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Association of the Timing of Postpartum Intrauterine Device Insertion and Breastfeeding With Risks of Intrauterine Device Expulsion

Mary Anne Armstrong, MA; Tina Raine-Bennett, MD; Susan D. Reed, MD, MPH, MS; Jennifer Gatz, PhD; Darios Getahun, MD, PhD, MPH; Juliane Schoendorf, MD; Debbie Postlethwaite, MPH, RNP; Michael J. Fassett, MD; Jeffrey F. Peipert, MD, PhD; Catherine W. Saltus, MA, MPH; Maqdooda Merchant, MSc, MA; Amy Alabaster, MPH, MS; Xiaolei Zhou, PhD; Laura Ichikawa, MS; Jiaxiao M. Shi, PhD; Vicki Y. Chiu, MS; Fagen Xie, PhD; Shannon Hunter, MS; Jinyi Wang, MStat; Mary E. Ritchey, PhD; Giulia Chillemi, MS; Theresa M. Im, MPH; Harpreet S. Takhar, MPH; Federica Pisa, MD, MStat; Alex Asiimwe, PhD; Mary S. Anthony, PhD

Abstract

IMPORTANCE Intrauterine device (IUD) expulsion increases the risk of unintended pregnancy; how timing of postpartum IUD insertion and breastfeeding are associated with risk of expulsion is relevant to the benefit-risk profile.

OBJECTIVE To evaluate the association of postpartum timing of IUD insertion and breastfeeding status with incidence and risk of IUD expulsion.

DESIGN, SETTING, AND PARTICIPANTS The Association of Perforation and Expulsion of Intrauterine Devices (APEX-IUD) cohort study included women aged 50 years or younger with an IUD insertion between 2001 and 2018. The breastfeeding analysis focused on a subcohort of women at 52 or fewer weeks post partum with known breastfeeding status. The study was conducted using data from electronic health records (EHRs) at 4 research sites with access to EHR: 3 Kaiser Permanente sites (Northern California, Southern California, Washington) and the Regenstrief Institute (Indiana). Data analysis was conducted from June to November 2019.

EXPOSURES Timing of IUD insertion post partum was categorized into discrete time periods: 0 to 3 days, 4 days to 6 or fewer weeks, more than 6 weeks to 14 or fewer weeks, more than 14 weeks to 52 or fewer weeks, and non–post partum (>52 weeks or no evidence of delivery). Breastfeeding status at the time of insertion was determined from clinical records, diagnostic codes, or questionnaires from well-baby visits.

MAIN OUTCOMES AND MEASURES Incidence rates and adjusted hazard ratios (aHRs) were estimated using propensity scores to adjust for confounding.

RESULTS The full cohort included 326 658 women (mean [SD] age, 32.0 [8.3] years; 38 911 [11.9%] Asian or Pacific Islander; 696 [0.2%] Hispanic Black; 56 180 [17.2%] Hispanic other; 42 501 [13.0%] Hispanic White; 28 323 [8.7%] non-Hispanic Black; 137 102 [42.0%] non-Hispanic White), and the subcohort included 94 817 women. Most IUDs were levonorgestrel-releasing (259 234 [79.4%]). There were 8943 expulsions. The 5-year cumulative incidence of IUD expulsion was highest for insertions 0 to 3 days post partum (10.73%; 95% CI, 9.12%-12.61%) and lowest for insertions more than 6 weeks to 14 or fewer weeks post partum (3.18%; 95% CI, 2.95%-3.42%). Adjusted HRs using women with non–post partum IUD insertion as the referent were 5.34 (95% CI, 4.47-6.39) for those with postpartum insertion at 0 to 3 days; 1.22 (95% CI, 1.05-1.41) for those with postpartum insertion at 4 days to 6 or fewer weeks; 1.06 (95% CI, 0.95-1.18) for those with postpartum insertion at more than 6 to 14 or fewer weeks; and 1.43 (95% CI, 1.29-1.60) for those with postpartum insertion at more than 14 to 52 or fewer weeks. In the subcohort, 5-year cumulative incidence was 3.49% (95% CI,

(continued)

Key Points

Question Are timing of intrauterine device (IUD) insertion post partum and breastfeeding associated with the risk of IUD expulsion?

Findings In this cohort study of 326 658 women, 5-year cumulative incidence of IUD expulsion was highest among women with postpartum IUD insertions at 0 to 3 days and lowest for those with insertions at more than 6 weeks to 14 or fewer weeks. IUD expulsion was higher for women who were not breastfeeding.

Meaning In this study, immediate postpartum IUD insertion was associated with increased risk of IUD expulsion relative to later insertions, and breastfeeding was associated with lower expulsion risk.

+ Supplemental content

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Abstract (continued)

3.25%-3.73%) for breastfeeding women and 4.57% (95% CI, 4.22%-4.95%) for nonbreastfeeding women; the adjusted HR for breastfeeding vs not breastfeeding was 0.71 (95% CI, 0.64-0.78).

CONCLUSIONS AND RELEVANCE In this study of real-world data, IUD expulsion was rare but more common with immediate postpartum insertion. Breastfeeding was associated with lower expulsion risk.

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Introduction

Intrauterine devices (IUDs) are highly effective contraception, with failure rates of less than 1% in the first year of use.[1,2] IUDs are commonly placed at postpartum visits, typically 4 to 6 weeks after delivery but increasingly are being placed immediately post partum, within 3 days of delivery.[3] Immediate postpartum insertion of IUDs is supported by US clinical guidelines and is considered safe, effective, and convenient for women.[3,4]

An important reason for IUD failure and unintended pregnancy is unrecognized expulsion of the IUD following insertion. For women considering IUDs, timing of IUD insertion post partum as well as breastfeeding may affect expulsion risk and should be factored into decisions about IUD insertion in the postpartum period. Evidence from a meta-analysis suggests that rates of IUD expulsion vary by postpartum timing of insertion, with rates of 13.2% observed for early inpatient postplacental insertion (>10 minutes to <72 hours) and 10.2% for immediate postplacental insertion (≤10 minutes). Lower rates were observed for insertion 4 or more weeks post partum (1.8%), and no complete expulsions were observed after early outpatient insertion (72 hours to <4 weeks).[3] Given that breastfeeding is associated with short-term and longer-term maternal endocrine and genitourinary changes after birth (including changes to uterine morphology, peristalsis, the uterotonic effect of oxytocin released during breastfeeding, and pituitary-induced amenorrhea secondary to breastfeeding), breastfeeding status may also be associated with expulsion risk for IUDs placed post partum.[5-7] While postpartum women with copper IUDs who were breastfeeding have been reported to experience similar or lower risks of expulsion relative to those who were not breastfeeding,[8] the association of breastfeeding with expulsion rates for other IUD types has not been extensively evaluated.

We present findings from a multisite US study evaluating the incidence and risk of IUD expulsion in a cohort of more than 325 000 women, grouped by postpartum status and timing at IUD placement and, among postpartum women, comparing those who were and were not breastfeeding at the time of IUD insertion. The Association of Perforation and Expulsion of Intrauterine Devices (APEX-IUD) cohort study evaluated the association of breastfeeding and timing of IUD insertion post partum with the outcome of IUD expulsion in routine clinical care settings in the United States.

Methods

Study Setting and Dates

The cohort study included IUD insertions between January 1, 2001, and April 30, 2018, using data from 3 health care systems—Kaiser Permanente Northern California (KPNC), Kaiser Permanente Southern California (KPSC), and Kaiser Permanente Washington (KPWA)—and a research site accessing data from a health care information exchange in Indiana—the Regenstrief Institute (RI). Study methods, including study size calculations, development of propensity scores to control for bias from measured confounding, and validation of outcomes and exposures, have been described in detail previously.[9,10] All research sites received either institutional review board approval or an

exemption for the conduct of this study, which qualified for a waiver of informed consent requirements because of the use of deidentified data and/or minimal risk to participants. KPSC also received approval from California state agencies for use of vital statistics data. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Sources of Data

This study was conducted using electronic health records (EHRs), including women's records and linked mother-infant records. As described previously,[9] both structured EHR data (ie, data that have been organized into a formatted database that are ready to use, including *International Classification of Diseases, Ninth Revision* [*ICD*-9] and *International Statistical Classification of Diseases, Tenth Revision, Clinical Modification* [*ICD-10-CM*] diagnostic and procedural codes, medication codes, *Current Procedural Terminology* codes, and Healthcare Common Procedural Coding System codes) and unstructured data (eg, clinical notes) were used. Operational definitions were developed that included code lists for structured data and search terms for unstructured data using natural language processing (NLP).

Study Population

The study population included women aged 50 years or younger at the time of IUD insertion with at least 12 months of health care plan enrollment before IUD insertion (for KPNC, KPSC, and KPWA) or a clinical visit within 12 months before insertion (for RI) to enable identification of baseline preinsertion covariates. The first eligibility date for inclusion in the study varied by research site (2001, RI; 2007, KPWA; 2009, KPSC; 2010, KPNC); the last eligibility date at all sites was April 30, 2018. Only the first IUD insertion during the study period for each woman was considered for this analysis; the date of insertion is referred to as the index date.

Women were followed up from the date of IUD insertion to documented IUD expulsion or were censored at the earliest of the following: IUD-related uterine perforation, removal, reinsertion, or expiration (range, 3-10 years, depending on device); pregnancy; hysterectomy or other sterilization procedures; disenrollment from the health care system (KP sites) or last clinical encounter (RI); end of the study period (June 30, 2018); or death. The full study cohort included all women with an IUD insertion (N = 326 658). A subcohort of women with an IUD insertion at 52 or fewer weeks post partum and information on breastfeeding status at IUD insertion was also created (n = 94 817). Incidence and risk of IUD expulsion were evaluated by postpartum status and timing of IUD insertion in the full cohort and by breastfeeding status in the subcohort (**Figure 1**).

Exposures

The 2 primary exposures of interest were postpartum timing at IUD insertion and breastfeeding status, which were ascertained using algorithms developed and validated for this purpose.[10] For the full study cohort, timing of IUD insertion was categorized into 4 discrete time periods after delivery: 0 to 3 days, 4 days to 6 or fewer weeks, more than 6 weeks to 14 or fewer weeks, more than 14 weeks to 52 or fewer weeks. The nonpostpartum group included women with no evidence of delivery in the 52 weeks preceding IUD insertion. While 4 discrete time periods initially were planned for the postpartum timing exposure as specified a priori by the US Food and Drug Administration, the earliest being 0 days to 6 or fewer weeks, this exposure was refined post hoc to a 5-category variable (splitting the ≤6-week category further to 0-3 days and 4 days to ≤6-weeks).

In the subcohort of women who were 52 or fewer weeks post partum at IUD insertion, breastfeeding status was determined using NLP (all sites), *ICD-9* and *ICD-10-CM* codes (KPWA, RI), well-baby visit questionnaires (KPNC, KPSC), and lactation status from clinical encounters (KPNC, KPSC). Breastfeeding status was defined as yes if breastfeeding had been documented within 30 days before IUD insertion or anytime following insertion; as no if there was documentation of not breastfeeding at insertion or if breastfeeding data were missing at insertion and the most recent

documentation of breastfeeding (yes) was more than 30 days before insertion; and as missing in all other circumstances. The 3007 postpartum women with missing breastfeeding status were excluded from the subcohort.

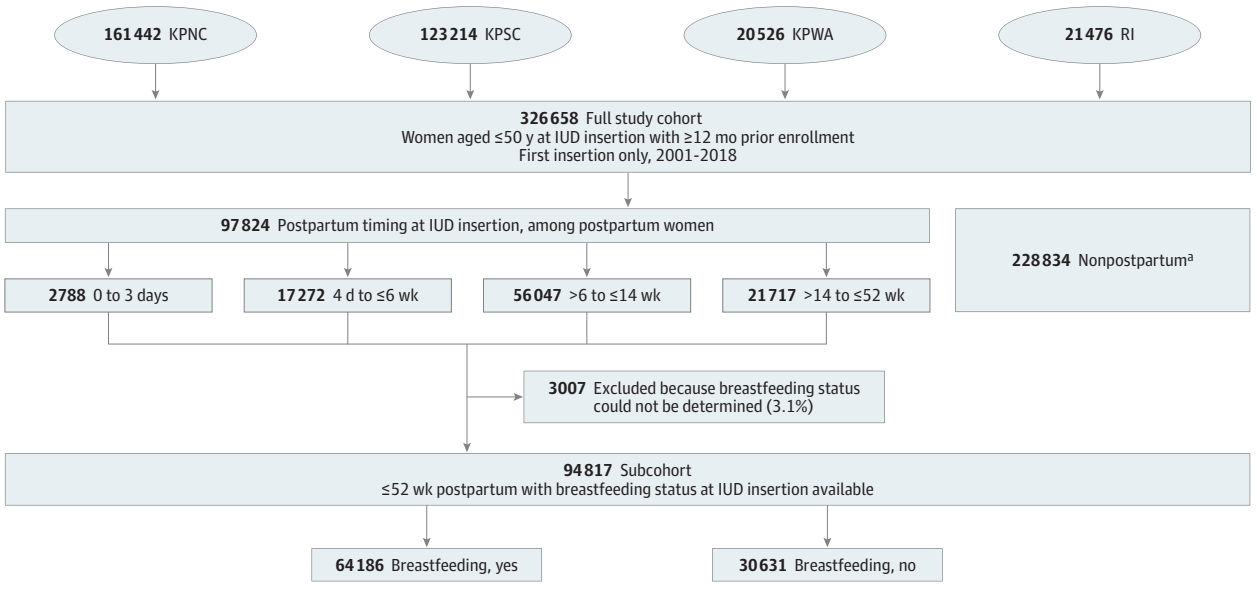
Outcome

The primary outcome of interest was IUD expulsion, defined as the spontaneous, unintended expulsion of the IUD, and was determined from the EHR, including clinical notes, using algorithms developed and validated for this purpose.[10] IUD expulsions recorded in the EHR from KPNC and KPWA were further classified as complete, partial, or undetermined. Complete expulsion was defined as an IUD located in the vagina, not present in the uterus or abdomen on imaging, or by documented reports by women that the IUD was expelled or "fell out." Partial expulsion was defined as visualization of the IUD extruding from external cervical os or present in the cervix on imaging. If the IUD was malpositioned in the uterine cavity (eg, imaging demonstrated IUD in lower uterine segment but not the cervix), it was not considered an expulsion unless it was removed by the clinician. All expulsions (complete, partial, and undetermined) were considered in the primary outcome analysis, and the date of the expulsion is the date it came to medical attention.

Covariates

Covariates of interest were used in descriptive analyses of the study population and in propensity score models (eTable 1 in the Supplement). Variables included baseline characteristics, such as research site, demographic characteristics, and risk factors at time of IUD insertion, including smoking status during the past 12 months, body mass index (BMI), reproductive history, gynecologic factors, and information about the IUD insertion procedure (year, IUD type, indicators of difficult insertion). Race and ethnicity were self-reported within the health care systems using prespecified categories of race and, separately, ethnicity (with additional data on race and ethnicity taken from death data if self-reported race or ethnicity data were missing, for some sites). Racial categories were

Figure 1. Study Population



At the time of this study, the electronic health records identified biologic sex, not gender. We recognize that intrauterine (IUD) insertions occur among individuals with a uterus, most of whom identify as women, but a small proportion of individuals in our cohort may identify as a different gender. KPNC indicates Kaiser Permanente Northern California; KPSC, Kaiser Permanente Southern California; KPWA, Kaiser Permanente Washington; RI, Regenstrief Institute.

[a] Nonpostpartum women had no evidence of delivery within 52 weeks before IUD insertion, and included women more than 52 weeks post partum and nulliparous women.

American Indian or Alaska Native, Asian or Pacific Islander, Black, Native American, White, and other. American Indian or Alaska Native, Native American, and other were collapsed into other given small sample size. Ethnicity categories were Hispanic and non-Hispanic. These self-identified categories are recorded in participants' EHRs. Differences in risk of IUD expulsion have been reported by race and ethnicity, and therefore race and ethnicity were used as a variable within the propensity scores to address potential confounding. Clinician experience was based on number of IUD insertions in the prior year. Covariates were assessed on or before the index date using all available information during the look-back period (12 months minimum)[11,12] from the earliest enrollment date (KP sites) or first clinical encounter (RI) to index date.

Statistical Analysis

Descriptive analyses for the variables of interest are presented overall; characteristics stratified by research site are published elsewhere.[9] For categorical variables, frequencies and percentages are presented; for continuous variables, mean, SD, and minimum and maximum are presented. Missing data were treated as missing; no imputation was performed. All analyses were performed using SAS software version 9.3 or higher (SAS Institute).

IUD expulsions were analyzed in the full study cohort by postpartum timing interval at insertion and in the subcohort of women with breastfeeding status. We estimated incidence rates, cumulative incidence, and crude and adjusted hazard ratios (HRs) and their 95% CIs for risk of IUD expulsion. The 95% CI for incidence rates was calculated based on the relationship between the Poisson distribution and the χ^2 distribution.[13] Cumulative incidence was estimated using the Kaplan-Meier method. The HRs were estimated using Cox proportional hazards models. The proportional hazards assumption was met through follow-up, except for the group with IUD insertions at 0 to 3 days post partum, for whom data were sparse. Adjusted HRs were calculated using propensity score overlap weighting to adjust for confounding.[14] Propensity score models were developed separately for exposure-outcome pairs. Covariates for inclusion in the propensity score models were assessed based on their association with the study outcome and the confounding effect; if imbalance remained between groups within a data source, interaction terms with the data source were included. Details have been described previously.[9] A multinomial logistic regression model was used to calculate propensity scores for categorical timing of IUD insertion and a binary logistic regression model for breastfeeding status; eTable 1 in the Supplement presents the variables used in the propensity score models and additional details. After weighting, the standardized difference between 3 postpartum groups and the group with IUD insertion more than 52 weeks post partum or with no delivery was small (<0.20) for all key covariates, but the group with IUD insertion at 0 to 3 days post partum differed in some characteristics (eg, race and ethnicity, BMI, and clinician experience). Breastfeeding could not be included in the propensity score model for timing of IUD insertion because no woman was categorized as breastfeeding in the category of IUD insertion at more than 52 weeks post partum; therefore, adjustment for breastfeeding status was accomplished by including it as a covariate in the Cox model additional to propensity score overlap weighting to estimate fully adjusted HRs.

Results

Participants

The full study cohort included 326 658 women with at least 1 IUD insertion identified during the study period (KPNC, 161 442 [49.4%]; KPSC, 123 214 [37.7%]; KPWA, 20 526 [6.3%]; and RI, 21 476 [6.6%]). Mean (SD) age was 32.0 (8.3) years; 38 911 (11.9%) were Asian or Pacific Islander; 696 (0.2%), Hispanic Black; 56 180 (17.2%), Hispanic other; 42 501 (13.0%), Hispanic White; 28 323 (8.7%) non-Hispanic Black; 137 102 (42.0%) non-Hispanic White; and 16 357 (5.0%) of other or multiple races/ethnicities (**Table**). The subcohort of women with IUD insertion at 52 or fewer weeks post partum with known breastfeeding status included 94 817 women (KPNC, 45 353 [47.8%]; KPSC,

Table. Characteristics of the Study Population at the Time of IUD Insertion

Characteristic	Participants, No. (%)	
	Full cohort (N = 326 658)	Subcohort with known breastfeeding status (n = 94 817))
Person-years at risk, No.	641 427	182 738
Breastfeeding	64 186 (19.6)	64 186 (67.7)
Postpartum time of IUD insertion		
0-3 d	2788 (0.9)	2647 (2.8)
4 d to ≤6wk	17 272 (5.3)	16 933 (17.9)
>6 to ≤14 wk	56 047 (17.2)	54 697 (57.7)
>14 to ≤52 wk	21 717 (6.6)	20 540 (21.7)
Nonpostpartum (>52 wk or no delivery)	228 834 (70.1)	NA
Age, y		
Mean (SD)	32.0 (8.3)	29.3 (5.7)
≤28	119 469 (36.6)	40 360 (42.6)
>28 to ≤36	107 871 (33.0)	44 643 (47.1)
>36 to ≤50	99 318 (30.4)	9814 (10.4)
Race and ethnicity[a]		
Asian/Pacific Islander	38 911 (11.9)	12 335 (13.0)
Hispanic		
Black	696 (0.2)	208 (0.2)
Other	56 180 (17.2)	15 066 (15.9)
White	42 501 (13.0)	20 159 (21.3)
Non-Hispanic		
Black	28 323 (8.7)	7255 (7.7)
White	137 102 (42.0)	34 092 (36.0)
Other or multiple	16 357 (5.0)	4741 (5.0)
Recent smoking[b]	32 623 (10.0)	7519 (7.9)
BMI		
Mean (SD)	28.5 (6.99)	28.7 (6.18)
Category[c]		
Underweight, <18.5	3689 (1.1)	541 (0.6)
Normal weight, 18.5-24.9	113 675 (34.8)	28 587 (30.1)
Overweight, 25.0-29.9	96 181 (29.4)	32 628 (34.4)
Obesity, >30.0	107 674 (33.0)	32 883 (34.7)
Dysmenorrhea in the past year	15 266 (4.7)	2249 (2.4)
Menorrhagia in the past year	32 552 (10.0)	898 (0.9%)
Uterine fibroids	17 416 (5.3)	3617 (3.8)
Parity[d]		
≤1	128 577 (39.4)	31 789 (33.5)
>1	148 985 (45.6)	57 376 (60.5)
Cesarean delivery any time before IUD insertion[e]	54 295 (16.6)	25 792 (27.2)
Cesarean delivery for most recent delivery before IUD insertion[f]	23 245 (7.1)	22 551 (23.8)
IUD type[g]		
Levonorgestrel-releasing	259 234 (79.4)	72 201 (76.1)
Copper	63 664 (19.5)	22 004 (23.2)
Concomitant gynecological procedure[h]	26 234 (8.0)	1561 (1.6)
Indicator of difficult insertion[i]	29 777 (9.1)	2763 (2.9)
Annualized IUD insertions performed by clinician in previous year, mean (SD), No.	52.0 (73.70)	49.5 (79.52)

(continued)

Table. Characteristics of the Study Population at the Time of IUD Insertion (continued)

Characteristic	Participants, No. (%)	
	Full cohort (N = 326 658)	Subcohort with known breastfeeding status (n = 94 817))
Duration of look-back period, mo		
Mean (SD)	56.8 (42.3)	48.2 (35.0)
Median (IQR) [range]	46.3 (26.1-76.6) [12-435]	38.7 (23.0-64.2) [12-391]
Duration of follow-up, median (range), y	1.4 (0.0-10.3)	1.4 (0.0-10.3)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NA, not applicable; IUD, intrauterine device.

[a] Race and ethnicity were as reported in electronic health records. The other and unknown categories included both those who self-identified as other and groups with very small numbers in this study (eg, non-Hispanic Native American and non-Hispanic American Indian or Alaska Native). Unknown or missing: postpartum cohort, 2.0%; breastfeeding cohort, 1.0%.

[b] Unknown or missing: full cohort, 1.7%; breastfeeding cohort, 0.3%.

[c] Unknown or missing: full cohort, 1.7%; breastfeeding cohort, 0.2%.

[d] Unknown or missing: full cohort, 15.0%; breastfeeding cohort, 6.0%.

[e] Unknown or missing: full cohort, 11.9%; breastfeeding cohort, 0.0%.

[f] No delivery in the past year in the postpartum cohort: 70.1%.

[g] Unknown or missing: full cohort, 1.2%; breastfeeding cohort, 0.6%.

[h] At least 1 of the following: abortion, aspiration and curettage, dilation and curettage, excision or biopsy of cervix or uterus, ablation, colposcopy and other cervical procedures, hysteroscopy procedure, laminaria procedure, laparoscopy, lysis adhesions, myomectomy, nerve procedure, salpingectomy, or oophorectomy.

[i] Including need for cervical dilation, ultrasound guidance, paracervical block, use of misoprostol, and clinician indicating difficulty.

40 706 [42.9%]; KPWA, 4839 [5.1%]; RI, 3919 [4.1%]). Total follow-up time was 641 427 person-years for the full cohort and 182 738 person-years for the subcohort; median duration of follow-up after IUD insertion was 1.4 years (range, 0.0-10.3 years) in both the full cohort (IQR, 0.5-3.0 years) and the subcohort (IQR, 0.6-2.9 years). The most common censoring events were end of the study period (104 591 [32.0%]), removal and/or replacement of IUD (104 342 [32.0%]), and end of enrollment or follow-up (83 745 [25.6%]).

In the full cohort, most women (228 834 [70.1%]) had no delivery in the year before IUD insertion, and 97 824 (29.9%) had a delivery. Among women with a delivery in the year before IUD insertion, most insertions were more than 6 weeks to 14 or fewer weeks post partum (56 047 [17.2% of full cohort]) and the fewest had insertions at 0 to 3 days post partum (2788 [0.9%]). Most insertions (310 134 [94.9%]) occurred in 2010 to 2018; eFigure 1 in the Supplement presents the postpartum day of insertion for women with insertions 6 or fewer weeks post partum by insertion year. The percentage of IUD insertions within 0 to 3 days post partum, although small, increased from 112 of 31 563 (0.4%) in 2010 to 215 of 15 550 (1.4%) in 2018, with most of these insertions (2746 of 2788 [98.5%]) occurring on day 0 (eFigure 1 in the Supplement). Most women had a levonorgestrel-releasing IUD (full cohort: 259 234 [79.4%]; subcohort: 72 201 [76.1%]).

IUD Expulsion in All Women and by Timing of Postpartum IUD Insertion in the Full Cohort

There were 8943 IUD expulsions in the full cohort, for a crude incidence rate of 13.94 (95% CI, 13.65-14.23) per 1000 person-years. eTable 2 in the Supplement presents the number of events by postpartum status. Not all sites classified IUD expulsions as complete or partial, but among the 5471 expulsions that were further classified, 2616 (47.8%) were considered complete, 2480 (45.3%) partial, and 375 (6.9%) undetermined. Cumulative 1-year and 5-year incidence of expulsion was 2.29% (95% CI, 2.24%-2.35%) and 4.57% (95% CI, 4.45%-4.68%), respectively.

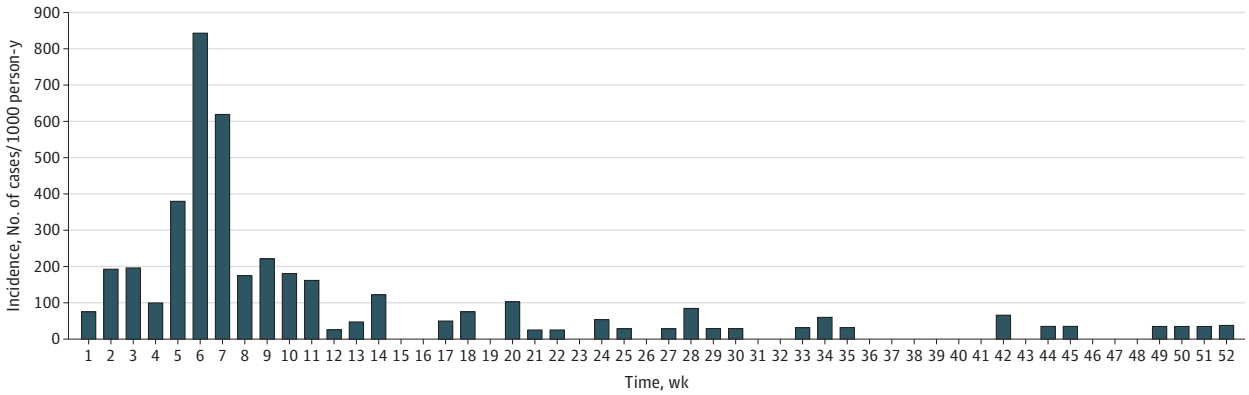
Crude incidence rates of IUD expulsion were highest for women with IUD insertions 0 to 3 days postpartum (46.54 [95% CI, 40.54-53.18] per 1000 person-years) (eTable 2 and eFigure 2A in the Supplement). Within the group with IUD insertions 0 to 3 days post partum, the highest expulsion rates were discovered within 12 weeks of insertion, with the highest incidence rate occurring at week 6 (844 per 1000 person-years), a time women are commonly seen post delivery (**Figure 2**). Crude incidence rates were lowest among women with IUD insertions at 4 days to 6 or fewer weeks postpartum (10.88 [95% CI, 9.78-12.08] per 1000 person-days) and more than 6 weeks to 14 or fewer weeks post partum (9.29 [95% CI, 8.73-9.87] per 1000 person-years) (eTable 2 and eFigure 2A in the Supplement). Cumulative incidence of IUD expulsion was highest in women with insertions at 0 to 3 days post partum (1 year: 7.84% [95% CI, 6.83%-9.00%]; 5 years: 10.73% [95% CI, 9.12%-12.61%]) (**Figure 3**A); many of those expulsions were recognized soon after insertion.

Compared with insertions in nonpostpartum women (referent group), insertions 0 to 3 days post partum had the highest risk of expulsion (**Figure 4**A) in crude analyses (HR, 2.95; 95% CI, 2.57-3.38) and in analyses adjusted for propensity scores (HR, 3.77; 95% CI, 3.23-4.40) and adjusted for propensity scores plus breastfeeding status (HR, 5.34; 95% CI, 4.47-6.39). Compared with nonpostpartum insertions, IUDs inserted 4 days to 6 or fewer weeks post partum had HRs less than 1 in both crude analyses and analyses adjusted for propensity scores but HR greater than 1 after adjustment for propensity scores and breastfeeding status (HR, 1.22; 95% CI, 1.05-1.41). Relative to nonpostpartum insertions, insertions more than 14 to 52 or fewer weeks post partum had no increased risk of IUD expulsion in crude analyses (HR, 0.94; 95% CI, 0.86-1.02) but a higher risk in analyses adjusted for propensity scores (HR, 1.20; 95% CI, 1.09-1.33) and analyses adjusted for propensity score and breastfeeding status (HR, 1.43; 95% CI, 1.29-1.60).

IUD Expulsion by Breastfeeding Status in the Subcohort

For the subcohort of women who were 52 or fewer weeks post partum at IUD insertion and had breastfeeding status available, crude incidence rates of IUD expulsion per 1000 person-years of follow-up were 10.23 (95% CI, 9.68-10.81) and 14.58 (95% CI, 13.62-15.59), respectively, in women who were and were not breastfeeding (eTable 2 and eFigure 2B in the Supplement). The crude 5-year cumulative incidence was almost 25% lower in breastfeeding women (3.49%; 95% CI, 3.25%-3.73%) compared with nonbreastfeeding women (4.57%; 95% CI, 4.22%-4.95%) (Figure 3B). The risk of IUD expulsion was lower for women who were breastfeeding vs not breastfeeding (adjusted HR, 0.71; 95% CI, 0.64-0.78) (Figure 4B).

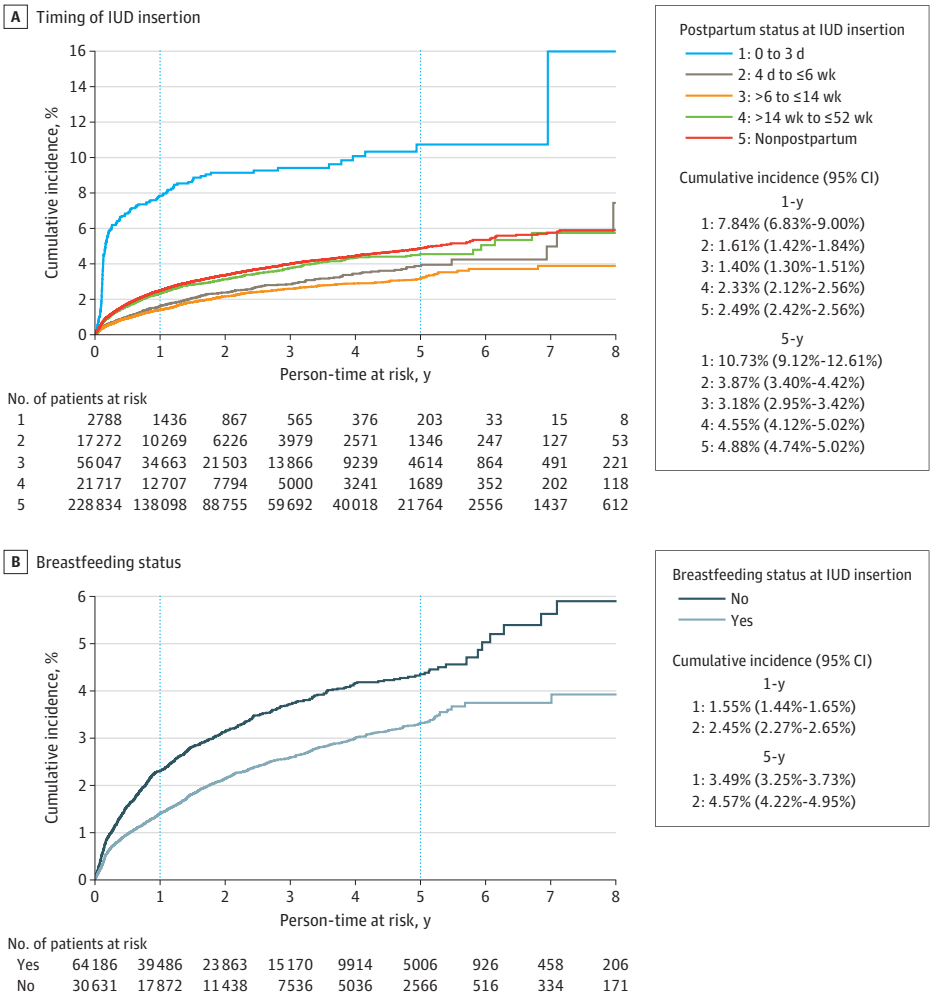
Figure 2. Incidence Rate of Expulsion Detected by Week in the First Year Since Intrauterine Device Insertion for Women With Intrauterine Devices Inserted at 0 to 3 Days Post Partum



Discussion

This US cohort study found that the IUD expulsion rate was highest if the IUD was inserted during the early postpartum period (≤3 days after delivery), a practice currently recommended by the American College of Obstetricians and Gynecologists to reduce the risk of eventual unintended and short-interval pregnancies.[4] The overall rates of IUD expulsion were low in the full study cohort, at 13.94 (95% CI, 13.65-14.23) per 1000 person-years. Among women with IUDs inserted 6 or fewer weeks after delivery or more than 14 weeks to 52 or fewer weeks after delivery, IUD expulsion risk was higher than among nonpostpartum insertions, and breastfeeding (vs not) at IUD insertion was associated with approximately a 30% lower risk of IUD expulsion after adjustment for covariates. Women with IUDs placed immediately post partum (ie, ≤3 days after delivery) had the greatest expulsion risk, more than 5 times greater than nonpostpartum women. Nevertheless, for the immediate postpartum group with the highest risk of expulsion, cumulative 5-year incidence was low at 10.73% (95% CI, 9.12%-12.61%). For those with immediate insertions, most expulsions were discovered in the 12 weeks after insertion, with the highest incidence of expulsion identified at 6 weeks, the time when most US women have their first postpartum visit (eFigure 2 in the Supplement).

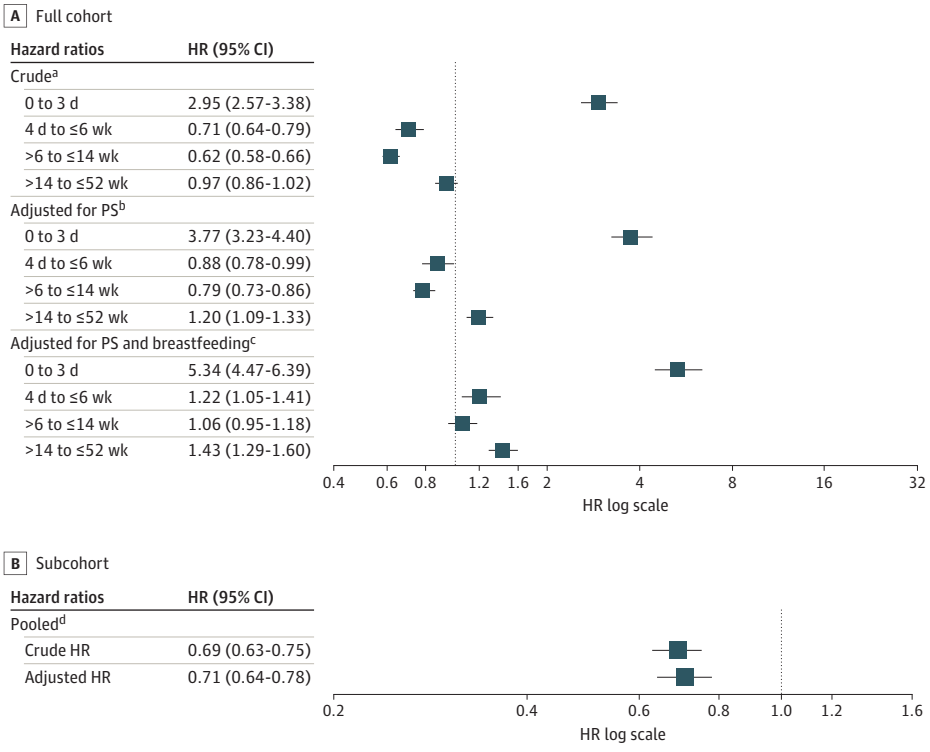
Figure 3. Cumulative Incidence of Intrauterine Device (IUD) Expulsion by Timing of IUD Insertion and Breastfeeding Status



To our knowledge, APEX-IUD is the largest study to date to examine associations of postpartum timing of IUD insertion and breastfeeding at insertion with risk of IUD expulsion. While previously published data are scarce, our findings in a cohort of women primarily using levonorgestrel-releasing IUDs are consistent with the lower risk in breastfeeding women using copper IUDs observed by some studies.[8] Findings regarding the increased risk of expulsion following immediate postpartum IUD insertion are consistent with the results of previously published observational studies and trials.[3,15,16] For IUDs placed immediately post partum, the size of the uterine cavity may increase the likelihood of malpositioning, potentially contributing to expulsion risk.[3,17]

Differential rates of IUD expulsion based on timing of insertion post partum warrant consideration in benefit-risk evaluations and should be an important part of IUD preinsertion counseling. In fully adjusted analyses, increased risk of expulsion compared with nonpostpartum status during the early puerperal period (4 days to ≤6 weeks) was less than that during the immediate postpartum period; however, perforation risk also must be considered during this period. IUD expulsion itself does not constitute a serious harm if recognized; however, women experience the inconvenience of another IUD insertion and may be discouraged from continued use of an IUD, particularly women with challenges accessing care. Most importantly, unrecognized expulsion may result in unintended pregnancy. Approximately half of expulsions identified in this study were partial and half were complete. Limited evidence suggests that the unintended pregnancy rate is greater among women whose IUDs are expelled or removed than in women with malpositioned IUDs that remain in situ.[18] The fact that most expulsions in the immediate postpartum group occurred early presents an opportunity to mitigate risk of unrecognized expulsion and unintended pregnancy via counseling on signs of expulsion and follow-up examination. Most trials show higher IUD utilization rates and lower pregnancy rates for immediate insertion vs later time points, despite higher expulsion risk.[19] We found that breastfeeding was associated with a lower expulsion risk. A potential mechanism to explain this finding may be the protective effect of lactational amenorrhea: as IUD

Figure 4. Crude, Propensity Score (PS)–Adjusted, and Fully Adjusted Hazard Ratios (HRs) for Intrauterine Device Expulsion for Full Cohort and Subcohort



A, Reference group was women who were non–post partum. B, Reference group was women who were not breastfeeding.

[a] PS variables were intrauterine device type; menorrhagia; age (in tertiles); race and ethnicity, calendar year index date; body mass index (categorical); dysmenorrhea; uterine fibroids; parity; concomitant gynecologic procedures; difficult insertion; clinician experience; site; and age × site, calendar year × site, parity × site interactions.

[b] Adjusted for PSs using overlap weighting.[14]

[c] Adjusted for PSs[14] and breastfeeding status.

[d] PS variables were postpartum timing, intrauterine type, menorrhagia, age (in tertiles), race and ethnicity, calendar year index date, body mass index (categorical), dysmenorrhea; uterine fibroids; parity; concomitant gynecologic procedures; difficult insertion; clinician experience; live birth in 52 weeks before index date; site; and postpartum × site interaction.

expulsion often occurs with menstrual bleeding[20] and often occurs during the first months of IUD use, women who are breastfeeding during the first months of IUD use and have lactational amenorrhea may be at a lower risk for expulsion.

Future research could evaluate risk factors for partial vs complete expulsions, the association of preinsertion counseling with recognition of potential expulsions and corresponding IUD failure rates, and whether ultrasound verification of IUD position in the uterus after insertion is associated with expulsion risk. While women who accept immediate postpartum IUD placement report high satisfaction rates,[21,22] information on women's preferences and satisfaction associated with different timing of postpartum placement would also be helpful to understand the benefit-risk profile.

Strengths and Limitations

Key strengths of the study include its large size and demographically diverse cohort of women across US regions. Use of linked mother-infant records enabled identification of study exposures, and EHRs allowed more accurate identification of the outcomes.[10] The retrospectively collected data analyzed in the study reflect US clinical practice, minimizing the selection and recall biases that can occur with prospective studies with long intervals between data-collection interviews.

This study has limitations. Misclassification of exposures and the study outcome is possible, particularly for breastfeeding in the early postpartum period, when women might be lactating regardless of their decision to breastfeed. The study did not collect information on lactational amenorrhea, which may be associated with expulsion risk. The study period spanned the use of both *ICD-9* and *ICD-10* codes, but no difference in the proportions of expulsions was identified between these two time periods.[9] Complete and partial expulsions were combined in the analyses, and we did not stratify the analysis by mode of delivery. The date of IUD expulsion reflects the date it came to medical attention, not necessarily the time of the expulsion. Ascertainment bias is possible: women with immediate postpartum insertions may have been exposed to more routine follow-up in the immediate postpartum time periods, whereas for later postpartum insertions, IUD expulsions might be underestimated due to a lack of timely clinical encounters and expulsions not being recognized. There is the potential for unmeasured confounding. Some variables have a high rate of missingness (eg, in the postpartum cohort, parity [15%] and cesarean delivery any time before IUD insertion [12%]). APEX-IUD data on postpartum timing did not differentiate postplacental insertions (ie, ≤10 minutes after delivery) with insertions at later time points on the day of delivery, although the clinical importance of this distinction has been questioned[23] and may not be relevant. The study cohort was identified from 4 health care systems; thus, the results may not be generalizable to an uninsured population.

Conclusions

In this study, risk of IUD expulsion was low overall, but highest in those with IUD insertions 0 to 3 days post partum in both crude and adjusted comparative analyses. Most expulsions were recognized within 12 weeks after insertion. Among women who were 52 or fewer weeks post partum with known breastfeeding status at the time of IUD insertion, adjusted analysis showed breastfeeding (vs not) at IUD insertion was associated with an approximately 30% lower risk of IUD expulsion. The potential association of lactational amenorrhea with expulsion risk among postpartum women who are breastfeeding warrants future study. Data from this study should inform preinsertion counseling.

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Corresponding Author: Mary Anne Armstrong, MA, Division of Research, Kaiser Permanente Northern California, 2000 Broadway, Oakland, CA 94612 (maryanne.armstrong@kp.org).

Author Affiliations: Division of Research, Kaiser Permanente Northern California, Oakland (Armstrong, Raine-Bennett, Postlethwaite, Merchant, Alabaster, Chillemi); Department of Health Systems Science, the Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, California (Raine-Bennett, Getahun); University of Washington, Seattle (Reed); Regenstrief Institute, Indianapolis, Indiana (Gatz); Department of Research & Evaluation, Kaiser Permanente Southern California, Pasadena (Getahun, Shi, Chiu, Xie, Im, Takhar); Bayer OY, Espoo, Finland (Schoendorf); Department of Obstetrics & Gynecology, Kaiser Permanente West Los Angeles Medical Center, Los Angeles, California (Fassett); Department of Clinical Science, the Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, California (Fassett); Indiana University, Indianapolis (Peipert); RTI Health Solutions, Waltham, Massachusetts (Saltus); RTI Health Solutions, Research Triangle Park, North Carolina (Zhou, Hunter, Wang, Ritchey, Anthony); Kaiser Permanente Washington Health Research Institute, Seattle (Ichikawa); Bayer AG, Berlin, Germany (Pisa, Asiimwe).

Author Contributions: Drs Zhou and Anthony had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Armstrong, Reed, Gatz, Getahun, Schoendorf, Postlethwaite, Peipert, Ritchey, Takhar, Asiimwe, Anthony.

Acquisition, analysis, or interpretation of data: Armstrong, Raine-Bennett, Reed, Gatz, Getahun, Schoendorf, Postlethwaite, Fassett, Peipert, Saltus, Merchant, Alabaster, Zhou, Ichikawa, Shi, Chiu, Xie, Hunter, Wang, Ritchey, Chillemi, Im, Pisa, Asiimwe, Anthony.

Drafting of the manuscript: Armstrong, Reed, Getahun, Pisa, Asiimwe, Anthony.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Armstrong, Getahun, Alabaster, Zhou, Shi, Chiu, Xie, Hunter, Wang, Ritchey, Asiimwe, Anthony.

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Administrative, technical, or material support: Raine-Bennett, Gatz, Getahun, Postlethwaite, Peipert, Saltus, Merchant, Xie, Wang, Ritchey, Chillemi, Im, Takhar, Asiimwe, Anthony.

Supervision: Armstrong, Reed, Getahun, Schoendorf, Postlethwaite, Chiu, Takhar, Pisa, Asiimwe.

Conflict of Interest Disclosures: Mss Armstrong, Postlethwaite, Alabaster, and Chillemi; Drs Raine-Bennett, Reed, Gatz, Getahun, Schoendorf, and Ritchey; and Mrs Merchant reported receiving grants from Bayer AG during the conduct of the study. Dr Raine-Bennett reported becoming chief executive officer of Medicines360, which holds a new drug application for a hormonal intrauterine device, on July 1, 2021, after work for this study was complete. Dr Gatz reported receiving grants from Bayer AG outside the submitted work. Dr Schoendorf reported receiving personal fees from Bayer AG during the conduct of the study and outside the submitted work. Drs Fassett, Shi, and Xie; Mss Chiu and Im; and Mr Takhar reported receiving grants from Bayer AG as employees of Kaiser Permanente Southern California (KPSC) during the conduct of the study. Dr Peipert reported receiving grants from Bayer, Merck, and CooperSurgical outside the submitted work. Mss Saltus and Wang, Drs Zhou and Anthony, and Mrs Hunter reported receiving support from Bayer AG and being employees of RTI Health Solutions, which provides consulting and other research services to pharmaceutical, device, governmental and nongovernmental organizations, during the conduct of the study. Dr Ritchey reported receiving personal fees from Bayer outside the submitted work and consulting for various pharmaceutical, medical device, and database companies regarding real-world use of data and conducting real-world data studies. Drs Pisa and Asiimwe reported being employees of Bayer during the conduct of the study and outside the submitted work. No other disclosures were reported.

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SUPPLEMENT.

eAppendix. Supplementary Methods
eTable 1. Variables Included in Propensity Score Models
eTable 2. Number of IUD Insertions, Follow-up Time, Expulsion Events, and Crude Incidence Rate by Postpartum Interval and Breastfeeding Status at Time of IUD Insertion
eFigure 1. Proportion of Total Annual IUD Insertions by Postpartum Day to 6 Weeks
eFigure 2. Crude Incidence Rates of IUD Expulsion by Postpartum Timing and Breastfeeding Status
eReferences.