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More US women are using IUDs than ever before. With more use comes the potential for complications and more requests related to non-contraceptive benefits. New information provides contemporary insight into rare IUD complications and the use of hormonal IUDs for treatment of HMB.

The first intrauterine device (IUD) to be approved in the United States, the Lippes Loop, became available in 1964. Sixty years later, more US women are using IUDs than ever before, and numbers are trending upward (FIGURE, page 38).<sup>1,2</sup> Over the past year, contemporary information has become available to further inform IUD management when pregnancy occurs with an IUD in situ, as well as counseling about device breakage. Additionally, new data help clinicians expand which patients can use a levonorgestrel (LNG) 52-mg IUD for heavy menstrual bleeding (HMB) treatment.

As the total absolute number of IUD users increases, so do the absolute numbers of rare outcomes, such as pregnancy among IUD users. These highly effective contraceptives have a failure rate within the first year after placement ranging from 0.1% for the LNG 52-mg IUD to 0.8% for the copper 380-mm<sup>2</sup> IUD.<sup>3</sup> Although the possibility for extrauterine gestation is higher when pregnancy occurs while a patient is using an IUD as compared with most other contraceptive

methods, most pregnancies that occur with an IUD in situ are intrauterine.<sup>4</sup>

The high contraceptive efficacy of IUDs make pregnancy with a retained IUD rare; therefore, it is difficult to perform a study with a large enough population to evaluate management of pregnancy complicated by an IUD in situ. Clinical management recommendations for these situations are 20 years old and are supported by limited data from case reports and series with fewer than 200 patients.<sup>5,6</sup>

Intrauterine device breakage is another rare event that is poorly understood due to the low absolute number of cases. Information about breakage has similarly been limited to case reports and case series.<sup>7,8</sup> This past year, contemporary data were published to provide more insight into both intrauterine pregnancy with an IUD in situ and IUD breakage.

Beyond contraception, hormonal IUDs have become a popular and evidence-based treatment option for patients with HMB. The initial LNG 52-mg IUD (Mirena)

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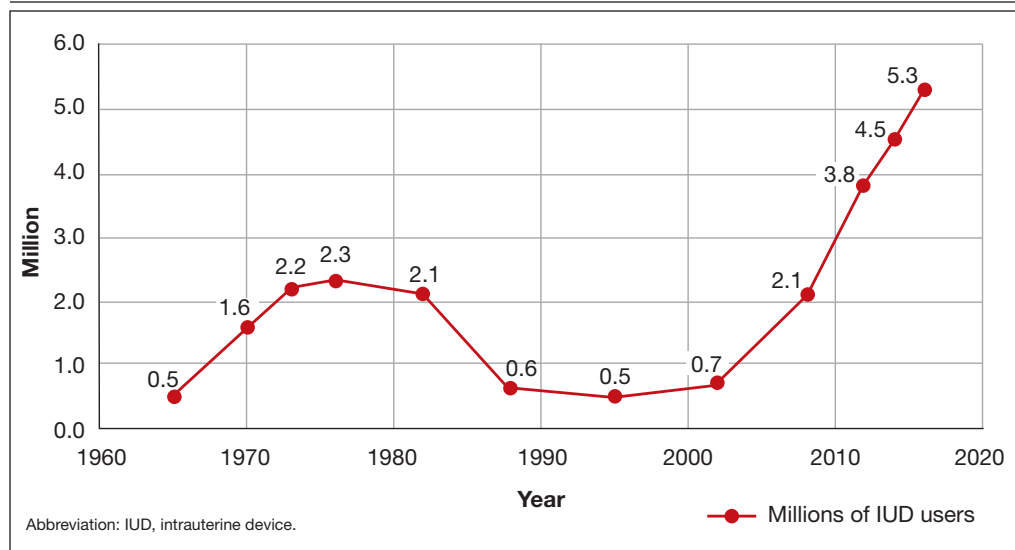
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**FIGURE** Number of IUD users (in millions), United States, 1965–2016<sup>1,2</sup>



regulatory approval studies for HMB treatment included data limited to parous patients and users with a body mass index (BMI) less than 35 kg/m<sup>2</sup>.<sup>9</sup> Since that time, no studies have explored these populations. Although current practice has commonly

extended use to include patients with these characteristics, we have lacked outcome data. New phase 3 data on the LNG 52-mg IUD (Liletta) included a broader range of participants and provide evidence to support this practice.

## Removing retained copper 380-mm<sup>2</sup> IUDs improves pregnancy outcomes



Panchal VR, Rau AR, Mandelbaum RS, et al. Pregnancy with retained intrauterine device: national-level assessment of characteristics and outcomes. *Am J Obstet Gynecol MFM*. 2023;5:101056. doi:10.1016/j.ajogmf.2023.101056

Karakuş SS, Karakuş R, Akalın EE, et al. Pregnancy outcomes with a copper 380 mm<sup>2</sup> intrauterine device in place: a retrospective cohort study in Turkey, 2011–2021. *Contraception*. 2023;125:110090. doi:10.1016/j.contraception.2023.110090

To update our understanding of outcomes of pregnancy with an IUD in situ, Panchal and colleagues performed a cross-sectional study using the

Healthcare Cost and Utilization Project's National Inpatient Sample. This data set represents 85% of US hospital discharges. The population investigated included hospital deliveries from 2016 to 2020 with an ICD-10 (International Classification of Diseases, Tenth Revision) code of retained IUD. Those without the code were assigned to the comparison non-retained IUD group.

The primary outcome studied was the incidence rate of retained IUD, patient and pregnancy characteristics, and delivery outcomes including but not limited to gestational age at delivery, placental abnormalities, intrauterine fetal demise (IUFD), preterm premature rupture of membranes

(PPROM), cesarean delivery, postpartum hemorrhage, and hysterectomy.

attempted removal in relation to measured pregnancy outcomes.

### Outcomes were worse with retained IUD, regardless of IUD removal status

The authors found that an IUD in situ was reported in 1 out of 8,307 pregnancies and was associated with PPRM, fetal malpresentation, IUFD, placental abnormalities including abruption, accreta spectrum, retained placenta, and need for manual removal (TABLE 1). About three-quarters (76.3%) of patients had a term delivery ( $\geq 37$  weeks).

Retained IUD was associated with pre-viable loss, defined as less than 22 weeks' gestation (adjusted odds ratio [aOR], 5.49; 95% confidence interval [CI], 3.30–9.15) and periviable delivery, defined as 22 to 25 weeks' gestation (aOR, 2.81; 95% CI, 1.63–4.85). Retained IUD was not associated with pre-term delivery beyond 26 weeks' gestation, cesarean delivery, postpartum hemorrhage, or hysterectomy.

Important limitations of this study are the lack of information on IUD type (copper vs hormonal) and the timing of removal or

### Removal of copper IUD improves, but does not eliminate, poor pregnancy outcomes

Karakus and colleagues conducted a retrospective cohort study of 233 patients in Turkey with pregnancies that occurred during copper 380-mm<sup>2</sup> IUD use from 2011 to 2021. The authors reported that, at the time of first contact with the health system and diagnosis of retained IUD, 18.9% of the pregnancies were ectopic, 13.2% were first trimester losses, and 67.5% were ongoing pregnancies.

The authors assessed outcomes in patients with ongoing pregnancies based on whether or not the IUD was removed or retained. Outcomes included gestational age at delivery and adverse pregnancy outcomes, assessed as a composite of preterm delivery, PPRM, chorioamnionitis, placental abruption, and postpartum hemorrhage.

Of those with ongoing pregnancies, 13.3% chose to have an abortion, leaving 137 (86.7%) with continuing pregnancy. The IUD was able to be removed in 39.4% of the sample, with an

**TABLE 1** Pregnancy and delivery outcomes related to retained IUD (composite of both hormonal and nonhormonal devices)

Outcome	Outcome rate (%)		aOR (95% CI) <sup>a</sup>
	Removed IUD	Retained IUD	
Placental abnormalities			
Abruption	1.1	4.7	3.24 (2.25-4.66)
Accreta spectrum	0.1	0.7	4.82 (1.99-11.65)
Retained	0.4	2.5	4.45 (2.70-7.36)
Manual removal	0.6	3.2	4.81 (3.11-7.44)
IUFD	0.8	2.6	2.21 (1.37-3.57)
PPROM	2.7	9.2	3.15 (2.41-4.12)
Cesarean delivery	32.4	31.2	0.87 (0.73-1.03)
Postpartum hemorrhage	4.0	5.9	1.36 (0.98-1.88)
Hysterectomy	0.2	0.6	0.83 (0.22-3.21)
Fetal malpresentation	7.2	10.9	1.47 (1.15-1.88)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; IUD, intrauterine device; IUFD, intrauterine fetal demise; PPRM, preterm premature rupture of membranes.

<sup>a</sup>Adjusted for negative presence of listed outcome.

Source: Panchal VR, Rau AR, Mandelbaum RS, et al. Pregnancy with retained intrauterine device: national-level assessment of characteristics and outcomes. *Am J Obstet Gynecol MFM*. 2023;5:101056.

**TABLE 2** Approximate ongoing pregnancy rate by gestational age with retained and removed copper 380-mm<sup>2</sup> IUD

Gestational age (weeks)	Ongoing pregnancy rate (%) <sup>a</sup>	
	Removed copper IUD	Retained copper IUD
10	80	63
15	74	55
22	65	36
26	65	34
34	58	28
37	55	25

Abbreviation: IUD, intrauterine device.

<sup>a</sup>Percent approximated from published Kaplan-Meier survival estimates.

Source: Karakuş SS, Karakuş R, Akalin EE, et al. Pregnancy outcomes with a copper 380 mm<sup>2</sup> intrauterine device in place: a retrospective cohort study in Turkey, 2011-2021. *Contraception*. 2023;125:110090.

average gestational age of 7 weeks at the time of removal.

Compared with those with a retained IUD, patients in the removal group had a lower rate of pregnancy loss (33.3% vs 61.4%;  $P < .001$ ) and a lower rate of the composite adverse pregnancy outcomes (53.1% vs 27.8%;  $P = .03$ ). **TABLE 2** shows the approximate rate of ongoing pregnancy by gestational age in patients with retained and removed copper 380-mm<sup>2</sup> IUDs. Notably, the largest change occurred periviable, with the proportion of patients with an ongoing pregnancy after 26 weeks reducing to about half for patients with a retained IUD as compared with patients with a removed IUD; this proportion of ongoing pregnancies held through the remainder of gestation.

**WHAT THIS EVIDENCE MEANS FOR PRACTICE**

These studies confirm that a retained IUD is a rare outcome, occurring in about 1 in 8,000 pregnancies. Previous US national data from 2010 reported a similar incidence of 1 in 6,203 pregnancies (0.02%).<sup>10</sup> Management and counseling depend on the patient’s desire to continue the pregnancy, gestational age, intrauterine IUD location, and ability to see the IUD strings. Contemporary data support management practices created from limited and outdated data, which include device removal (if able) and counseling those who desire to continue pregnancy about high-risk pregnancy complications. Those with a retained IUD should be counseled about increased risk of preterm or preivable delivery, IUFD, and placental abnormalities (including accreta spectrum and retained placenta). Specifically, these contemporary data highlight that, beyond approximately 26 weeks’ gestation, the pregnancy loss rate is not different for those with a retained or removed IUD. Obstetric care providers should feel confident in using this more nuanced risk of extreme preterm delivery when counseling future patients. Implications for antepartum care and delivery timing with a retained IUD have not yet been defined.

## Do national data reveal more breakage reports for copper 380-mm<sup>2</sup> or LNG IUDs?



Latack KR, Nguyen BT. Trends in copper versus hormonal intrauterine device breakage reporting within the United States’ Food and Drug Administration Adverse Event Reporting System. *Contraception*. 2023;118:109909. doi:10.1016/j.contraception.2022.10.011

Latack and Nguyen reviewed postmarket surveillance data of IUD adverse events in the US Food and Drug Administration’s (FDA) Adverse Event Reporting System (FAERS) from 1998 to 2022. The FAERS is a voluntary, or passive, reporting system.

PHOTO: DOOMU/SHUTTERSTOCK

## Study findings

Of the approximately 170,000 IUD-related adverse events reported to the agency during the 24-year timeframe, 25.4% were for copper IUDs and 74.6% were for hormonal IUDs. Slightly more than 4,000 reports were specific for device breakage, which the authors

grouped into copper (copper 380-mm<sup>2</sup>) and hormonal (LNG 52 mg, 19.5 mg, and 13.5 mg) IUDs.

The copper 380-mm<sup>2</sup> IUD was 6.19 times more likely to have a breakage report than hormonal IUDs (9.6% vs 1.7%; 95% CI, 5.87–6.53).

### WHAT THIS EVIDENCE MEANS FOR PRACTICE

The overall proportion of IUD-related adverse events reported to the FDA was about 25% for copper and 75% for hormonal IUDs; this proportion is similar to sales figures, which show that about 15% of IUDs sold in the United States are copper and 85% are hormonal.<sup>11</sup> However, the proportion of breakage events reported to the FDA is the inverse, with about 6 times more breakage reports with copper than with hormonal IUDs. Because these data come from a passive reporting system, the true incidence of IUD breakage cannot be assessed. However, these findings should remind clinicians to inform patients about this rare occurrence during counseling at the time of placement and, especially, when preparing for copper IUD removal. As the absolute number of IUD users increases, clinicians may be more likely to encounter this relatively rare event.

Management of IUD breakage is based on expert opinion, and recommendations are varied, ranging from observation to removal using an IUD hook, alligator forceps, manual vacuum aspiration, or hysteroscopy.<sup>7,10</sup> Importantly, each individual patient situation will vary depending on the presence or absence of other symptoms and whether or not future pregnancy is desired.

## Data support the LNG 52-mg IUD for HMB in nulliparous and obese patients

Creinin MD, Barnhart KT, Gawron LM, et al. Heavy menstrual bleeding treatment with a levonorgestrel 52-mg intrauterine device. *Obstet Gynecol.* 2023;141:971-978. doi:10.1097/AOG.0000000000005137

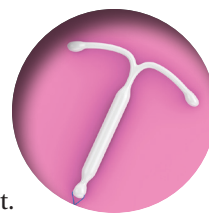
Creinin and colleagues conducted a study for US regulatory product approval of the LNG 52-mg IUD (Liletta) for HMB. This multicenter phase 3 open-label clinical trial recruited nonpregnant participants aged 18 to 50 years with HMB at 29 clinical sites in the United States. No BMI cutoff was used.

Baseline menstrual flow data were obtained over 2 to 3 screening cycles by

collection of menstrual products and quantification of blood loss using alkaline hematin measurement.

Patients with 2 cycles with a blood loss exceeding 80 mL had an IUD placement, with similar flow evaluations during the third and sixth postplacement cycles.

Treatment success was defined as a reduction in blood loss by more than 50% as compared with baseline (during screening) and measured blood loss of less than 80 mL. The enrolled population (n=105) included 28% nulliparous users, with 49% and 28% of participants having a BMI of 30 kg/m<sup>2</sup> or higher and higher than 35 kg/m<sup>2</sup>, respectively.



**Treatment highly successful in reducing blood loss**

Participants in this trial had a 93% and a 98% reduction in blood loss at the third and sixth cycles of use, respectively. Additionally, during the sixth cycle of use, 19% of users had no bleeding. Treatment success occurred in about 80% of participants overall and occurred regardless of parity or BMI.

To assess a subjective measure of success, participants were asked to evaluate their menstrual bleeding and dysmenorrhea severity, acceptability, and overall impact on quality of life at 3 time points: during prior typical menses, cycle 3, and cycle 6. At cycle 6, all participants reported significantly improved acceptability of bleeding and

uterine pain and, importantly, decreased overall menstrual interference with the ability to complete daily activities (**TABLE 3**).

**IUD expulsion and replacement rates**

Although bleeding greatly decreased in all participants, 13% (n=14) discontinued before cycle 6 due to expulsion or IUD-related symptoms, with the majority citing bleeding irregularities. Expulsion occurred in 9% (n=5) of users, with the majority (2/3) occurring in the first 3 months of use and more commonly in obese and/or parous users. About half of participants with expulsion had the IUD replaced during the study. ●

**TABLE 3 LNG 52-mg IUD for treatment of HMB: Study participant assessment of changes in menstrual bleeding, dysmenorrhea, and daily activities<sup>a</sup>**

<b>Visual analog scale question</b> <i>Anchors: 0 cm, 10 cm</i>	<b>Baseline</b> <i>(n=89)<sup>b</sup></i>	<b>Cycle 3</b> <i>(n=87)<sup>c,d</sup></i>	<b>Cycle 6</b> <i>(n=80)<sup>c,d</sup></i>
<b>How heavy was your bleeding?</b> <i>No flow, heaviest flow I ever experienced</i>	8.2 (7.4–9.0)	1.9 (0.7–2.9)	1.0 (0.2–2.3)
<b>How acceptable was your bleeding?</b> <i>Not acceptable, completely acceptable</i>	1.8 (0.8–3.0)	8.7 (6.3–9.6)	9.2 (8.0–9.8)
<b>How much cramping pain did you have?</b> <i>No pain, worst pain I ever experienced</i>	6.3 (3.9–7.4)	1.4 (0.3–3.2)	0.8 (0.1–2.4)
<b>How much did it affect your ability to sleep?</b> <i>No effect, I do not get any sleep</i>	5.3 (2.1–7.1)	0.3 (0.0–0.8)	0.2 (0.0–0.8)
<b>How much did it interfere with your ability to do daily activities?</b> <i>No effect, I cannot do any daily activities</i>	6.2 (4.4–7.8)	0.5 (0.1–1.3)	0.2 (0.0–1.1)

Data are median (interquartile range).

Abbreviations: HMB, heavy menstrual bleeding; IUD, intrauterine device; LNG, levonorgestrel.

<sup>a</sup>Based on a 10-cm visual analog scale; includes participants with any follow-up bleeding evaluations.

<sup>b</sup>Participant asked to assess “typical menses.”

<sup>c</sup>Participant asked to assess experience for preceding 4 weeks.

<sup>d</sup>One participant did not complete questionnaire at cycle 3 or cycle 6; 1 additional participant at each visit did not complete questionnaire (all with treatment success).

Source: Creinin MD, Barnhart KT, Gawron LM, et al. Heavy menstrual bleeding treatment with a levonorgestrel 52-mg intrauterine device. *Obstet Gynecol.* 2023;141:971-978.

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### WHAT THIS EVIDENCE MEANS FOR PRACTICE

Interestingly, both LNG 52-mg IUDs have been approved in most countries throughout the world for HMB treatment, and only in the United States was one of the products (Liletta) not approved until this past year. The FDA required more stringent trials than had been previously performed for approval outside of the United States. However, a benefit for clinicians is that this phase 3 study provided data in a contemporary US population. Clinicians can feel confident in counseling and offering the LNG 52-mg IUD as a first-line treatment option for patients with HMB, including those who have never been pregnant or have a BMI greater than 35 kg/m<sup>2</sup>.

Importantly, though, clinicians should be realistic with all patients that this treatment, although highly effective, is not successful for about 20% of patients by about 6 months of use. For those in whom the treatment is beneficial, the quality-of-life improvement is dramatic. Additionally, this study reminds us that expulsion risk in a population primarily using the IUD for HMB, especially if also obese and/or parous, is higher in the first 6 months of use than patients using the method for contraception. Expulsion occurs in 1.6% of contraception users through 6 months of use.<sup>12</sup> These data highlight that IUD expulsion risk is not a fixed number, but instead is modified by patient characteristics. Patients should be counseled regarding the appropriate expulsion risk and that the IUD can be safely replaced should expulsion occur.

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