Review

Extended use of the intrauterine device: a literature review and recommendations for clinical practice☆,☆☆

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Abstract

There are multiple advantages to “extended use” of the intrauterine device (IUD) use beyond the manufacturer-approved time period, including prolongation of contraceptive and non-contraceptive benefits. We performed a literature review of studies that have reported pregnancy outcomes associated with extended use of IUDs, including copper IUDs and the levonorgestrel intrauterine system (LNG-IUS). Among parous women who are at least 25 years old at the time of IUD insertion, there is good evidence to support extended use of the following devices: the TCu380A and the TCu220 for 12 years, the Multiload Cu-375 for 10 years, the frameless GyneFix® (330 mm²) for 9 years, the levonorgestrel intrauterine system 52 mg (Mirena®) for 7 years and the Multiload Cu-250 for 4 years. Women who are at least 35 years old at the time of insertion of a TCu380A IUD can continue use until menopause with a negligible risk of pregnancy. We found no data to support use of the LNG-IUS 13.5 mg (Skyla®) beyond 3 years. When counseling about extended IUD use, clinicians should consider patient characteristics and preferences, as well as country- and community-specific factors. Future research is necessary to determine the risk of pregnancy associated with extended use of the copper IUD and the LNG-IUS among nulliparous women and women less than 25 years old at the time of IUD insertion. More data are needed on the potential effect of overweight and obesity on the long-term efficacy of the LNG-IUS.

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Keywords: Intrauterine device; Copper IUD; Levonorgestrel intrauterine system; LNG-IUS; Extended use; Prolonged use; Copper T

1. Introduction

The intrauterine device (IUD) is the most widely used reversible form of contraception in the world [1], although it remains underutilized in North America, South Asia, Oceania and sub-Saharan Africa [2]. Given its long-acting properties and excellent efficacy, the IUD is also the most cost-effective reversible contraceptive method [3]. Widespread use of the IUD beyond the manufacturer-approved time period could have a significant public health impact by decreasing the rate of unintended pregnancy at a population level. Other advantages of extended IUD use include patient convenience, cost-savings, extension of non-contraceptive benefits and avoidance of potential complications associated with re-insertion of another IUD including pelvic inflammatory disease in the immediate post-insertion period [4] and the rare but real risk of uterine perforation [5]. We conducted a literature review of currently published studies regarding “extended IUD use”, that is, continuous use of an IUD beyond the manufacturer-approved time period. The focus of this review is not to recommend one IUD type over another; IUD selection must be based upon patient characteristics and preferences, provider skills and IUD types available. When possible, we encourage selection of IUDs associated with the highest contraceptive efficacies (the TCu380A, the GyneFix®, the LNG-IUS) [6–8].

We focus our discussion on the copper IUD and the levonorgestrel intrauterine system (LNG-IUS) to address the following questions:

1. Based upon prior studies, what is the risk of pregnancy associated with extended IUD use?
2. How do the pharmacokinetic properties of the LNG-IUS and the copper IUD contribute to our understanding of the potential lifetimes of these IUDs?
3. What are current gaps in the literature regarding extended IUD use?

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E-mail address: wuju1@rwjms.rutgers.edu (J.P. Wu).
4. What research initiatives are necessary to address these gaps?

5. What recommendations should be made to women regarding extended IUD use based upon the current literature?

2. Materials and methods

We searched PubMed and Medline for articles in all languages using the following MeSH terms and combination of terms: (1) “intrauterine device”, “IUD”, “IUCD”, “copper IUD”, “copper T IUD,” “copper release”, “levonorgestrel IUD”, “Mirena IUD”, “levonorgestrel IUS”, “Skyyla”, “LNG-IUS; and/or (2) “extended use” or “prolonged use”. We retrieved 762 citations. The authors (J.W. and S.P.) independently reviewed each abstract and when necessary, the entire paper itself, to identify studies that reported the following: (1) pregnancy outcomes for any copper IUD or LNG-IUS in current use worldwide; and (2) pregnancy outcomes beyond the manufacturer approved time period for that IUD. Using this strategy, we identified seven manuscripts (all published in English) that met eligibility criteria and were reviewed in entirety. To ensure we did not miss articles relevant to IUDs less widely used than the TCu380A and the LNG-IUS (e.g., frameless IUDs and other copper IUD types), we repeated the same search strategy using the following MeSH terms and combinations of terms: (1) “frameless intrauterine device”, “GyneFix”, “FlexiGard”, “Cu-Fix”, “Multiload intrauterine device”, “Fibroplant LNG-IUS”, “Nova-T”; and/or (2) “extended use” or “prolonged use”. Using this strategy, we retrieved 593 citations, from which we identified an additional five papers (all published in English) that met our eligibility criteria. Each article’s reference section was reviewed for citations that may have been missed initially. We also reviewed the bibliographies of all currently published Cochrane reviews containing the word “IUD” or “intrauterine device” in the title (13 in total) and did not retrieve any additional articles of relevance. When necessary, we contacted authors via email for clarification regarding data findings and interpretations. In total, we identified eight papers regarding copper IUDs and four papers regarding the LNG-IUS. When possible, we abstracted data regarding the total period of observation (in woman-years) and the period of observation considered to be “extended use” for that device. Pregnancy outcomes are reported by pregnancy rates per 100 women and/or gross numbers of pregnancies that occurred during a period of observation.

3. Results

3.1. Based upon prior studies, what is the risk of pregnancy associated with extended IUD use?

Table 1 summarizes eight papers that describe extended use of copper IUDs. Nulliparous women were excluded from all studies. Collectively, the mean age of subjects in the copper IUD studies ranged from 26.7–38.8 years at the time of IUD insertion. The first two studies, a Brazilian study [9] and a multi-center, international randomized controlled trial (RCT) conducted by the World Health Organization/United Nations (WHO/UN) [10], collectively provide the largest body of evidence regarding extended use of the TCu380A (Paragard®). There were no pregnancies reported among parous women who used the TCu380A for 11–16 years; the number of women who were followed from Years 12–16 was small (n=39) [10]. A smaller Population Council Study also reported no pregnancies among parous women who used the TCu380Ag up to 20 years [11].

While not as widely used as the TCu380A, we included data regarding extended use of the TCu220, a “first generation” copper IUD [6]. Given the smaller amount of copper surface area, the efficacy of the TCu220 is inferior to that of the TCu380A (cumulative pregnancy rates of 7.2/100 versus 2.2 pregnancies/100 women at 10 years, respectively) [10]. Nevertheless, the TCu220 has been used by millions of women worldwide, most prevalently in China where the cost of the TCu220 is half the cost of the TCu380A [12]. The same WHO/UN RCT mentioned previously included a study arm of women who used the TCu220 for 12 years; three pregnancies (two intrauterine, one ectopic) occurred during Years 10–12 [10]. The majority of pregnancies that occurred during the entire 12-year period occurred prior to Year 8, and the three pregnancies that occurred during Years 10–12 minimally affected the cumulative pregnancy rate (7.2/100 at Year 10, 7.6/100 at Year 12) [10].

We identified two articles regarding extended use of the frameless GyneFix® IUD (330 mm² of copper), which is approved for 5 years of use [13]. Both papers describe RCTs comparing the GyneFix® with the TCu380A. Based upon data among 521 women who used the GyneFix® up to 8 years in a multi-center RCT, Meirik et al. reported a negligible increase in the pregnancy rate from Year 6 (2.4/100 women) to Year 7 (2.5/100 women) without any subsequent pregnancies occurring during Years 7–8 [14]. In a Chinese-based RCT, Cao et al. reported no pregnancies among 139 parous women who used the GyneFix® up to nine years; only 1 woman was lost to follow-up (0.64%) [15].

The Multiload is a horseshoe shaped copper IUD with serrated “fins” designed to minimize the risk of expulsion [16]; the Multiload Cu-375 (MLCu-375) is approved for 5 years of use and the Multiload Cu-250 (MLCu-250) is approved for 3 years of use [17]. A WHO sponsored RCT observed 352 parous women who used the MLCu-375 up to 10 years [18]; data isolated to Years 5–10 (the period that would be considered “extended”) were not available. Based upon data from Years 3 and 10, there was a small increase in the cumulative pregnancy rate (2.9/100 in Year 3–5.3/100 in Year 10) [18,19]. Similar to the MLCu-375, the MLCu-250 has demonstrated contraceptive efficacy beyond its approved time period; a Singapore based RCT (with only 5.2% lost to follow-up) reported no additional pregnancies...
among women using the MLCu-250 from Years 3–4 [20]. A small study of 52 women conducted in an Indonesian gynecology office also reported no pregnancies among women using the MLCu-250 up to 9 years [21]; it is unclear based upon the paper whether this was a retrospective chart review or a prospective study, and details regarding lost to follow-up and demographics were not reported.

3.1. Levonorgestrel intrauterine system (LNG-IUS)

Table 2 summarizes four studies regarding extended use of the LNG-IUS, which is approved for 5 years of use. Based upon cumulative, international data, the LNG-IUS (the 60 mg device and the 52 mg device) appears to be highly effective for pregnancy prevention up to 7 years among parous women whose mean age is greater than 25 at the time of insertion; no pregnancies were reported between Years 5–7 in all four studies [22–25].

3.2. How do the pharmacokinetic properties of the copper IUD and the LNG-IUS contribute to our understanding of the potential lifetimes of these IUDs?

3.2.1. Copper IUD

The copper IUD exhibits its contraceptive effect through the dissolution of copper ions, which creates a spermicidal, sterile inflammatory response at the level of the endometrium and copper-rich cervical mucus that decreases sperm motility [26–29]. In utero and in vivo studies of the copper IUD demonstrate a “burst release” of cupric ions after insertion, followed by a stabilization of copper release over time [30–35]. Multiple factors influence the rate of copper release, including uterine fluid pH [26,33,36], the phase of the menstrual cycle [37,38], hemoglobin release during menses [37] and local concentrations of intrauterine urea, protein and oxygen [37,39]. Uterine fluid complexity and variability make it challenging to predict the rate of copper release over the lifespan of an IUD for any given individual.

Based upon decades of cumulative data from clinical trials, we know that greater amounts of active copper surface area are associated with superior contraceptive efficacy [40], as reflected by the fact that the TCu380A has lower associated pregnancy rates compared to that of the MLCu250, TCu220 or TCu200 [6]. However, the total length of time that copper can be released from a copper IUD in a concentration high enough to provide contraceptive efficacy is unknown. A small study of copper IUDs placed in simulated uterine environments after being in utero did not demonstrate different copper release rates in IUDs removed from women who experienced accidental pregnancy compared to IUDs removed from non-pregnant women who had similar durations of IUD use [41]; these data need to be confirmed in larger studies.

3.2.2. LNG-IUS

The LNG-IUS consists of a polyethylene frame with a central reservoir containing levonorgestrel (52 mg total in the Mirena®) [42]. Immediately after insertion, the LNG-IUS releases approximately 20 μg/day of LNG, which declines slowly over the lifetime of the IUD [42,43]. The contraceptive effect of LNG is exerted via local via anti-proliferative effects on the endometrium [44] and cervical mucus thickening [45]. LNG is a lipophilic substance and distributes rapidly into fatty tissue [46].

Low levels of systemic absorption of LNG do occur, however, and are responsible for adverse hormonal effects such as headache, hirsutism and mood changes [42]. In a recent pharmacokinetic study, Austrian researchers evaluated serum levonorgestrel levels among 110 women who used the LNG-IUS (52 mg) for a mean of 3.8 years (±971 days) [47]. LNG plasma levels declined over time, with the greatest relative drop occurring between Years 2–3 followed by a plateau from Years 4–8 [47]. Women who used the LNG-IUS for ≥6 years had significantly lower LNG serum levels than women who used the LNG-IUS ≤5 years (126±44 pg/mL vs.157±62 pg/mL respectively, p=.014); there were no pregnancies reported in either group [47]. These data must be interpreted with caution because the study was underpowered to detect differences in pregnancy rates and the cohort was comprised of predominately older (mean age of 42.3±8.2 years) and thus less fertile women, some nearing peri-postmenopause by the end of the study. However, the findings are consistent with our current understanding that LNG-IUS exerts its contraceptive effect locally and not systemically. Vaginal bleeding patterns were not correlated with serum LNG levels [47], providing further support for the importance of local endometrial effects. Given the lipophilic properties of LNG, mean serum levels of LNG were lower in obese women (BMI ≥25) compared to leaner women [47]. This trend did not reach significance likely due to the small number of women in the highest BMI categories. Overall, participants were relatively lean (63% of women had BMI <25) [47]; therefore, this cohort is no representative of overweight and obese women.

One final consideration regarding the potential lifespan of the copper IUD and the LNG-IUS is the fact that inert IUDs (i.e., unmedicated IUDs such as the Lippes Loop) have demonstrated contraceptive efficacy [48,49] via the local inflammatory effect on the endometrium [50], raising the theoretic possibility that medicated IUDs such as the TCu380A and the LNG-IUS may exert some of contraceptive effect even after copper concentrations and LNG concentrations are undetectable, respectively. However, we cannot directly extrapolate findings from unmedicated IUDs to medicated IUDs given variations in the material composition and design of different devices. Therefore, the exact period of time one could rely on possible inert properties of a medicated IUD for contraceptive efficacy is unknown.

3.3. What are current gaps in the literature regarding extended IUD use?

We currently lack data regarding extended IUD use among women who are less than 25 years old at the time of initial insertion. While most of the studies in this review did
<table>
<thead>
<tr>
<th>Study Author</th>
<th>IUD type</th>
<th>Study setting and design</th>
<th>No. of participants, parity and age</th>
<th>Observation period (Obs) in woman-years (wy) and pregnancy rates (per 100 women)</th>
<th>Lost to follow-up at end of year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bahamondes et al. (2005)</td>
<td>TCu380A</td>
<td>- Family planning clinic in Brazil - Prospective observational study, enrolled women who had TCu380A in place &gt;10 years</td>
<td>- Of 228 parous women, 142 observed for 12 years, 31 for 14 years, 8 for 16 years - Mean age 38.8 ± S.D. 5.6 years *</td>
<td>Total cumulative obs at Year 16: na Cumulative pregnancy rate at Year 16: na (women enrolled after Year 10) Obs Years 11–16 only: 366 wy Pregnancy rate Years 11–16 only: 0.0</td>
<td>11 years: 1.6% 12 years: 3.7% 13 years: 6.2% 14 years: 9.6% 15 years: 9.6% 16 Years 9.6%</td>
</tr>
<tr>
<td>World Health Organization/United Nations (1997)</td>
<td>TCu380A</td>
<td>- Multicenter, international - RCT of TCu380A vs. TCu220C - TCu380A arm observed for 12 years</td>
<td>- Of 1396 parous women, 172 observed to 12 years - Mean age 28.7± S.D. 4.6 years</td>
<td>Total cumulative obs at Year 12: 7159 wy Cumulative pregnancy rate at Year 12: 2.28% Obs Years 10–12 only: 392 wy **</td>
<td>8 years: 21.8% 10 years: 31.1% 12 years: 38.4%</td>
</tr>
<tr>
<td>World Health Organization/United Nations (1997)</td>
<td>TCu220</td>
<td>- Multicenter, international - Data combined from 2 RCTs with TCu220 arms observed for 12 years</td>
<td>- Of 3277 parous women, 341 observed to 12 years RCT #1: Mean age 28.7 ± S.D. 5.0 years RCT #2: Mean age 29.0 ± S.D. 4.5 years</td>
<td>Total cumulative obs at Year 12: 17,098 Cumulative pregnancy rate: - at Year 10: 7.2, at Year 12: 7.6 Obs Years 10–12 only: 1012 wy ** Pregnancy rate Years 10–12 only: nr</td>
<td>No. of pregnancies Years 10–12 only: 3 pregnancies (2 intrauterine, 1 ectopic)</td>
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<tr>
<td>Sivin (2007)</td>
<td>TCu380Ag</td>
<td>- Population Council study - Observational study of women who used the TCu380Ag &gt;10–20 years</td>
<td>No. of women observed: nr Parity: nr Mean age: nr</td>
<td>Total cumulative obs at Year 12: 17,098 Cumulative pregnancy rate: Obs Years 10–12 only: 224 wy ** Pregnancy rate Years 10–12 only: 0.0</td>
<td>10 years: 28.9% 12 years: 35.4%</td>
</tr>
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<td>Cao et al. (2000)</td>
<td>GyneFix® 330 mm²</td>
<td>- Family planning clinic in China - RCT of GyneFix® vs. TCu380A - Gynefix® arm observed for 9 years</td>
<td>- Of 157 parous women, 139 observed to 9 years - Mean age 30 ± S.D. 4.14 years</td>
<td>Total cumulative obs at Year 9: 1093 wy Cumulative pregnancy rate at Year 9: 0.0 Obs Years 5–9 only: 1 woman Pregnancy rate Years 5–9 only: 0.0</td>
<td>9 years: 0.64% (representing 1 woman)</td>
</tr>
<tr>
<td>Meirk et al. (2009)</td>
<td>GyneFix® 330mm²</td>
<td>- Multi-site, international - RCT of GyneFix® vs. TCu380A - Gynefix® arm observed for 8 years</td>
<td>- Of 1984 parous women, 521 observed to 8 years - Mean age 29.9 ± S.D. 4.7 years</td>
<td>Total cumulative obs at Year 8: 9696 wy Cumulative pregnancy rate at Year 8: 2.5% Obs Years 5–8 only: 2068 wy Cumulative pregnancy rate at Year 5: 2.4 Pregnancy rate Years 5–8 only: nr</td>
<td>5 years: 11% 6 years: 12% 7 years: 21% 8 years: 32%</td>
</tr>
<tr>
<td>World Health Organization (2003)</td>
<td>MLCu-375</td>
<td>- Multicenter, international study - RCT of MLCu-375 vs. TCu380A - MLCU-375 arm observed for 10 years</td>
<td>- Of 1832 parous women, 352 observed to 10 years - Mean age 30.2 ± S.D. 4.5 years</td>
<td>Total cumulative obs at Year 10: 10,019 Cumulative pregnancy rate at Year 10: 5.3 Cumulative pregnancy rate at Year 5: 2.9 Obs Years 5–10 only: nr Pregnancy rate Years 5–10 only: nr</td>
<td>10 years: 12.2%</td>
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Table 1 (continued)

<table>
<thead>
<tr>
<th>Study Author</th>
<th>IUD type</th>
<th>Study setting and design</th>
<th>No. of participants, parity and age</th>
<th>Observation period (Obs) in woman-years (wy)</th>
<th>Lost to follow-up at end of year</th>
<th>Pregnancy rates (per 100 women) at end of year</th>
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</thead>
</table>
| McCarthy et al. (1987) | MLCu-250 | Singapore-based RCT of MLCu-250 vs. Nova T 200 mm² | All parous | Obs for Years 3–4 only: 1729 | 3 years: 4.6% | Cumulative pregnancy rate at Year 4: 1.6
| | | - Devices placed immediately post-abortion | - Mean age: 26.7 ± 4.2 years | - nr (age range 20–40 years) | - nr | - Total cumulative obs at Year 9: nr |
| Soeprono (1988) | MLCu-250 | Private gynecologist office in Indonesia | 52 parous women | Obs for Years 4–9 only: nr | 3 years: 5.2% | Cumulative pregnancy rate at Year 9: 0.0
| | | - Cannot determine study design | | - Mean age: 20.7 ± SD | - nr | - Total cumulative obs at Year 9: nr |

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not have age-based exclusion criteria, collectively, women were on average older at the time of IUD insertion (>25 years); this finding reflects the fact that only parous women, who were on average older than nulliparous women, were eligible. Another reason for the relative lack of data on younger women is that younger women as a group experienced higher rates of IUD discontinuation than older women for all reasons, most often for planning pregnancy [24]. Collectively, older women have lower baseline fertility than their younger cohorts [51], which contributed to the low to zero pregnancy rates observed.

All studies in this review excluded nulliparous women. It is not known whether parity would affect pregnancy risk in IUD users, even after controlling for age. If nulliparous IUD users have a higher risk of expulsion, they could be at higher risk for pregnancy than parous IUD users. A retrospective study of 828 women using the LNG-IUS reported that nulliparous women did not experience higher rates of expulsion compared to parous women (hazard ratio 1.40, 95% CI 0.57–3.43) [52]. However, data were missing on approximately one-third of participants and the study was not powered to detect differences <16% [52]. A large trial (n=2254) of women using the TCu380A reported only a slightly higher risk of expulsion for nulliparous women compared to parous women [53].

Individual variations in fertility, regardless of age, also influence the risk of pregnancy with extended IUD use. In the trials reviewed, we do not know if and how the women who used the IUD for an extended period differed from women who removed the IUD at an earlier time with respect to fertility. The fact that most pregnancies occurred during the early years of IUD use suggests that women who were more fertile became pregnant earlier, leaving a cohort of less fertile women that contributed data to the extended years of use.

While overweight and obese LNG-IUS users exhibit lower levels of serum LNG compared to leaner LNG-IUS users [47], it is unclear how this affects pregnancy risk since LNG exerts its contraceptive effect at the level of the endometrium. There are no data regarding whether overweight and obese copper IUD users experience different rates of copper release compared to leaner copper IUD users. However, based upon our current understanding of the local contraceptive effect of copper, we do not believe there is a physiologic basis to support concerns regarding weight-based differences in copper IUD users.

3.4. What research initiatives are necessary to address these gaps?

There is a need for prospective and adequately powered studies regarding extended use of the copper IUD and the LNG-IUS among young women (≤25 years at time of insertion) and nulliparous women. For the LNG-IUS, similar trials are necessary to estimate the risk of pregnancy with extended use among overweight and obese women. These trials can also provide data regarding non-pregnancy related
Table 2

Studies of extended use of the levonorgestrel intrauterine system (LNG-IUS)

<table>
<thead>
<tr>
<th>Study author (year of publication)</th>
<th>IUD type</th>
<th>Study setting and design</th>
<th>No. of participants, parity and age</th>
<th>Observation period (Obs) in woman-years (wy) and pregnancy rates (per 100 women)</th>
<th>Lost to follow-up at end of year</th>
</tr>
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<tbody>
<tr>
<td>Diaz J et al. (1993)</td>
<td>LNG-IUS 60 mg</td>
<td>- Family planning clinic in Brazil</td>
<td>- Of 293 parous women, 50 observed for 7 years, Mean age 25.3 ± S.D. 4.7 years</td>
<td>Total cumulative obs at Year 7: 899 wy Cumulative pregnancy rate at Year 7: 0.0 Obs Years 5–7 only: 122 wy* Pregnancy rate Years 5–7 only: 0.0</td>
<td>5 years: 11.6% 6 years: 11.9% 7 years: 13.7%</td>
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<td></td>
<td>(approved for 5 years use)</td>
<td>- RCT of LNG-IUS vs. copper T IUD</td>
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<td>- LNG-IUS arm observed for 7 years</td>
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<td>Sivin et al. (1991)</td>
<td>LNG-IUS 60 mg</td>
<td>- Multi-center, international</td>
<td>- Of 897 parous women, 172 observed for 7 years, Mean age 26.6 years (S.E. 0.1)</td>
<td>Total cumulative obs at Year 7: 2831 wy Cumulative pregnancy rate at Year 7: 0.5 Obs Years 6–7 only: nr Pregnancy rate Years 6–7 only: 0.0</td>
<td>7 years: 11.5%</td>
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<tr>
<td></td>
<td>(approved for 5 years use)</td>
<td>- RCT of LNG-IUS vs. copper T IUD</td>
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<tr>
<td></td>
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<td>- LNG-IUS arm observed for 7 years</td>
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<td>Ronnerdag and Odlind (1999)</td>
<td>LNG-IUS 52 mg</td>
<td>- Swedish center</td>
<td>- Of 100 parous women, all 100 observed for 6.6 years, Mean age 32.7 (range 22–38 years)</td>
<td>Total cumulative obs at Year 6.6: nr Cumulative pregnancy rate at Year 6.6: nr Obs Years 5–6.6 years only: nr Pregnancy rate Years 5–6.6 years only: 0.0</td>
<td>5 years: 6.3% 6.6 years: 6.3%</td>
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<tr>
<td></td>
<td>(approved for 5 years use)</td>
<td>- RCT of LNG-IUS vs. Nova-T IUD</td>
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<tr>
<td></td>
<td></td>
<td>- LNG-IUS arm observed for 6.6 years</td>
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<td>Hidalgo et al.** (2009)</td>
<td>LNG-IUS 52 mg</td>
<td>- OBGYN Clinic in Brazil</td>
<td>- Of 86 parous women, 67 observed for 7 years, Mean age of 34.3± S.D. 0.8 years</td>
<td>Total cumulative obs at Year 7: na Cumulative pregnancy rate at Year 7: na (women enrolled after 5 years of use) Obs Years 5–7 only: 469 Pregnancy rate Years 5–7 only: 0.0</td>
<td>7 years: 22.1%</td>
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<tr>
<td></td>
<td>(approved for 5 years use)</td>
<td>- Observational study re: endometrial thickness in LNG-IUS users</td>
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<tr>
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<td></td>
<td>- Extended observation of subsample who had used IUD at least 5 years</td>
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na, not applicable; nr, not reported; wy, woman-years; Obs, observation. All observation periods refer to periods of continuous IUD use from the time of insertion. *When necessary, we hand-calculated woman years of observation based on data available. **Additional data obtained via personal communication with L Bahamondes, February 3, 2014. For data points noted to be nr (not reported), we made attempts to obtain the data from the corresponding author(s), and/or the author contact information was not available in the paper or could not be found elsewhere.
outcomes that are clinically significant to women as they age (e.g. blood pressure, weight, menstrual loss, anemia). A prospective study of 82 women who used the LNG-IUS continuously for a mean time period of 12.2 years reported that on average, hemoglobin increased, blood pressure increased slightly and body weight increased with a mean increase of 0.49 kg/year [25]. In the Population Council Study of women using the TCu380Ag continuously beyond 10 years, there was a 2–3% increase in discontinuations secondary to perimenopausal bleeding patterns between the first and second decade of use, although no discontinuations occurred secondary to anemia [11]. These data must be confirmed with a comparative group of non-IUD users with similar baseline characteristics.

Research efforts are underway that will contribute to our understanding of and ability to offer extended IUD use to more women. The “EPIC” (The Effectiveness of Prolonged Use of IUD/Implant for Contraception) Study is currently tracking long-term outcomes of adolescents and women (without parity or age-related restrictions) who have chosen to extend use the TCu380A IUD and the LNG-IUS beyond the approved period; study outcomes should provide critical information regarding prolonged IUD use among nulliparous and younger women (personal communication, J. Peipert, July 25, 2013). Copper IUDs that can release sufficient copper ions for at least 25 years are now being evaluated, (personal communication, D. Wildemeersch, February 9, 2014), which have the potential to offer a safe alternative to surgical sterilization.

3.5. What recommendations should be made regarding extended IUD use?

We recommend that clinicians engage in a shared decision making process with patients who may be interested in extended IUD use. Shared decision making has been shown to be preferred by women undergoing contraceptive counseling and involves three phases to which both the clinician and patient contribute (1) information sharing, (2) deliberation and (3) decision making [54]. We also acknowledge the importance of country- and community-specific factors, particularly in developing nations and resource poor areas. For example, in countries where access to safe abortion and/or IUD devices is difficult or restricted, the risk of unintended pregnancy with the removal of an IUD should be strongly considered. Based upon the studies described in this review, we make the following recommendations:

**Level A Recommendation (based on consistent and good quality patient oriented evidence) [55].**

- Clinicians should counsel that extended IUD use is currently an off-label practice, but likely highly effective among parous women who are at least 25 years old at the time of IUD insertion.

- Clinicians can recommend extended use of the following IUDs:
  a. TCu380A: for 12 years (women who are ≥35 years at the time of initial TCu380A IUD insertion can continue use until menopause with only a small, theoretical risk of pregnancy)
  b. TCu220: for 12 years
  c. Multiload Cu-375: for 10 years
  d. frameless GyneFix® (330 mm²): for 9 years
  e. LNG-IUS: for 7 years
  f. Multiload Cu-250: for 4 years

**Level B Recommendation (based on inconsistent or limited-quality patient oriented evidence) [55].**

- When counseling about extended IUD use, clinicians should consider patient characteristics and personal preferences, as well as country- and community-specific factors.
- Extended use of the Copper IUD or the LNG-IUS can be offered to overweight and obese women.
- For women who are satisfied with the IUD, clinicians should not advocate switching to a less effective, short-acting method.

**Level C Recommendation (based upon consensus, usual practice, disease-oriented evidence, case series and/or opinion) [55].**

- Among women who are less than 25 years old and/or nulliparous at the time of either LNG-IUS or copper IUD insertion, clinicians should discuss the lack of data regarding extended use in these situations and that their risk of pregnancy may be higher than noted in prior studies.
- For women who have no barriers to IUD access and cannot accept the small potential risk of pregnancy with extended use, clinicians may recommend replacing the IUD at the recommended time period.

4. Summary

Among parous women who are at least 25 years or older at the time of initial IUD insertion, there is good evidence to support extended use of the TCu380A and TCu220, the Multiload Cu-375, the frameless GyneFix® (330 mm²), the LNG-IUS 52 mg, and the Multiload Cu-250 (for 12, 10, 9, 7 and 4 years, respectively). If practiced widely, extended IUD use could have a significant public health impact by decreasing rates of unintended pregnancy worldwide. Research efforts regarding extended IUD use among nulliparous and young women as well as development of longer acting IUDs are underway. More studies regarding the effect of overweight and obesity on the contraceptive efficacy of the LNG-IUS are necessary.
References


