Intrauterine Contraception: The Pendulum Swings Back
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Everything we can do to give women control over their bodies and their fertility enhances their health and also changes the world for the better.
—Malcom Potts, Presidential Address, Annual Clinical Meeting of the American College of Obstetricians and Gynecologists, May 2, 2005

Intrauterine contraception use in the United States and worldwide

Intrauterine contraception (IUC) is the most widely used method of reversible fertility regulation in the world. Over 100 million women worldwide use it for contraception [1]. IUC is undergoing a renaissance in the United States (US) due to recognition of its many benefits and safety. As more new devices and intrauterine hormonal systems are developed and introduced into the US market, IUC utilization will continue to expand. Liberalization of previously overly restrictive product labeling and medical protocols will encourage a new age of modern IUC use in the US.

Unmet need for contraception and the role of intrauterine contraception

The unmet need for contraception in the US and worldwide constitutes a public health crisis. The scope of this unmet need is evident: worldwide, an estimated 60 million unintended pregnancies occur annually. These unintended pregnancies result in an estimated 26 million births, 26 million abortions, and 8 million miscarriages worldwide [2]. In the US, nearly half of all
pregnancies—an estimated 3 million annually—are unintended, and nearly half of these end in abortion [3]. Over half of unintended pregnancies are a result of contraceptive failure or misuse [3]. Because the intrauterine device (IUD) rarely fails and is difficult to misuse, more widespread use of IUC could have a powerful effect in reducing unintended pregnancy in the US.

Patterns of intrauterine contraception use in the United States and abroad

Many cultures have addressed the unmet need for successful fertility regulation by embracing and expanding IUC. IUC is one of the most popular methods of contraception in Europe and Latin America, ranging from 10% to 30% of women contraceptors. In Cuba, Egypt, and North Korea, IUC use accounts for more than 50% of contraceptive use. In China, 83% of married women use contraception, and 36% of these use IUDs [1]. In Germany and Denmark, where unintended pregnancy and abortion rates are dramatically lower than in the US, IUC is used by 20% of contraceptors [5].

Despite its popularity worldwide, IUC is just beginning to be appreciated by US clinicians, and perhaps more importantly, by US women. Currently only 2% of US women contraceptors use IUC [4]. Women physicians have consistently used IUDs more than age- and income-matched women, even before the marketing of the levonorgestrel intrauterine system (LNG IUS). In the 1995 “Women’s Physician Health Study,” approximately 1% of women in the general population used IUDs, whereas 5% of female physicians and 9% of female obstetrician/gynecologists used them [6]. Now, more than a decade later and with the availability of the LNG IUS, female physicians choose IUC more than ever. Female fellows of the American College of Obstetricians and Gynecologists indicated they would choose IUC as their first choice contraceptive method when childbearing was completed and as their second choice, after oral contraceptives, if desiring to space their children [7]. US women who have the most knowledge to make their contraceptive decisions—obstetrician/gynecologists—choose IUC far more frequently than their patients do (Fig. 1).

Intrauterine contraception available in the United States today

Only two FDA-approved intrauterine devices are available in the United States today, the copper T380A (Paragard, Duramed, Barr Pharmaceuticals, Cincinnati, Ohio) and the LNG IUS (Mirena, LNG 20, Bayer HealthCare Pharmaceuticals, Wayne, New Jersey). Many of the important qualities of IUC—effectiveness, safety, and acceptability—are shared by the two methods.

The copper T380A consists of a T-shaped frame made of a polyethylene blend. The active component is 380 mm$^2$ of exposed copper surface area in the form of copper wire wound on the stem and copper collars on the
horizontal arms. The copper ions released into the endometrium are toxic to sperm and provide the prefertilization contraceptive effect [8,9]. Of the many copper devices available worldwide, the copper T380A is more effective than, and has a similar side-effect profile to, other framed copper devices such as the Nova T, TCu220, and MLCu250, MLCu375 [10]. The copper T380A was approved by the US Food and Drug Administration (FDA) in 1984, and prescribing information was updated in 2005 (Fig. 2).

The LNG IUS is also a T-shaped device, but the active ingredient, LNG, is contained in a steroid reservoir around the stem. The reservoir releases 20 μg per day of LNG directly into the uterine cavity. The high local LNG concentrations cause uniform suppression of endometrial proliferation, which creates decidualization of the stroma and an inactive histology. Similar to the uterine effects obtained with copper devices, these alterations in the uterine environment are hostile to sperm viability and motility as well as fertilization. Antifertilization mechanisms of the LNG IUS are being elucidated: LNG concentrations in the uterus have been shown to alter zona pellucida binding site expression on human spermatozoa [11]. The T-frames of both IUDs contain barium sulfate, making them visible on radiograph examination. The Mirena was approved in Finland, its country of origin, in 1990 and by the US FDA in 2000 (Fig. 3).

**Determinants of contraceptive effectiveness**

To accurately compare real-life effectiveness of different contraceptive methods, and how IUC fits in, several factors must be considered. First, how well does a method biologically prevent pregnancy? Second, how difficult or easy is it to be compliant with the method in order that use will be consistent and accurate? Third, what is the method’s continuation rate?
Continuation of a method over time may be the most important, yet often underappreciated, cause of unintended pregnancy. Continuation rates provide one proxy of acceptability of a given method. If side effects or cumbersome compliance requirements make women discontinue or use a method erratically, effectiveness over time plummets. The real-life contraceptive effectiveness equation helps put the many important factors influencing effectiveness into perspective (Box 1) [12].

IUC demonstrates high contraceptive effectiveness because it scores so well on all three attributes in the numerator of the real-life contraceptive effectiveness equation. IUC has high biologic efficacy, it requires almost no compliance—in fact it takes a volitional act to discontinue protection rather than to use protection—and it has the highest continuation rate of any reversible method. The impact of continuation rates on contraceptive success cannot be underestimated. Women spend most of their reproductive years—on average 40 years—trying to avoid pregnancy. The copper IUD continuation rate is 78%, and the LNG IUS continuation rate is 81% at the end of 1 year of use [13]. In contrast, oral contraceptive continuation rates at 1 year range from 50% [14] to 68% [13]. Although the efficacy of depo-provera is considered top-tier [13], the overall continuation rate at 1 year is only 56% [13] and is as low as 22% in some populations [15]. Compliance and continuation can have more impact than perfect-use efficacy in determining a method’s overall success.
Although continuation rates with the two IUDs are similar, reasons for discontinuation differ. More women discontinue the copper device because of bleeding and cramping complaints, whereas more women discontinue the LNG IUS because of amenorrhea and hormonal complaints. Overall, continuation rates are similar [16].

**Observed effectiveness of intrauterine contraception**

IUC is among the most effective reversible methods of contraception. Its efficacy rivals that of permanent sterilization [13]. IUC “compliance” is limited to string checks, which are helpful in detecting unnoticed expulsions that could result in pregnancy. Because IUC compliance is minimal, perfect and typical use are nearly identical. Similar first-year typical-use (or perfect-use) pregnancy rates are observed in LNG-IUS users and copper T380A users: 0.8 to 0.6 and 0.1 per 100 women, respectively [16].

Data suggest that efficacy persists longer than current product labeling indicates for the copper IUD and the LNG IUS. Twelve-year data for the copper IUD and 7-year data for the LNG IUS provide cumulative pregnancy rates of 1.9 per 100 women for the copper IUD [18] and 1.1 to 1.4 pregnancies per 100 women with the LNG IUS [17]. The cumulative 10-year probability of pregnancy after tubal ligation is 1.8 per 100 women, not clinically different [19]. Modern IUC can be considered “reversible sterilization”—without the risk of anesthesia, surgery, or regret for the woman or her partner (Table 1).

**Barriers to intrauterine contraception use: safety and liability**

Despite the best real-life effectiveness of any reversible contraceptive method, IUC has come up against impressive barriers to widespread use in the US. Primarily, unfounded safety and liability concerns resulted in restrictive product labeling and medical protocols and overly conservative candidate selection criteria [20–22].

**Safety concerns**

Misperceptions about the risks associated with IUD use are well documented [21,23]. Although every contraceptive intervention has it’s risks,
including failure and the much greater medical risks associated with pregnancy and childbirth, the overall safety profile of modern IUC is among the best in the contraceptive armamentarium. [21,23]. It is discouraging that the problematic IUD of the 1970s, the Dalkon Shield, off the market for over 30 years, still tarnishes the reputation of modern IUC. Despite extensive testing establishing the safety of modern IUDs, clinicians and women confuse the risks of the Dalkon Shield with the currently available IUDs. Safety concerns about IUC focus on the risk of pelvic inflammatory disease (PID) with subsequent infertility and risk of ectopic pregnancy.

<table>
<thead>
<tr>
<th>Method</th>
<th>Percentage of women experiencing an unintended pregnancy within the first year of use (Typical Use[^b])</th>
<th>Percentage of women continuing use at one year[^a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>No method[^c]</td>
<td>85</td>
<td>—</td>
</tr>
<tr>
<td>Male condoms[^d]</td>
<td>15</td>
<td>53</td>
</tr>
<tr>
<td>Combined pill and minipill</td>
<td>8</td>
<td>68</td>
</tr>
<tr>
<td>Evra Patch</td>
<td>8</td>
<td>68</td>
</tr>
<tr>
<td>NuvaRing</td>
<td>8</td>
<td>68</td>
</tr>
<tr>
<td>Depo-Provera</td>
<td>3</td>
<td>56</td>
</tr>
<tr>
<td>IUC</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>ParaGard (copper T)</td>
<td>0.8</td>
<td>78</td>
</tr>
<tr>
<td>Mirena (LNG-IUS)</td>
<td>0.1</td>
<td>81</td>
</tr>
<tr>
<td>Female Sterilization</td>
<td>0.5</td>
<td>100</td>
</tr>
<tr>
<td>Male Sterilization</td>
<td>0.15</td>
<td>100</td>
</tr>
</tbody>
</table>

Emergency Contraceptive Pills: Treatment initiated within 72 hours after unprotected intercourse reduces the risk of pregnancy by at least 75%.

[^a]: Among couples attempting to avoid pregnancy, the percentage who continue to use a method for 1 year.

[^b]: Among *typical* couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason. Estimates of the probability of pregnancy during the first year of typical use for spermicides, withdrawal, periodic abstinence, the diaphragm, the male condom, the pill, and Depo-Provera are taken from the 1995 National Survey of Family Growth corrected for underreporting of abortion; see the text for the derivation of estimates for the other methods.

[^c]: The percentages becoming pregnant in columns (2) and (3) are based on data from populations where contraception is not used and from women who cease using contraception in order to become pregnant. Among such populations, about 89% become pregnant within 1 year. This estimate was lowered slightly (to 85%) to represent the percentage who would become pregnant within 1 year among women now relying on reversible methods of contraception if they abandoned contraception altogether.

[^d]: Without spermicides.

Risk of pelvic inflammatory disease

Clinicians’ most deeply rooted fear about the IUD is an association between IUD use and the development of PID. A large body of evidence refutes this association and is summarized in a Cochrane review [24]. The review concludes that the risk of PID after the first 20 postinsertion days is small and reflects baseline risk in the population. One of the most convincing studies reviewed 22,908 copper IUD insertions. This study identified a background risk of PID of 1.4 cases per 1000 woman-years of use compared with 9.7 cases per 1000 woman-years in the first 20 days after IUD insertion [25]. Rates of PID fell to the background level after the first 20 days postinsertion and remained low and stable for 8 years of follow-up monitoring, demonstrating the uncommonness of PID in IUD users. Further, these 22,908 IUD insertions occurred in clinical settings with variable resources for testing for current sexually transmitted infections (STIs) and cervicitis. In a US study in which over 2000 women were randomized to prophylactic antibiotics for IUD insertion, PID rates were not elevated above baseline rates [26]. The most important conclusion from this study was that even during the 20-day postinsertion period—the possibly high risk time frame—the absolute rate of PID was 1/1000, approximating the background rate of PID.

The two IUDs do not appear to differ in PID risk, although data are conflicting. The LNG IUS has demonstrated a trend toward protection against PID. Biologic plausibility for PID protection lies in progestin’s effect of thickening cervical mucus and decidualizing the endometrium, creating a barrier to ascending infection. A protective benefit has not consistently reached statistical significance. In one of the few randomized, long term studies comparing a copper device, the Nova T (similar to the copper T380A), to the LNG-IUS, 5-year cumulative gross removal rates for PID were similar [27].

Risk of infertility

Fear of infertility because of clinical or subclinical tubal infection or inflammation has been the main barrier to widespread use of IUC in young and/or nulliparous women. Although some initial reports from the 1980s suggested an increased risk of infertility in women who used IUDs, the heightened risk disappeared when controlling for number of sexual partners and STIs. Research consistently demonstrates no difference in fertility rates in multiparous women who discontinued various methods of contraception, including IUC [28,29]. Further, fertility rates are not statistically different in women who discontinue IUC because of planning pregnancy compared with those who discontinue because of a complication [30,31]. A recent follow-up prospective study examined time to pregnancy and need for fertility evaluations in women randomized to two investigational copper devices in Norway. There was no difference in these 2 fertility outcomes in women who had their IUD removed to become pregnant compared to women who discontinued the IUD because of problems [31a]. In the best-designed study
examining the association between IUD use and infertility, 1895 women who had primary tubal infertility were compared with several control groups. Previous copper IUD use was not found to be associated with an increased risk of tubal occlusion in nulligravid women. Rather, presence of chlamydia antibodies, indicating past chlamydia infection, was associated with tubal occlusion [32].

Ectopic pregnancy

Ectopic pregnancy risk in women using different contraceptive methods remains misunderstood. Highly effective methods that protect against pregnancy protect against both intrauterine and ectopic pregnancy. Although the IUD protects better against intrauterine than tubal pregnancy, IUC may still provide better long-term protection against ectopic pregnancy than other methods because it’s effectiveness and continuation rates are higher than other reversible methods.

Cohort data from US trials with both the CuT380A and the LNG IUS have shown an ectopic pregnancy rate of 0.2 to 0.4 per 1000 women per year, compared with an ectopic pregnancy rate of 3.25 to 4.5/1000 among women who do not use contraception [17]. Given this low risk, even a history of ectopic pregnancy should not be considered a contraindication to IUC. In fact, women who have a history of ectopic pregnancy should be counseled towards methods with the highest real-life effectiveness to prevent another ectopic pregnancy. The World Health Organization (WHO) [33] contraceptive eligibility criteria support the routine use of both currently available IUDs in women who have a past history of ectopic pregnancy.

Liability concerns

Fear of liability has often been cited by clinicians as a barrier to more liberal prescribing practices [21,23,34]. In a survey of fellows of the American College of Obstetricians and Gynecologists in 2002, Stanwood and colleagues [21] found a significant correlation between fear of litigation and a lower number of IUC insertions in the previous year. In actual practice, litigation related to the IUD is uncommon. Although few studies examine the incidence of litigation and the IUD, a 1996 commentary from the Vice President for Medical Affairs of Planned Parenthood Federation of America cited a small number of IUD-related “events” since the Paragard was introduced in 1989 [35]. The risk-management group was notified of approximately 125 events per year, and these events occurred in a large national health system that used more liberal criteria for candidate selection than recommended by the package insert. Half the events were related to excess bleeding and expulsion, 30% were related to pregnancies with an IUD in place, 10% were related to “other,” and 10% were related to infection. The commentary concludes that the method does not seem to pose “major expense to the malpractice insurance company of the provider.” The lack of publicized litigation related to the
IUD—either against the companies that manufacture them or against clinicians—should reassure concerned providers.

Addressing barriers

Restrictive labeling has created unnecessary barriers to effective contraceptive provision [20] by reinforcing the safety and liability concerns previously described. Restrictive labeling creates discomfort in clinicians who have to practice “off-label” and encourages the development of rigid medical protocols. Unfortunately, the FDA process for updating package inserts is cumbersome and expensive, creating a disincentive to make updates. Additionally, manufacturers may err on the side of caution because of product liability fears [20].

Update of the Cu T380A package insert

Fortunately, FEI Womens Health, the makers of ParaGard in 2004, chose to update the package insert for the copper IUD to reflect the large body of research that had accumulated over the prior 20 years. The company chose a nonprofit group, “The Reproductive Health Technologies Project,” to convene a panel of experts to rewrite the ParaGard label to better reflect current evidence. As there had been no major changes to the ParaGard label for 20 years, a label up-date was long overdue. Most changes proposed by the panel were approved by the FDA. Further, the product-specific consent form was removed in the 2004 ParaGard label revision, eliminating another cumbersome step in IUD provision.

Restrictions on age, parity, and monogamy in the recommended patient profile of the old label were mainly related to unsubstantiated fears about IUC playing a causal role in ascending PID and resultant infertility. In fact, the CuT380A was named “ParaGard” specifically because it was designed for use in parous women. With better understanding of contributing factors to PID and tubal infertility, eliminating the recommended patient profile restrictions based on parity, and certain contraindications was warranted (Box 2).

Sexual behavior

The restriction of IUC to women in mutually monogamous relationships was present in both the original CuT380A and the current US LNG IUS package inserts. Overall, contraceptive choice has little or no impact on the risk of STIs and PID, unless the woman’s choice for both pregnancy and STI prevention is consistent long-term condom use.

The copper IUD label now warns against current risky sexual behavior because of the possible increased risk of PID in the peri-insertion time frame and the increased background risk of PID related to increased risk for STIs. In the old package label, a history of PID (even in the remote past)
was considered a contraindication to IUD use. Now only women with current high-risk behavior for new STI acquisition around the time of the insertion period are considered less-favorable candidates for copper IUD insertion.

**Nulliparity**

Once STIs were established as the causal agents for PID, the restriction against use of IUC for nulliparous women had no basis in evidence. Both

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**Box 2. Comparison of “contraindications” in new and old label for ParaGard. Adapted from the ParaGard package insert**

<table>
<thead>
<tr>
<th>Old Label</th>
<th>New Label</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended patient profile</strong></td>
<td><strong>Contraindications</strong> (highlighting only differences)</td>
</tr>
<tr>
<td>The ParaGard T 380 A is recommended for women who have had at least one child, are in a stable, mutually monogamous relationship, and have no history of pelvic inflammatory disease.</td>
<td>Acute PID or history of PID</td>
</tr>
<tr>
<td>Postpartum endometritis or infected abortion in past 3 months</td>
<td>Postpartum or postabortal endometritis in the past 3 months</td>
</tr>
<tr>
<td>Untreated acute cervicitis or vaginitis</td>
<td>Mucopurulent cervicitis</td>
</tr>
<tr>
<td>Patient or partner with multiple partners</td>
<td>Known or suspected uterine or cervical malignancy</td>
</tr>
<tr>
<td>Increased susceptibility to infection (AIDS, leukemia, intravenous drug abuse)</td>
<td></td>
</tr>
<tr>
<td>Genital actinomycosis</td>
<td></td>
</tr>
<tr>
<td>Uterine or cervical cancer or unresolved abnormal Pap smear</td>
<td></td>
</tr>
</tbody>
</table>

Data from ParaGard product labelling, 1984 and revised 2005.
safety and efficacy of IUC in nulliparous women has been established in clinical trials outside the US where IUC use in nulliparous women is both common and on-label [36,37,38]. Current research is now focussing on the acceptability of IUC in nulliparous women, trying to quantify any increased rates of expulsion and early removals for pain and bleeding [36].

To address the increased expulsion rates and side effects observed in some studies of nulliparous women, new devices are being developed and tested that are uniquely designed for the nulliparous uterus [36,38]. A study from Mexico, where copper IUC use approaches 50% in some family-planning facilities, compared the copper T380A with two devices designed for nulliparous women: T Nul, a small T-shaped device, similar to the T380A with the same amount of copper but a smaller shaped T frame (8.4 mm shorter on the cross arms and 6.7 mm shorter on the vertical stem); and a third device that is not T-shaped but rather horseshoe-shaped and called the Multiload CU-375. The authors found high effectiveness with a failure rate of 1.2% at 1 year, and low overall expulsion rates (1.8% in both the T Nul and the Multiload, compared with 3.3% in the CU T380A). The expulsion rates in the nulliparous women in this study are comparable to expulsion rates in parous women (ParaGard package insert). Further, the Nul copper IUD had fewer removals for pain and bleeding. Although 1172 nulliparous participants were randomized, clinicians were not blinded to IUD type and may have been biased toward more early removals in the traditional IUD group, the copper T380A [37]. The most important study finding was that nulliparous women experienced excellent safety, efficacy, and acceptability with all three IUDs studied.

Efficacy and continuation rates of the LNG IUS are similar in nulliparous and parous women, regardless of age. In one study of nulliparous women randomized to the LNG IUS or oral contraceptive pills, continuation rates at 1 year were 80% for the LNG IUS versus 68% for the oral contraceptive group [38]. In addition to the long-acting and excellent protection against unplanned pregnancy, many of the health benefits of the LNG IUS, namely the reduced menstrual blood loss and diminished dysmenorrhea, make this method particularly useful in young nulliparous women intending to postpone pregnancy.

Even if nulliparous women experience more expulsions or side effects than parous women with the 2 IUDs currently available to them, after plugging all variables into the contraceptive effectiveness equation, it is clear nulliparous IUD users will enjoy excellent contraceptive success.

Many of the revisions of the copper IUD package insert would apply to the LNG IUS, but no application has been made to the FDA to update the label (see Box 2). In other countries, the many restrictions in the US FDA package insert do not exist. Organizations that develop evidence-based practice guidelines, such as the WHO medical eligibility criteria, Faculty of Family Planning & Reproductive Health Care of the Royal College of Obstetricians & Gynecologists, have all adjusted eligibility criteria to reflect
the large body of evidence supporting the copper IUD label update and the evidence supporting more liberalized use of both IUDs.

**Intrauterine contraception use in women who have medical problems**

As IUC becomes more accepted as an appropriate first choice method for many women throughout their reproductive lives, regardless of age or parity, it is also being studied in women who have complex medical conditions in whom IUC use was previously considered contraindicated.

In 2003, the Expert Working Group for the WHO’s Reproductive Health and Research Department WHO made changes to recommendations for IUD use in settings whereby HIV and other STIs are common. The main conclusions of the group were (1) the IUD does not increase a woman’s chance of acquiring HIV; (2) the IUD does not increase HIV transmission to sexual partners; and (3) a woman can generally initiate IUC even if she is HIV-infected, at high risk of HIV infection, or has AIDS but is clinically well on anti-retroviral therapy [39–41].

Limited data exist on IUC use in women who have relative immunosuppression, but the data of IUC use in different HIV and AIDs populations have documented no increase in infectious morbidity. The ParaGard label has removed “increased susceptibility of infections with micro-organisms… such as AIDS, leukemia, or intravenous drug abuse” from the contraindications section and “relative immunosuppression from chronic steroid use or insulin-dependent diabetes” from the precautions section (ParaGard package insert [33]). The WHO medical eligibility criteria considers IUC use in women with insulin dependent-diabetes mellitus generally safe, even for women with vascular complications [33]. The theoretic risks of infectious complications related to IUD use were so pervasive, and yet when studied in high-risk settings, increased in infectious problems related to IUD use or worsening of disease were not observed [41a,41b]. Many women who have medical problems have few contraceptive choices; now clinicians and women can feel more secure in using IUC in many of these complex medical scenarios whereby pregnancy can pose life-threatening risk.

**Noncontraceptive benefits of intrauterine contraception**

The increasing list of noncontraceptive benefits of IUC, mostly with LNG IUS, will encourage further appreciation of IUC. Currently all noncontraceptive use of IUC is off-label in the US, but in many European countries, therapeutic uses of LNG IUS are common and on-label.

**Endometrial cancer protection**

IUC with various devices has been associated with a decreased risk of endometrial cancer both across study designs and IUD type. Nine case control
and one large cohort study all show a relative risk of 0.4 to 0.6 of endometrial cancer in IUD users versus nonusers. In a systematic review, Hubacher and Grimes [42] rated the mostly II-2 evidence illustrating the IUD’s protective effect against endometrial cancer.

In a recent cohort study of 2,037,883 woman-years of follow-up from 1989 to 1998 in China, ever-use of an IUD was associated with a decreased risk of endometrial cancer with an adjusted OR of 0.6 (95% CI 0.3–0.9) [43]. Although IUD types are not specified in this large cohort, a combination of copper T IUDs and stainless steel rings were the most frequently used devices in this population. The mechanism of protection for copper and inert IUDs remains unclear. All IUDs create an inflammatory response in the uterus. Copper IUDs also release copper ions into the endometrial cavity, and the LNG IUS exposes the endometrium to a high local level of the potent progestogen, LNG. Any or all of these effects may reduce the risk of neoplasia.

Although biologic plausibility supports the LNG protective effect against endometrial cancer, the LNG IUS has not been in widespread use long enough to document direct evidence of its impact on endometrial cancer risk. New evidence examines molecular markers for the mechanism by which LNG and other progestins protect against endometrial cancer [44]. The LNG IUS may eventually be used for treatment of early endometrial cancers [44].

**Therapeutic indications for the levonorgestrel intrauterine system**

In addition to providing top-tier contraception, the LNG IUS is being studied for various uses including treatment of idiopathic menorrhagia, menorrhagia and/or pain symptoms secondary to fibroids, endometriosis, adenomyosis, and hyperplasia. A recent comprehensive review examines the evidence for these therapeutic uses [45].

The LNG IUS is already approved for treatment of menorrhagia in 102 countries and for hormonal protection of the endometrium during postmenopausal estrogen use in 93 countries. Two Cochrane reviews have evaluated medical treatment with LNG IUS compared with endometrial resection [46] and hysterectomy [47] for the treatment of menorrhagia. Satisfaction rates at 1 year were similar for the IUS and endometrial resection [47].

Extrapolating from the therapeutic effects of the LNG for such conditions as menorrhagia, research is examining a possible role for the LNG as a preventive and/or therapeutic agent for other gynecologic problems, such as dysmenorrhea, endometriosis, adenomyosis, infertility, and fibroids (Table 2). Future devices will test intrauterine delivery of other steroid hormones, such as progestogen receptor modulators to prevent disease in high-risk women and to treat symptomatic women medically instead of surgically [48].

The expanding use of the LNG IUS for prevention of and therapy for a large array of common gynecologic conditions may result in a decrease in surgery for benign gynecologic disorders, including sterilization procedures,
myomectomy, and hysterectomy. These trends have already been observed in the UK, with expanding use of LNG IUS suspected as the cause [48].

Practical considerations

A clinician’s approach to counseling and insertion of IUDs may have a major impact on successful use of the method. Proactive counseling, experience with insertion of both devices, same-day insertion, and avoidance of cumbersome screening protocols will help expand IUC use.

Helping women choose the right Intrauterine device

Duration of action and suppression of menstruation are often the factors that most influence women’s choice of IUD. Many clinicians and women consider the IUD as a child-spacing method, useful for 1 to 5 years for the LNG IUS and 1 to 10 years for the copper IUD. Because return to fertility is immediate with both IUDs [28,30], both are appropriate for any duration of time a women desires contraception throughout the reproductive years. Other considerations that may influence choice of IUD include the desire to have regular periods versus the desire to suppress menstruation and, for some women, the desire to use a completely hormone-free method.

Most side effects, including cramping and heavier bleeding with the copper IUD, irregular bleeding with the LNG IUS, as well as expulsion and pelvic

Table 2
Indications for use of the LNG IUS for possible prevention of gynecologic symptoms and disease

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Potential underlying cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heavy menstrual bleeding</td>
<td>Previous ovulatory or anovulatory dysfunctional uterine bleeding</td>
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<tr>
<td></td>
<td>Polycystic ovary syndrome</td>
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<td></td>
<td>Intramural or subserous fibroids</td>
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<td>Adenomuosis and endometriosis disorders of haemostasis</td>
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<td></td>
<td>Menopause transition</td>
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<td>Irregular menstrual bleeding</td>
<td>Previous endometrial polypys</td>
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<td></td>
<td>Previous endometrial hyperplasia</td>
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<td></td>
<td>Endometrial adenocarcinoma</td>
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<td>Pelvic pain</td>
<td>Primary dysmenorrhoea</td>
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<td>Recurrent enometriosis</td>
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<td></td>
<td>Adenomyosis</td>
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<tr>
<td></td>
<td>Acute episodes of pelvic infection</td>
</tr>
<tr>
<td>Infertility</td>
<td>Endometriosis</td>
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<td></td>
<td>Acute episodes of pelvic infection</td>
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<td>Uterine fibroids</td>
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infection, all occur in the first few months after insertion. Hormonal side effects are reported by some women in the early months of LNG IUS use (Mirena package insert). Follow-up and surveillance during these first few months on an as-needed basis rather than on any specific schedule, may detect any IUD-related complications and allow for early treatment and support.

**Copper intrauterine device**

The copper IUD is hormone free and may be ideal for women who either prefer a hormone-free method or who have the few relative contraindications, such as breast cancer and severe cardiovascular disease (WHO medical eligibility criteria), to even the low dose of hormone in the LNG. The discontinuation for pain and bleeding is higher with the copper IUD. Although worsened periods often occur only with the first few menses and may be treated successfully with nonsteroidal anti-inflammatory drugs [49], they are the most common reason for early discontinuation of the copper IUD. Prophylactic nonsteroidal anti-inflammatory drugs at a dose of 400 mg twice daily did not show a change in early removals for pain/bleeding [50].

**Levonorgestrel intrauterine system**

In contrast, the LNG IUS is ideal for women who have dysmenorrhea, heavy periods, or who prefer oligo- or amenorrhea. Side effects that may lead to early discontinuation include hormonal side effects and amenorrhea: 12% and 6%, respectively, over 5 years [27]. Anticipatory guidance about possible transient hormonal side effects and about the expectation of major changes in bleeding patterns may prevent early removals [51]. The additional role of the LNG IUS in treating many gynecologic complaints, especially dysmenorrhea and menorrhagia, may determine the choice of IUD.

The importance of preinsertion counseling for both IUDs is critical: when women’s expectations match the known change in menstrual pattern and side-effect profile, compliance, continuation rates, and satisfaction are optimized.

**Timing of interval insertion**

A simple way to improve the efficiency of IUC provision is to remove the requirement that women return during their menses for insertion. Either the copper or the LNG IUD can be placed safely, and possibly with a lower expulsion rate at times other than menses [52]. Pregnancy must be ruled out and is usually accomplished with a sensitive urine pregnancy test. Historical factors assist the clinician in ruling out pregnancy with a high degree of certainty: patient history of abstinence, highly compliant oral contraceptive or condom use, transitioning from a contraceptive implant, immediately postpartum, and fully breastfeeding during the early postpartum period. Waiting for a regular menstrual period between contraceptive methods invites an unintended pregnancy.
**Pap smear screening**

Cervical cytology is an example of a screening test that is not related to IUC initiation and should not delay insertion. If the IUC visit coincides with her cervical cancer screening schedule, both can be done at the same time. If a patient has a history of cervical dysplasia or recent screening results indicate low-grade dysplasia, inserting the IUD is a reasonable option. Women undergoing colposcopic surveillance or treatment of cervical dysplasia have an additional need for highly effective contraception. If a patient has a high-grade lesion or inspection of the cervix reveals lesions suspicious for high-grade dysplasia or cancer, it is prudent to postpone insertion until cervical cancer is ruled out (ParaGard Package Insert).

**Sexually transmitted infection (STI) screening**

Screening for STIs should also be individualized to the patient population. Evidence does not support routine screening for gonorrhea and chlamydia in populations at low risk of STIs [52]. Factors that indicate high risk include history of a new sexual partner, age under 25, or recent history of STIs. If screening is indicated, it can be done at the time of the insertion, and the patient can be called back for treatment and encouraged to employ dual usage of protection: her IUC for pregnancy protection and consistent condom use for STI protection. The IUD should not be removed because its presence does not change the PID risk in the face of a new STI. Case studies of women who tested positive for chlamydia at the time of IUD insertion and were treated promptly revealed no higher risk of PID in those who screened negative at the time of insertion [53,54]. Prophylactic antibiotics have not been shown to lower peri-insertion infectious complications [26], but may have a role in settings in which STI screening is not available or efficient.

**Postpartum and postabortion insertion**

IUC can be initiated immediately postpartum and postabortion. Several advantages of insertion in these settings include the assurance that the patient is not pregnant, the high motivation to begin a contraceptive method, and diminished discomfort with insertion. Immediate postpartum insertion with copper T devices is common outside the US and, if performed within 10 minutes of delivery of the placenta, appears safe and effective [55,56]. Neither bleeding nor infectious complications nor increased perforations have been associated with immediate insertion with copper devices [57]. The main disadvantage of immediate postpartum insertion is increased expulsion. In one recent study, expulsion risk was 12.3% at 1 year after immediate post-placental insertion with the copper IUD [55].

In older studies, insertion of an IUD after the immediate postpartum period and before 4 weeks postpartum was associated with more uterine perforations. IUDs should therefore be inserted within 10 minutes of placental delivery or after 4 weeks postpartum [13,33].
Immediate IUD insertion after spontaneous or induced abortion is both practical and safe [58]. As with postpartum insertion, expulsion rates may be increased, depending on the duration of pregnancy at the time of abortion. IUC after early first trimester abortion has the same expulsion rate as interval insertion, no higher complication rates, and high continuation rates [59,60]. When immediate postabortion studies include abortion up to 12 weeks gestational age [61], higher cumulative expulsion rates at 1 year of 7% to 12%, have been observed. Randomized trials in the US are currently underway with both IUDs to better define the differences in expulsion rates in immediate versus delayed postpartum and postabortion insertion. The role of ultrasound guidance in assuring fundal placement in postpartum or postabortion insertion is also under investigation. Because the local effect of the LNG IUS on involution of the uterus is unknown, it is not recommended until some of these data become available [53]. WHO medical eligibility criteria rates immediate insertion after an uncomplicated first trimester abortion a category 1 for both IUDs and a category 2 after a second trimester abortion—only because of the increasing risk of expulsion after placement in larger uteri [56]. Many medical protocols as well as product labeling Package Insert (Para-Gard [33]), now support IUC initiation immediately following spontaneous or induced abortion, by both surgical methods or medication abortion [62].

The future of intrauterine contraception

Research and development in the US and globally will increase the types of IUC in the US if industry perceives a demand from women and their physicians. In 2004, Chinese women had 21 types of IUDs to choose from. Examples of innovations in IUC include smaller less-bulky devices intended for the smaller nulliparous uterus, frameless copper IUDs anchored to the endometrium with a suture, devices with movable joints in the cross bars to help them expand and contract with uterine contractions and adapt to different uterine sizes and contours, and some that have cervical components and cervical anchoring systems [63,64]. Smaller devices appropriate for the smaller atrophic postmenopausal uterus are also under development. These investigational systems are medicated with copper, silver, combinations of metals, LNG, other progestins, and steroid receptor modulators. All these modifications are aimed at reducing expulsions and side effects while maintaining the exceptionally high effectiveness and safety profiles. Combining the different frame designs of different sizes and shapes with various active substances for pregnancy prevention and/or other desired effects on the endometrium will supply US women with many more options for fertility regulation.

Summary

IUC is poised to meet the contraceptive needs of many more US women and will expand as new devices and systems are developed, and as old biases
among clinicians and women are erased. Unintended pregnancy and abortion in the US could diminish as a result of increasing IUD use. Successful fertility regulation is a defining factor of the health of a population; the expanded use of IUC can help achieve that public health success.

References

