Annotated Bibliography: Hormonal Intrauterine Device (IUD)

A compilation of journal articles and reports with a focus on emerging evidence from low-income countries

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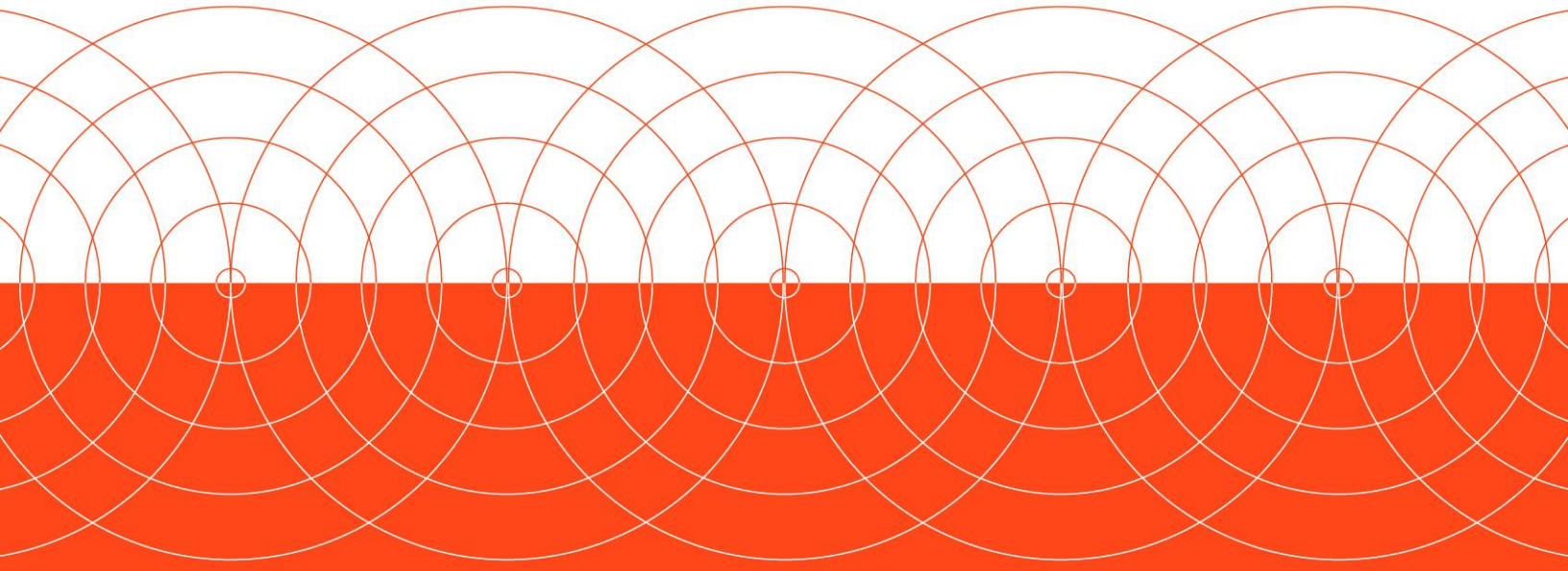

The Hormonal Intrauterine Device (IUD)
Resources with a Focus on Emerging Evidence from Low-income Countries

This annotated bibliography contains research articles, toolkits, reports, and other resources relating to the hormonal intrauterine device (IUD) published between 2000 and 2024. These resources focus particularly on use and availability of this method in low-resource settings, including insights about acceptability among clients and providers and supply-side facilitators and barriers to access. Some resources highlight potential next steps to increase method uptake at the country level. This compilation was last updated in February 2024; to submit additional resources for inclusion in this list, please email afratus@fhi360.org. For additional information including about efforts to expand access to the hormonal IUD globally, please visit the Hormonal IUD Access Portal at www.hormonaliud.org

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Summary of LMIC Pilot Learning

Rademacher KH, Sripipatana T, Danna K, et al. What Have We Learned? Implementation of a Shared Learning Agenda and Access Strategy for the Hormonal Intrauterine Device. *Glob Health Sci Pract.* 2022;10(5):e2100789. 2022 Oct 31. Available here.

ABSTRACT: In 2015, a global learning agenda for the hormonal intrauterine device (IUD) was developed with priority research questions regarding use of the method in low- and middle-income countries. In addition, members of the Hormonal IUD Access Group aligned on a strategy to expand access in the context of volunteerism and contraceptive method choice. This article synthesizes evidence generated since then and describes steps taken to address demand- and supply-side barriers to access. Findings demonstrated high continuation rates and satisfaction among hormonal IUD users that are comparable to other long-acting reversible contraceptives (LARCs). Across studies, a sizable number of users reported they would have chosen a short-acting method or no method at all if the hormonal IUD were not an option, which suggests that women did not see the hormonal IUD as interchangeable with other LARC options and thus it may fill an important niche in the market. With several countries now poised to scale up the method, resource mobilization will be key. On the demand side, investments in implementation research will be critical to understanding how best to launch and scale the method,

while ensuring the sustainability of multiple quality-assured suppliers with affordable public-sector pricing will be necessary on the supply side.

Global Perspectives

These resources provide global perspectives on the hormonal IUD, including benefits and challenges to introduction.

1. Bahamondes L, Fernandes A, Monteiro I, Bahamondes MV. Long-acting reversible contraceptive (LARCs) methods. *Best Pract Res Clin Obstet Gynaecol*. 2020 Jul; 66:28-40. Available here.
ABSTRACT: Unplanned pregnancy (UP) is a public health problem, which affects millions of women worldwide. Providing long-acting reversible contraceptive (LARC) methods is an excellent strategy to avoid or at least reduce UP, because the effectiveness of these methods is higher than other methods, and is indeed comparable to that of permanent contraception. As the initial introduction of the inert plastic intrauterine device (IUD) and of the six-rod implant, pharmaceutical companies have introduced a copper IUD (Cu-IUD), different models of levonorgestrel-releasing intrauterine system (LNG IUS), and one and two-rod implants, which certainly improved women's LARC options. The main characteristic of LARCs is that they provide high contraceptive effectiveness with a single intervention, and that they can be used for a long time. Emerging evidence from the last few years has demonstrated that it is possible to extend the use of the 52 mg LNG IUS and of the etonogestrel-implant beyond five- and three years, respectively, which adds new value to these LARCs.

2. Benova L, Cleland J, Daniele MAS, et al. Expanding Method Choice in Africa with Long-Acting Methods: IUDs, Implants or Both? *Int Perspect Sex Reprod Health.* 2017; 43(4): 183–191. Available here.
ABSTRACT: Improving women's access to a wider range of methods—including long-acting reversible methods (LARCs), defined here as the IUD and the implant—will give women more choice and should reduce unmet need, which is increasingly the result of discontinuation of short-acting methods. LARCs are typically used for longer durations than the injectable or the pill, and thus are particularly appropriate for the growing number of women who want to cease childbearing altogether. Women may use LARCs longer because those who choose them are more committed to long-term avoidance of pregnancy; another reason may be that LARC discontinuation requires a firm decision and a visit to a health facility, where health staff may encourage clients to persist with the method. According to a randomized, controlled trial in the United States, characteristics of the method rather than of the user account for the difference in discontinuation between LARCs and other reversible methods.
Major initiatives to increase access to LARCs in Africa—funded by bilateral donors and foundations, and implemented with input from such international nongovernmental organizations as Marie Stopes International (MSI) and Population Services International (PSI)—have been launched in the past decade. Some of these projects were designed for the general population, whereas others were focused on women who had recently given birth or had an abortion, those living with HIV, those affected by conflict

and the young. Many placed equal emphasis on the IUD and the implant, but some were dedicated to one or the other.
The objective of this article is to review key components of LARC uptake in Sub-Saharan Africa with the aim of guiding policies and programs. We assess trends in access to the IUD and implant, including method knowledge and availability at facilities; examine trends in use, source of supply, discontinuation and characteristics of users; and discuss the prospects for expanding method choice by increasing the availability of LARCs in national programs and the policy implications of our results.

3. Brull E, Machado HC, Bahamondes L, Juliato CRT. Expulsion and continuation rates of the levonorgestrel 52 mg intrauterine system was similar among nulligravid and parous users. *Int J Gynaecol Obstet*. 2021. Available here.
OBJECTIVE: To compare the expulsion and continuation rates of the levonorgestrel (LNG) 52 mg intrauterine system (IUS) in a cohort of nulligravid and parous users.
METHODS: We conducted a retrospective cohort study that included 996 participants in whom we placed an LNG-IUS, and the participants were monitored for up to 5 years after device placement. We identify 498 nulligravid participants in the medical record database between 2012 and 2020. Each nulligravida was paired with a parous users who had an LNG-IUS inserted on the same day, just before or after the nulligravida. The Kaplan-Meier method and the log-rank test were used to compare the survival curves of the two groups.
RESULTS: By the fifth year of use, the expulsion rates were 7.6/100 and 8.2/100 women-years (W-Ys) and the continuation rates were 641/100 W-Ys and 65.4/100 W-Ys without difference among nulligravid and parous users, respectively (P = 0.782 and P = 0.564, respectively). We observed 29 and 31 expulsions among nulligravid and parous users, respectively.
CONCLUSION: Nulligravid and parous participants who used the 52 mg LNG-IUS showed similar expulsion and continuation rates during five years of use.

4. Creinin MD, Schreiber CA, Turok DK, Cwiak C, Chen BA, Olariu AI. Levonorgestrel 52 mg intrauterine system efficacy and safety through 8 years of use. *Am J Obstet Gynecol*. 2022;S0002-9378(22)00366-0. E-Publication ahead of print available here.
BACKGROUND: Extending hormonal intrauterine system duration will allow users to have less need for procedures to provide long-term contraception.
OBJECTIVE: This study aimed to evaluate the efficacy and safety of the levonorgestrel 52 mg intrauterine system during years 7 and 8 of use.
STUDY DESIGN: A total of 1751 nulliparous and multiparous participants aged 16 to 45 years enrolled in a phase 3, multicenter trial to evaluate the efficacy and safety of the use of the Liletta levonorgestrel 52 mg intrauterine system for up to 10 years. Participants aged 36 to 45 years at enrollment underwent safety evaluation only. After the first year, we evaluated participants every 6 months for intrauterine system location confirmation and urine pregnancy testing at each visit. We assessed the Pearl Indices in years 7 and 8 and the life-table analysis for cumulative pregnancy rates through 8 years of use. For the primary efficacy analyses, all participants aged 16 to 35 years at enrollment were included through year 6; years 7 and 8 included only users aged ≤39 years at the start of each use year. Safety outcomes were assessed in all participants regardless of duration of use. We assessed amenorrhea rates, defined as no bleeding or spotting in the 90 days before the end of the year.

RESULTS: After intrauterine system placement, we followed 1568 participants aged 16 to 35 years and 146 participants aged 36 to 45 years. The 16- to 35-year-old participants included 986 (57.5%) nulliparous and 433 (25.3%) obese users. Overall, 569 participants started year 7478 completed year 7 (380 aged ≤39 years at beginning of year) and 343 completed year 8 (257 aged ≤39 years at beginning of year); 77 completed 10 years of use. Eleven pregnancies occurred over 8 years, 7 (64%) of which were ectopic. Two pregnancies occurred in year 7 (Pearl Index, 0.49; 95% confidence interval, 0.06-1.78), 1 in a participant with implantation 4 days after a desired removal; no pregnancies occurred in year 8. The cumulative life-table pregnancy rate in the primary efficacy population through year 8 was 1.32 (95% confidence interval, 0.69-2.51); without the postremoval pregnancy, the rate was 1.09 (95% confidence interval, 0.56-2.13). Two perforations (0.1%) occurred, none noted after year 1. Expulsion occurred in 71 (4.1%) participants overall, with 3 in year 7 and 2 in year 8. Pelvic infection was diagnosed in 16 (0.9%) participants during intrauterine system use, 1 each in years 7 and 8. Only 44 (2.6%) participants overall discontinued because of bleeding complaints (4 total in years 7 and 8) with rates per year of 0.1% to 0.5% for years 3 to 8. Amenorrhea rates were 39% at both years 7 and 8.
CONCLUSION: The levonorgestrel 52 mg intrauterine system is highly effective over 8 years of use and has an excellent extended safety profile. This report details the longest period of efficacy and safety data for continuous use of a levonorgestrel 52 mg intrauterine system for contraception.

5. Dethier D, Qasba N, Kaneshiro B. Society of Family Planning Clinical Recommendation: Extended Use of Long Acting Reversible Contraception. *Contraception*. 2022;S0010-7824(22)00162-7. E-Publication ahead of print available here.

In this clinical recommendation, the Society of Family Planning reviews the evidence supporting the use of the copper intrauterine device, levonorgestrel intrauterine devices and etonogestrel subdermal implant beyond the Food and Drug Administration approved duration of use for contraception (extended use). Clinicians should discuss effectiveness as well as other clinical considerations with patients to allow them to make contraceptive decisions that support their reproductive goals and clinical needs. Extended use of long acting reversible contraception may be a safe, effective and desirable option for many patients.

6. Furlani RM, Garcia E, Castro S, Machado HC, Bahamondes L, Monteiro I. Expulsion rates of the levonorgestrel 52 mg intrauterine system are similar among women with heavy menstrual bleeding and users for contraception. *Contraception*. 2021 Sep 5:S0010-7824(21)00374-7. Available here.
OBJECTIVE: To compare the expulsion rates of the levonorgestrel (LNG) 52 mg intrauterine system (IUS) among women with heavy menstrual bleeding versus women using solely for contraception.
STUDY DESIGN: We conducted an audit study of 548 (8.8%) women with heavy menstrual bleeding and 5655 (91.2%) users for contraception (comparison group) for 4 years in Campinas, Brazil. We retrieved sociodemographic data, expulsion rates, and variables associated to device placement. Among women with heavy menstrual bleeding, we placed the devices after the cessation of bleeding or after the reduction of menstrual flow.
RESULTS: Thirty-one of 548 (5.6%) women with heavy menstrual bleeding and 315 of 5655 (5.6%) from the comparison group expelled the device. This constituted 7.8 expulsions/100 women-years in women with heavy menstrual bleeding and 10.3 expulsions/100 women-years from the comparison group (p =

0.94). Expulsion risk was associated with previous cesarean delivery in both groups (OR 1.93, 95% CI 1.36;2.74).
CONCLUSIONS: Expulsion rates of the LNG IUS among women with heavy menstrual bleeding whose IUS was placed after the cessation or reduction of bleeding were similar to expulsion rates among users for contraception. Previous cesarean delivery was a risk factor for expulsion.
IMPLICATIONS: We recommend the 52 mg LNG IUS placement after the cessation of bleeding or a reduction of menstrual flow among women with heavy menstrual bleeding because this strategy was associated with similar risk of expulsion when compared to users for contraception.

7. Hashem AT, Mahmoud M, Aly Islam B, et al. Comparative efficacy of lidocaine-prilocaine cream and vaginal misoprostol in reducing pain during levonorgestrel intrauterine device insertion in women delivered only by cesarean delivery: A randomized controlled trial. *Int J Gynaecol Obstet*. 2022;10.1002/ijgo.14157. E-Publication ahead of print available here.

OBJECTIVE: To compare efficacy of lidocaine-prilocaine (LP) cream versus misoprostol versus placebo before levonorgestrel-releasing intrauterine device (LNG-IUD) insertion.
METHODS: This randomized controlled trial (RCT) was conducted in a tertiary referral hospital from April 30, 2020 to March 1, 2021 on 210 parous women willing to receive LNG-IUD and delivered only by elective cesarean delivery (CD). Participants received 200 µg vaginal misoprostol or 5 ml of LP cream 5% or placebo 3 h before LNG-IUS insertion. Primary outcome was pain during LNG-IUD insertion, while secondary outcomes were pain 10 min post-procedure, ease of insertion, patient satisfaction, insertion time, and drug side effects.
RESULTS: Pain during LNG-IUS insertion was reduced in LP group and misoprostol group compared to placebo group (2.1 ± 1.0 vs 3.7 ± 1.6; p <0.001) and (2.3 ± 1.3 vs 3.7 ± 1.6; p <0.001), respectively. Ease of procedure and patient satisfaction were significantly higher in LP and misoprostol groups than placebo (P <0.001). Need for additional analgesia was significantly higher in placebo group than in the other two groups (P = 0.009). Adverse events were not significantly different between the three groups except vomiting and abdominal cramps, which were higher with misoprostol.
CONCLUSION: LP cream and 200 µg of vaginal misoprostol administration before LNG-IUD insertion in women delivered only by elective CD effectively reduced pain during insertion and 10 min post-procedure with easier insertions, high patient satisfaction, and tolerable side effects. Pain reduction with LP cream was clinically significant.

8. Hubacher D. The Levonorgestrel Intrauterine System: Reasons to Expand Access to the Public Sector of Africa. *Glob Health Sci Pract.* 2015; 3(4): 532-7. Available here.

The levonorgestrel intrauterine system has: (1) excellent effectiveness, (2) high satisfaction levels, (3) non-contraceptive benefits, and (4) potential to help reinvigorate interest in intrauterine contraception. The time is ripe for ministries and donor agencies to work together to make the product widely available across Africa. This paper outlines 6 main reasons why donor agencies should purchase the LNG IUS and why family planning programs should incorporate the method into their services.

9. Jacobstein R, Shelton JD. The levonorgestrel intrauterine system: a pragmatic view of an excellent contraceptive. *Glob Health Sci Pract*. 2015;3(4):538–543. Available here.

The levonorgestrel intrauterine system (LNG IUS) has major advantages and could be a “game-changer” in improving contraceptive choice and use. It faces important challenges, however, including: (1) high

commodity cost; (2) often-strong provider resistance to IUDs and difficult programmatic requirements; (3) need for demand creation, including assessing if markedly reduced menstrual bleeding is attractive to clients; and (4) the many requirements for introducing any new contraceptive. A good next step would be a well-focused and multifaceted "learning introduction" to assess the LNG IUS's potential in several low-income countries, with rapid scale-up if results are promising.

10. Pires MLL, Souza AI, Dantes MLBR, Soriano GD, Henriques CV, Ferreira ALCG. Indications and reasons for discontinuing the levonorgestrel-releasing intrauterine system (LNG-IUS). ***Rev Bras Saude Mater Infant.*** **2020;20(2):479-484. Available here.**

OBJECTIVES: to identify the main indications and reasons for discontinuing the use of the Levonorgestrel-Releasing Intrauterine System (LNG-IUS). Methods: a cross-sectional study was carried out from medical records of 327 women who used the LNG-IUS 52mg between January 2011 and December 2016 at a public hospital in the Northeast of Brazil.
RESULTS: the main indications for the use of the LNG-IUS were: contraception (32.7%), myoma/metrorrhagia (28.7%) and endometriosis/pelvic pain (22.3%). Of the 327 women, 68 (20.8%) had discontinued using the device. The most frequent reasons for discontinuation were: expulsion (9.2%), LNG-IUS expiration (3.7%), bleeding (2.4%) and pain (1.5%). Most patients had no difficulty in the insertion and did not require anesthesia/sedation. Among the 30 women who expelled the device, 17 (56.7%) had used it for metrorrhagia and myoma, 8 (26.7%) for contraception, and 5 (16.6%) for endometriosis/pelvic pain.
CONCLUSIONS: the LNG-IUS is a well-accepted contraceptive method, with therapeutic applications for some gynecological conditions and a low expulsion rate.

11. Rademacher KH, Sripipatana T, Pfitzer A, Mackay A, Thurston S, Jackson A, Menotti E, Traeger H. A Global Learning Agenda for the Levonorgestrel Intrauterine System: Addressing Challenges and Opportunities to Increase Access. ***Glob Health Sci Pract*****. 2018;6(4):635-643. Available here.**

The LNG IUS is one of the most effective forms of reversible contraception and has important noncontraceptive benefits but is currently not used at scale in any FP2020 focus country. A global working group developed a shared learning agenda to answer critical questions, harmonize approaches, avoid duplication, and facilitate introduction of the method within the context of informed choice. This paper reviews current challenges to LNG IUS access in low- and middle-income countries (LMICs), describes an introduction coordination platform that was launched in 2015 to help address these challenges and answer critical questions about the LNG IUS through a shared global learning agenda, and discusses some of the advantages and disadvantages of this type of method-specific coordination platform and provide a call to action for other organizations that are considering introducing or scaling up the LNG IUS.

12. Rowe P, Farley T, Peregoudov A, et al. Safety and efficacy in parous women of a 52-mg levonorgestrel-medicated intrauterine device: a 7-year randomized comparative study with the TCu380A. Contraception 2016; 93: 498–506. Available here.

OBJECTIVE: To compare rates of unintended pregnancy, method continuation and reasons for removal among women using the 52-mg levonorgestrel (daily release 20 microg) levonorgestrel IUD (LNG-IUD) or the copper T 380 A (TCu380A) intrauterine device.
STUDY DESIGN: This was an open-label 7-year randomized controlled trial in 20 centres, 11 of which in China. Data on 1884 women with interval insertion of the LNG-IUD and 1871 of the TCu380A were analysed using life tables with 30-day intervals and Cox proportional hazards models.
RESULTS: The cumulative 7-year pregnancy rate of the LNG-IUD was 0.5 (standard error 0.2) per 100, significantly lower than 2.5 (0.4) per 100 of the TCu380A, cumulative method discontinuation rates at 7 years were 70.6 (1.2) and 40.8 (1.3) per 100, respectively. Dominant reasons for discontinuing the LNG-IUD were amenorrhea (26.1 [1.3] per 100) and reduced bleeding (12.5 [1.1] per 100), particularly in Chinese women and, for the TCu380A, increased bleeding (9.9 [0.9] per 100), especially among non-Chinese women. Removal rates for pain were similar for the two intrauterine devices (IUDs). Cumulative rates of removal for symptoms compatible with hormonal side effects were 5.7 (0.7) and 0.4 (0.2) per 100 for the LNG-IUD and TCu380A, respectively, and cumulative losses to follow-up at 7 years were 26.0 (1.4) and 36.9 (1.3) per 100, respectively.
CONCLUSIONS: The LNG-IUD and the TCu380A have very high contraceptive efficacy, with the LNG-IUD significantly higher than the TCu380A. Overall rates of IUD removals were higher among LNG-IUD users than TCu380A users. Removals for amenorrhea appeared culturally associated.
IMPLICATIONS: The 52-mg LNG-IUD and the TCu380A have very high contraceptive efficacy through 7 years. As an IUD, the unique side effects of the LNG-IUD are reduced bleeding, amenorrhea and symptoms compatible with hormonal contraceptives.

13. Zgliczynska M, Kocaj K, Szymusik I, Dutsch-Wicherek MM, Ciebiera M, Kosinska-Kaczynska K. Levonorgestrel-Releasing Intrauterine System as a Contraceptive Method in Nulliparous Women: A Systematic Review. *J Clin Med*. 2020;9(7):2101. Available here.
ABSTRACT: The aim of this review was to summarize the available evidence about the use of levonorgestrel-releasing intrauterine system (LNG-IUS) as a contraceptive method in nulliparous women. For this purpose, studies evaluating the efficacy, safety, bleeding pattern, satisfaction and discontinuation of the levonorgestrel-releasing intrauterine system in nulliparous women were analyzed. Only original research articles published in English between 1990–27th March 2020 were considered eligible. Reviews, book chapters, case studies, conference papers, opinions, editorials and letters were excluded. The systematic literature search of PubMed/MEDLINE, Scopus, Embase and Cochrane Library databases identified 816 articles, 23 of which were analyzed. The available evidence indicates that LNG-IUS is an effective and safe contraceptive method for nulliparous women that achieves high levels of satisfaction among patients. Moreover, nulliparous women seem to experience fewer expulsions than parous ones. Bleeding pattern is acceptable for the majority of patients, and bleeding disorders mainly occur in the first months after the insertion. More in-depth, long-term prospective studies are needed in this patient group to determine risk factors for the occurrence of side effects and associated discontinuations, which should not, however, delay the wider use of the method in this group, given the number of advantages.

Country Introduction Experiences

These resources provide country-specific insights on strategies for introducing the hormonal IUD into healthcare systems effectively. Sources include analyses of potential barriers and challenges for introduction as well as user and provider perspectives.

1. Brunie A, Nwala AA, Stankevitz K, et al. Factors affecting uptake of the levonorgestrel-releasing intrauterine device: A mixed-method study of social franchise clients in Nigeria. *PLoS One*. 2021 Sep 29;16(9):e0257769. Available here.

BACKGROUND : Despite the positive characteristics of the levonorgestrel-releasing intrauterine device (IUD)–a long-acting, highly effective contraceptive with important non-contraceptive attributes–the method has not been widely available in low- and middle-income countries. This study of hormonal IUD, copper IUD, implant and injectable users in Nigeria compares their characteristics, reasons for method choice, and experiences obtaining their method.

METHODS : We conducted a phone survey with 888 women who received a hormonal IUD, copper IUD, contraceptive implant or injectable from 40 social franchise clinics across 18 states in Nigeria. We analyzed survey data descriptively by method and assessed factors associated with hormonal IUD use through multivariate logistic regression models. Follow-up in-depth interviews conducted with 32 women were analyzed thematically.

RESULTS : There were few differences by method used in the socio-demographic profiles and contraceptive history of participants. Among users choosing a long-acting, reversible method, the top reasons for method choice included perceptions that the method was “right for my body,” long duration, recommended by provider, recommended by friends/family, few or manageable side effects, and high effectiveness. Among hormonal IUD users, 17% mentioned reduced bleeding (inclusive of lighter, shorter, or no period), and 16% mentioned treatment of heavy or painful periods. Qualitative data supported these findings. Among survey respondents, between 25% and 33% said they would have chosen no method if the method they received had not been available. Both quantitative and qualitative data indicated that partner support can affect contraceptive use, with in-depth interviews revealing that women typically needed partner permission to use contraception, but men were less influential in method choice.

CONCLUSIONS : Expanding access to the hormonal IUD as part of a full method mix provides an opportunity to expand contraceptive choice for women in Nigeria. Findings are timely as the government is poised to introduce the method on a wider scale.

2. Brunie A, Rademacher KH, Nwala AA, et al. Provision of the levonorgestrel intrauterine system in Nigeria: Provider perspectives and service delivery costs. *Gates Open Res*. 2020 Aug 6;4:119. Available here.

BACKGROUND: Several organizations in Nigeria are leading pilot introduction programs of the levonorgestrel intrauterine system (LNG-IUS). We conducted a qualitative assessment of providers' experiences across the five programs and an analysis of service delivery costs in one program.
METHODS: We conducted 20 in-depth interviews (IDIs) with providers. We used project expenditure records to estimate incremental direct service delivery costs of introducing the LNG-IUS in 40 social franchise clinics supported by the Society for Family Health (SFH). We then compared the direct service delivery costs per couple years of protection (CYP) for the LNG-IUS to other family planning methods.
RESULTS: Providers appreciated the therapeutic benefits of the LNG-IUS, especially reduction of heavy bleeding. They said that women generally accepted bleeding changes with counseling but noted complaints about spotting and mixed acceptability of amenorrhea. Providers indicated being comfortable with both the insertion and removal process and believed their equipment and infection prevention protocols were adequate. Lack of awareness among women, limited availability, current pricing, and resistance to uterine placement among some women were perceived as barriers. The estimated direct service delivery cost of introducing the LNG-IUS in pilot settings, inclusive of up-front provider training costs, was USD 34 per insertion. Direct service delivery costs at a 'steady state' (i.e., without training costs included for any method) of the LNG-IUS per CYP was similar to that of other contraceptive methods distributed in Nigeria.
CONCLUSION: Providers' positive experiences with the LNG-IUS and direct service delivery costs per CYP that align with those for other methods suggest that the LNG-IUS could be an important addition to the method mix in Nigeria. Product introduction strategies will need to address both the supply and the demand sides, as well as consider appropriate pricing of the LNG-IUS relative to other methods and particularly the copper IUD.

3. Brunie A, Stankevitz K, Nwala AA, et al. Expanding long-acting contraceptive options: a prospective cohort study of the hormonal intrauterine device, copper intrauterine device, and implants in Nigeria and Zambia. *Lancet Glob Health*. 2021 Oct;9(10):e1431-e1441. Available here.
BACKGROUND: 30 years after the introduction of the levonorgestrel-releasing intrauterine device in Europe, several sub-Saharan African countries are seeking to broaden access to this contraceptive method. In this study, we aimed to assess 12-month continuation of the hormonal intrauterine device, copper intrauterine device, and implants, as well as to assess women's experiences and satisfaction using these methods in the private sector in Nigeria and the public sector in Zambia.
METHODS: We did a prospective cohort study of long-acting reversible contraceptive users across 40 private sector clinics in Nigeria and 21 public sector clinics in Zambia. Eligible women were aged 18–49 years in Nigeria and 16–49 years in Zambia, had chosen to receive the hormonal intrauterine device, copper intrauterine device, or implant (either a 5-year levonorgestrel-releasing subdermal implant or a 3-year etonogestrel-releasing subdermal implant), and, in Nigeria only, had access to a telephone. Women were interviewed within 100 days of receiving their contraceptive method either via telephone in Nigeria or in person in Zambia, with follow-up surveys at 6 months and 12 months. The primary outcomes were method-specific, 12-month continuation rates—ie, continuation rates of the hormonal intrauterine device, copper intrauterine device, and implant across Nigeria and Zambia. We used Kaplan-Meier methods to estimate the cumulative probabilities of method-specific continuation and a log-rank test to compare contraceptive methods. We analysed self-reported satisfaction and experiences as a secondary outcome.

FINDINGS: Between June 25 and Nov 22, 2018, we enrolled a total of 1542 women (n=860 in Nigeria and n=682 in Zambia) receiving a long-acting reversible contraceptive. In total, 835 women (266 [32%] hormonal intrauterine device users, 274 [33%] copper intrauterine device users, and 295 [35%] implant users) in Nigeria and 367 (140 [38%] hormonal intrauterine device users, 149 [40%] copper intrauterine device users, and 78 [21%] implant users) in Zambia were included in the study analysis. The 12-month cumulative continuation rates were 86·8% (95% CI 82·1–90·4) for the hormonal intrauterine device, 86·9% (82·1–90·4) for the copper intrauterine device, and 85·0% (80·2–88·7) for implants in Nigeria. In Zambia, the 12-month cumulative continuation rates were 94·7% (89·2–97·4) for the hormonal intrauterine device, 89·1% (82·3–93·4) for the copper intrauterine device, and 83·1% (72·2–90·1) for implants. At least 71% of respondents across the timepoints were very satisfied with their method, and at least 55 (79%) of 70 reported having recommended their contraceptive method to someone else. Across the methods, the most commonly self-reported positive aspect of long-acting reversible contraceptive use at 12 months was effectiveness in Nigeria (range 93–94%) and long-lasting duration in Zambia (48–60%). Between 124 (50%) of 248 and 136 (59%) of 230 Nigerian participants and 26 (42%) of 62 and 66 (57%) of 117 Zambian participants reported nothing negative about their contraceptive method.
INTERPRETATION: Our study showed high continuation rates and satisfaction across long-acting reversible contraceptives, including the hormonal intrauterine device, a method that has been largely underused in sub-Saharan Africa. This finding supports the inclusion of the hormonal intrauterine device as a valuable addition to the mix of contraceptive methods in Nigeria and Zambia.

4. Brunie A, Lydon M, Stankevitz K, et al. What are the prospects for the hormonal IUD in the public sector? A mixed-method study of the user population in Zambia. *BMC Womens Health*. 2022;22(1):178. Available here.

BACKGROUND: The levonorgestrel-releasing intrauterine device (IUD)-also known as the hormonal IUD-is a highly effective contraceptive method that has not been widely available in the public sector in Zambia. Early introduction efforts can provide critical insights into the characteristics of users, reasons for method choice, and experiences getting their method.
METHODS: We conducted a survey with 710 public sector clients who received a hormonal IUD, copper IUD, implant or injectable in two provinces of Zambia, and additional in-depth interviews with 29 women. We performed descriptive analyses of survey data and fitted multivariable logistic regression models to assess factors associated with hormonal IUD use. Qualitative interviews were analyzed thematically.
RESULTS: Factors associated with hormonal IUD use included full-time or self-employment (relative to both implant and copper IUD use), as well as being older, wealthier, and partner not being aware of method use (relative to implant use only). Common reasons for choosing long-acting methods were duration, perception that the method was "right for my body," and convenience. In addition, a portion of hormonal IUD acceptors mentioned effectiveness, potential for discreet use, few or manageable side effects, and treatment for heavy or painful periods. Between 83 and 95% of women said that they were counseled about menstrual changes and/or non-bleeding side effects; however, more hormonal IUD acceptors recalled being counseled on the possibility of experiencing reduced bleeding (88%) than amenorrhea (43%). Qualitative interviews indicate that women seek methods with minimal or tolerable

side effects. While most women reported their partner was aware of method use, men may be more consistently involved in the decision to use contraception rather than in the choice of a particular method. Qualitative results show an appreciation of the lifestyle benefits of reduced bleeding (especially lighter bleeding), although amenorrhea can be cause for concern.
CONCLUSIONS: Initial efforts to introduce the hormonal IUD can provide valuable learnings that can inform broader method introduction to expand choice and better suit women's needs in Zambia and elsewhere. Scale-up plans should include emphasis on high quality counseling and demand generation.
The government of Zambia is committed to increasing access to high-quality contraception and making more choices available to users. To date, the hormonal IUD, a highly effective, long-lasting contraceptive has not been widely available in the country. A study in pilot introduction settings provided insights into why women chose the methods, their characteristics, and their experiences getting their methods. The 710 women in the study received family planning services in public sector settings in two provinces in Zambia. Women in the study who received a hormonal IUD, copper IUD, implant, or injectable completed a quantitative survey; in-depth interviews were also conducted with 29 women. Results showed common reasons for choosing the long-acting methods (hormonal IUD, copper IUD or implants) were their duration, perception that the method was "right for my body," and convenience. In addition, some hormonal IUD acceptors indicated that they were attracted to the method's effectiveness, potential for discreet use, few or manageable side effects, and treatment for heavy or painful periods. Qualitative interviews with women also showed that women want contraceptive methods that lead to minimal or tolerable side effects. Male partners were typically aware of contraceptive use; however, men were less involved with decisions about the particular method women selected. Use of the hormonal IUD can lead to reduced menstrual bleeding, and in the interviews, women indicated that they liked reduced bleeding (especially lighter bleeding), although amenorrhea (paused bleeding) can be cause for concern. The results can help inform broader method introduction.

5. Danna, K, Jackson, A, Mann, C, Harris, D. Expanding Effective Contraceptive Options: Lessons Learned from the Introduction of the Levonorgestrel Intrauterine System (LNG-IUS) in Zambia and Madagascar. Report. 2019. Available here.
Expanding Effective Contraceptive Options (EECO) is a USAID project with funding from 2013-2022 that supports the introduction of new contraceptive options, like the SILCS diaphragm, and dual protection methods, like the women's condom. Each product in the EECO portfolio is designed to address one or more method-related reasons for non-use of contraception. Among these methods is the Levonorgestrel Intrauterine System (LNG-IUS), a contraceptive option with a side effect profile that differs from other methods and may appeal to women seeking reduced menstrual bleeding. EECO conducts pilot introductions of new contraceptive products, like the LNG-IUS, in countries that have high levels of unmet need for contraception such as Madagascar, Malawi, Niger, Nigeria, and Zambia. By the project's end, EECO will have produced step-by-step roadmaps for product introduction which can be used to scale up access to the products or expand introduction to additional countries. This program brief focuses on the lessons learned through each stage of the project's pilot introductions of the LNG-IUS in Zambia and Madagascar from 2016 to 2018.

6. Danna K, Jaworski G, Rahaivondrafahitra B, et al., Introducing the hormonal Intrauterine Device in Madagascar, Nigeria, and Zambia: Results from a pilot study. *BMC Reproductive Health*. 2022;19(1):4. Available here.

BACKGROUND: The hormonal Intrauterine Device (IUD) is a highly effective contraceptive option growing in popularity and availability in many countries. The hormonal IUD has been shown to have high rates of satisfaction and continuation among users in high-income countries. The study aims to understand the profiles of clients who choose the hormonal IUD in low-and middle-income countries (LMICs) and describe their continuation and satisfaction with the method after 12 months of use.
METHODS: A prospective longitudinal study of hormonal IUD acceptors was conducted across three countries— Madagascar, Nigeria, and Zambia—where the hormonal IUD had been introduced in a pilot setting within the context of a broad mix of available methods. Women were interviewed at baseline immediately following their voluntary hormonal IUD insertion, and again 3 and 12 months following provision of the method. A descriptive analysis of user characteristics and satisfaction with the method was conducted on an analytic sample of women who completed baseline, three-month, and 12-month follow-up questionnaires. Kaplan-Meier cumulative hazard models were used to estimate method continuation rates up to 12 months post-insertion.
RESULTS: Each country had a unique demographic profile of hormonal IUD users with different method use histories. Across all three countries, women reported high rates of satisfaction with the hormonal IUD (67-100%) and high rates of continuation at the 12-month mark (91-93%).
CONCLUSIONS: Rates of satisfaction and continuation among hormonal IUD users in the study suggest that expanding method choice with the hormonal IUD would provide a highly effective, long-acting method desirable to many different population segments, including those with high unmet need.

7. Eva G, Nanda G, Rademacher KH, Mackay A, Negedu O, Taiwo A, Dal Santo L, Saleh M, Palmer L, Brett T. Experiences with the Levonorgestrel Intrauterine System among Clients, Providers and Key Opinion Leaders: A Mixed-Methods Study in Nigeria. *Glob Health Sci Pract*. 2018;6(4):680-692. Available here.

BACKGROUND: The levonorgestrel intrauterine system (LNG IUS) is one of the most effective contraceptive methods, and it has noncontraceptive health benefits, including treatment for women with heavy menstrual bleeding. In 2016, Marie Stopes International Organisation Nigeria (MSION) expanded LNG IUS provision through training and support to 9 mobile outreach teams, 105 social franchise clinics, and 20 public-sector providers in 17 states. Information about the LNG IUS was added to awareness-raising materials, and community mobilizers provided information on the LNG IUS alongside other voluntary family planning methods.
METHODS: In 2016, Marie Stopes International, MSION, and FHI 360 examined clients' and providers' experiences with the LNG IUS to assess the potential for further scale-up of the method as part of a comprehensive approach to family planning in Nigeria. A mixed-methods approach was used including analysis of routine service data, supplemental data specific to LNG IUS clients, and in-depth interviews with LNG IUS clients, providers, and key opinion leaders.
RESULTS: Just under 1,000 LNG IUS were inserted from September 2016 to December 2017 in 16 states in channels supported by MSION, representing 0.4% of all long-acting and reversible contraceptive (LARC) services provided by the participating providers during this time frame. The vast majority (82%)

of LARCs provided were implants. A small pool of providers was responsible for providing almost half of the LNG IUS services. Common reasons for women choosing the LNG IUS were reduced menstrual bleeding (61%), long-acting duration (52%), effectiveness (49%), and discreetness (42%). Almost 80% of the users first heard about the method from a provider. Almost all users and providers reported positive experiences with the method, noting the noncontraceptive benefits and fewer side effects compared with other methods. All providers who were interviewed said they would continue offering the LNG IUS. Several key opinion leaders mentioned a total market approach incorporating both public and private sectors would be needed to successfully scale up the LNG IUS.
CONCLUSION: Reduced menstrual bleeding and fewer side effects compared with other methods were identified as important attributes of the LNG IUS by clients, providers, and key opinion leaders. Challenges to uptake of the LNG IUS include difficulty with introducing a new method within a busy service delivery infrastructure and limited awareness and demand-generation activities on the LNG IUS specifically. A comprehensive product introduction approach with coordinated demand- and supply-side activities may be required for this method to reach its full potential.

8. FHI 360, Society for Family Health, PSI, WomanCare Global. Market Assessment for Potential Introduction of a New Hormonal IUCD in Zambia. Report. 2016. Report available here.

The hormonal IUCD is not available in the public sector in Zambia and is only available on a very limited basis in the private sector. High quality, affordable LNG-IUS products are now being introduced in the global market. As a result, partners embarked on a national market assessment in Zambia. The market assessment included an analysis of the current reproductive health landscape in Zambia including the current market for IUDs, interviews with Key Opinion Leaders (KOLs), healthcare providers and potential users including women currently using a short-acting family planning method, women currently using a long-acting family planning method, postpartum women and non-users of contraception; and an assessment of the regulatory landscape and documentation of partners' initial plans for introduction of a new, more affordable, quality assured hormonal IUCD product.

9. Harris DM, Dam A, Morrison K, et al. Barriers and Enablers Influencing Women's Adoption and Continuation of Vaginally Inserted Contraceptive Methods: A Literature Review. *Stud Fam Plann*. 2022;53(3):455-490. Available here.

ABTRACT: Most vaginally inserted methods have limited availability and use despite offering characteristics that align with many women's stated preferences (e.g., nonhormonal and/or on demand). The objective of this review was to identify enablers and barriers to women's adoption and continuation of vaginally inserted contraceptive methods in low- and middle-income countries (LMICs). We searched three databases (PubMed, Embase, and Web of Science) and 18 websites using keywords related to five vaginally inserted contraceptive methods (diaphragm, vaginal ring, female condom, copper intrauterine device [IUD], hormonal IUD) and terms associated with their adoption and continuation. Searches were limited to resources published between January 2010 and September 2020. Studies eligible for inclusion in our review presented results on women's use and perspectives on the enablers and barriers to adoption and continuation of the vaginally inserted contraceptive methods of interest in LMICs. Relevant studies among women's partners were also included, but not those of providers or other stakeholders. Data were coded, analyzed, and disaggregated according to a framework grounded in family planning (FP) literature and behavioral theories common to FP research

and program implementation. Our initial search yielded 13,848 results, with 182 studies ultimately included in the analysis. Across methods, we found common enablers for method adoption, including quality contraceptive counseling as well as alignment between a woman's preferences and a method's duration of use and side effect profile. Common barriers included a lack of familiarity with the methods and product cost. Notably, vaginal insertion was not a major barrier to adoption in the literature reviewed. Vaginally inserted methods of contraception have the potential to fill a gap in method offerings and expand choice. Programmatic actions should address key barriers and enable voluntary use.

10. Homan R, Rademacher RH, Stankevitz, Brunie A. Cost-effectiveness of including the hormonal IUD in the contraceptive method mix in Nigeria and Zambia: Summary of results. Final brief. November 2021. Available here.

This analysis estimates the incremental cost-effectiveness of the hormonal IUD compared to other contraceptive methods available in Nigeria and Zambia over a 5-year and 10-year period. Separate models were built for Nigeria and Zambia reflecting the different service delivery contexts, contraceptive prevalence, and current method mix. Costs were estimated from the perspective of the health system as well as from the societal perspective.

11. Hubacher D, Akora, V., Masaba, R., Chen, M., Veena, V. Introduction of the levonorgestrel intrauterine system in Kenya through mobile outreach: review of service statistics and provider perspectives. *Global Health: Science and Pract*. 2014;2(1):47-54. Available here.

BACKGROUND: The levonorgestrel intrauterine system (LNG IUS) was developed over 30 years ago, but the product is currently too expensive for widespread use in many developing countries. In Kenya, one organization has received donated commodities for 5 years, providing an opportunity to assess impact and potential future role of the product.

METHODS: We reviewed service statistics on insertions of the LNG IUS, copper intrauterine device (IUD), and subdermal implant from 15 mobile outreach teams during the 2011 calendar year. To determine the impact of the LNG IUS introduction, we analyzed changes in uptake and distribution of the copper IUD and subdermal implant by comparing periods of time when the LNG IUS was available with periods when it was not available. In addition, we interviewed 27 clinicians to assess their views of the product and of its future role.

RESULTS: When the LNG IUS was not available, intrauterine contraception accounted for 39% of long-acting method provision. The addition of the LNG IUS created a slight rise in intrauterine contraception uptake (to 44%) at the expense of the subdermal implant, but the change was only marginally significant ($P = .08$) and was largely attributable to the copper IUD. All interviewed providers felt that the LNG IUS would increase uptake of long-acting methods, and 70% felt that the noncontraceptive benefits of the product are important to clients.

CONCLUSIONS: The LNG IUS was well-received among providers and family planning clients in this population in Kenya. Although important changes in service statistics were not apparent from this analysis (perhaps due to the small quantity of LNG IUS that was available), provider enthusiasm for the product was high. This finding, above all, suggests that a larger-scale introduction effort would have strong support from providers and thus increase the chances of success. Adding another proven and

highly acceptable long-acting contraceptive technology to the method mix could have important reproductive health impact.

12. Hubacher D, Masaba R, Manduku CK, Chen M, Veena V. The levonorgestrel intrauterine system: cohort study to assess satisfaction in a postpartum population in Kenya. *Contraception*. 2015 Apr;91(4):295-300. Available here.

BACKGROUND**:** The levonorgestrel intrauterine system (LNG IUS) may become the next long-acting contraceptive to be introduced in public sector programs of resource-poor countries. Whereas service provision for subdermal implants and intrauterine devices is growing, little is known about how the LNG IUS might fit in.

STUDY DESIGN**:** We conducted a cohort study of 313 women in Kenya who were 6–12 weeks postpartum when they started using these methods: subdermal implant (205), LNG IUS (93), and copper intrauterine device (15). Participants returned for visits at 6 and 12 months to share information on bleeding patterns, side effects, satisfaction, and continued use of the products. We used Kaplan–Meier techniques to estimate method continuation rates and chi-square tests of association to identify differences in experiences with the methods.

RESULTS**:** The 12-month continuation rate for the LNG IUS was 89.1 (95% confidence interval [CI] = 86.9–94.9) and statistically equivalent to that of the subdermal implant (91.8: 95% CI = 80.6–94.0). Nearly 87% of LNG IUS users were very satisfied with the method at 6 months compared to 75% of implant users; this gap closed somewhat at 12 months as satisfaction levels of implant users rose. At 12 months 78% of LNG IUS users felt that their bleeding pattern was highly acceptable compared with about 66% of implant users.

CONCLUSIONS: This study found that the LNG IUS compared favorably to the subdermal implant in terms of satisfaction levels and continued use. The LNG IUS will provide another long-acting option for postpartum women.

IMPLICATIONS: The LNG IUS may soon be purchased by international donor agencies for use in public sector programs in sub-Saharan Africa and other resource-poor countries. The results of this study suggest that the product will be successful in future introduction activities.

13. Hubacher, D., Masaba, R., Manduku, C., Veena, V. Uptake of the levonorgestrel intrauterine system among recent postpartum women in Kenya: factors associated with decision-making. *Contraception.* 2013;88(1):97-102. Available here.

BACKGROUND: The levonorgestrel intrauterine system (LNG IUS) may become more available in the public sector of resource-poor countries, but it is unclear what product features might be attractive to users and what factors will influence uptake.

STUDY DESIGN: We recruited 671 women in Kenya who were seeking contraception at 6–12 weeks postpartum and gave them an opportunity to try the LNG IUS. We asked why they did or did not choose it, relative to the alternative options. χ^2 tests of association were done to examine participant characteristics and decision-making associated with choice.

RESULTS: Participants chose the following methods: LNG IUS (16%), injectable (36%), subdermal implant (30%), progestin-only pills (15%) and copper intrauterine device (IUD) (3%). Reasons for not choosing the LNG IUS included fear of pain/injury/discomfort (34%), modesty issues regarding insertion (33%) and fear of hormonal/health side effects (31%). Nearly a third of LNG IUS acceptors said they would have

chosen a short-acting method if the LNG IUS were not available, and only 21% would have chosen the copper IUD.
CONCLUSION: The LNG IUS could be an ideal method for increasing uptake of long-acting methods among recent postpartum women. Product attributes and comparisons to other contraceptive options are important factors in decision-making. Even among women comfortable with intrauterine contraception, great distinctions and preferences are apparent. Addressing specific misconceptions and fears with better information can help women make the best personal choices.

14. Hussein S, Khalil A, Alharbi S. Knowledge and attitude about intrauterine contraceptive devices among patients attending the National Guard Hospital in Jeddah, Saudi Arabia: a cross-sectional study. *Eur J Contracept Reprod Health Care*. 2022;27(1):9-15. Available here.

OBJECTIVES: To investigate women's knowledge and attitudes regarding the use of the intrauterine device (IUD) for contraceptive purposes and to explore eventual misconceptions about its benefits, and disadvantages.
METHODS: A cross-sectional study was conducted in the Obstetrics and Gynaecology (OB/GYN) outpatient department at King Khalid National Guard Hospital in King Abdul-Aziz Medical City, Jeddah, Saudi Arabia. It involved women aged 15-55 years, who attended the outpatient OB/GYN clinic from July 2018 till May 2019. A validated self-structured questionnaire was used to collect demographic data and clinical data; including, medical and surgical history, obstetrical and gynaecological history.
RESULTS: Of 269 participants, 32.3% reported a positive history of unintended pregnancy, and 28.6% declared using or having used IUD, with copper being the most frequent type (17.8%). A majority (81.4%) of the respondents viewed IUD as a contraceptive method only. In comparison, more than 70% declared not knowing the type of IUD used for bleeding control, cycle regulation, endometriosis treatment, cervix cancer prevention, and endometrial hyperplasia. Further, 21.9% and 55.4% believed that IUD increases the risk of ectopic pregnancy and infections, respectively.
CONCLUSION: Women attending outpatient clinics in our centre had poor knowledge levels about IUDs, with several misconceptions and apprehensions, especially regarding the risk of genital infections and ectopic pregnancy, which may constitute a significant psychological barrier use.

15. Iyengar S, Iyengar K, Anand A, Suhalka V, Jain M. Observational study of feasibility and acceptability of the levonorgestrel-releasing intrauterine device as a long-acting reversible contraceptive in a primary care setting in India. Contracept X. 2022;4:100079. 2022 Jun 30. Available here.

OBJECTIVES: The levonorgestrel-releasing intrauterine device (LNG-IUD) is a well-accepted contraceptive across developed countries, yet there is limited experience in use and acceptance amongst women living in low-resource, developing country settings. We studied the feasibility of providing the LNG-IUD through a primary care service, and its acceptability amongst women living in a low-income, rural-tribal community in India.
DESIGN: We conducted an observational study of feasibility and acceptability at four health facilities (three rural, and one urban) in Rajasthan, India. Women seeking contraception were offered the LNG-IUD in addition to existing contraceptive methods. We followed all those who adopted LNG-IUD from August 2015 to September 2019 (n= 1266) till discontinuation or 12 months, whichever was earlier. The

primary outcome was continuation rate and acceptability, and the secondary outcome was change in hemoglobin levels, which we measured before insertion and at 12-month follow-up, using Sahli's method.
RESULTS: Most users lived in villages, were illiterate, belonged to marginalized groups, had 2 or more children, and wished to limit births when they adopted the method. The 12-month continuation rate was 87.6%. Amongst all users, 7.4% of women sought removal for side effects and 2% for change in reproductive intention, while another 2% reported spontaneous expulsion. Most continuing users reported hypomenorrhea (54%) or amenorrhea (42%) by 12 months of use. User satisfaction was high at 91.6%, with 92% of women rating their experience as equaling or exceeding expectations. Moderate and severe anemia reduced, and mean hemoglobin levels increased by 0.7 g/dL ($p < 0.01$).
CONCLUSIONS: Primary care clinics can feasibly deliver LNG-IUD, with high acceptability amongst women living in low resource settings. Given the paucity of long-acting reversible contraceptive options and high prevalence of anemia among women in India and similar countries, the method should be piloted through the public health system.
IMPLICATIONS: Long duration of contraceptive action, ability to reduce menstrual bleeding and reduce anemia, reversibility, and easy removal, combine to make LNG-IUD acceptable to women, especially in regions with high prevalence of anemia. This study demonstrates the feasibility and acceptability of introducing LNG-IUD in a low resource, primary care setting.

16. Laporte M, Charles CM, Metelus S, Peloggia A, Paez GO, Juliato CT, Bahamondes L. Reasons reported by women for choosing the levonorgestrel intrauterine system as a contraceptive method. *Int J Gynaecol Obstet*. 2021. E-Publication ahead of print available here.

OBJECTIVE: To assess the reasons provided by women for choosing the use of the 52 mg levonorgestrel intrauterine system (LNG-IUS) as a contraceptive method.
METHODS: We conducted a cross sectional study from January 2021 to August 2021 at the University of Campinas, Campinas, SP, Brazil. Women who had never used the 52 mg LNG-IUS and were requesting it for contraception answered a questionnaire asking for their sociodemographic characteristics, the last contraceptive method in use, how they received information about the device, and their main reasons for choosing the method.
RESULTS: We enrolled 516 women, 365 (70.7%) of whom were under the age of 35 and 352 (68.2%) of whom were parous. The last contraceptive method in use was a short-acting reversible method among 387 (80.8%) women, 454 (88%) reported that they wanted to use the IUS only for contraception, and the main source of information was their health care providers. The main reported reasons for choosing the method were because it is safe, has high contraceptive efficacy, and reduces menstrual bleeding.
CONCLUSION: Health care providers should continue their efforts to provide guidance about the LNG-IUS, including the non-contraceptive benefits, which may contribute to a reduction in the number of unplanned pregnancies.

17. Laporte M, Charles CM, Metelus S, Souza RB, Peloggia A, Bahamondes L. Reasons for satisfaction with the use of the 52-mg levonorgestrel intrauterine system. *Int J Gynaecol Obstet*. 2022;10.1002/ijgo.14214. E-Publication ahead of print available here.

OBJECTIVES: To assess the reasons to use, reasons they liked, satisfaction with, and possibilities of recommendation to other women of the levonorgestrel 52-mg intrauterine system (LNG-IUS) by users.
MATERIALS AND METHODS: A cross-sectional study was conducted at the University of Campinas, Campinas, Brazil from January to July 2021. We enrolled users who came to the clinic, and we applied a pre-tested structured questionnaire with open-ended questions. We performed descriptive analyses of the variables, assessing the level of satisfaction with, and the reasons regarding the possibility of continuing to use, the IUS.
RESULTS: Of the 517 enrolled women, 251 (48%) were aged 35 years or older (mean age 33.9 ± 9.0 years), 276 (53%) were white, 14 (3%) were adolescents, 155 (30%) were nulligravidas, and 307 (59.4%) reported experiencing amenorrhea in the last 90 days. Common reasons why women liked to use the LNG-IUS included both the reduction of menstrual bleeding (419 women; 81%) and dysmenorrhea (290 women; 56.1%). Nine out of 10 users (517 women; 91%) were satisfied with the method, and the majority would recommend it to other women.
CONCLUSION: We found a high satisfaction rate among LNG-IUS users mainly due to the reduction of both menstrual bleeding and dysmenorrhea.

18. Laporte M, Metelus S, Ali M, Bahamondes L. Major differences in the characteristics of users of the copper intrauterine device or levonorgestrel intrauterine system at a clinic in Campinas, Brazil. *Int J Gynaecol Obstet*. 2021 Apr. Available here.
OBJECTIVE: To compare the sociodemographic characteristics of users of the copper intrauterine device (Cu-IUD) and the levonorgestrel intrauterine system (LNG-IUS) at a family planning clinic in Campinas, SP, Brazil.
METHODS: A retrospective audit study was conducted to analyze the characteristics of new users of IUDs at the clinic of the Department of Obstetrics and Gynecology, University of Campinas. Data covered insertions performed between 1979 and 2006 when only the Cu-IUD was offered at the clinic, and between 2007 and 2019 when the LNG-IUS was also offered, both free of charge to women. Logistic regression analysis was performed.
RESULTS: There were 31 385 insertions. Cu-IUD: n = 17 156 (1979-2006) and n = 2013 (2007-2019); LNG-IUS n = 12 216 (2007-2019). Up to 2006, Cu-IUD users were less likely to be nulligravidas, more likely to be younger than 40 years of age, and with fewer years of schooling. Following introduction of LNG-IUS, the sociodemographic characteristics of users presented major changes over time. Comparing the period 1979-2006 with 2007-2019, new users of the LNG-IUS were more likely to be older than 40 years of age, with fewer years of completed schooling, and to be nulligravidas.
CONCLUSION: Major changes in sociodemographic characteristics of users were noted according to preference over time. Introduction of the LNG-IUS presents a major opportunity to increase IUD use.
19. Laporte M, Peloggia A, Marcelino AC, de Carvalho LS, Bahamondes L. Perspectives of health care providers regarding the levonorgestrel-releasing intrauterine system. *Eur J Contracept Reprod Health Care*. 2021. E-Publication ahead of print available here.

OBJECTIVES: The aims of the study were to assess the number of insertions per month of the 52 mg levonorgestrel-releasing intrauterine system (LNG-IUS) and gauge the knowledge and opinions of health

care providers with regard to some of its characteristics and the reasons why women liked using the method.
METHODS: An online questionnaire survey was conducted between January and July 2021 at the University of Campinas, Brazil. The survey comprised physicians and nurses from centres that had requested and received donated devices.
RESULTS: A total of 65 health care providers answered the questionnaire (41 physicians and 24 nurses). The main misconceptions were related to insertion after an ectopic pregnancy: 60/65 (92.3%) answered that users with previous ectopic pregnancy must have frequent follow-up. Wrong answers were also given on the occurrence of acne (37/65, 56.9%) and depression (32/65, 49.2%). Participants reported that the LNG-IUS was highly effective (100%), long-acting (93.9%) and an appropriate method for controlling uterine bleeding (90.8%) and that it had few side effects (86.2%).
CONCLUSION: Our study suggests that health care providers from centres that requested and received LNG-IUS donations, even though they reported adequate knowledge about the device, still had misconceptions with regard to its clinical management.

20. Miranda L, Townsend J, Faúndes A, Bahamondes L. The benefits and limitations of donating new contraceptive technology: The case of the International Contraceptive Access (ICA) Foundation and the LNG IUS Program in Brazil. *Contraception*. 2020 Jun;101(6):367-369. Available here.
The International Contraceptive Access (ICA) Foundation was established in Finland in December 2003 as a public–private partnership between Bayer AG, a global pharmaceutical company, and the Population Council, an international nonprofit nongovernmental organization. The objective of the Foundation was to provide public service-delivery organizations with the levonorgestrel 52 mg intrauterine system (LNG IUS) on a not-for-profit basis to serve the reproductive needs of women in resource-poor settings in developing countries.

By the end of 2018, the ICA Foundation had donated nearly 130,000 units of LNG IUS to organizations serving low income communities and humanitarian settings, public hospitals training physicians and nurses in family planning, and global partners with a network of service delivery facilities in 36 low income or developing countries in Asia, Africa and Latin America and the Caribbean [1]. Annual donations in 2018 reached nearly 25,000 units globally. Brazil has been the country which has received the largest number of LNG IUS, with 32,740 units until February 2019 [2]. Other large donations were made to service delivery organizations in Nigeria and Kenya and through NGO networks such as International Planned Parenthood Federation, Population Services International, and Marie Stopes International. The objective of our commentary was to describe the benefits and limitations of the donations of the LNG IUS to Brazil.

21. Nanda, G, Brennan C, Brunie A et al., Adolescent Girls' and Young Women's Perspectives on the LNG-IUS in Nigeria. Final report. May 2020. Available here.
This presentation provides an overview of the methods and findings from focus group discussions conducted among adolescent girls and young women (AGYW) in Nigeria. The FGDs examined the potential acceptability of and interest in the hormonal IUD among AGYW, and how the method's characteristics and side effect profile might meet the unique reproductive health needs of both married and unmarried adolescents. FGD participants in Nigeria identified the potential for reduced or no

menstrual bleeding while using the method as a key advantage, along with the duration of effectiveness, insertion/placement process, and the possibility of fewer side effects than other contraceptive methods. While more participants discussed benefits or positive characteristics of the method than potential disadvantages, some AGYW expressed concerns about insertion or placement (noting pain, an invasive or overly intimate procedure, or health problems as potential issues), the potential for amenorrhea or other bleeding changes, and the lack of protection from STIs if solely using the hormonal IUD. Participants in Nigeria were divided on whether they felt it was easy for girls to obtain access to contraception in general and identified several key barriers to accessing any contraceptive method and the hormonal IUD in particular.

22. Nanda, G, Brennan C, Brunie A, et al., Adolescent Girls' and Young Women's Perspectives on the LNG-IUS in Zambia. Final report. May 2020. Available here.

This presentation provides an overview of the methods and findings from focus group discussions conducted among adolescent girls and young women (AGYW) in Zambia. The FGDs examined the potential acceptability of and interest in the hormonal IUD among AGYW, and how the method's characteristics and side effect profile might meet the unique reproductive health needs of both married and unmarried adolescents. More than half of the participants believed other AGYW would consider the potential for reduced or no menstrual bleeding to be a desirable characteristic of the method, and also cited the associated lower need to buy menstrual hygiene products and reduced menstrual cramps or menstrual pain as advantages. Approximately 1/3rd of the participants believed that other AGYW might consider the potential for amenorrhea to be an *undesirable* characteristic of the method, and 1/4th expressed concerns about the insertion or placement process. Overall, fewer AGYW expressed concerns or dislikes about the hormonal IUD than described positive aspects or benefits of the method. Participants identified girls with heavy or painful periods as the most likely user group for the method. Counseling emerged as an important aspect of girls' decisions about whether or not to use a hormonal IUD, and participants believed girls would need comprehensive information about the method in order to make a decision.

23. Nanda G, Rademacher KH, Solomon M, Mercer S, Wawire J, Ngahu R. Experiences with the Levonorgestrel Intrauterine System (LNG-IUS) in Kenya: Qualitative Interviews with Mirena Users and their Partners. *Eur J Contracept Reprod Health Care*. 2018;10:1-6. Available here.

1) OBJECTIVES: The levonorgestrel-releasing intrauterine system (LNG-IUS) is an underused contraceptive method in sub-Saharan Africa. A recent market assessment in Kenya found that if a more affordable version of the method were available it may increase demand and uptake of the method. We therefore aimed to examine attitudes and perceptions around the LNG-IUS and experiences of method use, including exploring attributes such as bleeding changes, contraceptive-related amenorrhoea and perceived non-contraceptive benefits.
2) METHODS: Qualitative interviews were conducted among 29 women who were current or recent users of the LNG-IUS, and among a subset (n = 9) of their husbands/partners.
3) Results: Our findings indicate that women's main reason for choosing the LNG-IUS for contraception was their perception that the method had fewer side effects compared with other contraceptive

methods. Women had favourable attitudes towards using the LNG-IUS. Husbands were also very positive about their partner's use of the method.
4) CONCLUSION: Understanding the motivations and experiences of early adopters of the LNG-IUS can help inform the development of demand creation and communication strategies to influence uptake and continuation of the LNG-IUS both in Kenya and perhaps more broadly. Communication efforts that emphasise the positive attributes of the LNG-IUS could help promote wider use of the method, especially if new, more affordable product(s) become available.
5)

24. Nyarko P, Adohinzin C, Tapsoba P, Esantsi S, Townsend J, Kanlisi N, et al. Acceptability and promotion strategies for LNG-IUS in Ghana: a public health assessment. Accra, Ghana: Population Council, Regional Office for Sub-Saharan Africa. 2009. Available here.

The main objectives of the study were to evaluate client knowledge and acceptability of Levonorgestrel intrauterine contraceptives, provider training and competence, product affordability and accessibility. The study also explored promotion and sustainability strategies that would enhance the integration of the product into the family planning method mix. The results indicate that the product is universally accepted by women who had had the product inserted. More than 90 percent of LNG-IUS clients expressed satisfaction with the colour, shape, size and overall packaging of the product. The overall mean satisfaction score was very high, with four out of five women expressing satisfaction with the product. Providers and non-LNG-IUS users also had similar views. Both users and providers were quite knowledgeable about the product. In addition, providers had the skills to insert and remove the product, although a few were unsure of their competence. Non-users, on the other hand, mostly did not know about the existence of the product and those who had heard about the product were not adequately informed about it. Almost a third (28%) of LNG-IUS acceptors were new acceptors of contraception. The rest had mostly switched from the injectable, IUD, pill and natural family planning method.

25. Rademacher KH, Solomon M, Brett T, Bratt JH, Pascual C, Njunguru J, Steiner MS. Expanding access to a new, more affordable levonorgestrel intrauterine system in Kenya: A comparison of service delivery costs and perspectives from Key Opinion Leaders. *Glob Health Sci Pract*. 2016;4 Suppl 2:S83-S93. Available here.

BACKGROUND: The levonorgestrel intrauterine system (LNG IUS) is one of the most effective forms of contraception and offers important non-contraceptive health benefits. However, it is not widely available in developing countries, largely due to the high price of existing products. Medicines360 plans to introduce its new, more affordable LNG IUS in Kenya. The public sector transfer price will vary by volume between US$12 to US$16 per unit; for an order of 100,000 units, the public-sector transfer price will be approximately US$15 per unit.
METHODS: We calculated the direct service delivery cost per couple-years of protection (CYP) of various family planning methods. The model includes the costs of contraceptive commodities, consumable supplies, instruments per client visit, and direct labor for counseling, insertion, removal, and resupply, if required. The model does not include costs of demand creation or training. We conducted interviews with key opinion leaders in Kenya to identify considerations for scale-up of a new LNG IUS, including strategies to overcome barriers that have contributed to low uptake of the copper intrauterine device.
RESULTS: The direct service delivery cost of Medicines360's LNG IUS per CYP compares favorably with other contraceptive methods commonly procured for public-sector distribution in Kenya. The cost is

slightly lower than that of the 3-month contraceptive injectable, which is currently the most popular method in Kenya. Almost all key opinion leaders agreed that introducing a more affordable LNG IUS could increase demand and uptake of the method. They thought that women seeking the product's non-contraceptive health benefits would be a key market segment, and most agreed that the reduced menstrual bleeding associated with the method would likely be viewed as an advantage. The key opinion leaders indicated that myths and misconceptions among providers and clients about IUDs must be addressed, and that demand creation and provider training should be prioritized.
CONCLUSION: Introducing a new, more affordable LNG IUS product could help expand choice for women in Kenya and increase use of long-acting reversible contraception. Further evaluation is needed to identify the full costs required for introduction—including the cost of demand creation—as well as research among potential and actual LNG IUS users, their partners, and health care providers to help inform scale-up of the method.

26. Routes2Results, PSI and FHI 360. Understanding End-user and Healthcare Provider preference for the hormonal IUS contraceptive in Nigeria and Kenya. November 2019. Available here.

This presentation from November 2019 outlines findings from quantitative market research in Kenya and Nigeria. The quantitative analysis, authored by Routes2Results and PSI, followed qualitative market research on views of the hormonal IUD, and was designed to gather information on access to and demand for the method, and forecast potential demand and market environment impact. The analysis found that the provided description of the hormonal IUD was easy to understand, that impressions of the method were very positive among women and healthcare providers (HCPs) in both Nigeria and Kenya, and that HCPs believed that the method would be appealing to their clients (though for slightly different reasons in the two assessed countries) and were highly likely to provide the method.

27. Routes2Results, PSI and FHI 360. Understanding the market potential of the hormonal IUS in Kenya and Nigeria. February 2019. Available here.

This presentation from April 2019 outlines findings from qualitative market research in Kenya and Nigeria. Focus group discussions were held to understand perspectives about potential advantages and disadvantages of the hormonal IUS and to refine the method profile description. This analysis, authored by Routes2Results and PSI, helped create a framework for follow-on quantitative evaluations of market demand.

28. Sitrin D, Pfitzer A, Ndirangu G, et al. Expanding contraceptive method choice with a hormonal intrauterine system: results from mixed methods studies in Kenya and Zambia. *Glob Health Sci Pract*. 2021;9(1):89-106. Available here.

INTRODUCTION: Few women in low- and middle-income countries have access to the hormonal intrauterine system (IUS). Past research from a small number of facilities and the private sector suggest the IUS could be an important addition to the contraceptive method mix because it is the only long-acting method some women will adopt and users report high satisfaction and continuation. We aimed to determine whether these promising results were applicable in public facilities in Kenya and Zambia.
METHODS: We used a mixed-methods approach with program monitoring data, interviews with women who received an IUS, and qualitative focus group discussions with providers. Data were collected in 2017–2019.
RESULTS: Facilities in Kenya and Zambia reported 1,985 and 428 IUS insertions, respectively. If the IUS had not been available, 30% of adopters would have chosen a short-acting method. Women and providers gave diverse reasons for adopting the IUS, with the desire for fewer side effects being

frequently mentioned in focus group discussions. Many IUS adopters first heard of the method on the day it was inserted (70% in Kenya, 47% in Zambia), yet providers reported that many women were unwilling to try a method they were just hearing about for the first time. Satisfaction and continuation were high: 86% of adopters in Kenya were still using the method 3–6 months after insertion and 78% were in Zambia (average 10 months post insertion). Providers also reported that most IUS adopters were satisfied; they rarely returned with complaints that could not be addressed with additional counseling.
CONCLUSION: Expanding IUS access through the public sector shows promise to increase contraception use and continuation in low- and middle-income countries. Efforts to strengthen availability should consider demand and engage directly with various communities, including youth, around availability of a new long-acting option.

29. Todd CS, Jones HE, Langwenya N, Hoover DR, Chen PL, Petro G, Myer L. Safety and continued use of the levonorgestrel intrauterine system as compared with the copper intrauterine device among women living with HIV in South Africa: A randomized controlled trial. *PLoS Med*. 2020 May 22;17(5):e1003110. Available here.

BACKGROUND: Women living with HIV (WLHIV) have lower rates of contraceptive use than noninfected peers, yet concerns regarding contraceptive efficacy and interaction with antiretroviral therapy (ART) complicate counseling. Hormonal contraceptives may increase genital tract HIV viral load (gVL) and sexual transmission risk to male partners. We compared gVL, plasma VL (pVL), and intrauterine contraceptive (IUC) continuation between the levonorgestrel intrauterine system (LNG-IUS) and copper intrauterine device (C-IUD) in Cape Town, South Africa.
METHODS: In this double-masked, randomized controlled noninferiority trial, eligible WLHIV were ages 18–40, not pregnant or desiring pregnancy within 30 months, screened and treated (as indicated) for reproductive tract infections (RTIs) within 1 month of enrollment, and virologically suppressed using ART or above treatment threshold at enrollment (non-ART). Between October 2013, and December 2016, we randomized consenting women within ART groups, using 1:1 permuted block randomization stratified by ART use, age (18–23, 24–31, 32–40), and recent injectable progestin contraceptive (IPC) exposure, and provided the allocated IUC. At all visits, participants provided specimens for gVL (primary outcome), pVL, RTI, and pregnancy testing. We assessed gVL and pVL across 6 and 24 months controlling for enrollment measures, ART group, age, and RTI using generalized estimating equation and generalized linear models (non-ART group pVL and hemoglobin) in as-treated analyses. We measured IUC discontinuation rates with Kaplan-Meier estimates and Cox proportional hazards models. We enrolled 71 non-ART (36 LNG-IUS, 31 C-IUD; 2 declined and 2 were ineligible) and 134 ART-using (65 LNG-IUS, 67 C-IUD; 1 declined and 1 could not complete IUC insertion) women. Participant median age was 31 years, and 95% had 1 or more prior pregnancies.
RESULTS: Proportions of women with detectable gVL were not significantly different comparing LNG-IUS to C-IUD across 6 (adjusted odds ratio [AOR]: 0.78, 95% confidence interval [CI] 0.44–1.38, p = 0.39) and 24 months (AOR: 1.03, 95% CI: 0.68–1.57, p = 0.88). Among ART users, proportions with detectable pVL were not significantly different at 6 (AOR = 0.83, 95% CI 0.37–1.86, p = 0.65) and 24 months (AOR = 0.94, 95% CI 0.49–1.81, p = 0.85), whereas among non-ART women, mean pVL was not significantly different at 6 months (−0.10 log10 copies/mL, 95% CI −0.29 to 0.10, p = 0.50) between LNG-IUS and C-IUD users. IUC continuation was 78% overall; C-IUD users experienced significantly higher expulsion (8% versus 1%, p = 0.02) and elective discontinuation (adjusted hazard ratio: 8.75, 95% CI 3.08–24.8, p < 0.001) rates.

Sensitivity analysis adjusted for differential IUC discontinuation found similar gVL results. There were 39 serious adverse events (SAEs); SAEs believed to be directly related to IUC use (n = 7) comprised 3 pelvic inflammatory disease (PID) cases and 4 pregnancies with IUC in place with no discernible trend by IUC arm. Mean hemoglobin change was significantly higher among LNG-IUS users across 6 (0.57 g/dL, 95% CI 0.24–0.90; p < 0.001) and 24 months (0.71 g/dL, 95% CI 0.47–0.95; p < 0.001). Limitations included not achieving non-ART group sample size following change in ART treatment guidelines and truncated 24 months' outcome data, as 17 women were not yet eligible for their 24-month visit at study closure. Also, a change in VL assay during the study may have caused some discrepancy in VL values because of different limits of detection.
CONCLUSIONS: In this study, we found that the LNG-IUS did not increase gVL or pVL and had low levels of contraceptive failure and associated PID compared with the C-IUD among WLHIV. LNG-IUS users were significantly more likely to continue IUC use and had higher hemoglobin levels over time. The LNG-IUS appears to be a safe contraceptive with regard to HIV disease and may be a highly acceptable option for WLHIV.

Menstrual Bleeding Changes

These resources provide data about the incidence and impact of bleeding changes among users of the hormonal IUD, a non-contraceptive side-effect of the method that may positively or negatively influence uptake and acceptability. For additional resources on contraceptive-induced menstrual changes, please refer to a separate annotated bibliography on this topic available here.

1. Alves R, Rabelo M, Andrade V, Cabral R, Merriman J, Brito M. The influence of the levonorgestrel-releasing intrauterine system position on bleeding patterns in reproductive age women. *Int J Gynaecol Obstet.* 2019;147(3):326-331. Available here.
OBJECTIVE: To determine whether users of the non-fundal levonorgestrel-releasing intrauterine system (LNG-IUS) present with unfavorable bleeding patterns more frequently than fundal LNG-IUS users.
METHODS: A prospective cohort was conducted from June, 2016 to January, 2018 involving women aged 18-45 years who wished to use the LNG-IUS as contraception and had no contraindications, endometrial polyps, submucosal myomas, irregular menstrual cycle, or anticoagulant use. Two study groups comprised women using fundal insertion and non-fundal insertion LNG-IUS. Bleeding was evaluated using a diary and pictogram chart.
RESULTS: Of the 92 women who participated in the study, those with non-fundal LNG-IUS insertion sustained bleeding at rates greater than 83% (31) in the first 3 months of use, and 58% (14) at 6 months, versus 51% (22) at 3 months and 33% (19) at 6 months in those with fundal insertion (P=0.002 at 3 months; P=0.037 at 6 months). Blood loss in the non-fundal LNG-IUS group was higher than in the fundal LNG-IUS group according to pictograms drawn by participants.
CONCLUSION: Women with non-fundal LNG-IUS placement had a higher frequency of sustained bleeding and blood loss volume according to self-reported charts than those with fundal LNG-IUS placement.

2. Beckert V, Ahlers C. Bleeding patterns with the 19.5 mg LNG-IUS, with special focus on the first year of use: implications for counselling. *Eur J Cont Rep Health Care.* 2019;24(4): 251-259. Available here.
Objective: The aim of the study was to provide an additional, detailed description of early bleeding patterns with the 19.5 mg levonorgestrel-releasing intrauterine system (LNG-IUS). Methods: We conducted a pooled analysis of the bleeding diaries of participants in a previously reported phase II randomised controlled study (n = 741) and a phase III study (n = 2904), with 2-year extension phase (n = 707), of the 19.5 mg LNG-IUS. Main outcome measures were the median number of bleeding and/or spotting days per 30-day reference period for 12 months and the influence of the previous contraceptive method and levonorgestrel dose on bleeding patterns. Results: The pooled analysis comprised 1697 women. There was a progressive decline in the number of bleeding and/or spotting days from month 1: the proportion of women with </=4 bleeding and/or spotting days per month increased from 6.2% in month 1 to 15.8% in month 2, 26.0% in month 3, 39.3% in month 6 and 54.1% in month 12. The median number of bleeding and/or spotting days in month 1 was lowest in women who had previously been using an LNG-IUS. Conclusion: Analysis of bleeding diaries using 30-day reference periods provides detailed insight into bleeding changes in the first months following placement of the 19.5 mg LNG-IUS. This insight may prove useful when counselling women about contraceptive choice and method continuation.

3. Darney PD, Stuart GS, Thomas MA, Cwiak C, Olariu A, Creinin MD.
Amenorrhea rates and predictors during 1 year of levonorgestrel 52 mg intrauterine system use.
***Contraception*. 2018;97(3):210-214. Available here.**
OBJECTIVE: The objective was to evaluate amenorrhea patterns and predictors of amenorrhea during the first year after levonorgestrel 52 mg intrauterine system (IUS) placement.
STUDY DESIGN: This cohort analysis includes 1714 nulliparous and parous women who received a Liletta® levonorgestrel 52 mg IUS in a multicenter trial to evaluate efficacy and safety for up to 8 years. Participants maintained a daily diary with bleeding information. We assessed bleeding patterns in 90-day intervals; amenorrhea was defined as no bleeding or spotting in the preceding 90 days. We employed multivariable regression to identify predictors of amenorrhea at 12 months. The predictor analysis only included women not using a levonorgestrel IUS in the month prior to study enrollment.
RESULTS: In the month before enrollment, 148 and 1566 women, respectively, had used and not used a levonorgestrel IUS. Prior users averaged 50±19 months of use before IUS placement; 38.4% of these women reported amenorrhea at 12 months. Amenorrhea rates for non-prior-users at 3, 6, 9 and 12 months were 0.2%, 9.1%, 17.2% and 16.9%, respectively. During the first 12 months, 29 (1.7%) women discontinued for bleeding irregularities; no women discontinued for amenorrhea. The only significant predictor of amenorrhea at 12 months was self-reported baseline duration of menstrual flow of fewer than 7 days vs. 7 or more days (18.2% vs. 5.2%, adjusted odds ratio 3.70 [1.69, 8.07]). We found no relationships between 12-month amenorrhea rates and age, parity, race, body mass index, baseline flow intensity or hormonal contraception use immediately prior to IUS placement.
CONCLUSIONS: Amenorrhea rates during the first year of levonorgestrel 52 mg IUS use are similar at 9 and 12 months. Amenorrhea at 12 months is most common among women with shorter baseline duration of menstrual flow.

4. Fraser IS. Non-contraceptive health benefits of intrauterine hormonal systems. *Contraception*. 2010 Nov;82(5):396-403. Available here.
ABSTRACT: Non-contraceptive health benefits are now recognized as an important aspect of the overall impact of all hormonal contraceptives. The levonorgestrel-releasing intrauterine systems (LNG IUS) are particularly effective at producing a number of health benefits for women using the LNG IUS as a contraceptive (reduced menstrual bleeding; reduced dysmenorrhea and the potential for prevention of a number of gynecological conditions in the longer term, such as iron-deficiency anemia, endometrial hyperplasia, uterine fibroids, acute episodes of pelvic inflammatory disease, endometriosis and perhaps others). The LNG IUS also has the potential to specifically treat a range of pre-existing gynecological conditions such as heavy menstrual bleeding due to a wide range of underlying causes, endometrial hyperplasia, uterine fibroids, adenomyosis, and endometriosis. These health benefits should be recognized as a key component in the decision-making process for individual women in choosing a specific type of hormonal or other contraceptive. Investment in research into the very substantial health benefits of hormonal contraceptives, such as the LNG IUS, has generally been ignored in comparison with the massive investment into understanding the often subtle or rare complications of hormonal contraceptive use. Both are important, but there is a real need to define more accurately those women who will benefit most from these health benefits.
5. Frenz AK, Ahlers C, Beckert V, Gerlinger C, Friede T. Predicting menstrual bleeding patterns with levonorgestrel-releasing intrauterine systems. *Eur J Contracept Reprod Health Care*. 2021;26(1):48-57. Available here.
PURPOSE: To develop a bleeding-pattern prediction model to inform counselling on amount and regularity of bleeding after levonorgestrel-releasing intrauterine system (LNG-IUS) placement.
MATERIALS AND METHODS: Fixed-cluster and regression-tree models were developed using bleeding data pooled from two clinical trials of LNG-IUSs. Models were trained and cross-validated on LNG-IUS 12 data, then applied to LNG-IUS 20 and LNG-IUS 8 data. Three clusters were generated for the fixed-cluster model: predominantly amenorrhoea; predominantly spotting; and predominantly bleeding. A random-forest model predicted the future-bleeding cluster, then the probability of cycle regularity was calculated. In the regression-tree model, women were assigned by the model to less- or more-bleeding groups.
RESULTS: With LNG-IUS 12 (n = 1351) in the fixed-cluster model, 70.4% of women were correctly classified. The correct classification rates for LNG-IUS 20 (n = 216) and LNG-IUS 8 (n = 1300) were 72.2% and 69.0%. The probability distribution for cycle regularity showed regular and irregular bleeding were best separated with LNG-IUS 12 data, and less well with LNG-IUS 20 and LNG-IUS 8 data. In the regression-tree model there was high variability in the more- and less-bleeding group distributions with LNG-IUS 12 data.
CONCLUSIONS: A fixed-cluster model predicted bleeding patterns better than a regression-tree model in women using LNG-IUS, yielding understandable, informative output.
6. Goldthwaite LM, Creinin MD. Comparing bleeding patterns for the levonorgestrel 52 mg, 19.5 mg, and 13.5 mg intrauterine systems. *Contraception*. 2019 Aug;100(2):128-131. Available here.
OBJECTIVE: Compare bleeding patterns for levonorgestrel 52 mg, 19.5 mg, and 13.5 mg intrauterine system (IUS) products using the World Health Organization Belsey definitions.
Study design: We extracted available data on bleeding patterns from published sources. Lower dose products had published data at 1 and 3 years; the 52 mg IUS had available data for 1, 2 and 3 years for

amenorrhea and 1 and 2 years for other bleeding patterns. We interpolated 2-year data for the lower dose products based on 1- and 3-year data and compared bleeding pattern rates using Fisher exact testing.
RESULTS: The studies evaluated bleeding patterns in 1700, 1566 and 1531 women using levonorgestrel 52 mg, 19.5 mg and 13.5 mg products, respectively. Amenorrhea rates were greater by 180 days after insertion for 52 mg IUS users (11%) as compared to 19.5 mg (5%, p<.0001) and 13.5 mg (3%, p<.0001). Infrequent bleeding rates were higher for 52 mg users by the end of year 1 (31%) compared to 19.5 mg (26%, p=.01) and 13.5 mg (20%, p<.0001). Irregular bleeding rates were higher with the lower dose products by 90 days after insertion with continued lower rates at the end of year 1 for 52 mg users (6%) compared 19.5 mg (17%, p<.0001) and 13.5 mg (23%, p<.0001). Frequent and prolonged bleeding patterns were similar over the first 2 years for all products, although the rates were statistically higher for levonorgestrel 13.5 mg IUS users compared to 19.5 mg and 52 mg IUS users (p≤.03 for all time points after 90-days post-insertion).
CONCLUSIONS: Levonorgestrel 52 mg IUS users have more amenorrhea and infrequent bleeding and less irregular bleeding compared to women using lower dose levonorgestrel IUS products.
Implications statement: All women considering levonorgestrel IUS placement should receive counseling on the differences in bleeding patterns related to the various available doses. Women who are interested in maximizing the likelihood of favorable bleeding should consider a levonorgestrel 52 mg IUS over the lower dose alternatives.

7. Polis CB, Hussain R, Berry A. There might be blood: a scoping review on women's responses to contraceptive-induced menstrual bleeding changes. *Reprod Health*. 2018;15(1):114. Available here.

1) INTRODUCTION: Concern about side effects and health issues are common reasons for contraceptive non-use or discontinuation. Contraceptive-induced menstrual bleeding changes (CIMBCs) are linked to these concerns. Research on women's responses to CIMBCs has not been mapped or summarized in a systematic scoping review.
2) METHODS: We conducted a systematic scoping review of data on women's responses to CIMBCs in peer-reviewed, English-language publications in the last 15 years. Investigator dyads abstracted information from relevant studies on pre-specified and emergent themes using a standardized form. We held an expert consultation to obtain critical input. We provide recommendations for researchers, contraceptive counselors, and product developers.
3) RESULTS: We identified 100 relevant studies. All world regions were represented (except Antarctica), including Africa (11%), the Americas (32%), Asia (7%), Europe (20%), and Oceania (6%). We summarize findings pertinent to five thematic areas: women's responses to contraceptive-induced non-standard bleeding patterns; CIMBCs influence on non-use, dissatisfaction or discontinuation; conceptual linkages between CIMBCs and health; women's responses to menstrual suppression; and other emergent themes. Women's preferences for non-monthly bleeding patterns ranged widely, though amenorrhea appears most acceptable in the Americas and Europe. Multiple studies reported CIMBCs as top reasons for contraceptive dissatisfaction and discontinuation; others suggested disruption of regular bleeding patterns was associated with non-use. CIMBCs in some contexts were perceived as linked with a wide range of health concerns; e.g., some women perceived amenorrhea to cause a buildup of "dirty" or "blocked" blood, in turn perceived as causing blood clots, fibroids, emotional disturbances, weight gain, infertility, or death. Multiple studies addressed how CIMBCs (or menstruation) impacted daily

activities, including participation in domestic, work, school, sports, or religious life; sexual or emotional relationships; and other domains.
CONCLUSIONS: Substantial variability exists around how women respond to CIMBCs; these responses are shaped by individual and social influences. Despite variation in responses across contexts and sub-populations, CIMBCs can impact multiple aspects of women's lives. Women 's responses to CIMBCs should be recognized as a key issue in contraceptive research, counseling, and product development, but may be underappreciated, despite likely – and potentially substantial – impacts on contraceptive discontinuation and unmet need for modern contraception.

8. Rademacher KH, Sergison S, Glish L, Maldonado LY, Mackenzie A, Nanda G, Yacobson I. Menstrual Bleeding Changes are NORMAL: Proposed Counseling Tool to Address Common Reasons for Non-Use and Discontinuation of Contraception. *Glob Health Sci Pract*. 2018;6(3)603-610. Available here.

A new family planning counseling tool uses the simple mnemonic device "NORMAL" to help family planning counselors and providers communicate to their clients key messages about menstrual bleeding changes associated with use of hormonal contraception and the copper IUD. The authors noted that development of a counseling tool could help health care providers better communicate with clients about potential bleeding changes associated with contraceptive use. The work described here was undertaken to address this gap.

9. Sergison JE, Maldonado LY, Gao X, Hubacher D. Levonorgestrel Intrauterine System associated amenorrhea: a systematic review and meta-analysis. *Amer Journal of Obstet and Gynecol*. 2018. Available here.

OBJECTIVE DATA: Amenorrhea is a polarizing noncontraceptive effect of the levonorgestrel intrauterine system. Composite amenorrhea prevalence estimates that summarize all clinical data for the first-year after insertion currently are not available. The purpose of this study was to investigate the validity of existing prevalence estimates by the systematic calculation of amenorrhea measures for a general population of levonorgestrel intrauterine system users and to provide 90-day interval point estimates for the first year of use.
STUDY: We identified clinical trials, randomized controlled trials, and randomized comparative trials that were published in English between January 1970 and September 2017 through electronic searches of 12 biomedical and scientific literature databases that included MEDLINE and ClinicalTrials.gov.
STUDY APPRAISAL AND SYNTHESIS METHODS: We considered studies that clearly defined amenorrhea per World Health Organization standards (the complete cessation of bleeding for at least 90 days), collected data from written daily bleeding diaries (the gold standard data collection technique on menstrual bleeding changes), and evaluated levonorgestrel intrauterine system devices that released 20 μg of levonorgestrel per day. We assessed study quality using guidelines established by the US Preventive Services Task Force and Cochrane handbook for systematic reviews of interventions. Two reviewers independently conducted all review stages; disagreements were resolved by a third reviewer. Where possible, data were pooled with the use of a random-effects model.
RESULTS: Of 2938 potentially relevant studies, we included 9 in our meta-analysis. We calculated amenorrhea prevalence, which was weighted for inter- and intrastudy variance, for 4 90-day intervals and months 0–12. Our results demonstrated few levonorgestrel intrauterine system users (0.2%; 95%

confidence interval, 0.0–0.4) experienced amenorrhea during the first 90 days after insertion; however, prevalence increased to 8.1% (95% confidence interval, 6.6–9.7) on days 91–180. Finally, 18.2% (95% confidence interval, 14.9–21.5) of users experienced amenorrhea for at least 1 90-day interval during the first year. Although interstudy heterogeneity limited reliability of days 181–271 and 272–365 measures, prevalence increased from 13.6% (95% confidence interval, 9.3–18.0) to 20.3% (95% confidence interval, 13.5–27.0), respectively.
CONCLUSION: Approximately 20% of levonorgestrel intrauterine system users experience amenorrhea during at least 1 90-day interval by the first year after insertion. This composite estimate is consistent with the product labeling and demonstrates that most users do not experience amenorrhea during the first year. These results provide accurate summary measures to facilitate counselling and informed method selection.

10. Maldonado LY, Sergison JE, Gao X, Hubacher D. Menstrual bleeding and spotting with the Levonorgestrel Intrauterine System (52 mg) during the first-year after insertion: a systematic review and meta-analysis. Am J Obstet Gynecol. 2020;222(5):451-468.e9. Available here.

BACKGROUND: Changes in menstrual bleeding concern many users of the 52 mg Levonorgestrel Intrauterine System. Prescribing information for Levonorgestrel Intrauterine System devices describe an overall decrease in bleeding and spotting days over time; however, estimates derived from a variety of existing clinical data are currently unavailable.
OBJECTIVE: The objective of the study was to systematically calculate the mean days of bleeding-only, spotting-only, and bleeding and/or spotting experienced by a population of reproductive-aged Levonorgestrel Intrauterine System users with normal regular menses prior to insertion during the first year of use.
Data Sources: We identified clinical trials, including randomized controlled trials and randomized comparative trials, as well as cohort studies published in English between January 1970 and November 2018 through searching 12 biomedical and scientific literature databases including MEDLINE and ClinicalTrials.gov.
STUDY ELIGIBILITY CRITERIA: We considered studies that reported data on Levonorgestrel Intrauterine System devices releasing 20 μg of levonorgestrel per day, collected daily menstrual bleeding data for at least 90 consecutive days, defined bleeding and spotting per World Health Organization standards and evaluated participants with normal regular menses prior to insertion.
STUDY APPRAISAL AND SYNTHESIS METHODS: We assessed study quality using established guidelines. Two reviewers independently conducted all review stages and rated the quality of evidence for each article; any disagreements were resolved by a third. Where possible, we pooled data using a random-effects model.
RESULTS: Among 3403 potentially relevant studies, we included 7 in our meta-analysis. We calculated the mean days of bleeding-only, spotting-only, and bleeding and/or spotting for the first four 90 day intervals after Levonorgestrel Intrauterine System insertion. Combined menstrual bleeding and/or spotting days gradually decreased throughout the first year, from 35.6 days (95% confidence interval, 32.2-39.1) during the first 90 day interval to 19.1 (95% confidence interval, 16.6-21.5), 14.2 (95% confidence interval, 11.7-16.8), and 11.7 days (95% confidence interval, 9.7-13.7) in the second, third,

and fourth intervals. Measures for bleeding-only and spotting-only days similarly decreased throughout the first year, with the greatest decreases occurring between the first and second intervals.
CONCLUSION: Our study provides 90 day reference period measures that characterize menstrual patterns for Levonorgestrel Intrauterine System users with normal regular menses prior to insertion during the first year of use. Our findings provide broader generalizability and more detail than patterns described in the prescribing information. These findings quantify an overall decrease in menstrual bleeding days with longer duration of use, with the greatest decrease occurring between months 3 and 6. Accurately establishing expectations with the Levonorgestrel Intrauterine System may improve informed selection and decrease discontinuation.

11. Schreiber CA, Teal SB, Blumenthal PD, Keder LM, Olariu AI, Creinin MD. Bleeding patterns for the Liletta® levonorgestrel 52 mg intrauterine system. *The European Journal of Contraception & Reproductive Health Care*. 2018;23(2):116-120. Available here.

PURPOSE: Evaluate bleeding patterns for the Liletta® levonorgestrel 52 mg intrauterine system (IUS) using the World Health Organization Belsey definitions.
MATERIAL AND METHODS: This prospective multicenter trial evaluates the efficacy and safety of Liletta® (Clinicaltrials.gov NCT00995150). We evaluated bleeding patterns for 1700 nulliparous and multiparous women using a daily diary completed by participants for the first 2 years and by questionnaire every 3 months thereafter. We assessed amenorrhea rates over 3 years and the proportion of subjects with infrequent, frequent, prolonged and irregular bleeding per 90-day reference period over 2 years for the entire study population as well as comparing nulliparous and parous women and obese and non-obese women.
RESULTS: Amenorrhea rates at 1 and 3 years in levonorgestrel 52 mg IUS users were 19 and 37%, respectively. The infrequent bleeding rate increased from 14% in the first 90 days to 30% at the end of Year 1, and was maintained at the same rate through Year 2. Frequent, prolonged and irregular bleeding declined to low levels by the end of the first year. Discontinuation for bleeding-related complaints occurred in 35 (2.1%, 95% CI 1.3–2.7%) women during the first 36 months; only one subject discontinued for amenorrhea (in Year 2). Outcomes did not vary for nulliparous versus parous or obese versus non-obese women.
CONCLUSIONS**:** Among Liletta users, amenorrhea and infrequent bleeding become more prevalent over time and amenorrhea rates continue to increase after the first year of use. Bleeding patterns do not differ significantly by parity or by obesity-status. Discontinuation for bleeding concerns is uncommon with this product.

12. Yang H, Wang S, Fu X, Lan R, Gong H. Effect of modified levonorgestrel-releasing intrauterine system in human adenomyosis with heavy menstrual bleeding. *J Obstet Gynaecol Res*. 2022;48(1):161-168. Available here.
AIM: The levonorgestrel-releasing intrauterine (LNG-IUS) system is an effective primary treatment for adenomyosis; however, it has high expulsion rates. We aimed to modify the system-allowing affixion to the myometrium-and evaluate the expulsion rate, effectiveness, and side effects in patients with adenomyosis and heavy menstrual bleeding.

METHODS: This study included patients with adenomyosis and heavy menstrual bleeding who underwent implantation of: a modified LNG-IUS (experimental group, n = 47); and the original system after gonadotropin-releasing hormone agonist treatment (control group, n = 47), between January 2014 and April 2016.
RESULTS: In the experimental group, two device expulsions occurred 12-18 months post implantation. In the remaining 45 patients, the system was safely removed after the 60-month validity period, and no extrauterine device movement or infection occurred. In the control group, downward displacement and expulsion of the device occurred in eight (17%) patients within 60 months. The 5-year total expulsion rates were 4.3% and 17.0% in the experimental and control groups, respectively ($p = 0.045$). There were significant changes in the pretreatment severity of dysmenorrhea, menstrual volume, uterine volume (cm3), and hemoglobin level in each group compared with after 1 year ($p < 0.01$ in all groups). The severity of dysmenorrhea, menstrual volume, uterine volume, and hemoglobin level after 1 year were similar between the two groups ($p > 0.05$ in all groups).
CONCLUSIONS: Use of the modified LNG-IUS is a safe, cost-effective, and simple method for reducing the downward movement and expulsion rate in patients with adenomyosis and heavy menstrual bleeding.

General Resources

These resources contain general information about the hormonal IUD

1. WHO Essential Medicines List addition of the hormonal IUD: available here.
This page contains information and peer review reports about the hormonal IUD, as well as the method's application for addition to the WHO Essential Medicines List, which was approved in 2015.

2. WHO Statement on hormonal IUD nomenclature: available here.
In this 2021 statement, the WHO proposes greater clarity for the terminology surrounding intrauterine devices, including a recommendation that the term "hormonal IUD" be used to categorize both the current levonorgestrel-releasing IUD and any new hormone-releasing IUDs that are under development. The Society for Family Planning released a complimentary statement in 2022 with additional recommendations for nomenclature, available here.

3. Announcement of introduction of hormonal IUD products to USAID and UNFPA product catalogs: available here.

In June 2021, the FP2030 global partnership announced the addition of two hormonal IUD products – Mirena™, supplied by Bayer AG, and Avibela™, supplied by Impact RH360 - to the USAID and UNFPA product catalogues, additions which enable broader hormonal IUD introduction in low- and middle-income countries.

4. Hormonal IUD Access Portal Resource Library: available here.

Developed and maintained by the Hormonal IUD Access Group, the Resource Library compiles published resources produced by the global community focused on perspectives on and experiences with the hormonal IUD, as well as costing, coordination, training, and marketing tools.

5. Training Resource Package for providers for the hormonal IUD: available here.

This module, co-developed by a consortium of organizations led by USAID, WHO, and UNFPA, is designed to train family planning service providers (primarily nurses, nurse-midwives, and PCPs) in low- and middle-income countries to accurately and effectively counsel clients about selecting and using the hormonal IUD.