Experiences of the use of the levonorgestrel intrauterine device for heavy menstrual bleeding: Device discontinuation rates and reasons for discontinuation among users at a regional hospital in the Western Cape - A seven-year review

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Background. Medical management for heavy menstrual bleeding (HMB) in low- and middle-income countries is limited. The National Institute for Health and Care Excellence recommends the levonorgestrel intrauterine device (LNG-IUD) as first-line management for HMB. However, since 2019, South Africa's (SA) Essential Medicines List (EML) guidelines have listed it as the last medical treatment option in the public health sector. An economic analysis conducted from a payer's perspective found the LNG-IUD dominant at 5 years and more cost-effective at 1 year than other medical treatment options. However, it would no longer be dominant if the 5-year discontinuation rate exceeded 40%. Assumptions about continuation rates of the LNG-IUD for HMB were made, as no local SA data are available.
Objectives. To assess the discontinuation rate of the LNG-IUD for HMB after 1 year and explore the reasons for discontinuation.
Methods. This was a retrospective, folder-based study of patients who received the LNG-IUD for HMB at Tygerberg Hospital, Cape Town, SA between 2014 and 2020.
Results. The hospital records of all women who received the LNG-IUD were reviewed. Incomplete records, duplications or prescriptions for contraception were excluded. Complete records were available for 100 patients, of whom 68 reported symptom improvement after 1 year and continued use. Thirty-two patients discontinued use, of whom eight experienced spontaneous expulsions and 24 requested removals. Reasons for discontinuation included ongoing symptoms (*n*=18), adverse effects (*n*=4) and the desire for fertility (*n*=2). Fourteen of the 24 patients who requested removal had a hysterectomy. The study showed a 68% continuation rate for the LNG-IUD, which is lower than in higher-income countries (82 - 88%). This rate is considered sufficient to endorse the affordability of LNG-IUD for HMB over 5 years.
Conclusion. Offering LNG-IUD as the primary treatment may potentially improve the continuation rate. Further research is needed to assess the feasibility of recommending LNG-IUD as the first-line treatment in national policy, following patient discussion.

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Heavy menstrual bleeding (HMB) and irregular or intermenstrual bleeding, collectively known as abnormal uterine bleeding (AUB), affect 5 - 13% of women in their reproductive years globally.[1] AUB has a major impact on women's lives, especially in low- and middle-income countries (LMIC), where management options are limited. For HMB, the available medical management options are systemic hormones, non-steroidal anti-inflammatory drugs or tranexamic acid.

The levonorgestrel intrauterine device (LNG-IUD) was added to South Africa's (SA) Essential Medicine List for public sector use in 2019. A health impact model showed that over 5 years, the LNG-IUD was cheaper than other medications.[2] However, the model assumed that patients using the LNG-IUD for a year would likely continue using it for 5 years. Since the discontinuation rate in SA is unknown, the model indicated that if women discontinue LNG-IUD usage within 1 year, it would no longer be the dominant strategy and would become the least cost-effective compared with conventional therapy.

The LNG-IUD is a 32 mm T-shaped plastic device containing 52 mg of levonorgestrel around the vertical stem. Levonorgestrel is released into the uterine cavity at a rate of 20 µg/day, decreasing to ~10 µg/day after 5 years.[3] Originally developed as a contraceptive device in the 1990s,[4] it has been extensively studied for its

non-contraceptive benefits such as the management of HMB, dysmenorrhea, small uterine fibroids, adenomyosis and endometrial hyperplasia. It is over 99% effective at preventing pregnancy for up to 7 years,[5] but is more expensive than other contraceptive methods in SA's public sector.

In most women with HMB, the cause is anovulation. The National Institute for Health and Care Excellence (NICE) guideline on HMB recommends pharmacological treatment based on history and physical examination only. Diagnostic interventions such as histology, hysteroscopy or ultrasound, are reserved for cases with a suggestive history of uterine abnormalities or a higher risk for cancer.[6] The guideline recommends the LNG-IUD as the first-line treatment for HMB. If unsuitable, alternatives include non-hormonal options (tranexamic acid or non-steroidal anti-inflammatory drugs) and hormonal options (combined oral contraception, cyclical oral progesterone or intramuscular progesterone preparations).[6] The LNG-IUD improves HMB in 92% of patients after six cycles.[7]

In the SA public sector, only essential medicines listed on the National Essential Medicines List (EML) may be prescribed. The ministerially appointed National Essential Medicines List Committee (NEMLC) reviews and recommends adding or removing medicines from the EML. The EML concept aligns with SA's Constitution ensuring that all South Africans have fair access to essential and affordable medicines.[8] The 1996 National Drug Policy and the 2023 National Department of Health's *Health Technology Assessment* (HTA) Methods Guide outline the criteria for selecting medicines for the EML.[9]

Medical management of HMB, excluding LNG-IUD, was the standard of care in SA's public sector until 2019. However, in 2015, an evidence review was conducted to determine whether LNG-IUD should be included in the Standard Treatment Guidelines (STGs) and EML for treating HMB.[10] The review found that 'LNG-IUD provides a clinically relevant reduction in menstrual blood loss due to HMB, with greater patient retention at 2 years than with medical therapy'. Despite superior evidence of the effectiveness of the LNG-IUD compared with conventional therapy, the committee decided not to recommend its inclusion at that time owing to uncertainty around affordability and potential for use for non-approved indications such as contraception.

Subsequently, a health technology assessment was conducted in 2018/2019 to further inform NEMLC's decision.[2] The recommendation was to provide the LNG-IUD as last-line pharmaceutical therapy for AUB in women failing the current standard of care as recommended in the Adult Hospital Level Standard Treatment Guidelines (STGs) and EML.[11] A cost-effectiveness analysis showed that the LNG-IUD is the dominant strategy at 5 years. The incremental cost per quality-adjusted life year for the LNG-IUD at one year was ZAR 6 443.26 for younger women in their fertile years and ZAR 19 235.43 for women in pre- or peri-menopausal stages. Women who want to fall pregnant require early removal of the LNG-IUD. Furthermore, a threshold analysis showed that the model shifts from being dominant to having an incremental cost for the additional benefit when the probability of patients discontinuing treatment reaches 60% or higher. There is a paucity of local data on the uptake, satisfaction and discontinuation of the LNG-IUD among SA women in the public sector.[2] The literature suggests that the LNG-IUD reduces menstrual blood loss by 86% after 3 months and 97% after 12 months.[12]

Continuation rates for the LNG-IUD in high-income countries, where it was primarily used for contraception, show high retention. In the US, among ~80 000 users, the continuation rate was 88% at 12 months, with abnormal menstruation being the most frequent complication.[13] A study from Finland,[14] where the LNG-IUD was provided free of charge, reported a discontinuation rate of 24.2 per 100 women years after 2 years (95% CI 21.7 - 26.9). The most common reason for discontinuation was bleeding irregularities (21%) and abdominal pain (20%). In a study from Switzerland,[15] the highest rate of discontinuation for the LNG-IUD was 18% within the first year, mostly among younger women.

For devices inserted to treat HMB, a study in Japan[16] showed an expulsion risk of 8.7%. In the Netherlands, the discontinuation rate at two years was 46%.[17] A retrospective study[18] from Brazil showed an 88.8% continuation rate for multiparous women and a 90.2% continuation rate for nulliparous women after 5 years. Another Brazilian study[19] found higher 1-year continuation rates for contraceptive users (85.8%) compared with those using it for HMB (83.4%).

A randomised controlled trial from SA,[20] comparing copper IUD with the LNG-IUD in women living with HIV disease, reported that LNG-IUD users were significantly more likely to continue using the method, had higher haemoglobin levels and found the method safe for women living with HIV. The overall continuation at 30 months for both copper IUD and LNG-IUD was 78%. Similar pilot studies conducted in Madagascar and Zambia reported satisfaction rates of 67 - 100% and 1-year continuation rates of 82 - 90%.[21]

The primary objectives of the present study were to assess the one-year discontinuation rate of the LNG-IUD for first-time users with HMB at Tygerberg Hospital, Western Cape, SA. The secondary objectives included exploring the reasons for discontinuation as well as the success rate, defined as satisfaction with the treatment and resolution of symptoms.

Methods

This was a retrospective, folder-based study of women who had the LNG-IUD inserted for non-contraceptive indications at Tygerberg Hospital in the Western Cape between January 2014 and December 2020. Eligible patients were diagnosed with HMB or AUB. AUB was defined as heavy, irregular and intermenstrual bleeding. HMB was defined as heavy regular menses. At the time, the FIGO PALM COEIN classification was not yet universally adopted, therefore patients were included regardless of the underlying cause.[22]

Before 2019, the LNG-IUD was prescribed on a named-patient basis at Tygerberg Hospital. The pharmacy and head of general specialist services kept a record of the names of women who received a device as part of routine clinical governance. Total population sampling was conducted, which involved reviewing the file of every woman who received a device for HMB as part of the audit. The audit focused on the initial visit and the 1-year follow-up visit. Patients with incomplete records and those who received the device for contraceptive reasons (e.g. patients with cardiac disease) were excluded from the audit.

Data was analysed using simple formulas within Excel 365 and exported for analysis in IBM SPSS (IBM Corp., USA).

Ethical approval was received from the Stellenbosch University Health and Research Ethics Committee (HREC), the CEO of Tygerberg Hospital and the head of the health department for the Western Cape Province (ref. no. S21/08/160).

Results

The folders of all women who received the LNG-IUD were reviewed and incomplete records, duplications or prescriptions for other reasons were excluded.

The median age of patients who received the LNG-IUD was 38 (range 13 - 65) years. One 13-year-old patient received a device due to intellectual impairment and HMB after menarche. Three patients received a device for postmenopausal bleeding after excluding significant pathology. The median parity was 2, with a range of 0 - 7. A total of 21 nulliparous patients received a device. On average, patients visited the Tygerberg Gynaecology outpatient department 2.6 times (range 1 - 8 visits). This count does not include visits before being referred to a tertiary hospital. Patients underwent extensive evaluations before receiving a device—all 100 patients had at least one ultrasound and cervical cytology smear. Additionally, 40% had a hysteroscopy before device insertion. 11% of patients had significant bleeding, requiring a blood transfusion at some point. Most of the devices (66%) were inserted by registrars, who received insertion technique training.

At the initial visit, the most common symptoms reported by patients were AUB (36%), a combination of pelvic pain with abnormal bleeding (27%), HMB (25%), dysmenorrhoea (7%), postmenopausal bleeding (3%) and chronic pelvic pain (2%). On average, patients experienced these symptoms for 4 years (range 3 months - 12 years) before LNG-IUD insertion. Most patients (62%) received a combination of treatments prior to device insertion including various combinations of intramuscular medroxyprogesterone, combined oral contraceptives (COC), progesterone-only pill (POP), non-steroidal anti-inflammatory drugs (NSAIDs) and tranexamic acid. Other patients only received one treatment modality, either intramuscular medroxyprogesterone (19%), tranexamic acid (7%), COC (5%), NSAIDs (4%) or POP (3%).

After 1 year, 68 patients continued using the device and reported an improvement in their symptoms, while 32 discontinued use. Of the 32 that discontinued use, 8 patients experienced spontaneous expulsion and 24 requested removals of the LNG-IUD. Unfortunately, specific reasons for the expulsion could not be ascertained owing to unclear record-keeping regarding ultrasound findings including the size, location and number of fibroids. Of the 24 patients who requested removal of the device, 18 cited ongoing symptoms as the reason for their request. Four patients reported adverse effects, mainly worsening abnormal bleeding (unscheduled bleeding) and headaches, while two patients desired fertility. Among the 24 patients who requested removal, 14 underwent surgical management in the form of hysterectomy. The histology of the 14 hysterectomies showed that 50% had leiomyomas, 43% had adenomyosis and 7% had no pathology.

Discussion

The study showed a 68% device continuation rate and a 32% discontinuation rate by the 1-year follow-up. Compared with high-income countries, the continuation rates were lower. Possible contributing factors for the lower continuation rates include insufficient time for the LNG-IUD to work, patient despondency from previous failed treatments, patient expectations not managed appropriately with inadequate counselling prior to insertion and hysterectomies booked too soon. Most devices were inserted by registrars, thus clinician experience may have also played a role. The two patients who desired fertility within the first year were inadequately counselled before insertion. The spontaneous expulsion rate was 8 per 100 women, which is similar to another real-world study conducted in Japan, which reported a cumulative incidence of expulsion of 8.7% after 1 year of insertion.[16] If all the patients who had spontaneous expulsion returned for reinsertion, the estimated continuation rate of 78% would be comparable to studies done in Brazil, where continuation rates were between 83 and 90%.[19] Patients in the current study who requested removal usually did so at the 6-week or 3-month follow-up, even though it is expected that there might be unscheduled bleeding for the first few months after device insertion.[24] Patients who opted for hysterectomy experienced a delay of a few months before their surgery date, during which time they continued to retain the device. At their pre-op admission, it was documented that their AUB had improved, but they still proceeded with the hysterectomy as they wanted definitive management, indicating that the device continuation rate may have been higher if more time was allowed for the device to work.

Despite the high discontinuation rates, the LNG-IUD resolved symptoms in 68% of cases, thereby avoiding surgical management. The total cost of surgical management and hospital stay exceeds that of one device, and the few data available in the literature suggest that LNG-IUD is potentially cheaper and more effective than surgical interventions.[25] A Cochrane review on progestogen-releasing intrauterine systems for HMB could only identify three studies that showed the LNG-IUD was more cost-effective than hysterectomy.[24] Patients requesting surgery in the current study also received a device as a last option, after undergoing extensive diagnostic evaluation and regular follow-up. If patients were offered a device earlier after their initial presentation, several costs could have been avoided, including the expenses related to diagnostic workups such as ultrasound, hysteroscopy and laboratory investigations, regular doctor visits, alternative treatment modalities, blood transfusion and economic costs associated with missed work days owing to symptoms and travel expenses to the hospital.

The main strength of the present study is that, to the best of our knowledge, it is the first reported review of retention rates of LNG-IUD for HMB in a local real-world setting. The study has some limitations such as incomplete patient records, its retrospective nature and a limited number of patients. Future prospective research is recommended, allowing for the collection of all relevant data from the outset and follow-up of all patients for more than a year. Additionally, the feasibility of early treatment of HMB with LMG-IUD should be examined.

Conclusion

The study demonstrated that the LNG-IUD is a suitable treatment option for SA women with HMB in the public sector, despite the lower continuation rate compared with higher-income countries. The 68% continuation rate at one year endorses the affordability of LNG-IUD as the dominant strategy compared with conventional therapy. Potential options to lower discontinuation rates include the provision of LNG-IUD as first-line management for HMB, managing initial breakthrough bleeding with NSAIDs and tranexamic acid and proactive management of patient expectations through shared decision-making. Surgical management should only be considered after sufficient time has been given for the device to work.

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Data availability statement. The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.

Conflicts of interest. None.

1. Harlow SD, Campbell OMR. Epidemiology of menstrual disorders in developing countries: A systematic review. Br J Obstet Gynaecol 2004;111(1):6-16. https://doi.org/10.1111/j.1471-0528.2004.00012.x
2. Miot J. LNG-IUD- health economics and budget impact analysis. Department of Health: South Africa; 2018:07-20. https://www.knowledgehub.org.za/system/files/elibdownloads/2020- 07/LNG-IUD%20_EconomicEvaluationReport_1December2018.pdf (accessed 13 July 2023).
3. Joo JK, Shin JH, Lee JR, et al. Levonorgestrel-releasing intrauterine system use in perimenopausal women. J Menopausal Med 2021;27(2):49-57. https://doi.org/10.6118/jmm.20038
4. Luukkainen T, Toivonen J. Levonorgestrel-releasing IUD as a method of contraception with therapeutic properties. Contracep 1995;52(5):269-276. https://doi.org/10.1097/aog.0000000000005466
5. Bayer. Mirena® IUD Effectiveness. Mirena US. https://www.mirena-us.com/about-mirena/mirena-effectiveness/ (accessed 10 January 2022).
6. National Institute for Health and Care Excellence. Heavy menstrual bleeding: assessment and management | Guidance | NICE. NICE; 2018. https://www.nice.org.uk/guidance/ng88 (accessed 18 August 2023)
7. Chen BA, Eisenberg DL, Schreiber CA, et al. Bleeding changes after levonorgestrel 52-mg intrauterine system insertion for contraception in women with self-reported heavy menstrual bleeding. Am J Obstet Gynecol 2020;S888(e1-S888.e6). https://doi.org/10.1016/j.ajog.2019.11.1288
8. The Constitution of the Republic of South Africa | South African Government. 1996. https://www.gov.za/documents/constitution/constitution-republic-south-africa-1996-1
9. National Department of Health. HTA Methods Guide, September 2023. https://knowledgehub.health.gov.za/ (accessed September 2024).
10. National Department of Health. Adult Hospital Medicine review: LNG-IUS for endometriosis. 2015. https://www.knowledgehub.org.za/ (accessed)
11. Department of Health. Hospital-Level (Adults) Standard Treatment Guidelines and Essential Medicines List 2nd Edition - 2019: Department of Health Knowledge Hub. 2019 https://knowledgehub.health.gov.za/elibrary/hospital-level-adults-standard-treatment-guidelines-and-essential-medicines-list-2nd (accessed 20 June 2023).
12. Andersson JK, Rybo G. Levonorgestrel-releasing intrauterine device in the treatment of menorrhagia. Br J Obstet Gynaecol 1990;97(8):690-694. https://doi.org/10.1111/j.1471-0528.1990.tb16240.x
13. Berenson AB, Tan A, Hirth JM. Complications and continuation rates associated with 2 types of long-acting contraception. Am J Obstet Gynecol 2015;212(6):761.e1-761.e8. https://doi.org/10.1016/j.ajog.2014.12.028
14. Saloranta TH, Gyllenberg FK, But A, et al. Free-of-charge long-acting reversible contraception: Two-year discontinuation, its risk factors, and reasons. Am J Obstet Gynecol 2020;223(6):886.e1-886.e17. https://doi.org/10.1016/j.ajog.2020.06.023
15. Bachofner M, Blickenstorfer K, Hutmacher J, et al. Intrauterine device continuation rates and reasons for discontinuation in a Central European clinic with a high standard of care and ultrasound follow-up: A retrospective cohort study. Eur J Contracept; Reprod Health Care 2018;23(6):407-414. https://doi.org/10.1080/13625187.2018.1539164
16. Harada T, Ota I, Kitawaki J, et al. Real-world outcomes of the levonorgestrel-releasing intrauterine system for heavy menstrual bleeding or dysmenorrhea in Japanese patients: A prospective observational study (J-MIRAI). Contracep 2022;116:22-28. https://doi.org/10.1016/j.contraception.2022.08.006
17. Beelen P, Den BMJ, Herman MC, et al. Predictive factors for failure of the levonorgestrel releasing intrauterine system in women with heavy menstrual bleeding. BMC Women's Health 2021;9:21(1). https://doi.org/10.1186/s12905-021-01210-x
18. 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 Organ Int Fed Gynaecol Obstet 2022;158(2):318-324. https://doi.org/10.1002/ijgo.13998
19. Miranda L, de SMH, Faundes A, Juliato C. Continuation rates of the 52-mg levonorgestrel-releasing intrauterine system according to the primary reason for its use. Rev Bras Ginecol E Obstetrícia 2021;43:291-296. https://doi.org/10.1055/s-0041-1726056
20. Todd CS, Jones HE, Langwenya N, et al. 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 randomised controlled trial. PLoS Med 2020;17(5):e1003110. https://doi.org/10.1371/journal.pmed.1003110
21. Danna K, Jaworski G, Rahaivondrafahitra B, et al. Introducing the hormonal intrauterine device in Madagascar, Nigeria, and Zambia: Results from a pilot study. Reprod Health 2022;19(1):4. https://doi.org/10.1186/s12978-021-01300-x
22. Munro MG, Critchley HOD, Broder MS, Fraser IS, FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Int J Gynaecol Obstet 2011;113(1):3-13. https://doi.org/10.1016/j.ijgo.2010.11.011
23. Brull E, Machado HC, Bahamondes L, Juliato CRT. Expulsion and continuation rates of the 52 mg levonorgestrel intrauterine system in adolescents and adult women. Eur J Contracept Reprod Health Care Off J Eur Soc Contracept 2023;28(4):210-215. https://doi.org/10.1080/13625187.2023.2215366
24. Lethaby A, Hussain M, Rishworth JR, Rees MC. Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. Cochrane Database Syst Rev 2015(4):CD002126. https://doi.org/10.1002/14651858.CD002126.pub3
25. Bhattacharya S, Middleton LJ, Tsourapas A, et al. Hysterectomy, endometrial ablation and Mirena® for heavy menstrual bleeding: A systematic review of clinical effectiveness and cost-effectiveness analysis. Health Technol Assess Winch Engl 2011;15(19):iii–xvi, 1-252. https://doi.org/10.18203/2320-1770.ijrcog20173145

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