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Long-Acting Reversible Contraception

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Long-acting reversible contraceptive (LARC) methods are effective options for pregnancy prevention. Currently available products in the United States include an etonogestrel implant, a copper intrauterine device (IUD), and several levonorgestrel IUDs. With increasing prevalence and duration of use, our understanding of efficacy, risks, and benefits has evolved. In addition to a brief discussion on nomenclature and LARC use within a framework of bodily autonomy and reproductive justice, this review covers clinical challenges with placement and removal, evidence-based duration of use, and how to mitigate side effects. Although all obstetrician–gynecologists as well as primary care clinicians can safely provide LARCs, complex family planning specialists are an expert referral source for challenging cases and evidence-based care as contraceptive technology continues to develop.

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Long-acting reversible contraceptive (LARC) methods are effective options that can be used by most patients seeking to prevent pregnancy. Long-acting reversible contraceptives prevent pregnancy for 1 year or longer with a single administration.[1] Currently marketed LARC products include implants, nonhormonal intrauterine devices (IUDs), and hormonal IUDs.

Long-acting reversible contraceptive use has been increasing since the early 2000s, with 18% of contraceptors reporting use of an IUD (14%) or implant (4%) in 2016.[2] Unintended pregnancy, although declining in incidence, continues to account for 45% of U.S. pregnancies, and rates remain disproportionately high among people with less financial means.[3] Although multiple factors contribute to unintended pregnancy rates, increasing LARC use correlates with declining rates and is likely a contributing factor.[4,5]

Currently available LARCs in the United States are described in Table 1. Given the expansion of available IUD products, consistent and clear IUD nomenclature is critical. In this review, we will refer to IUDs according to Society of Family Planning guidelines.[6] Per these recommendations, IUD categories should be referred to as nonhormonal and hormonal. The specific types of IUDs should be denoted as copper or hormone-type (eg, levonorgestrel), followed by the dose.

In addition, we would like to contextualize LARC use within a lens of bodily autonomy and reproductive justice. Over the past decade, there has been significant research and funding pertaining to LARCs, with the intention of increasing education and access for people desiring pregnancy prevention. As a community reflecting on our efforts to provide tools for reproductive health goals, it is vital that we approach contraception, especially methods that require a clinician for initiation and discontinuation, within the framework of our patient's preferences and goals. Long-acting reversible contraceptives, although an effective choice, are not the best choice for everyone. In addition, we must remember the history of racism, eugenics, and coercion in contraceptive technology when we consider how we discuss and promote LARC use.[7]

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This article discusses Liletta, which is scheduled for approval for 8-year use by the U.S. Food and Drug Administration in November 2022.

Each author has confirmed compliance with the journal's requirements for authorship.

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Table 1. Long-Acting Reversible Contraceptive Methods Currently Available in the United States and First-Year Efficacy

Device	Brand Name(s)	% of Users Experiencing Pregnancy in the 1st Year[1]	
		Perfect Use	Typical Use
Etonogestrel 68-mg implant	Organon (Jersey City, NJ)	0.1	0.1
Copper 380-mm^2 IUD	Paragard (Cooper Surgical, Trumbull, CT)	0.6	0.8
Levonorgestrel IUD			
13.5-mg	Skyla (Bayer, Whippany, NJ)	0.3	0.4
19.5-mg	Kyleena (Bayer, Whippany, NJ)	0.2	0.2
52-mg	Liletta (Medicines360, San Francisco, CA; and AbbVie, North Chicago, IL) Mirena (Bayer, Whippany, NJ)	0.1	0.1

IUD, intrauterine device.

SPECIFICATIONS AND MECHANISMS OF ACTION

Although all LARC methods are highly effective contraception, they prevent pregnancy in different ways. The etonogestrel implant is a single flexible radiopaque rod measuring 4 cm long and 2 mm in diameter containing 68 mg of 3-ketodesogestrel, otherwise known as etonogestrel, within a core surrounded by a rate-controlling membrane. When placed subdermally, etonogestrel diffuses from the implant into systemic circulation at concentrations that inhibit ovulation by preventing the mid-cycle luteinizing hormone surge.[8] Ovarian activity is not fully suppressed, as evidenced by near normal levels of follicle stimulating hormone and estradiol with continued use.

Intrauterine devices do not exert their main effect through systemic mechanisms; rather, they work locally. As a foreign body, all IUDs create a sterile inflammatory response in the endometrial cavity that is spermicidal and prevents fertilization.[9] In the United States, available IUDs add copper or hormones to increase efficacy, and IUD frames are one of two types. The copper 380-mm^2 IUD is available on a rigid Tatum-T polyethylene frame in which the arms and the stem meet in a true "T"; for placement, the arms bend downward toward the stem to load into the inserter. The hormonal IUDs are all available on a more flexible Nova-T polyethylene frame; for placement, the arms fold upward above the stem into the inserter.

The copper 380-mm^2 IUD is 32-mm wide by 36-mm long, with 380 mm^2 of exposed copper surface area. Unlike earlier versions of the copper IUD that contained copper only on a thin wire wrapped around the stem, this IUD has bands of copper on each arm. These bands dissolute much more slowly than the copper wire, significantly extending the duration of action. The copper ions adversely affect sperm motility and viability.[9]

The levonorgestrel IUDs have a steroid-releasing reservoir covered by a rate-limiting membrane over the stem.[10] The levonorgestrel 13.5-mg and 19.5-mg IUD frames are 28-mm wide by 30-mm long, and the levonorgestrel 52-mg IUD frame is 32-mm wide by 32-mm long.[11] Although levonorgestrel IUDs cause foreign-body reactions and progestin-mediated endometrial changes, the latter being the mechanism through which they decrease bleeding frequency, pregnancy is prevented by thickening of cervical mucous as a barrier to sperm penetration.[12,13]

EFFICACY

Given that LARCs are not user-dependent after placement, perfect-use and typical-use failure rates are similar. The percentage of people experiencing pregnancy in the first year of use is presented in Table 1. Although these first-year rates are often cited in marketing, efficacy over the duration of action is equally important for LARC methods (Table 2).

Although LARCs are very effective at preventing fertilization, in the rare situation in which pregnancy occurs, ectopic pregnancy must be excluded. Compared with non–contraceptive users, the risk of ectopic pregnancy in LARC users is much lower because the likelihood of fertilization is very low; however, if pregnancy occurs, the likelihood of an extrauterine gestation is higher than the 1% rate in the general population.[14,15] During 11 international clinical trials, no pregnancies occurred in people with the

Table 2. Long-Acting Reversible Contraceptive Extended Duration of Use Summary

Device	FDA-Approved Duration (y)	Evidence-Based Duration (y)	Cumulative Pregnancy Rate Through Evidence-Based Duration
Etonogestrel 68-mg implant (Nexplanon)	3	5 (without obesity)[125,126] 4–5 (with obesity)[126]	0.6 (0.2–1.8)[125]
Copper 380-mm^2 IUD (Paragard)	10	12[127,128] (consider 15 if aged 45 y or older)[129]	2.2*,[127]
Levonorgestrel IUD			
13.5-mg (Skyla)	3	3†	0.9 (upper limit CI 1.7%)†
19.5-mg (Kyleena)	5	5‡	1.45 (0.82–2.53)‡
52-mg (Mirena)	8	8[65]	1.37 (0.71–2.62)§,[65]
52-mg (Liletta)	6‖	8[65]	1.37 (0.71–2.62)§,[65]

FDA, U.S. Food and Drug Administration; IUD, intrauterine device.
Data are % (95% CI) unless otherwise specified.
* No 95% CI provided.
† Skyla prescribing information, Bayer Healthcare, 2021.
‡ Kyleena prescribing information, Bayer Healthcare, 2021.
§ 1.09 (0.56–2.13) if one pregnancy 4 days after IUD removal during year 7 excluded.
‖ Liletta is expected to receive FDA approval for 8 years of use in November 2022.

etonogestrel implant in place; thus, no rate of ectopic pregnancy could be determined.[16] In IUD clinical trials for regulatory approval, approximately 6% of pregnancies were ectopic in copper 380-mm^2 IUD users (Paragard prescribing information, CooperSurgical, 2020) and 50% of pregnancies were ectopic in levonorgestrel IUD users regardless of dose (Skyla prescribing information, Bayer Healthcare, 2021; Kyleena prescribing information Bayer Healthcare, 2022; Mirena prescribing information, Bayer Healthcare, 2022; Liletta prescribing information, Allergan USA Inc. and Medicines360, 2019). In population-based studies, ectopic pregnancy rates were 20% in a systematic review including 240,000 implant users, 15% in a cohort of approximately 17,000 copper IUD users, and 27% in a cohort of approximately 41,000 levonorgestrel 52-mg IUD users.[17,18] Because population-based rates are likely more reflective of patients in clinical practice, these rates should be used when counseling regarding ectopic pregnancy risk.

With the rise of the obesity epidemic, it is also important to examine contraceptive efficacy in the context of a typical user. According to the Centers for Disease Control and Prevention, almost half of all U.S. adults have obesity and an additional quarter have overweight.[19] In response to increasing rates of overweight and obesity in contraceptive users in the United States, the U.S. Food and Drug Administration (FDA) recommended in 2007 that hormonal contraceptive studies include participants with overweight and obesity to remain representative of the population who will use the product.[20] The efficacy of some contraceptive methods, such as the patch and emergency contraception pills, are known to be affected by weight.[21,22] Contraceptive implants rely on ovarian suppression as their primary mechanism of action but have other progestin-mediated effects that may contribute to pregnancy prevention at lower serum etonogestrel levels. No studies have primarily assessed implant efficacy in users with overweight and obesity; secondary analyses from a population-based study of 1,168 implant users, of whom 28% had overweight and 30% had obesity, provide evidence that there is no clinically significant correlation between contraceptive failure and body mass index (BMI, calculated as weight in kilograms divided by height in meters squared).[23] Conversely, given that IUDs have a local mechanism of action, it follows that their efficacy should not change in relation to body weight; this is also supported by findings from 4,200 users of the copper or levonorgestrel IUD, of whom 27% had overweight and 35% had obesity, in the aforementioned cohort study.[23]

INITIATION CONTRAINDICATIONS AND CONSIDERATIONS

If pregnancy has been reasonably excluded, LARCs can be initiated in most people. Uterine cavity anomalies, untreated cervical cancer, and active pelvic infection are contraindications to IUD placement.[24] Uterine cavity anomalies, including congenital anomalies (eg, septate and bicornuate uterus) and other structural anomalies (eg, cavity-distorting leiomyoma, uterine synechiae), may increase the risk of complications such as expulsion and decrease contraceptive efficacy. A review of the literature assessing the safety

and efficacy of IUD use in patients with müllerian anomalies or uterine synechiae found 19 case reports or case series with reported complications of expulsion, pregnancy, bleeding, perforation, and pain; some cases did not report complications.[25] Regarding leiomyoma, a systematic review evaluated eight studies that reported on hormonal IUD expulsion rates among women with uterine leiomyomas and concluded that expulsion rates may be higher in this group, although no comparative studies achieved a statistically significant difference in expulsion rates between women with leiomyomas and those without leiomyomas.[26] Given the limited data, IUDs cannot be recommended for patients with uterine cavity distortion seeking contraception. Intrauterine devices may be considered for those seeking only noncontraceptive IUD benefits who are willing to accept the possible increased risk of expulsion or other complications.

Implant and hormonal IUD use is restricted in some medical conditions, such as breast cancer, severe decompensated liver disease, hepatocellular adenoma, and malignant liver tumors.[24] Certain enzyme-inducing anticonvulsants may decrease the efficacy of an etonogestrel implant, and drug interactions were found to account for 4% of method failures in a study of 234 reported pregnancies during implant use.[27] Age and parity should not affect eligibility for LARC use. Implants and IUDs are appropriate and recommended if desired by adolescents and young people without a history of prior pelvic examination or pregnancy.[28,29]

After placement, follow-up with a health care professional for a routine IUD string check in an asymptomatic patient is not recommended by the U.S. Selected Practice Recommendations for Contraceptive Use[30]; furthermore, counseling patients to self-check their IUD strings has been shown to have limited clinical utility and may lead to increased patient anxiety and unnecessary visits.[31] Instead, counseling patients on unexpected symptoms and signs of expulsion may permit patients to self-identify a problem and present for follow-up.

PLACEMENT TIMING

Although interval placement (anytime 4 weeks or more postpregnancy) is the most common time for LARC initiation, postpregnancy placement has been increasingly studied and performed. Implant placement at the time of medication abortion or immediately after early pregnancy uterine aspiration is safe.[32–35] Placing an implant at the time of initiating medication abortion with mifepristone does not change treatment outcome and should be considered based on patient preference and plan for follow-up.[34] Two population studies report decreased repeat pregnancy and abortion in the 2 years after immediate postabortion implant placement.[33,35] Intrauterine devices can be placed immediately after uterine evacuation in the first or second trimester or at time of completed medication abortion; immediate placement reduces rapid repeat pregnancy without increasing infection or expulsion risk compared with delayed placement.[35–39]

Both postpartum implant placement before hospital discharge and immediate postplacental IUD placement are safe, convenient, and result in high method-continuation rates and low repeat-pregnancy rates within the first year.[40,41] Despite theoretical concerns about the effects of exogenous progestins on breastfeeding, data suggest that the etonogestrel implant and levonorgestrel IUD and have no effect on breastfeeding initiation, continuation, or infant growth.[42–46] An important caveat is that perforation risk is higher in people who are breastfeeding; a systematic review concludes that the risk of perforation during IUD placement in people who are breastfeeding is 6–10 times greater than in those who are not breastfeeding.[47] There are limited data regarding perforation risk with immediate postplacental IUD placement.

Expulsion is one significant disadvantage of immediate postplacental IUD placement. According to a systematic review and meta-analysis, among IUDs placed immediately after vaginal birth, the expulsion rate was 27% for the levonorgestrel 52-mg IUD and 12% for the copper IUD; on average, this represents an eightfold increase over expulsion rates after interval placement.[48] Expulsion rates were greater in placement after vaginal birth compared with cesarean birth (adjusted risk ratio 4.57) and greater with levonorgestrel compared with copper IUDs (adjusted risk ratio 1.9). This meta-analysis included studies with various durations of follow-up from 1 month to 5 years, though expulsion rates did not differ for studies with follow-up at 3–6 months compared with greater than 6 months, implying that most expulsions occurred early. In addition, a recent population-based study shows that, compared with IUDs placed more than 1 year from birth, the adjusted hazard ratio for expulsion was highest for placements 0–3 days postpartum (5.34), lower at 4 days–6 weeks postpartum (1.22), and lowest at 6–14 weeks postpartum (1.06).[49] Other concerns after immediate postpartum IUD placement include malposition and missing strings;

in one cohort of 348 people who underwent immediate postpartum IUD placement and were monitored for 12 months, 21% of IUDs in situ lacked visible strings.[50]

The ability to follow up may be a key factor when weighing the risks and benefits of immediate postplacental IUD placement. Among participants who completed follow-up, two U.S. randomized controlled trials comparing immediate postplacental IUD placement with delayed placement found no difference in use at 6 months[51] and 12 months[52] after allowing for postexpulsion replacement. In both clinical trials and population-based studies, postpartum follow-up rates are higher in patients with private insurance and lower in those with Medicaid insurance.[53,54] In addition, for patients with Medicaid insurance, funding may be more reliable in the immediate and early postpartum period due to lack of Medicaid expansion in some states.[55] These findings suggest that those least likely to be able to attend follow-up appointments have the most potential benefit from immediate placement.

In summary, immediate postplacental IUD placement should be personalized as opposed to universal. If patients are likely to retain health care funding and attend their postpartum follow-up appointments, the risks of immediate postplacental placement may outweigh the advantages. Informing patients of the available data may empower them to choose the ideal type and timing of postpartum LARCs, if desired. Patients who choose immediate postpartum IUD placement should be thoroughly counseled on recognizing expulsion and given a plan for back-up contraception and follow-up if an expulsion is recognized. Furthermore, if an immediate postpartum LARC method is strongly desired but the expulsion risk is unacceptable to the patient, emphasis should be placed on the implant.

PLACEMENT COMPLICATIONS

Although placement and removal of LARC methods has become routine for most clinicians, growing experience has brought new clinical challenges for both implants and IUDs.

Implant

Implant placement can routinely cause a small scar and mild pain, swelling, and bruising. A pressure dressing applied for 24 hours may decrease bruising and swelling. Patients should be instructed to apply ice and use anti-inflammatory medications for postplacement discomfort. Infection at the placement site is extremely rare but could require oral antibiotics and consideration for removal depending on infection extent and response to treatment (Nexplanon prescribing information, Organon, 2021). Improper placement is arguably the most serious complication, because it can have lasting repercussions for the patient. The original implant inserter, introduced in 2006, was a two-handed inserter with the benefit of providing the clinician with an unobstructed view of the inserter needle. Subsequently, in 2010, the one-handed inserter was introduced, and barium sulfate was added to the implant to make it radiopaque.[56] This inserter features a depth guide designed to minimize risk of improper placement, although with the consequence of blocking the clinician's view of the inserter needle from above, requiring clinicians to attempt to view the inserter needle from the side.

Though most implants are easily removed, 14 per 1,000 removals are reported by health care professionals as difficult and 1 per 1,000 implants are nonpalpable.[57,58] The importance of postplacement implant palpation by the clinician and patient is highlighted by the fact that "missing implants" attributed to nonplacement accounted for 26% of 463 pregnancies in implant users in a population study.[27] The etonogestrel 68-mg implant is meant to be placed in the subcutaneous tissues of the upper arm over the triceps, 8–10 cm proximal to the medial epicondyle. Less than 8 cm from the medial epicondyle, the ulnar nerve is more superficial and could be injured by implant placement. The triceps region is a change from prior recommendations to place the implant over the sulcus, or the groove between the biceps and triceps muscles, and was made to improve safety because there are no neurovascular structures in this area.[59] If the implant cannot be easily palpated immediately after placement, it should be removed at that time and replaced through a different incision.

Intrauterine Device

Anticipated or perceived pain during IUD placement can be a barrier for some patients,[60] and an array of methods to improve pain with placement have been studied. A 2015 review concluded that there was no evidence of reduced pain with lidocaine 2% gel, misoprostol, and most nonsteroidal anti-inflammatory drugs (NSAIDs). Of the NSAIDs, oral naproxen was shown to reduce pain scores in one of two trials and intramuscular ketorolac reduced pain in a study for nulliparous patients only.[61]

Recent studies consistently show that a paracervical lidocaine block reduces pain in certain populations.[62–64] Randomized controlled studies in people who are nulliparous or nulligravid show that a 10–20-mL 1% lidocaine paracervical block decreased

pain during IUD placement. These studies included copper IUDs and all doses and sizes of hormonal IUDs; thus, they provide evidence of improved placement pain with paracervical block with all IUD types. Although a paracervical block may cause pain with injection and slight prolongation of the procedure, patients who are nulliparous or who may require cervical dilation should be offered this option.

Placement of IUDs with smaller frames and inserters may be presumed to be easier or less painful, but the available data do not favor a significant clinical difference. As stated previously, the levonorgestrel 13.5-mg and 19.5-mg IUD frames are 28-mm wide by 30-mm long, and the levonorgestrel 52-mg frame is 32-mm wide by 32-mm long. The outer diameter of the placement tube is 3.8 mm for the levonorgestrel 13.5-mg and 19.5-mg IUDs; it is 4.4 mm for the Mirena and 4.8 mm for the Liletta (Skyla prescribing information, Bayer Healthcare, 2021; Kyleena prescribing information Bayer Healthcare, 2022; Mirena prescribing information, Bayer Healthcare, 2022; Liletta prescribing information, Allergan USA Inc. and Medicines360, 2019). A randomized trial comparing the levonorgestrel 13.5-mg, 19.5-mg, and 52-mg IUDs found that, although more investigators evaluated placement as "easy" and more patients reported no pain with the levonorgestrel 13.5-mg and 19.5-mg IUDs, there were similarly low rates among the groups of "very difficult" placement or placement with "severe" pain.[11] Given that the levonorgestrel 52-mg IUDs have longer duration of use and significantly higher rates of absent or infrequent bleeding,[65] the levonorgestrel IUD 13.5-mg and 19.5-mg IUDs should be considered in appropriately counseled patients who do not prefer absence of bleeding or spotting or have other unique considerations (Table 3).

Perforation at time of IUD placement is rare; rates are 2 in 1,000 or less in clinical trials (Paragard prescribing information, CooperSurgical, 2020; Skyla prescribing information, Bayer Healthcare, 2021; Kyleena prescribing information Bayer Healthcare, 2021; Mirena prescribing information, Bayer Healthcare, 2022; Liletta prescribing information, Allergan USA Inc. and Medicines360, 2019) and approximately 2 per 1,000 in population-based studies.[66] Because patients may have minimal to no symptoms at time of perforation, a high index of suspicion must be maintained because the risks of laparoscopy to remove an intra-abdominal IUD far outweigh the risks of unnecessary removal and replacement. Signs of perforation may include a loss of resistance or greater than anticipated depth during sounding or IUD placement, unusual pain, or brisk bleeding. If perforation is suspected at time of placement, the IUD position should be confirmed by ultrasonography. If appropriate positioning cannot be confirmed, the IUD should be immediately removed. Uterine healing after perforation can be rapid, as evidenced by cases of laparoscopy shortly after identified perforations[67]; repeat placement should be delayed 2–6 weeks, and asymptomatic stable patients can often be discharged home with return precautions.

Although active pelvic infection is a contraindication to IUD placement, new pelvic infection is diagnosed in only 0.5% of people within 90 days.[68] Screening for sexually transmitted infections at time of IUD placement is recommended only if clinically indicated, and prophylactic antibiotics are not recommended. Traditional teaching was that infection risk is highest in the first 20 days after IUD placement, but recent evidence from a levonorgestrel 52-mg IUD clinical trial monitoring participants for 2 years after placement suggests that infections are infrequent and not temporally related to placement.[69] A 5-year randomized trial with people at low-risk for pelvic infection shows a significantly lower rate in participants aged 25 years or younger among levonorgestrel 52-mg IUD users compared with a comparator copper IUD; this suggests that progestin-mediated cervical thickening may play a role in infection prevention.[70] If pelvic infection develops in a patient with an IUD, treatment per Centers for Disease Control and Prevention guidelines should be provided. Only if the

Table 3. Comparison of Characteristics of Levonorgestrel Intrauterine Devices

Levonorgestrel IUD type	Frame Size (mm)	Inserter Diameter (mm)	Absence of Bleeding or Spotting Rate at 1 y[114,115]	Absence of Bleeding or Spotting Rate at 3 y[114,115]
13.5-mg (Skyla)	28×30	3.8	6	12
19.5-mg (Kyleena)	28×30	3.8	12	20
52-mg (Liletta)	32×32	4.8	19–20	36–37
52-mg (Mirena)	32×32	4.4	19–20	36–37

IUD, intrauterine device.
Data are % unless otherwise specified.

patient fails to improve after 48–72 hours should IUD removal be considered.[30]

REMOVAL CHALLENGES

Implant

After incision of the skin, implant removal can be accomplished with or without instruments and is best performed with techniques with which the operator feels most comfortable. Removal of palpable implants with a "pop-out" technique is well-described for multiple rod implants and is therefore a quick and efficient methodology with a single rod implant.[71] Regardless of technique, removal efficiency can be maximized by remembering a few key points. First, the local anesthetic should be injected under the implant tip, preferably while holding the proximal tip of the implant with the nondominant forefinger and elevating and stabilizing the distal tip with the dominant thumb. Using small amounts of anesthetic placed strategically will minimize fluid obliteration around the distal tip, which can make the implant difficult to palpate after injection. Second, the incision should always be made longitudinally in line with the long axis of the implant to prevent implant fracturing. Lastly, nonpalpable implant removal should be performed only by clinicians experienced with this complication.[72]

Three case series describe referral center experience with nonpalpable implant removal.[73–75] In these case series, approximately 90% of people referred were confirmed to have a nonpalpable implant. Almost all implants were able to be localized by high-frequency ultrasonography, with few requiring other imaging modalities. Although most implants were in the subcutaneous fat, approximately one third were found to be inserted below the fascia. Office removal by a specialist was successful at least 97% of the time if the implant was above the fascia, with slightly lower rates of success for subfascial implants (83–92% in the two-case series in which this rate was reported). In cases of unsuccessful office removal or if the implant is close to neurovascular structures, patients are referred to a surgeon specializing in arm and axillary dissection.

Lessons about proper placement can be learned from cases of difficult removal. Subfascial implants were more common in patients with underweight or normal weight (BMI lower than 25).[74] This is likely due to the thin layer of subcutaneous tissue between the dermis and the fascia in such individuals, and it makes awareness of appropriate subdermal placement per manufacturer's instructions even more crucial in this population. There are also data to suggest a potential association between replacement through a removal incision and subfascial placement. Although this has not been studied directly, the mechanism of decreased resistance through a prior incision makes causation plausible; thus, caution should be used, and replacement through a separate incision should be considered, especially in thin patients.

Intrauterine Device

There are few indications for IUD removal based on its position in the uterine cavity. Studies evaluating IUD location by ultrasonography have demonstrated spontaneous positional adjustments as well as changes in the appearance of positioning with normal growth and thinning of the endometrium.[76,77] Removal for partial expulsion should be reserved for patients with significant correlating symptoms such as increased bleeding or cramping, ultrasonographic evidence of the IUD stem in the cervical canal, or visualization of the stem protruding through the external cervical os. Embedment refers to penetration of an IUD into the myometrium without extension through the serosa. Recent advances in ultrasonographic technology and three-dimensional imaging have led to increased referrals for asymptomatic patients with possible IUD embedment. Although continued surveillance for the development of corresponding symptoms may be warranted in these circumstances, removal is not necessarily indicated.

Intrauterine devices available in the United States have strings that are meant to come through the external cervical os and sit in the upper vagina after placement. Intrauterine device strings are present to increase ease of removal, but lack of strings is not an indication for intervention. The copper 380-mm^2 IUD has white strings, the levonorgestrel 13.5-mg IUD has brown strings, the levonorgestrel 19.5-mg IUD has blue strings, and the levonorgestrel 52-mg IUDs have blue (Liletta) or brown (Mirena) strings (Paragard prescribing information, CooperSurgical, 2020; Skyla prescribing information, Bayer Healthcare, 2021; Kyleena prescribing information Bayer Healthcare, 2021; Mirena prescribing information, Bayer Healthcare, 2022; Liletta prescribing information, Allergan USA Inc. and Medicines360, 2019). Some IUDs available outside the United States do not have strings. A properly positioned IUD with missing or no strings can remain in situ until removal is desired or device expiration is reached. At time of removal, after confirmation of IUD location with ultrasonography, an in-office attempt is preferable if the patient is amenable. A paracervical block can be offered, and concurrent abdominal ultrasound guidance is helpful. An

IUD thread retriever can be used and may work up to 50% of the time.[78] Although there are case reports of successful T-shaped IUD removal with an IUD hook, this instrument is designed and intended for removal of ring IUDs.[79] Long, narrow instruments with jaws that open only at the distal end, such as alligator forceps or hysterographic grasping forceps, can be used with higher rates of successful removal (83–98%); if not successful, a manual vacuum aspiration device can be used to attempt removal through suction.[80–84] Intrauterine devices that appear to be embedded can still be removed in this manner,[85] although IUD fracturing, or breaking, can be noted.[86] In our experience, the Tatum-T IUD frames such as in the copper 380-mm^2 IUD are more prone to this complication. Given that IUDs are inert substances after depletion of their hormonal or copper components, careful consideration of fertility goals and counseling of risks and benefits should guide plans for operative removal, especially in those requiring destructive procedures to remove embedded IUD fragments.

When pregnancy occurs with an IUD in place, the risk of extrauterine location is significantly increased.[18] Therefore, the first and most important step is to rule out ectopic pregnancy. If ectopic pregnancy is confirmed, IUD removal is recommended; pregnancy with an IUD in place is rare, and one must wonder what made this particular IUD fail (eg, a manufacturing defect). A new IUD should be placed if the patient desires to continue this method. In all other pregnancies with an IUD in situ, a removal attempt should be considered as soon as possible regardless of pregnancy intentions. However, if the pregnancy is undesired, there are fewer concerns when attempting immediate removal. If the patient wishes to continue the pregnancy, the IUD should always be removed after appropriate counseling if strings are visible or if ultrasonography confirms its presence within the cervix. Pregnant patients with retained IUDs in pregnancy are at greater risk of spontaneous abortion, septic abortion, preterm delivery, and chorioamnionitis.[87] In a comparative cohort study of 144 pregnancies in patients with IUDs in situ, the combined risk of adverse pregnancy outcomes was significantly higher in patients who retained their IUD compared with those who had them removed during the first trimester (relative risk 2.0, 95% CI 1.3–3.3), especially in patients who retained an IUD in a low-lying position (relative risk 3.9, 95% CI 1.8–8.6); removal was performed only in patients with visible IUD strings.[88] If no strings are present and ultrasonography confirms an intrauterine IUD below the level of the pregnancy, ultrasound-guided removal with forceps or hysteroscopy can be attempted after thorough counseling of the risks and benefits of attempted IUD removal compared with the increased obstetric risks of IUD retention.[89] Removal should not be attempted if the IUD is superior to the gestational sac. If the IUD is not located on ultrasonogram, an X-ray of the abdomen and pelvis should be performed after the first trimester or pregnancy resolution to confirm expulsion.

Levonorgestrel IUD use in perimenopause and menopause is safe and has benefits in several clinical scenarios. During perimenopause, contraception remains necessary because occasional ovulation occurs.[90,91] In addition, people who are perimenopausal and experience heavy or frequent bleeding may undergo uncomfortable and time-consuming evaluation to rule out endometrial cancer; this may be avoided in those with lighter or absent bleeding with a levonorgestrel IUD in place through the menopausal transition. In patients with menopausal symptoms desiring hormone therapy, a levonorgestrel 52-mg IUD can be used for endometrial protection in place of a systemic progestin.[92–94] Because the copper IUD does not have hormonal benefits, removal is reasonable after confirmation of menopausal status. Although no studies have examined the risks of retaining an IUD long-term in asymptomatic people who are menopausal, retention of an inert IUD can be considered if removal risks outweigh benefits.[95]

INTRAUTERINE DEVICES AS EMERGENCY CONTRACEPTION

Emergency contraception, or contraception used after unprotected or inadequately protected intercourse to reduce the risk of pregnancy, continues to evolve. Methods such as ulipristal acetate and levonorgestrel pills are no more effective than placebo in individuals with BMIs of 35 or higher and 26 or higher, respectively.[22] In contrast, the copper IUD remains an effective method of emergency contraception unaffected by weight, with a window of at least 5 days after intercourse.[96] Consideration for placement after 5 days may be supported by an analysis of data from four studies in which no pregnancies occurred in patients with negative urine pregnancy test results who had copper 380-mm^2 IUDs placed after unprotected intercourse in the prior 6–14 days.[97] Placement of an IUD as emergency contraception has the benefit of providing long-term contraception, but use can be limited by barriers to access. Furthermore, people considering an IUD more commonly choose a levonorgestrel than a copper IUD, likely due to the hormonal effect on menstrual bleeding and dysmenorrhea.[98] A recent

randomized trial shows that the levonorgestrel 52-mg IUD was noninferior to the copper IUD for emergency contraception (0.3% vs 0% pregnancy rate).[99] Further study is needed to definitively understand differences in outcomes between the levonorgestrel IUD and the copper IUD for emergency contraception, although secondary analyses of this study have salient implications on recommendations for same-day levonorgestrel IUD placement as well as need for postplacement back-up contraception.[100,101]

BLEEDING PATTERNS

Implant

The etonogestrel implant is well known for its typically light yet unpredictable bleeding pattern; thus, it can be difficult to counsel patients on what to expect after placement. Continuous systemic progestin exposure can result in bleeding due to the atrophic endometrium with dilated, thin-walled vessels.[102] Although only 13% of patients discontinued implant use due to bleeding symptoms in U.S. phase 3 clinical trials,[103] clinical use in a population-based study in St. Louis shows a 44% discontinuation rate at 3 years, with approximately half of users citing bleeding changes as the reason for removal.[104] For a given 90-day reference period, approximately 50% of implant users experienced no or infrequent bleeding, with roughly 25% experiencing frequent or prolonged bleeding.[105] There was no consistent pattern of worsening or improving over time, although those who reported absent, infrequent, or normal frequency of bleeding within the first 3 months of use tended to continue these patterns over the next 2 years and those with frequent or prolonged bleeding initially had a 50% chance that their bleeding would improve in the subsequent 90 days.[106]

Because the implant has very high contraceptive efficacy, users may desire treatment for bleeding symptoms rather than removal. Several modalities have been studied and found to modestly or temporarily address bleeding symptoms. Investigated methods include cyclic and continuous combined oral contraceptive (COC) pills, progestin-only pills, NSAIDs, tranexamic acid, ulipristal acetate, and tamoxifen.[107,108] Combined oral contraceptive pills are easily accessible and well-studied compared with other options. Two randomized controlled trials investigated the effect of concurrent implant and continuous COC pill use.[109,110] Results show that a 14- to 28-day course of COCs improved bleeding in most users, although bothersome bleeding resumed after pill discontinuation. Furthermore, of users who desired removal initially, most requested removal after study completion despite bleeding improvement while on COCs.[109] For patients with no contraindication to estrogen use who prefer to attempt intervention before removal, initial management with continuous COCs for 4 weeks is reasonable, with the option to continue use if a desirable bleeding pattern is obtained. One small study evaluated combined implant and COC use for up to 6 months without any significant adverse effects.[111]

Intrauterine Device

The copper IUD is associated with increased dysmenorrhea and volume and length of menstrual bleeding, especially within the first several cycles after placement. These effects generally decrease over time[112] but are a reason for discontinuation in 2.4% of users in the first year.[113] Conversely, levonorgestrel IUDs decrease bleeding and improve dysmenorrhea through down-regulation of endometrial estrogen receptors and decreased endometrial proliferation.[12]

In levonorgestrel 52-mg IUD clinical trials, rates of absent bleeding, spotting, and light bleeding increased annually up to 3–5 years of use, at which time they accounted for 89% of bleeding patterns. *Absent bleeding or spotting* rates, defined as no bleeding within the previous 90 days, were 19% at 1 year, 37% at 3 years, and approximately 37–42% through 8 years of continuous use[65,114] Comparatively, levonorgestrel 13.5-mg and 19.5-mg IUD users had lower absent bleeding or spotting rates and infrequent bleeding rates.[115] At 1 year, absent bleeding or spotting rates were 6% and 12%, respectively, for the levonorgestrel 13.5-mg IUD and 19.5-mg IUD, increasing to 12% and 20%, respectively, at 3 years. Users of these IUDs also had higher rates of irregular bleeding at 3 years compared with levonorgestrel 52-mg IUD users (23% of levonorgestrel 13.5-mg IUD users, 17% of levonorgestrel 19.5-mg IUD users, and 6% of levonorgestrel 52-mg IUD users).

Given the favorable and consistent bleeding profile of the levonorgestrel 52-mg IUD as well as its ability to inactivate the endometrium, it has been used for multiple noncontraceptive benefits. These include management of heavy menstrual bleeding,[116] primary dysmenorrhea,[117] endometriosis,[118] leiomyoma,[119] adenomyosis,[120] menstrual bleeding in people with hemostatic disorders[121] or on anticoagulation,[122] and in patients with endometrial intraepithelial neoplasia and low-risk endometrial cancer.[123]

EVIDENCE-BASED DURATION OF USE

Ongoing research has shown that LARC methods are effective for contraception beyond their initial

approved duration of use (Table 2). The FDA supports off-label use in informed patients when adequate published evidence is available.[124] For people who desire long-term pregnancy prevention, extending duration of use minimizes removal and replacement procedures and decreases associated health care costs. All patients should be counseled regarding best evidence for LARC use. If clinicians are uncomfortable recommending extended duration based on the evidence, the patient can be referred for consultation with a complex family planning specialist. Clinicians should be aware that users may desire removal and replacement before evidence-based expiration; this practice should be individualized, with counseling of the risks and benefits of removal and replacement.

Implant

The etonogestrel 68-mg implant is FDA-approved for 3 years (Nexplanon prescribing information, Organon, 2021). Data support use up to 5 years in individuals without obesity. A World Health Organization study showed no pregnancies in years 4 and 5 of use, but only 6% of implants users who started the study had obesity.[125] The best data for extended use in users with obesity are provided by the Contraceptive CHOICE study. Approximately 100 users with obesity continued the implant for 4 years, and few continued to 5 years; no pregnancies occurred.[126] Although some institutions have chosen to recommend extended use of the etonogestrel 68-mg implant up to 5 years regardless of BMI, users with obesity should be counseled regarding available evidence when choosing to extend use past 4 years.

Intrauterine Device

Current FDA-approved use of the copper 380-mm^2 IUD is 10 years (Paragard prescribing information, CooperSurgical, 2020), but evidence supports at least 12 years of use. Data from the initial clinical trial included 78 people with use to 12 years, during which time no pregnancies occurred,[127] and the safety and efficacy of 12 years of use is supported by subsequent studies based on 1,204 woman-years of observations.[128] There are fewer data regarding use for between 12 and 15 years, with less than 100 woman-years of observations, and most users were aged 40 years or older at the time of 10 years of completed use.[129] In the context of decreased natural fertility, we recommend shared decision making for extending use to between 12 and 15 years in users aged 45 years and older.

The two U.S.-marketed levonorgestrel 52-mg IUDs are equivalent based on initial dose and release rates of their levonorgestrel component.[130] As such, data regarding duration of use can be applied equally to both products. Liletta is currently FDA-approved for 6 years of use (Liletta prescribing information, Allergan USA Inc. and Medicines360, 2019), and Mirena was approved for 8 years of use in 2022 (Mirena prescribing information, Bayer Healthcare, 2022). Liletta is expected to receive FDA approval for 8 years of use in November 2022. Recent data support the continued use of the levonorgestrel 52-mg IUD for at least 8 years, with low incidence of adverse events.[65] There is no evidence for extended use for the levonorgestrel 13.5-mg or 19.5-mg IUDs.

CONCLUSION

Although LARC methods are increasingly used for contraception, their use is not without clinical challenges. Notable updates include evidence-based duration of use, LARCs as emergency contraception, and guidance for implant placement and nonpalpable implant removals. An understanding of ongoing LARC developments is critical to providing patients with the most up-to-date and evidence-based counseling and care. Complex family planning has continued to grow as it takes a step forward as a subspeciality newly recognized by the American Board of Obstetrics and Gynecology.[131] Although all obstetrician–gynecologists as well as primary care clinicians can safely provide LARCs, complex family planning specialists are an expert referral source for challenging cases and evidence-based care as contraceptive technology continues to develop.

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