




OPEN ACCESS

More than just contraception: the impact of the levonorgestrel-releasing intrauterine system on public health over 30 years

Kristina Gemzell-Danielsson,¹ Ali Kubba,² Cecilia Caetano,³ Thomas Faustmann,⁴ Eeva Lukkari-Lax,⁵ Oskari Heikinheimo ⁶

¹Department of Women's & Children's Health, Karolinska Institutet, and Karolinska University Hospital, Stockholm, Sweden

²Department of Gynecology, Guys and St Thomas NHS Foundation Trust, London, UK

³Medical Affairs, Bayer Consumer Care AG, Basel, Switzerland

⁴Medical Affairs, Bayer AG, Berlin, Germany

⁵Clinical Development, Bayer Oy, Espoo, Finland

⁶Department of Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

Correspondence to

Dr Cecilia Caetano, Medical Affairs, Bayer Consumer Care AG, 4002 Basel, Switzerland; cecilia.caetano@bayer.com

Received 18 November 2020

Revised 12 January 2021

Accepted 13 January 2021

Published Online First

29 January 2021



© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Gemzell-Danielsson K, Kubba A, Caetano C, et al. *BMJ Sex Reprod Health* 2021;**47**:228–230.

ABSTRACT

Universal access to sexual and reproductive health services is essential to facilitate the empowerment of women and achievement of gender equality. Increasing access to modern methods of contraception can reduce the incidence of unplanned pregnancy and decrease maternal mortality. Long-acting reversible contraceptives (LARCs) offer high contraceptive efficacy as well as cost-efficacy, providing benefits for both women and healthcare systems. The levonorgestrel-releasing intrauterine system (LNG-IUS) first became available in 1990 with the introduction of Mirena (LNG-IUS 20), a highly effective contraceptive which can reduce menstrual blood loss and provide other therapeutic benefits. The impact of the LNG-IUS on society has been wide ranging, including decreasing the need for abortion, reducing the number of surgical sterilisation procedures performed, as well as reducing the number of hysterectomies carried out for issues such as heavy menstrual bleeding (HMB). In the context of the COVID-19 pandemic, Mirena can provide a treatment option for women with gynaecological issues such as HMB without organic pathology, minimising exposure to the hospital environment and reducing waiting times for surgical appointments. Looking to the future, research and development in the field of the LNG-IUS continues to expand our understanding of these contraceptives in clinical practice and offers the potential to further expand the choices available to women, allowing them to select the option that best meets their needs.

BACKGROUND

Sexual and reproductive health (SRH) constitutes a fundamental human right and plays a vital role in the empowerment of women and helping achieve

gender equality. Universal access to SRH services is essential to achieving this objective.^{1,2} Increasing access to modern, effective methods of contraception can reduce the incidence of unplanned pregnancy, decrease maternal mortality, and can also contribute to fighting poverty.^{1,3,4}

Long-acting reversible contraceptives (LARCs), such as implants, and hormonal and non-hormonal intrauterine devices (IUDs), are not only highly effective at preventing unintended pregnancy and subsequent abortion but are also cost-effective options that provide benefits for both women and healthcare systems.

Mirena (Bayer AG, Berlin, Germany) was the first levonorgestrel-releasing intrauterine system (LNG-IUS) of its kind. Developed by the Population Council's International Committee for Contraception Research, Mirena (also termed LNG-IUS 20 based on the average in vivo LNG release rate over the first year⁵) became available in 1990 in Finland under the name Levonova. Mirena is a highly effective contraceptive, with a long-lasting but reversible effect that does not require a daily routine. It also reduces menstrual blood loss, which women often find beneficial. Additionally, Mirena has therapeutic benefits; it is an effective treatment for heavy menstrual bleeding (HMB) without an organic cause and dysmenorrhoea, as well as providing endometrial protection for peri- and postmenopausal women receiving menopausal hormone therapy.

The impact of the LNG-IUS on society has been wide ranging: from decreasing the need for abortion (ie, unwanted pregnancy),^{6,7} to reducing the number of surgical sterilisation procedures

performed,⁸ as well as reducing the number of hysterectomies carried out for issues such as HMB without an organic cause,^{9,10} allowing women to avoid an invasive surgical procedure and maintain their fertility.

NOW MORE THAN EVER: THE ROLE OF LARCS IN THE CHANGING HEALTHCARE LANDSCAPE

With the COVID-19 pandemic causing widespread disruption to the provision of healthcare, including contraceptive services and supply chains, there are bound to be concerns regarding the potential for increased unintended pregnancies.¹¹

Unlike short-acting methods such as oral contraceptive pills, long-acting methods provide effective contraception for years after a single intervention that can mitigate concerns regarding access to and availability of contraceptive services.

As we seek to preserve capacity in healthcare systems and save valuable resources while increasing access to all, a shift towards medical treatment delivered in community settings for issues such as HMB is taking place in clinical practice. Medical options are less invasive than surgical treatments, generally preserve fertility, and in most cases can be prescribed and implemented rapidly and easily. In the context of the COVID-19 pandemic, the therapeutic benefits of Mirena provide an option for treating women with conditions such as HMB without an organic cause or dysmenorrhoea that minimises exposure to the hospital environment and reduces lengthy waits for surgical appointments.

BEYOND GYNAECOLOGICAL PRACTICE: HOW EFFECTIVE CONTRACEPTION CAN EMPOWER WOMEN

Increasing awareness and access to contraception can help women in low-income settings, by mitigating poverty and challenging gender inequalities. By providing discrete, effective contraception and reducing menstrual bleeding in the majority of users, the LNG-IUS can facilitate women's increased productivity and participation in society, as well as reducing some of the issues caused by limited access to sanitary protection (menstrual poverty) and providing freedom from social stigma and exclusion.

Effective contraception for women living with comorbidities, such as HIV/AIDS or anaemia, is also vital to ensure a well-timed pregnancy that occurs when they are in optimal health and is not associated with further negative health consequences. Not only does Mirena contribute to preventing unplanned pregnancy in these women, but the associated decrease in menstrual blood loss can have the additional benefit of reducing exposure to infected blood in the context of HIV/AIDS,^{12,13} and improving the body's iron stores in the context of anaemia.

The reduced number of visits to healthcare providers (eg, to obtain repeat prescriptions) and reduced need to purchase sanitary protection also decreases the

economic burden both to women and the healthcare system.

By decreasing the amount of sanitary protection, packaging and other waste products, the LNG-IUS and other long-acting methods can also be seen as 'green contraceptives' that reduce the traffic of non-biodegradable items to landfill sites.

THE FUTURE OF THE LNG-IUS AND PUBLIC HEALTH

With the popularity of LARCs, especially the LNG-IUS, continuing to increase it is good to know that research in this field is keeping pace. Real-world studies continue to deepen our understanding of how the LNG-IUS performs in clinical practice and further controlled trials offer the potential to expand or extend its use. Additionally, next-generation IUDs are being explored, which could further expand the options available to women, allowing them to choose the method that is best suited to their needs.¹⁴ Moving forward, it seems reasonable to hope that with further developments and ongoing initiatives, access to LARCs will become a possibility for women across the globe.

Contributors Kristina Gemzell-Danielsson, Ali Kubba, Oskari Heikinheimo and Cecilia Caetano developed the concept for the manuscript. Thomas Faustmann and Eeva Lukkari-Lax critically reviewed and refined the concept. All authors reviewed each subsequent draft and provided detailed feedback. All authors reviewed and approved the final draft for submission.

Funding The authors would like to acknowledge Highfield, Oxford, UK for providing medical writing assistance with funding from Bayer AG.

Competing interests Kristina Gemzell-Danielsson has been an ad hoc advisory board member or invited to give presentations for Merck (MSD), Bayer, Exelgyn, Actavis, Gedeon Richter, Mithra, Exeltis, Ferring, Natural Cycles, Azanta, Gynuity, Campus Pharma and HRA-Pharma. Oskari Heikinheimo serves occasionally on advisory boards for Bayer AG, Gedeon Richter, Sandoz and Vifor Pharma, and has lectured at educational events organised by these companies. Ali Kubba has taken part in sponsored educational activity and served on advisory boards for pharmaceutical companies including Bayer, Merck and Exeltis. Thomas Faustmann is an employee of Bayer AG, Berlin, Germany. Cecilia Caetano is an employee of Bayer Consumer Care AG, Basel, Switzerland. Eeva Lukkari-Lax is an employee of Bayer Oy, Espoo, Finland.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-

commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Oskari Heikinheimo <http://orcid.org/0000-0002-8671-130X>

REFERENCES

- European Parliamentary Assembly. Resolution 2331. Empowering women: promoting access to contraception in Europe, 2020. Available: [http://www.europeanrights.eu/public/atti/Resolution_2331_\(2020\)_ENG.pdf](http://www.europeanrights.eu/public/atti/Resolution_2331_(2020)_ENG.pdf) [Accessed 11 Sep 2020].
- United Nations. Sustainable Development Goals. Available: <https://www.un.org/sustainabledevelopment/sustainable-development-goals/> [Accessed 11 Sep 2020].
- Brunson J. Tool of economic development, metric of global health: promoting planned families and economized life in Nepal. *Soc Sci Med* 2020;254:112298.
- Sawhill IV, Guyot K. Preventing unplanned pregnancy: lessons from the States Brookings Institution, 2019. Available: <https://www.brookings.edu/wp-content/uploads/2019/06/Preventing-Unplanned-Pregnancy-2.pdf> [Accessed 11 Sep 2020].
- Hofmann BM, Apter D, Bitzer J, *et al.* Comparative pharmacokinetic analysis of levonorgestrel-releasing intrauterine systems and levonorgestrel-containing contraceptives with oral or subdermal administration route. *Eur J Contracept Reprod Health Care* 2020;25:417–26.
- Peipert JF, Madden T, Allsworth JE, *et al.* Preventing unintended pregnancies by providing no-cost contraception. *Obstet Gynecol* 2012;120:1291–7.
- Pohjoranta E, Suhonen S, Gissler M, *et al.* Early provision of intrauterine contraception as part of abortion care—5-year results of a randomised controlled trial. *Hum Reprod* 2020;35:796–804.
- Grimes DA, Mishell DR. Intrauterine contraception as an alternative to interval tubal sterilization. *Contraception* 2008;77:6–9.
- Dhamangaonkar PC, Anuradha K, Saxena A. Levonorgestrel intrauterine system (Mirena): an emerging tool for conservative treatment of abnormal uterine bleeding. *J Midlife Health* 2015;6:26–30.
- Meaidi A, Kuhr Skals R, Alexander Gerds T, *et al.* Decline in Danish use of oral tranexamic acid with increasing use of the levonorgestrel-releasing intrauterine system: a nationwide drug utilization study. *Contraception* 2020;101:321–6.
- Ferreira-Filho ES, de Melo NR, Sorpreso ICE. Contraception and reproductive planning during the COVID-19 pandemic. *Expert Rev Clin Pharmacol* 2020;13:615–22.
- Heikinheimo O, Lehtovirta P, Suni J, *et al.* The levonorgestrel-releasing intrauterine system (LNG-IUS) in HIV-infected women—effects on bleeding patterns, ovarian function and genital shedding of HIV. *Hum Reprod* 2006;21:2857–61.
- Kakaire O, Tumwesigye NM, Byamugisha JK, *et al.* Acceptability of intrauterine contraception among women living with human immunodeficiency virus: a randomised clinical trial. *Eur J Contracept Reprod Health Care* 2016;21:220–6.
- Grandi G, Farulla A, Sileo FG, *et al.* Levonorgestrel-releasing intra-uterine systems as female contraceptives. *Expert Opin Pharmacother* 2018;19:677–86.