Cost-effectiveness analysis of a low-dose contraceptive levonorgestrel intrauterine system in Sweden

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**Key words**
Long-acting reversible contraception, unintended pregnancy, levonorgestrel intrauterine system, cost-effectiveness analysis, unwanted pregnancy, abortion

**Abstract**

**Objective.** To evaluate the cost-effectiveness of a novel intrauterine system, levonorgestrel intrauterine system 13.5 mg vs. oral contraception, in women at risk of unintended pregnancy. **Design.** Cost-effectiveness model using efficacy and discontinuation data from published articles. **Setting.** Societal perspective including direct and indirect costs. **Population.** Women at risk of unintended pregnancy using reversible contraception. **Methods.** An economic analysis was conducted by modeling the different health states of women using contraception over a 3-year period. Typical use efficacy rates from published articles were used to determine unintended pregnancy events. Discontinuation rates were used to account for method switching. **Main outcome measures.** Cost-effectiveness was evaluated in terms of the incremental cost per unintended pregnancy avoided. In addition, the incremental cost per quality-adjusted life-year was calculated. **Results.** Levonorgestrel intrauterine system 13.5 mg generated costs savings of €311 000 in a cohort of 1000 women aged 15–44 years. In addition, there were fewer unintended pregnancies (55 vs. 294) compared with women using oral contraception. **Conclusion.** Levonorgestrel intrauterine system 13.5 mg is a cost-effective method when compared with oral contraception. A shift in contraceptive use from oral contraception to long-acting reversible contraception methods could result in fewer unintended pregnancies, quality-adjusted life-year gains, as well as cost savings.

**Abbreviations:** IUS, intrauterine system; LARC, long-acting reversible contraception; LNG-IUS, levonorgestrel intrauterine system; OC, oral contraception; QALY, quality-adjusted life-year; SARC, short-acting reversible contraception.

**Introduction**

Contraceptive methods are widely available in Sweden. However, the incidence of induced abortion, a possible proxy for unintended pregnancy, is the second highest in

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Europe (1). In 2011 there were approximately 38 000 induced abortions (20.9/1000 women) in Sweden, with women aged 20–24 and 25–29 years showing the highest rates, at 33/1000 women and 27/1000 women, respectively (2). The outcomes and implications of unintended pregnancy are not limited to induced abortions, but also include live birth, miscarriage, and ectopic pregnancy. Previous studies indicate that unintended pregnancy is associated with substantial health system costs (3), and may also impact quality-of-life (4,5). Avoiding unintended pregnancy is therefore important for the cost-effective allocation of healthcare resources.

A substantial proportion of women in Sweden use some form of contraception; however, many currently use short-acting reversible contraception [SARC; comprising oral contraception (OC), ring, patch, and injection]. SARC methods, which rely on user adherence for their effectiveness, have higher typical use failure rates than long-acting reversible contraception [LARC; comprising intrauterine contraceptive device, intrauterine system (IUS) and implant] (6). In Sweden there is a particularly pronounced uptake of SARC in younger age groups, with OC the most commonly used method (7,8), whereas LARC uptake remains low, with only 10% utilization within the 20– to 29-year age group (8). This distribution of use suggests that barriers to LARC uptake may exist. Furthermore, resistance to the provision of LARC appears to exist at the provider level, particularly for younger women, with a recent survey of midwives and gynecologists in Sweden indicating that <30% considered intrauterine contraception appropriate for younger women (9). The high uptake of adherence-dependent SARC methods in younger women may make this group particularly susceptible to unintended pregnancy.

The levonorgestrel intrauterine system (LNG-IUS) 13.5 mg (Jaydess®; Bayer Pharma, Berlin, Germany) is a novel low-dose hormonal intrauterine contraceptive system registered for up to 3 years of use. Compared with the existing hormonal IUS (Mirena®; Bayer Pharma), LNG-IUS 13.5 mg has a lower hormonal release rate, a smaller T-frame, and is placed with a narrower insertion tube. These are characteristics that could make this option more suitable for use in young women (10). The present analysis evaluates the cost-effectiveness of LNG-IUS 13.5 mg compared with OC in Sweden, reflecting the current contraceptive choices of women in Sweden.

Material and methods

An economic model was developed to assess the cost-effectiveness of LNG-IUS 13.5 mg compared with OC. Total costs, unintended pregnancies, and quality-adjusted life-years (QALYs) were estimated in each model arm over a 3-year time horizon and used to determine incremental cost-effectiveness ratios, expressed in the form of incremental cost per unintended pregnancy avoided, and incremental cost per QALY gained, respectively. Costs and QALYs were discounted at 3%, as per recommendations for Swedish cost-effectiveness analyses (11).

A Markov cohort model was constructed in Excel 2007 (Microsoft Corp., Redmond, WA, USA) to simulate the movement of women between health states following initiation of contraception. The three possible health states in the model were: initial method, unplanned pregnancy, and subsequent method, as presented in Figure 1. All women started the analysis in the initial method state. At the end of each 1-year model cycle, women could either remain in this state or transition to a subsequent method according to contraceptive-specific continuation probabilities (6) (Table 1). Upon entering the subsequent method state, women were assumed to initiate a market mix of possible alternative contraceptives, which included non-hormonal methods as well as hormonal methods, weighted to reflect current contraceptive use in Sweden (7,8). Women remained in this health state for the remainder of the model time horizon, unless they experienced an unintended pregnancy.

Women in both the initial and subsequent method states could transition to unplanned pregnancy, according to method-specific failure probabilities (6). All women who were modeled to experience an unintended pregnancy remained in this state for one cycle, during which they were assumed not to require contraception. In the following cycle these women transitioned to the subsequent method state.

The population included in the model comprised women aged 15–44 years, at risk of pregnancy, requiring reversible contraception. Further analyses were also undertaken in women aged 20–29 years.

Figure 1. Schematic representation of model health states.
The intervention arm of the model consisted of LNG-IUS 13.5 mg, whereas the comparator arm was OC. A scenario analysis comparing against a hormonal market mix of methods [comprising a weighted mixed bag of OC, ring, patch, injection, IUS (Mirena®), and implant], reflecting the contraceptive methods most likely to be displaced by potential LNG-IUS 13.5 mg uptake in Sweden, was conducted, as were analyses comparing against IUS (Mirena®). The relative uptake of each method within the hormonal market mix bag was derived using Swedish contraceptive use data (8).

Contraceptive failure and discontinuation rates for contraceptive methods included in the model were retrieved from published articles (6,12). Only first year data were available; efficacy rates were applied across all model years, whereas discontinuation rates after year one were assumed to be 20% of first year values, following clinician input. For LNG-IUS 13.5 mg the first year failure rate, determined from trial data (13), was also used and applied for the model duration, whereas discontinuation was conservatively assumed to be equivalent to that of the implant. All predicted discontinuation and failure rates are reported in Table 1.

Contraceptive ingredient costs were retrieved from electronic databases (14,15). Where several products were available within each contraceptive class, weighted average costs were derived using prescription volume data (8). The number of units of each contraceptive product required each year was derived using the product’s Summary of Product Characteristics data and a published article (16), and used to determine annual ingredient costs for each method. Barrier methods in the model were assumed to comprise condoms only, and annual costs associated with condom use (17) were used within the analysis for this contraceptive class. Contraceptive ingredient costs are presented in Table 2.

Contraceptive use is also associated with medical consultations, the frequencies of which were estimated using product Summary of Product Characteristics data and clinician input. All methods had an assumed initial consultation. For LARC methods insertion and follow-up costs were also modeled, whereas for SARC a half-hour consultation was assumed each year (i.e. on average a single, 1-h consultation every second year in clinical practice).

All consultations were assumed to be performed in one of three settings; a “primary” gynecology clinic, a women’s gynecology clinic, or a midwife department. Relative frequencies of 0.125, 0.125, and 0.75 for each type of visit, respectively, were assumed and used to derive a weighted average cost of consultation. The product of consultation frequency and consultation cost was used to generate total annual consultation costs for each method.

Four outcomes of unintended pregnancy were included in the model: live birth, induced abortion, miscarriage, and ectopic pregnancy. Costs for each of these unintended pregnancy outcomes were determined as weighted averages using diagnosis-related group cost (a system used in Sweden, as well as a number of other European countries, to show costs within the healthcare system) codes and recorded numbers of diagnosis-related group events within each pregnancy outcome class (18–20). For
miscarriage, in the absence of available data the cost was assumed to be equivalent to a gynecological consultation (21). Calculated costs of each unintended pregnancy outcome are presented in Table 3. The relative frequency of each unintended pregnancy outcome following contraceptive failure was subsequently determined using contraceptive-specific incidence data (for ectopic pregnancy and miscarriage) (16) as well as Swedish pregnancy outcome data (for live births and induced abortion, which were adjusted for the proportion of these outcomes that were due to unintended pregnancy) (22–24), and used to derive a weighted average cost of unintended pregnancy for each method in the model.

Indirect costs were determined on the basis of estimated work days lost from unintended pregnancy and contraceptive consultations (Table 4). Work days lost for each unintended pregnancy outcome and medical consultation were multiplied by Swedish mean daily wages for the age group of women included in each analysis (25) to estimate productivity losses. Live birth was assumed to fall under maternity leave and was therefore excluded from the indirect costs calculations.

Baseline population utility scores for women entering the model (aged 15–44 and 20–29 years) were derived from weighted averages of age-specific scores using EQ-5D™ (http://www.euroqol.org; a standardized measure of health-related quality of life) survey data (26). All women in the model who were not in the unintended pregnancy state were assigned this standardized baseline utility. The utility score for an unintended pregnancy event was retrieved from a published article (4). The reported unintended pregnancy utility was subsequently used to derive a utility decrement, which was applied to women in the unintended pregnancy state to model the impact of unintended pregnancy on quality-of-life. The total number of QALYs experienced by the cohort over the analysis duration was estimated by summing the utility values of women in every model state in each year of the model.

Table 3. Cost of unintended pregnancy outcomes (16–19).

| Pregnancy outcome | Cost in Swedish Crowns (SEK) |
|-------------------|------------------------------|
| Live birth        | 26 340.94                    |
| Induced abortion  | 9330.91                      |
| Miscarriage       | 1977.50 a                    |
| Ectopic pregnancy | 36 618.00                    |

aAssumed equivalent to cost of a gynecological consultation.

Table 4. Assumed work days missed from outcomes of unintended pregnancies and medical consultations.

| Event                | Days lost from work |
|----------------------|---------------------|
| Live birth           | –                   |
| Induced abortion     | 1                   |
| Miscarriage          | 1.5                 |
| Ectopic pregnancy    | 5.5                 |
| Initial consultation  | 0.125               |
| Follow-up consultation| 0.125              |
| Insertion/removal consultation | 0.125          |

Results

The LNG-IUS 13.5 mg was cost saving compared with OC over the 3-year analysis time horizon in a cohort of 1000 women. It exhibited lower total costs (€718 249 vs. €1 029 599; Figure 2) and fewer unintended pregnancies (55 vs. 294/1000 women), with similar overall QALYs (2467.6 vs. 2466.3; Figure 3). Costs savings stemmed principally from lower direct costs (€642 634 vs. €942 929), driven by reduced unintended pregnancy incidence, though indirect costs were also curtailed (€75 615 vs. €86 671) (Table 5). Cost data were converted from SEK to € using exchange rates from the currency exchange website http://www.XE.com (27/1/15).

Results from the one-way sensitivity analysis indicated that, when values of key input parameters used in the
model, such as contraceptive failure rates, were varied within plausible ranges, there were limited changes to the base-case results, with cost-effectiveness maintained across all inputs evaluated. This indicated that the base-case model findings were robust. Probabilistic sensitivity analysis outputs demonstrated that for 98.6% of model simulations, using LNG-IUS 13.5 mg was both cheaper and more effective than OC.

LNG-IUS 13.5 mg continued to show cost savings compared with OC in a cohort of women aged 20–29 years, generating fewer unintended pregnancies (1/C0242), greater QALYs (1.39) and lower costs (€241631). Changing the comparator to the hormonal market mix also continued to generate cost savings (€338331), reduce unintended pregnancies (€218), and greater QA-LYS (1.23). Modulating the distribution of methods in the hormonal market mix comparator to include successively increasing proportions of IUS (Mirena/C226), indicated that cost-effectiveness was maintained across a range of proportions tested (Table 6). The threshold for cost-effectiveness of LNG-IUS 13.5 mg compared with hormonal market mix was reached when the composition of the hormonal market mix was 89.0% IUS (Mirena/C226). A comparison with IUS (Mirena/C226) directly resulted in higher costs (€96433), as well as increased unintended pregnancies, and fewer QALYs (0.15). Total costs and QALYs for LNG-IUS 13.5 mg compared with all comparators are shown in Figures 2 and 3.

**Discussion**

LNG-IUS 13.5 mg was found to be cost-saving, to generate fewer unintended pregnancies, and to have similar overall QALYs when compared with OC from a societal perspective, over a 3-year time horizon, using a theoretical Markov model. The one-way sensitivity analysis and probabilistic sensitivity analysis results indicated that base-case outputs were robust to key parameter variation and that there was a nearly 100% probability that LNG-
IUS 13.5 mg resulted in cost savings and similar QALYs compared with OC. Cost savings and effectiveness gains were also demonstrated in a younger cohort of women aged 20–29 years, in whom the rate of induced abortions is highest (2). Cost-effectiveness was further demonstrated within a scenario analysis comparing the device against a mixed basket of hormonal methods likely to be displaced by LNG-IUS 13.5 mg uptake. Cost-effectiveness was not demonstrated against IUS (Mirena®). However, further analyses indicated that when the proportion of IUS (Mirena®) within the mixed hormonal basket comparator was increased to 89%, cost-effectiveness was still exhibited.

This study further adds to the evidence base supporting LARC use as a cost-effective means of reducing unintended pregnancies, additionally demonstrating the potential quality-of-life gains that could be achieved. Demonstration of cost-effectiveness in both younger women aged 20–29 years and a broader cohort aged 15–44 years indicates that the benefits associated with LARC may extend across a wide age spectrum. Furthermore, the incorporation of treatment discontinuation within the model enhances the external validity of analysis outputs.

There were, however, limitations to this analysis. In the absence of alternative data from European populations, typical use failure rates from a study in the USA were used in the model. Contraceptive failure rates may vary in US vs. European populations, hence cost savings compared with OC could potentially differ. Typical use failure rates were available for the first year of contraceptive use only, which were applied across all model years for all methods. Subsequent-year failure rates may be lower than in year one, so the estimated unintended pregnancy reduction compared with OC could be overstated.

Method switching after contraceptive discontinuation was included in the model to account for women’s changing contraceptive use over time. However, in the absence of robust data on switching preferences, women in the subsequent method state were allocated to a mixed contraceptive bag. A limited number of studies were available to inform the estimate of the utility score associated with an unintended pregnancy, none of which presented results in the Swedish setting. Further research to increase this evidence base may enhance the precision of subsequent cost-effectiveness analyses in this field. Utility scores were only applied to unintended pregnancy events. Future analyses might seek to include utility decrements associated with adverse events and invasive procedures associated with LARC methods requiring device insertion, as data become available.

Study results should be considered within the context of low current utilization of LARC vs. SARC methods in Sweden, particularly among younger women (8), who also have high rates of induced abortion (2). Existing barriers to LARC use may stem in part from anticipated discomfort from device insertion/removal (27). LNG-IUS 13.5 mg, which is smaller than the currently available IUS (Mirena®), with a narrower insertion tube, may help to shift contraceptive uptake from SARC to LARC in these age groups.

In conclusion, this analysis demonstrates that LNG-IUS 13.5 mg is cost-effective compared with OC in Sweden, generating both cost savings and a reduced number of unintended pregnancies. This finding held across all age groups evaluated, including among younger women, who are most susceptible to unintended pregnancies. The results contribute to the rapidly emerging evidence-base that LARC are cost-effective and prevent unintended pregnancies and their consequences more effectively than SARC.

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