Review of the safety, efficacy and patient acceptability of the levonorgestrel-releasing intrauterine system

Chandra Kailasam 1
David Cahill 2

1 Bristol Centre for Reproductive Medicine, Southmead Hospital, Bristol, UK; 2 Dept of Obstetrics and Gynaecology, University of Bristol, St Michael's Hospital, Bristol, UK

Correspondence: Chandra Kailasam
Bristol Centre for Reproductive Medicine, Southmead Hospital, BS10 9NB, UK
Email: chandra.kailasam@nbt.nhs.uk

Abstract: The levonorgestrel-containing intrauterine system is an extremely effective, reversible and safe form of long-term yet reversible birth control. In view of its efficacy, it is a safer alternative to permanent contraceptive methods such as sterilization. It is especially useful in situations where use of estrogen-containing contraceptives is contraindicated. While menstrual disturbances are a common side effect, proper counseling improves compliance. In addition to its contraceptive effect, the levonorgestrel intrauterine system offers potential therapeutic benefits in other clinical contexts, including menorrhagia, symptomatic fibroids, endometriosis, and endometrial protection.

Keywords: intrauterine device, levonorgestrel intrauterine device, contraception

Introduction

The levonorgestrel-containing intrauterine device is a very effective and safe form of reversible long-term birth control. In addition to its contraceptive effect, it offers potential non-contraceptive therapeutic benefits.

We reviewed the efficacy, safety and clinical applications of the levonorgestrel-containing intrauterine device (LNG-IUS, Mirena®). The search included the PubMed, Cochrane Controlled Trials Register and WHO publications on contraception. We included randomized controlled trials, controlled clinical trials and systematic/clinical reviews published in the English language in peer-reviewed journals and guidelines published by the WHO and the National Institute for Clinical Excellence (NICE). The key words used to search data included IUD, IUD-IUS, contraception.

Rationale for IUD

Among the several long-acting contraceptive methods, the intrauterine device (IUD) is the most popular and overall it is second most popular contraceptive method worldwide after sterilization (Progress in Reproductive Health Research 2002). The popularity of the IUD stems from the fact that in addition to providing long-lasting, highly effective, rapidly reversible contraception, it has no known effects on breast milk or breastfeeding; it does not interfere with sexual intercourse or with any type of medication; it is widely available throughout the world, it can used by women of any age or parity and following an abortion or miscarriage and finally once in place, its user can more or less forget about it with no further costs (WHO 2007). There is no evidence that use of IUD increases tubal infertility (Grimes 2000).
In addition to its contraceptive effect, the LNG-IUS offers potential therapeutic benefits in other clinical contexts, including menorrhagia, symptomatic fibroids, endometriosis, and endometrial suppression.

**Development and pharmacology of Mirena® intrauterine contraceptive device**

The aim of progesterone-releasing intrauterine systems initially was to reduce IUCD expulsion, by the addition of ‘uterine relaxing hormones’ (Odlind 1996). This led to the development of Progestasert® (the first hormonally impregnated device releasing 65 μg of progesterone per day) and Mirena® LNG-IUS (releasing 20 μg of levonorgestrel per day).

Mirena® LNG-IUS was developed by Leiras Oy, Turku, Finland, and was launched first in Finland in 1990. It has a T-shaped body (32 × 32 mm) made of polyethylene with an elastomer sleeve consisting a 1 to 1 mixture of polydimethylsiloxane and 52 mg of levonorgestrel mounted around its vertical part. The sleeve is covered with a drug-release-controlling membrane of medical grade polydimethylsiloxane that releases levonorgestrel over an extended time of up to 5 years at a practically constant rate. The initial release rate of levonorgestrel is 20 μg per 24 h, and at the end of 5 years the release rate is still above 10 μg per 24 h (Lähteenmäki et al 2000). The distal end of the T-frame contains 2 removal threads. The device also contains barium sulfate, which makes it visible on X-ray examination. Local delivery of LNG results in low but detectable serum levels of LNG (0.1–0.4 ng/mL), much lower than peak levels observed with LNG-IUS results in low but detectable serum levels of LNG makes it visible on X-ray examination. Local delivery of levonorgestrel (LNG) results in extensive decidualization of endometrial stromal cells, atrophy of the glandular and surface epithelium, and changes in vascular morphology (suppression of spiral artery formation and presence of large dilated vessels) along with down-regulation of sex steroid receptors in all cellular components (Guttinger and Critchley 2007). The result is a thin decidualized endometrium, an environment that is unsuitable for sperm survival, fertilization and implantation. The endometrial changes develop in the first month after insertion and persist until the device is removed (Guttinger and Critchley 2007). By inactivating the endometrium and suppressing proliferation, it also decreases menstrual blood loss (MBL) and pain. The levonorgestrel released locally alters the quality of cervical mucus, making it hostile to the movement of sperm through the cervix (Jonsson et al 1991). Thus, the number and quality of sperm reaching the site of fertilization in the tube seems to be reduced in LNG-IUS users.

Ovulation is not suppressed as it has little influence on ovarian activity; women have normal estradiol values from the time of insertion through its 5-year life span (Luukkainen et al 1990) ensuring that the LNG-IUS would not expose the user to hypoestrogenism leading to osteoporosis (Bahamondes et al 2006). Although the anovulation rate is almost 85% at the beginning of use, this rate falls to less than 15% at the end of the first year (Nilsson et al 1980). As ovulatory cycles occur in most, even amenorrhoeic, users, ovulation suppression is not the primary mode of action (Lähteenmäki et al 2000). Serum levels of LNG are usually not sufficient to suppress ovulation, as a release of 50 μg per 24 h of LNG would be necessary to completely inhibit ovulation (Lähteenmäki et al 2000). The local progestative effect of the LNG-IUS on the endometrium manifests within a period of 3 months and over after insertion (Zalel et al 2003). This means that it can take up to 3 months for the initial menstrual disturbances to settle. Women should be accordingly counseled so as to
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decrease the discontinuation rate of the LNG-IUS due to the
initial menstrual disturbances.

**Insertion**
The LNG-IUS can be inserted at any time in the menstrual
cycle if it is reasonably certain the woman is not pregnant.
However compared with the Cu-IUD that is effective imme-
diately, it takes 7 days to provide effective contraceptive
protection. Hence additional contraception or abstinence
should be advised for 7 days after inserting the LNG-IUS
unless inserted in the first 7 days of the cycle or when
switching from a different method of contraception unless
the current contraceptive method is still effective (FSRH
Guidance 2007). While the insertion procedure may be
relatively easy compared with insertion of other IUDs, some
women may need analgesia and cervical dilatation (Jensen
et al 2008). IUDs can be inserted immediately after first or
second trimester abortion and from 4 weeks post partum,
irrespective of the mode of delivery (El Tagy 2003; NICE
2005). In complicated valvular heart disease, prophylactic
antibiotics should be used at the time of insertion to prevent
endocarditis (WHO 2004).

**Contraindications**
The LNG-IUS should be avoided in patients with unexplained
vaginal bleeding. It is preferably avoided in the presence of
sexually transmitted diseases such as chlamydia and gonorrhea.
In a systematic review, Mohllajee et al (2006) reported
that with IUD insertion in the presence of chlamydia infection
or gonorrhea, subsequent pelvic inflammatory disease (PID)
rates were 0%–5%, compared with insertion in the absence
of infection (0%–2%).

**Therapeutic benefits of the LNG-IUS**

**Contraceptive benefits**
The LNG-IUS provides highly effective contraception and
is equally efficient in all age groups with the risk of failure
similar throughout the life span of the device. The 5-year
cumulative pregnancy rate per 100 users is 0.5 and the
5-year Pearl rate 0.11 (Backman et al 2004). The cumulative
pregnancy rate at 5 years is <0.5% (Thonneau and Almont
2008). Its use in lactating women provides highly effec-
tive and acceptable contraception and does not negatively
influence breast-feeding or the growth and development of
breast-fed infants (Shaamash et al 2005). Women with an
intrauterine pregnancy with an LNG-IUS in situ should be
advised to have the LNG-IUS removed before 12 completed
weeks’ gestation whether or not they intend to continue the
pregnancy (NICE 2005).

It can be safely used in women with a past history of PID
or ectopic pregnancy, women with fibroids, and in young
nulliparous women (WHO 2004). The LNG-IUS is medi-
cally safe for women to use if oestrogen is contraindicated
(NICE 2005).

The LNG-IUS is both safe and extremely efficacious for
use in nulliparous women with no greater risk of perforation
or expulsion (Prager and Darney 2007). In fact the LNG may
be protective against infection via thickening of the cervical
mucus (Jonsson et al 1991) and decreased menstrual blood
loss. Nulliparous users are at no increased risk for infection
and infertility than multiparous users and it is safe to offer
post-abortion placement of the LNG-IUS to nulliparous
women (Prager and Darney 2007). In a randomized study of
young nulliparous women (Suhonen et al 2004), the safety
and acceptability of the LNG-IUS for contraception was
observed to be as good as with oral contraceptives, with a
high continuation rate. The discontinuation rate in the first
year of the LNG-IUS is 20%, indicating that acceptability
is similar among nulliparous and parous women (Prager and
Darney 2007).

In contrast to the copper IUDs, the LNG-IUS is not
recommended for emergency contraception. The absence of
embryotoxic copper ions and the relatively low serum levels
of levonorgestrel obtained immediately following LNG-IUS
insertion compared with standard hormonal emergency
contraception suggests that it may not be effective (ESHRE
Capri Workshop Group 2008).

The LNG-IUS has been favorably compared with other
contraceptive methods. In randomized comparative trials
(RCTs), pregnancy rates were significantly lower with
the LNG-IUS than with copper devices (Sivin et al 1991;
Andersson et al 1994; Pakarinen et al 2003), though a
Cochrane review of 21 RCTs (French et al 2004) concluded
that there is insufficient evidence to conclude that the
LNG-IUS is more effective than copper IUDs. In a recent
systematic review of the Cochrane Library for all IUD-related
reviews (Grimes et al 2007), the LNG-IUS was found to
have comparable efficacy to that of IUDs with >250 mm²
of copper, immediate post-partum, and post-abortal inser-
tion appeared safe and effective and prophylactic antibiot-
ics at the time of insertion appeared unwarranted except in
populations with a high prevalence of sexually transmitted
infections (STIs). The LNG-IUS and tubal sterilization have
comparable high effectiveness, with the LNG-IUS a safer
option, and all women, particularly young women, who are
at high risk for sterilization regret, should be encouraged to consider the LNG-IUS in place of a surgical procedure that is potentially irreversible (Grimes and Mishell 2008).

Repeated use of the device has had favorable outcomes. The initial bleeding problems that are frequently observed after the insertion of the first LNG-IUS do not recur after an immediate change from the first IUS to the second IUS (Rönnerdag and Odlind 1999). In contrast to other long-acting progestin only contraceptives, LNG-IUS has no effect on bone mineral density (Inki et al 2007).

There does not seem to be a delay in the return of fertility following removal of the Mirena® coil with conception rates 79.1/100 women at 12 months after removal (Andersson et al 1992).

Non-contraceptive benefits of the LNG-IUS

Menorrhagia

Available medical treatments for menorrhagia include the LNG-IUS, non-steroidal anti-inflammatory drugs, antifibrinolytic drugs, progestogens, oral contraceptives, and danazol. The choice of medical treatment can depend on individual factors such as requirement for contraceptive and dysmenorrhea. However, first-line therapy with drugs has variable efficacy and, at best, oral medication reduces menstrual blood loss by only 50% (Istre and Qvigstad 2007). The immediate and intense suppression of the endometrium leads to over 90% reduction of menstrual blood loss over a period of 12 months (Anderson and Rybo 1990) along with significant beneficial increase in hemoglobin and ferritin levels (Xiao et al 2003).

In a randomized controlled trial (Hurskainen et al 2004) health-related quality-of-life outcomes associated with the LNG-IUS and hysterectomy was similar with financial benefits in favor of the LNG-IUS. In a Cochrane review of 10 randomized control trials (Lethaby et al 2005), the LNG-IUS was more effective than other medical interventions, with a 90% reduction from baseline in menstrual blood loss. Although the LNG-IUS results in a smaller reduction in menstrual blood loss than endometrial ablation, there are no differences in the women’s rates of satisfaction or quality of life. In a Cochrane systematic review of 8 trials (Marjoribanks et al 2006), use of LNG-IUS was more cost effective, with levels of satisfaction and quality of life with an LNG-IUS system similar to those after surgical treatment such as transcervical endometrial resection or balloon ablation or hysterectomy. Further long-term studies are needed to compare the effectiveness of the LNG-IUS against conservative surgical treatments.

Inherited bleeding disorders may be the cause of menorrhagia in up to 13% of women and the LNG-IUS is an effective treatment option in such women (Kadir and Chi 2007), as medical treatments may otherwise be contraindicated and surgery carries additional risks. It is also an effective treatment for menorrhagia in women receiving oral anticoagulation (Pisoni 2005).

The LNG-IUS is cost effective in the treatment of menorrhagia, while offering reliable contraception. Compared with oral contraceptives and surgical treatment, treatment strategies employing the LNG-IUS are the most cost-effective in managing dysfunctional uterine bleeding in women not desiring additional children (Blumenthal et al 2006). LNG-IUS followed by endometrial ablation may be the most cost-effective treatment for menorrhagia, when compared with immediate surgery (Clegg et al 2007).

Endometriosis

The LNG-IUS delivers significant amounts of levonorgestrel into the peritoneal fluid (Lockhat et al 2005) and this may explain the pain relief in patients with peritoneal endometriosis.

Medical treatments that are based on the reduction of lesions or on ovarian estrogen suppression, cause profound hypoestrogenism inducing a decrease in bone mineral density and hence treatment is limited 6 months (d’Arcangues 2006), although longer treatment with add-back hormone therapy is possible. In addition, there are systemic side effects, and the need for regular administration could affect compliance. In such patients the LNG-IUS can be a useful alternative.

In a systematic review on the use of LNG-IUS for symptomatic endometriosis following surgery, post-operative use of the LNG-IUS reduced the recurrence of painful periods in women who have had surgery for endometriosis while there was insufficient evidence for other benefits such as reduced likelihood of further surgery for endometriosis and improved long-term fertility (Abou-Setta et al 2006). In a randomized controlled trial, insertion of the Mirena® coil significantly reduced the medium-term risk of recurrence of moderate or severe dysmenorrhea compared with expectant management following operative laparoscopy for symptomatic endometriosis (Vercellini et al 2003). In another RCT (Petta et al 2005), LNG-IUS and depot-GnRH-analog were equally effective in significantly decreasing endometriosis-related pain. However an advantage with LNG-IUS is the fact that it does not provoke hypoestrogenism while being effective for 5 years. There is insufficient information on
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the efficacy of the LNG-IUS in the possible prevention of endometriosis recurrence.

Adenomyosis
The LNG-IUS has been reported to be useful in women with adenomyosis, although studies have been limited by small numbers. Its use may significantly reduce pain and abnormal bleeding associated with adenomyosis along with significantly reduced adenomyotic lesions, as evaluated by the thickness of the junctional zone (Braghetoa et al 2007). A long-term study showed that the use of the LNG-IUS led to significant pain relief, reduction in the uterine volume and menstrual blood loss volume, and improvements in hematologic indices in patients with adenomyosis (Cho et al 2008); however, there was a gradual increase in uterine volume, pain scores, and pictorial blood loss assessment chart scores at 2 years after insertion and the authors suggested that to maintain the efficacy of the LNG-IUS for the management of adenomyosis, a new device might be needed after 3 years.

Fibroids
The LNG-IUS appears safe and effective in the treatment of menorrhagia in women with uterine cavities distorted by submucosal fibroids (Soysal and Soysal 2005). A recent review (Kaunitz 2007) of the published literature suggested that, in women with uterine fibroids, with or without menorrhagia, the LNG-IUS reduces menstrual blood loss and likely reduces menstrual pain while maintaining high contraceptive efficacy. However, expulsion rates are higher and there is inconsistent evidence on whether the LNG-IUS decreases uterine/fibroid dimensions. Although symptomatic improvement may not be uniform, these findings indicate that the LNG-IUS is a useful therapeutic option for selected women with menstrual symptoms associated with uterine fibroids.

Endometrial protection
The targeted delivery of progestagen in the uterine cavity is a preferred route in women who need endometrial protection due to the absence of systemic side effects along with high efficacy.

Use of oral tamoxifen as adjuvant therapy for women with breast cancer has improved survival rates. However, it exerts weak estrogenic effect on the endometrium and hence is associated with endometrial pathologies such as polyps, hyperplasia and endometrial cancer. In view of its progestational effects, the LNG-IUS is an effective prophylaxis in the prevention of endometrial pathology in women receiving tamoxifen (Chan et al 2007; Gardner et al 2000).

The LNG-IUS adequately suppresses the endometrium during hormone replacement therapy with estrogens (Riphagen et al 2000) while avoiding the potential adverse systemic effects of progestogens. A literature review by Riphagen et al (2000) and a subsequent long-term study of post-menopausal women by Wildemeersch et al (2007a) highlighted the endometrial protection offered by the LNG-IUS in women receiving estrogen replacement therapy.

The LNG-IUS has been investigated in the treatment of non-atypical and atypical hyperplasia as a useful alternative to hysterectomy especially in younger women who still wish to become pregnant or in women who refuse operation or are in poor health. While studies (Wildemeersch et al 2007b; Varma et al 2008) suggest it may be an effective option for suppressing the endometrium, there have been reports of progression of atypical endometrial hyperplasia to adenocarcinoma despite intrauterine progesterone treatment with the levonorgestrel-releasing intrauterine system (Kresowick et al 2008). Hence extreme caution should be exercised and we need robust randomized controlled trials to evaluate the effectiveness of the LNG-IUS in treating endometrial hyperplasia.

Side effects
The adverse events of interest fall into 2 categories: those related to an intrauterine device, such as dysmenorrhea, irregular bleeding, ectopic pregnancy, and expulsion of the device; and those related to progestogens, such as bloating, weight gain, and breast tenderness. In a systematic review of the literature, reported cumulative discontinuation rates with the LNG-IUS were as high as 24% after 1 year and 33% after 2 years (NICE 2005).

Bleeding complications
Overall, the commonest reason for discontinuation is unacceptable bleeding patterns.

Up to 60% of women stop using the LNG-IUS within 5 years, which is similar to other IUDs, unacceptable vaginal bleeding and pain being the most common reasons for discontinuation (NICE 2005). Even though irregular bleeding and spotting are common during the first 6 months following LNG-IUS insertion, oligomenorrhea or amenorrhea is likely by the end of the first year of LNG-IUS use (NICE 2005). Since frequent irregular bleeding is common during the first few months following system insertion, proper counseling of the patient about possible bleeding patterns is crucial in
order to minimize premature LNG-IUS removals. Since amenorrhea is an expected outcome (occurring in about 20% of users at 12 months), adequate counseling provides reassurance that the absence of bleeding does not generally signify pregnancy or other problems leading to high continuation rate and high level of patient satisfaction (Jensen et al 2008).

Information received at the insertion visit is strongly associated with increased user satisfaction among the users of the LNG-IUS (Backman et al 2002), the association between high user satisfaction and advance information being strongest on the possibility of missing periods.

**Uterine perforations**
Incidence of uterine perforations related to the insertion of a LNG-IUS is around 2.6 per 1000 insertions (Van Houdenhoven et al 2006). Insertion in lactating women, even beyond 6 weeks after delivery, is an important risk factor. The manufacturer of the LNG-IUS currently recommends that post-partum insertions should be postponed until 8 weeks after delivery. Uterine perforation at insertion seems less likely to occur if a withdrawal rather than a push-out technique – the recommended technique for a LNG-IUS – is used.

**Expulsion and displacement**
Expulsion of an IUD occurs in approximately 1 in 20 women, and is most common in the first 3 months after insertion (NICE 2005). Patients at increased risk of expulsion include nulliparous women, women with severe dysmenorrhea, and those with insertions immediately post partum or post abortion. There is insufficient evidence to indicate that expulsion rates are lower with LNG-IUS (Chrisman et al 2007). There are no differences in the rates of expulsion between Cu-IUDs and the LNG-IUS (FSRH 2007). As expulsion generally occurs within the first few months, women should be encouraged to attend follow-up within 12 weeks of insertion.

It is rare for the LNG-IUS to get displaced and there is conflicting evidence on how best to manage these patients. Intra-peritoneal dislocated LNG-IUS results in plasma levonorgestrel levels 10 times higher (4.7 nmol/L) than those seen with LNG-IUS placed in utero. This high plasma levonorgestrel level suppresses ovulation and therefore it has been suggested that a misplaced LNG-IUS should be removed when pregnancy is desired, as opposed to the copper IUD that may be left intraperitoneally, especially if asymptomatic (Haimov-Kochman et al 2003). However pregnancies have also been documented with a displaced LNG-IUS (Budiman et al 2007).

**Ectopic pregnancy**
The LNG-IUS is a very effective contraceptive and the absolute risk of pregnancy (intrauterine and ectopic) is very low. A previous ectopic pregnancy is not a contraindication to the use of intrauterine contraception (FSRH 2007). The risk of ectopic pregnancy when using the LNG-IUS is lower than when using no contraception. The overall risk of ectopic pregnancy when using the LNG-IUS is very low, at about 1 in 1000 in 5 years. If a woman becomes pregnant with the LNG-IUS in situ, the risk of ectopic pregnancy is about 1 in 20 (NICE 2005). Similar rates of ectopic pregnancy are reported for the LNG-IUS and Cu-IUDs (French et al 2004).

**Infection**
The risk of developing PID following LNG-IUS insertion is very low (less than 1 in 100) in women who are at low risk of STIs and removals due to PID among LNG-IUS users is below 1% at 1 year, and below 1.5% at 5 years (NICE 2005). A systematic review reported that there is conflicting evidence on whether levonorgestrel IUD is associated with a lower risk of PID than other IUDs and any risk of upper-genital-tract infection after the first month is small (Grimes 2000). The protective effect of the LNG-IUS may be due to impenetrable cervical mucus, endometrial changes, or reduced retrograde menstruation (Toivonen et al 1991). If a woman was to develop PID with the IUD in place, it may be reasonable to offer initial treatment without immediate removal (WHO 2004). In rare cases of pelvic infection secondary to *Actinomyces israelii*, device removal in conjunction with antibiotic treatment is more successful at clearing the colonization than antibiotics alone (Bonacho et al 2001).

A woman who currently has an STI such as gonorrhea or chlamydia or is at very high risk should not have an IUD inserted as insertion may increase the risk of PID. If a high risk patient screens negative, then an IUD can be inserted and if the screen is positive, then an IUD can be inserted after treatment, if she is not at risk of reinfection by the time of insertion (WHO 2007). In exceptional circumstances, if other, more appropriate methods are not available or not acceptable, an IUD can be inserted in high risk individuals even if STI testing is not available. Presumptive treatment should be considered with a full curative dose of antibiotics effective against both gonorrhea and chlamydia and inserting the IUD after completion of treatment. The patient should be carefully checked for signs of infection at follow-up and treated accordingly while being advised to return at once if there are any signs of infection (WHO 2007).
Farley et al (1992) reported that PID among IUD users is most strongly related to the background risk of STI and hence screening for chlamydia should always be considered prior to inserting the LNG-IUS.

A systematic review to assess the effectiveness of prophylactic antibiotic administration before IUD insertion in reducing IUD-related complications and discontinuations within 3 months of insertion highlighted the low risk of IUD-associated infection, with or without use of antibiotic prophylaxis (Grimes and Schulz 2001). Another systematic review (Mohllajee et al 2006) suggested that women with chlamydial infection or gonorrhea at the time of IUD insertion were at increased risk of PID relative to women without infection, the absolute risk of PID being low for both groups. However, whether IUDs increase the risk of PID in women with an STI at the time of insertion is not known (Mohllajee et al 2006).

Ovarian cysts
The use of the LNG-IUS is associated with a small risk of development of ovarian cysts (Inki et al 2002). The precise mechanism by which the ovarian cysts are caused is not known, but may be secondary to disturbances in the normal growth and rupture of follicles during LNG-IUS use. However in a prospective, randomized trial by Inki et al (2002) these were symptomless and showed a high rate (94%) of spontaneous resolution and hence no routine ultrasound screening is necessary of women using the LNG-IUS.

Other rare side effects
Unrecognized retention in the uterine cavity of the active part (hormone-releasing capsule) of an LNG-IUS may lead to secondary amenorrhea. Although LNG-IUS are inserted and removed without particular difficulty in most cases, it may be prudent to check the device following removal to ensure that the capsule remains attached to the rest of the device (Forrest et al 2008).

Hormonal complications
The systemic absorption of levonorgestrel may have the potential to cause hormonal side effects. The LNG-IUS releases 20 μg per day of levonorgestrel and so drug-related adverse events are less frequent than with the oral preparations of progesterone, which result in higher serum concentrations.

However discontinuation due to hormonal (non-bleeding) problems is rare. While changes in mood and libido or weight gain are similar whether using the LNG-IUS or IUDs, there is an increased possibility of developing acne (NICE 2005). While some women may complain of headaches, women who have migraine with or without aura may use the LNG-IUS.

The use of the LNG-IUS has not been associated with an increased risk of breast cancer (Backman et al 2005). In women with a past history of breast cancer, Trinh et al (2007), reported that, overall, there was no increased risk of breast cancer recurrence associated with use of the LNG-IUS; subgroup analysis suggested that while the LNG-IUS is not associated with an increased risk of recurrence in patients who start using the LNG-IUS after completing their breast cancer treatment, women who developed breast cancer while using an LNG-IUS and who continued to use the LNG-IUS, showed a higher risk of recurrence of borderline statistical significance. Hence additional research is needed to confirm or refute these findings (Trinh et al 2007).

Conclusion
Women contemplating undergoing sterilization or hysterectomy seek a long-term solution for contraception or treatment of menorrhagia. The LNG-IUS is one of the most versatile forms of long-acting reversible method of contraception. New developments in the delivery of levonorgestrel-releasing intrauterine devices such as the Femilisk® (parous women), the Femilisk Slim® (nulliparous women), and the frameless FibroPlant® levonorgestrel LNG-IUS possess features that may solve the main problems encountered with conventional IUDs (eg, expulsion, abnormal or excessive bleeding, and pain) (Wildemeersch 2007). The LNG-IUS system is an extremely effective contraceptive and has many non-contraceptive health benefits, including suppression of menstruation, maintenance of iron stores, improvement in dysmenorrheal, and endometrial protection for women on estrogen replacement therapy.

Disclosures
Neither author has any conflicts of interest to disclose.

References
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