if unpublished manuscripts could be shared. ALM and MSH then performed full text screening to confirm studies met all inclusion criteria. A flow diagram of determinations regarding the reviewed abstracts and manuscripts are shown in Figure 1.

### 2.3 Quality determination

Authors ALM and MSH independently rated the quality of evidence in each study based on the Cochrane Risk of Bias Tool for Randomized Controlled Trials [9] and the National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies [10]; these authors then met to discuss and resolve discrepancies. Studies of fair quality or better were included.

### 2.4 Data extraction

We used the Cochrane Public Health Group Data Extraction and Assessment Template [11] to guide extraction of relevant data. Authors ALM and MSH extracted data separately and met to discuss and resolve discrepancies.

### 2.5 Data analysis

Data was analyzed with R software and the meta [12] and metaphor [13] packages. All statistical tests were performed with $p<0.05$ significance. To estimate pooled six-month continuation rates, a random-effects meta-analysis of proportions was performed. The logit transform was performed which is recommended when the observed proportions are >0.8 [14]. The DerSimonian and Laird [15] method was used to estimate between-study variance. Heterogeneity was assessed with $Tau^2$, $I^2$ and the Q-test. A forest plot was created to visualize the point estimates of the studies and their confidence intervals. Studentized residuals were screened to identify potential outlier studies (abs value $Z>2.0$). To determine the influence of outliers on model results, a "leave one out" analysis was

performed. Modifiers were assessed as possible sources of heterogeneity with subgroup analysis. Subgroup analysis of country as a modifier was done assuming a common variance between-study component (or pooled $tau^2$). Summary effects of each subgroup were compared with a mixed effect model. Secondary six-month outcome rates of expulsion, removal, bleeding, missing strings, and infection were pooled with a random effects meta-analysis. Double arcsine transformation was used for the rare outcome of infection. Otherwise, proportions were transformed with the logit transformation. Forest plots were created for each secondary outcome.

### 2.6 Ethics approval

As we used aggregated, de-identified data from other studies in which human subjects approval was obtained, we did not seek approval from an institutional review board or obtain consent from subjects.

## 3. Results

### 3.1 Study selection

The search strategy yielded 481 abstracts after duplicates were removed. After abstract screening was completed, 108 full-text studies were assessed for eligibility, and 11 studies [16-26] were included. See Figure 1 for screening flow diagram and reasons for exclusion. For the purposes of data analysis, one study [26] was divided into two as it took place in two different countries and presented separate data for each. Table 1 lists study details.

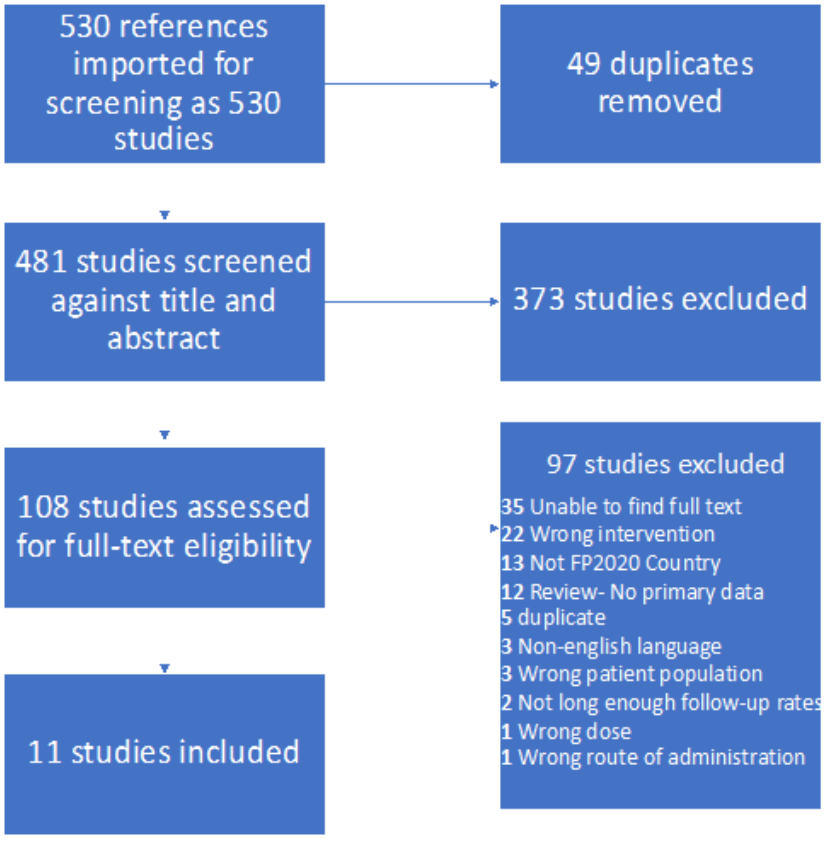


**Figure 1:** Screening flow diagram.

| Study number | Author, year | Methods | Participants | Interventions | Outcome(s) | Quality grading* |
|---|---|---|---|---|---|---|
| 1 | Rani, 2015 | Prospective cohort | 100 women delivering via Cesarean or vaginally in Patiala, India | Post-placental insertion of Cu380A IUD | Continuation rates, side effects, reasons for discontinuation | Fair |
| 2 | Dewan, 2017 | Prospective cohort | 348 women at least 18 years of age delivering via Cesarean or vaginally in New Delhi, India | Post-placental insertion of Cu380A IUD | Incidence of visible strings at follow-up and women's perceptions of missing strings; continuation, expulsion, removal rates at one year, reasons for removal | Good |
| 3 | Singal, 2014 | Prospective cohort | 300 primiparous women delivering via Cesarean in New Delhi, India | Post-placental insertion of Cu380A | Safety, efficacy, expulsion, and continuation rates | Good |
| 4 | Mishra, 2014 | Prospective cohort | 564 women, age 18-45 delivering via Cesarean or vaginally in bolangir, India | Post-placental insertion of Cu380A | Safety, efficacy, expulsion, continuation and removal rates, side effects/complaints | Fair |
| 5 | Mishra, 2017 | Retrospective cohort | 726 women delivering via Cesarean or vaginally in Bolangir, India | Post-placental insertion of Cu380A IUD | Incidence, clinical outcome, management of missing IUD strings; complications | Fair |
| 6 | Gupta, 2015 | Prospective cohort | 150 women delivery via cesarean or vaginally in New Delhi, India | Post-placental insertion of Cu380A IUD | Satisfaction, continuation, efficacy, safety, expulsion | Good |
| 7 | Bhat, 2016 | Prospective cohort | 680 women delivering via cesarean or vaginally in Pune, India | Post-placental (<10 min) or immediate postpartum (<48h) insertion of Cu380A IUD | Acceptance of intervention, retention, and expulsion rates; side effects/complications, satisfcation | Good |

| | | | | | | |
|---|---|---|---|---|---|---|
| 8 | Blumenthal, 2016 | Prospective cohort | 591 women delivering vaginally at sites of the Society for Family Health in Lusaka, Zambia | Immediate postpart-um (<48h) insertion of Cu380A IUD | Continuation; satisfaction, complications | Fair |
| 9 | El Beltagy, 2011 | Randomized-controlled trial | 300 women delivering vaginally at El-Shatby Maternity Hospital in Egypt | Immediate partum (<48h) insertion of Cu380A IUD (n= 150) vs Multiload 375 IUD (n=150) | Expulsion rates; side effects/complications | Fair |
| 10 | Lester, 2015 | Randomized-controlled trial | 68 women delivering via cesarean in Kampala, Uganda | Post-placental inser-tion vs delayed postpartum (>6wks) insertion of Cu380A IUD | Six-month utilization; satisfaction, removal, expulsion, adverse events | Good |
| 11 | Morrison, 1996 | Prospective cohort | 224 women in Kenya, and 110 women in Mali, delivering vaginally or via cesarean | Immediate (<10 min) vs late (up to 72h) postpartum insertion of Cu380A IUD (timing based on when patient requested IUD) | Expulsion, removal, discontinuation rates; adverse events | Fair |

*Quality of evidence determined by the Cochrane Risk of Bias Tool for Randomized Controlled Trials and the National Heart, Lunch, and Blood Institute (NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

**Table 1:** Study characteristics.

### 3.2 Description of studies

Of the 11 included studies, nine [16-23, 26] were prospective cohorts and two [24, 25] were randomized controlled trials. Six of the prospective cohorts [16, 17, 19-21] compared outcomes after post-placental (within ten minutes) copper IUD insertion between women delivering vaginally and via cesarean. Two prospective cohort study [22, 26] compared outcomes between post-placental insertion and later insertion (within 48 hours of delivery [22] or within 72 hours [26]; in women delivering vaginally or via cesarean. In the cohort that compared post-placenta insertion vs insertion up to 72 hours, only the data from the post-placental insertion group was used in analysis, as 72 hours was outside of the window for our inclusion criteria. One prospective cohort [18] recorded outcomes of post-placental insertion of copper IUDs in women undergoing cesarean deliveries only. Another prospective cohort [23] recorded outcomes after IUD insertion within 48 hours of vaginal delivery only. One randomized

controlled trial (RCT) compared outcomes between two different types of copper IUDs among women delivering vaginally; data from only the copper 380A IUD was used in our analysis [24]. The other RCT compared outcomes between post-placental insertion and delayed (>6 weeks) insertion; only data from post-placental insertion participants was used for our analysis [25].

### 3.3 Quality assessment

After initial independent quality assessment, MSH and ALM had two overall quality score discrepancies that were resolved through review and discussion. Ultimately, five studies were determined to be of good quality and six were of fair quality.

### 3.4 Primary outcome

The meta-analysis of all 12 studies (11 studies with Morrison, et al [26] considered as two) resulted in a pooled six-month continuation rate of 87% (0.87, 95% CI 0.80,0.92) (Figure 2). However, there is a significant (Q-test p= <0.0001) amount of heterogeneity ($tau^2$ = 0.76) which was mostly between studies ($I^2$ = 97%). The Mishra 2014 study was indicated as an outlier (abs z = 2.13). Removing this study resulted in less heterogeneity (tau2 = 0.45). However, this had little effect on the pooled proportion and confidence interval estimates (0.88, 95% CI 0.83,0.92). Therefore, no studies were removed as outliers in this analysis. Country (India vs other) was examined in moderator subgroup analysis to determine if it explained a significant amount of the heterogeneity of studies for six-month continuation rates because 7 of the 12 studies were executed in India. The pooled six-month continuation rates in the India studies did not differ significantly from that of studies from other countries (0.87, 95% CI 0.76,0.93] vs 0.87, 95% CI 0.74,0.94; p = 0.89).

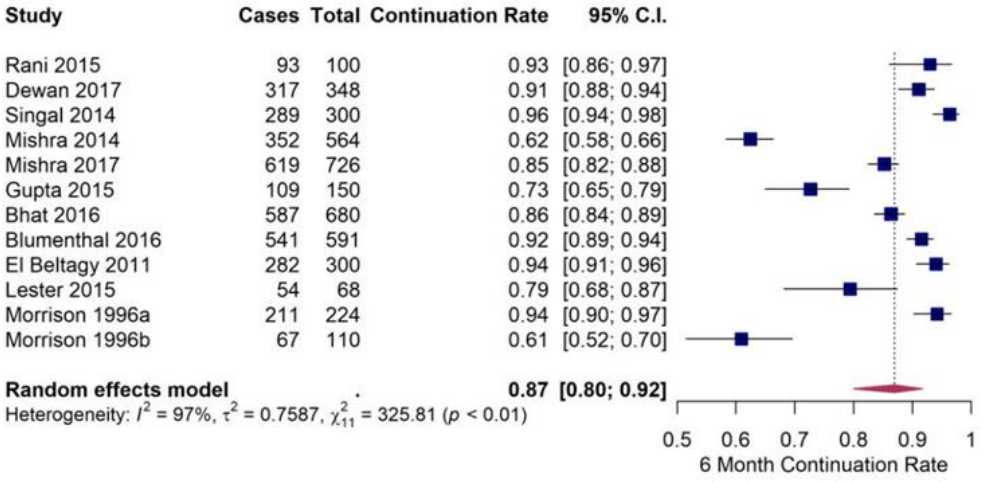


**Figure 2:** Forest Plot of Continuation Rates.

### 3.5 Secondary outcomes

The pooled estimated expulsion rate across all studies was 6% (0.06, 95%CI 0.05,0.09). The pooled removal rate for the 11 studies that included removal data was 5% (0.05, 95% CI 0.04,0.07). The pooled rate of bleeding at six months was 22% (0.22, 95% CI 0.07,0.52) for the six studies that had bleeding data. However, one study stood out on the forest plot with a bleeding proportion of 89%. Seven studies had data on six-month missing string rates; the pooled proportion

for those missing strings at six months was 17% (0.17, 95% CI 0.11,0.27). Four of the eight studies with infection data indicated no infection occurred. The pooled proportion for six-month infection was 0.2% (0.002, 95% CI 0.000,0.009).

## 4. Conclusions

This is the first meta-analysis, to our knowledge, of immediate postpartum copper IUD continuation rates in LMIC. Our finding of a six-month continuation rate of 87% is important to global public health because this rate is comparable to continuation rates found in higher-income countries [7]. This estimate did, however, have significant heterogeneity between studies. Secondary outcomes of expulsion, removal, and infection rates were low at 6%, 5%, and 0.2% respectively. This analysis has generalizability because the quality assessment performed on the studies included used validated quality assessment tools, and all the of studies were of fair or better quality. Studies that were excluded would not have been able to contribute to the primary outcome so we do not think the sample is biased by their exclusion. Additionally, as this was unfunded study, we were unable to translate non-English language manuscripts, of which there three; we did not use internet-based translating tools because the files of the manuscripts were images and not selectable text.

The results of this meta-analysis are important for future efforts to increase access to postpartum copper IUDs in LMIC. In a study of acceptability of post-partum IUDs among women in Nigeria, 50% of those who were offered a postpartum IUD accepted this method [27]. Since continuation rates can reflect satisfaction with a contraceptive method [7], our results add to the evidence that immediate postpartum copper IUD is acceptable to women in LMIC, and that women are likely to be very satisfied with this method. Notably, rates of complications, such as infection and expulsion, were low and consistent with data from higher-income countries [28-31]. These findings can be used to support programs that increase accessibility to postpartum copper IUD insertion in LMIC. Immediate postpartum copper IUD insertion has promise for improving birth spacing, unmet need for family planning, and resulting maternal, child, and neonatal morbidity and mortality [2]. When interpreting these results, it is important to consider alternative explanations for the high continuation rates. Specifically, in LMIC, it may be difficult for women to present to a care provider to have their IUD removed if they so desire [32]. However, the majority of these studies had little loss-to-follow-up, suggesting that these patients had adequate access to care. Another possible explanation for high continuation rates is provider coercion, which has been a global concern with contraception and sterilization among poor or otherwise marginalized people [33]. However, the studies included in this review reported following ethical research practices, including antenatal contraceptive counseling, and obtaining informed consent. Our focus on FP2020-committed countries can also provide reassurance that coercion is less likely, due to the initiative's focus on rights-based family planning programs; specifically, FP2020 initiatives aim to provide family planning services that aim to improve agency and autonomy, and prevent coercion [8].

The main strength of this study is that it is a novel investigation to summarize what is known about continuation rates of copper IUDs inserted postpartum in LMIC. Additionally, all data included in the meta-analysis were from published studies of fair or better quality. Additionally, collaborating with a librarian allowed for rational search strategy and identification of a comprehensive cohort of high-quality studies to screen and analyze. A weakness of the study is the heterogeneity identified between studies. This was reduced when one potential outlier was removed, but

this did not have a significant impact on the meta-analytic estimate of the six-month continuation rate. This heterogeneity could possibly be explained by differences between the six countries included in the study and in different timing of IUD insertion between studies. However, the potential outlier study was executed in India, where five other studies were also performed. Other limitations of this review are that included data was only from studies published in English from six countries, which limits our ability to generalize to more LMIC.

Another significant finding discovered during the systematic review was the extremely limited evidence on postpartum use of other LARC methods such as the levonorgestrel IUD and the progestin-containing implants. This may reflect cost differences, access or availability, and/or patient preferences, but more studies are needed to identify the feasibility of offering these additional methods in the immediate postpartum period in LMIC. Our findings can be used to educate providers about the public health relevance of immediate postpartum IUD initiation. Future knowledge, attitudes, and practice assessments of health care providers in LMIC will help with directing program implementation efforts to improve delivery and accessibility of postpartum IUD. It is also not known how often immediate postpartum IUD is being offered in LMIC. In regions where little is known about postpartum contraception, needs assessments and qualitative studies exploring patient and provider values may be considered for next steps in exploring postpartum IUD program implementation.

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## Conflict of Interest

The authors have no relationships to disclose that may be deemed to influence the objectivity of this paper and its review. The authors report no commercial associations, either directly or through immediate family, in areas such as expert testimony, consulting, honoraria, stock holdings, equity interest, ownership, patent-licensing situations or employment that might pose a conflict of interest to this analysis. Additionally, the authors have no conflicts such as personal relationships or academic competition to disclose. The findings presented in this paper represent the views of the named authors only, and not the views of their institutions or organizations.

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