The impact of discontinuation on the cost-effectiveness of long-acting reversible contraception - analysis based on an economic model developed for a NICE clinical guideline

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CES - HESG Workshop
2nd British-French meeting on health economics
London, 4-6 January 2006

Acknowledgments: This study was based on an economic model developed for a clinical guideline on *Long-Acting Reversible Contraception*, produced by the National Collaborating Centre for Women's and Children's Health (NCC-WCH) on the behalf of the National Institute for Health and Clinical Excellence (NICE). The author would like to thank the members of the Guideline Development Group for their expert advice on the development of the economic model.

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Abstract

Background: Long-acting reversible contraceptives (LARC) are highly effective. The relatively high costs associated with their initiation are offset by future savings from preventing a large number of unintended pregnancies. However, a significant number of women discontinue LARC, mainly due to changes in menstrual bleeding patterns and potential side effects. Discontinuation of LARC may have a strong impact on their cost-effectiveness, because of likely subsequent use of less effective/no contraceptive methods, and also because of a minimum period of time needed for the initial costs to be offset by future savings.

Aims: The objective of the analysis was to examine the cost-effectiveness of LARC licensed in the UK compared to the combined oral contraceptive pill (COC) and female sterilisation. In addition, cost-effectiveness across LARC was examined.

Methods: A decision analytic model was constructed in order to assess costs and benefits associated with use of LARC, COC and female sterilisation, over various time horizons. The model incorporated events such as contraceptive failure and discontinuation of LARC with subsequent use of another/no contraceptive method.

Results: LARC dominated COC after two years of use. Female sterilisation dominated LARC after 6 years of contraceptive protection. Cost-effectiveness between LARC varied over time. Results were sensitive to changes in discontinuation rates. Varying other factors such as failure rates and costs did not have a strong impact on the results.

Conclusions: LARC are shown to be cost-effective; however, discontinuation may affect their cost-effectiveness significantly. In order to reduce the risk of discontinuation, health professionals should provide women considering LARC use with sufficient information and enable them choose the method that is most suitable and acceptable to them.

Introduction

Use of contraception is widely adopted in the UK. It has been estimated that 53% of women of reproductive age (i.e. 16-49 years) use some form of reversible contraception, while another 22% have undergone permanent sterilisation (10%) or have a partner who has been sterilised (12%), thus raising the percentage of women that use protection against an unintended pregnancy at 75%[1]. Almost half of the women using reversible contraception take oral contraceptives (47%) and only 17% use one of the long-acting reversible contraceptives (LARC) available in the UK, i.e. the intrauterine device (IUD), the intrauterine system (IUS), the progestogen-only injectable, and the subdermal implant.

Although oral contraceptives are very effective in preventing unintended pregnancies, they have been associated with poor compliance[2], which, in many cases, has been responsible for contraceptive failure and unintended pregnancy[3,4]. In contrast, the effectiveness of LARC is much less dependent on users' compliance or correct use of other contraceptive methods[5].

Several studies have explored the cost-effectiveness of LARC methods in comparison to use of no method[6-10] and other contraceptive methods[11-14]. With the exception of one study[11] LARC methods were demonstrated to be cost-effective, as the relatively high costs associated with their initiation were offset by future cost savings from preventing a significantly large number of unintended pregnancies.

Only four of the above studies considered discontinuation in the estimation of costs and benefits associated with LARC use[9,12-14]. Nevertheless, a significant number of women discontinue LARC, mainly due to changes in menstrual bleeding patterns and potential side effects[15-18]. Discontinuation of LARC may have a strong impact on their cost-effectiveness, due to the subsequent use of a potentially less effective contraceptive method/no method, which increases the risk of an unintended pregnancy. Moreover, early discontinuation may not allow future cost savings from prevention of unintended pregnancies to offset the high initiation costs associated with LARC. Finally, discontinuation of a method may incur extra costs due to additional consultations with health professionals for premature removal of LARC and initiation of another contraceptive method.

The aim of this analysis was to assess the impact of discontinuation on the cost-effectiveness of LARC relative to the combined oral contraceptive pill (COC) and female sterilisation. These methods were selected as comparators for the analysis

as they are among the most widely used contraceptive methods in the UK. Moreover, it was believed that women of reproductive age who are likely to consider LARC as an option are mainly those already using COC, or those considering COC/female sterilisation as an alternative method. Besides these comparisons, the effect of discontinuation on the relative cost-effectiveness between LARC was examined.

Methods

A decision analytic Markov model was constructed in order to assess costs and benefits associated with use of LARC, COC and female sterilisation. The model was developed to assist decision-making at the development process of a NICE clinical guideline on Long-Acting Reversible Contraception[19]. The economic analysis considered multiple consecutive time frames, from 1 to 15 years of *intended* contraceptive use, so as to explore how the relative cost-effectiveness of LARC varied over time. The maximum time frame of 15 years was chosen to reflect the full duration of effect of female sterilisation.

According to the model structure, hypothetical cohorts of 1,000 sexually active women of reproductive age adopted each one of the contraceptive methods assessed and were subsequently followed for periods equal to the time frames of the analysis. Every year a proportion of women in each cohort were assumed to discontinue the examined method and switch to another method or no method. Therefore the *actual* duration of contraceptive use for each woman might differ (be shorter) from the initially *intended* period of contraceptive use (reflected in the time frame of the analysis) due to discontinuation of the method. During the simulation, women in each cohort either received the contraceptive benefits following use of contraception, or faced a contraceptive failure and the subsequent event of an unintended pregnancy. Four possible outcomes of unintended pregnancy were incorporated in the model: continuation of pregnancy leading to birth, miscarriage, abortion, and ectopic pregnancy.

The various methods adopted following discontinuation of initial form of contraception were summarised in the concept of the ‘average contraceptive method’. This concept was developed in order to consider the impact on cost effectiveness of discontinuation itself rather than of the patterns related to contraceptive method switching. In addition, there were no comprehensive data on switching patterns for LARC methods in the UK context. A limitation of this approach is that it did not

consider the fact that women who discontinue one method are not always eligible to use all other methods available. Women discontinuing IUD, for example, may not be able to use hormonal methods due to contraindications (which may have led to the use of an IUD in the first place). The failure rate of the 'average contraceptive method' was calculated as the average failure rate of all methods available in the UK, weighted according to data on contraceptive usage of women 'at risk of pregnancy'[1]. A weighted average method cost was also calculated using the same approach.

It was assumed that potential discontinuation of a method and switch to the average contraceptive method occurred in the middle of each year, i.e. at 6 months. For the first 6 months costs and contraceptive failure were attributed to the method examined. For the remaining 6 months of the year following discontinuation, costs and contraceptive failure referred to the average contraceptive method.

Costs were estimated from the perspective of the UK National Health Service (NHS). They consisted of contraceptive provision costs (ingredient costs, health professionals' time and equipment required for initiation/removal of LARC) and costs associated with possible outcomes of unintended pregnancy (continuation of pregnancy and birth plus additional neonatal care for unhealthy infants, miscarriage, abortion and ectopic pregnancy). Outcomes were expressed as the number of unintended pregnancies due to contraceptive failure *after* discontinuation had been taken into account. Thus, the overall effectiveness of each method was determined not only by its clinical effectiveness (expressed in the form of failure rate) but also by its discontinuation rate.

Cost data

Cost data associated with female sterilisation, antenatal care and birth until discharge of mother and infant, miscarriage, abortion and ectopic pregnancy were based on NHS reference costs[20]. Costs associated with miscarriages treated in GP practices were derived from the GP fee schedule[21]. LARC and COC ingredient costs were derived from the British National Formulary[22]. A weighted average COC ingredient cost was estimated utilising prescription data on COC use in England[23]. Resource use with respect to health professionals' time spent on contraceptive provision services was based on the expert opinion of the Guideline Development Group (GDG). Further data on resource use were derived from published literature[24,25]. Costs of sterile packs required at insertion and removal of some LARC

methods were also based on GDG consensus. Unit costs of GP consultations were derived from published unit costs of health and social care[26]. All estimated costs reflected 2004/05 prices. Cost data utilised in the analysis are presented in table 1.

Effectiveness data and other input parameters

Effectiveness data and other input parameters were taken from a summary of data reported in LARC guideline[19] and other published literature[5,27-32], in agreement with the GDG. Where evidence was limited, values of input parameters were based on GDG opinion. The estimation of probabilities for outcomes of unintended pregnancy was based on national statistics[33,34], a literature review on unintended pregnancy[35-38] and additional assumptions agreed with the GDG. Discounting was applied to both costs and outcomes at an annual rate of 3.5%, as recommended by NICE guidance on technology appraisal[39]. All effectiveness data and other clinical input parameters included in the analysis are provided in Table 2.

Sensitivity analysis

One-way sensitivity analyses were carried out to explore the robustness of the base-case results under the uncertainty characterising the input parameters. Parameters examined included LARC effectiveness and discontinuation rates, as well as COC and female sterilisation provision costs.

Results

Base-case analysis

Results of the analysis in terms of average annual costs and number of unintended pregnancies due to contraceptive failure per 1,000 women for 1 to 15 years of intended contraceptive use are presented in table 3. For each time frame all contraceptive methods have been ranked from the most to the least effective. Note that annual costs related to the IUD, the IUS and the implant are affected by the time frame of the analysis. This is caused to some extent by the time-dependency of the respective provision costs: (re)insertion of devices is associated with additional healthcare resource utilisation and therefore incurs extra costs. For intended periods of use ending soon after (re)insertion, average annual costs of the above methods are relatively high; these decrease as the intended period of use increases reaching the maximum licensed duration of use of each LARC device, as high costs of

(re)insertion are spread over longer time periods. Also note the increase in the annual number of unintended pregnancies over time at short time frames related to LARC and the COC use, owing to their high early discontinuation rates that lead to the use of less effective methods, and subsequently to higher rates of contraceptive failure.

Comparisons of LARC with COC

The analysis demonstrated that all LARC were more effective than COC across all time periods examined. For 1 year of use the IUD and the injectable were also less costly and dominated the COC, while the implant and the IUS incurred additional costs of £382 and £513 per additional unintended pregnancy averted, respectively. At 2 years of intended use and above all LARC dominated the COC.

Comparisons of LARC with female sterilisation

Female sterilisation was more effective than all LARC methods across all time frames. This is explained by the high discontinuation rates of LARC that lead to the use of less effective methods (summarised in the concept of average contraceptive method, as described) and the subsequent increase in the number of unintended pregnancies due to contraceptive failure. Female sterilisation was more costly than any of the LARC for time periods up to 4 years, incurring high incremental costs per pregnancy averted that reached £48,636 (versus the implant) for 1 year of contraceptive protection. However, incremental costs decreased as duration of effect increased (with all ICERs becoming lower than £2,000 per pregnancy averted at 4 years of contraceptive protection), until female sterilisation became the dominant option; this occurred at 5 years over the injectable, at 6 years over the implant and the IUS, and at 7 years over the IUD. Thus for 7 years of contraceptive use and above, female sterilisation dominated all LARC.

Comparisons between LARC

The injectable was dominated by the rest LARC for all time frames between 2 and 15 years. For 1 year of use, the injectable was the cheapest but also the least effective among LARC; the ICER of the IUD (the next most effective method *above* injectable in ranking) versus the injectable for this time frame was £339 per pregnancy averted.

The IUS was dominated by the implant at 1, 2, 3 and 6 years of use. It was also dominated by the IUD at 2, 3 and 4 years of use. For the rest time frames the IUS was dominated according to the rule of extended dominance (the ICER of the IUS versus the IUD was higher than the ICER of the implant versus the IUS).

The implant was the most effective while the IUD was the least costly among LARC. Between 1 and 4 years of intended use, the ICER of implant versus IUD lied within £14,000 and £18,000 per pregnancy averted. This ratio fell at £7,460 per pregnancy averted at 5 years of use, and decreased thereafter, reaching a cost of £1,323 per pregnancy averted at 15 years of use, with slight increases at 7, 10 and 13 years of use, due to implant reinsertion costs. The variation in the ICER of the implant versus the IUD over time is shown in figure 1.

Sensitivity analysis

Varying LARC failure rates

Results were rather insensitive to modest changes in LARC failure rates. The dominance of LARC over the COC remained unaffected by increasing LARC failure rates by 10% of the base-case values. Similarly, the relative cost-effectiveness between LARC and female sterilisation was not affected by decreasing LARC failure rates by 10% of the base-case values. Varying independently each of the LARC failure rates by ±10% of the base-case values did not affect ranking of LARC in terms of effectiveness, or cases of dominance (both absolute and extended) across LARC. Varying the IUD failure rate had a small impact on the ICER of the implant versus IUD only for short periods of contraceptive use (up to 3-4 years). This ratio was practically unaffected at longer time frames.

Varying provision costs of COC and female sterilisation

Using the lowest ingredient cost of the COC or reducing the health professionals' time in the follow-up consultations by 50% of the base-case estimate did not affect the results; cases of LARC dominance over the COC remained intact. A 20% increase in the female sterilisation procedure delayed its dominance over the injectable and the implant by 1 year, and over the IUS and the IUD by 2 years. Conversely, a 20% reduction in the cost of female sterilisation hastened the time over which female sterilisation became dominant by 1 year relative to the base-case analysis.

Varying LARC discontinuation rates

The cost-effectiveness of LARC relative to COC was not affected by substantial changes in their discontinuation rates: even an increase in the LARC discontinuation rates by 50% of the base-case values did not affect the dominance of LARC over the COC. In contrast, a 50% reduction in LARC discontinuation rates had a stronger impact on their relative cost-effectiveness compared to female sterilisation: female sterilisation dominated the injectable at 6 years, the implant at 8 years, the IUS at 10 years, and the IUD at 12 years. At the extreme scenario of no discontinuation related to LARC use, most LARC dominated female sterilisation for considerable periods of contraceptive protection; i.e. female sterilisation was dominated by the injectable, the implant and the IUS for 1-7 years, 1-12 years, and over the whole range of time frames examined (1-15 years), respectively. The IUD was only slightly less effective than female sterilisation (preventing a pregnancy less per 1,000 women annually) but with significant cost-savings, especially in the short term (e.g. about £70,000 per 1,000 women annually, at 8 years of contraceptive protection).

The impact of a decrease in LARC discontinuation rates on the cost-effectiveness of LARC versus female sterilisation is demonstrated in figure 2, which provides cost-effectiveness planes for various levels of LARC discontinuation. Every graph contains 15 points (squares) for each LARC, which represent the 15 time horizons examined (1 to 15 years of contraceptive protection). The planes have been reversed (with the horizontal axis representing difference in costs and the vertical representing difference in effectiveness in terms of additional number of pregnancies averted), so that successive points, reflecting consecutive time frames (from 1 to 15 years), are placed from the left to the right; therefore, each plane shows the cost-effectiveness of LARC versus female sterilisation over time, at a given level of discontinuation. At each level of discontinuation, consecutive points for each LARC move substantially from the left to the right (cost difference decreases in favour of female sterilisation over time), especially at short time frames. As the level of discontinuation falls, points for each LARC move western and northern (LARC become less costly and more effective), until they fall within the NW/NE quadrants, as at zero discontinuation (SW in the case of IUD).

The robustness of the relative cost-effectiveness between LARC following changes in their discontinuation rates was also tested in one-way sensitivity analyses.

Under this scenario, each method's discontinuation rates were varied by ±10% of their base-case values, while the rest methods' rates were kept intact. The majority of the base-case results were very sensitive to such a hypothesis, with the exception of the injectable, which remained dominated by all other LARC after 1-2 years of use.

Increasing the discontinuation rates of IUS by 10% of the base-case values resulted in IUS being constantly dominated by the IUD, across all time horizons examined. Reducing the discontinuation rates of IUS by 10% of the base-case values made IUS the dominant option over the implant starting from 3 years of use and above. The ICER of IUS versus IUD ranged between £61 (14 years) and £8,855 (3 years) per pregnancy averted; at 10 and 15 years of use the IUS dominated the IUD.

A 10% rise in the base-case values of discontinuation rates of IUD was followed by a significant decrease in the ICERs of the implant versus the IUD (e.g. £12,315 and £3,389 per pregnancy averted at 1 and 3 years respectively). No extended dominance over IUS existed after 3 years of use. The ICER of IUS versus IUD ranged between £3,581 (4 years) and £45 (13 years) per pregnancy averted. Moreover, the IUS became dominant over IUD at 10, 14, and 15 years of use. When IUD discontinuation rates were reduced by 10% of their base-case values, the IUD constantly dominated the IUS for all time horizons examined; it also dominated the implant between 2 and 6 years of use. For the rest time horizons, the ICER of the implant versus the IUD was significantly higher than that derived from the base-case analysis (£50,467 per pregnancy averted at 7 years of use, falling at £9,432 at 15 years of use).

Finally, a 10% increase in the implant discontinuation rates led to IUS dominating the implant at 4 years of use and above; under this scenario the IUD also dominated the implant for 2-5 years of use. The ICER of the implant versus the IUD rose up to £29,134 per pregnancy averted at 1 year, and fell at approximately £5,600 per pregnancy averted at 15 years of use. A 10% reduction in the discontinuation rates of implant substantially reduced its ICERs versus IUD compared with the base-case analysis (£12,021 per pregnancy averted at 1 year, falling at £413 at 15 years).

Discussion

According to the analysis, LARC dominated the COC for most of the time frames examined (starting at 1-2 years of use and above). Despite their relatively high initiation costs, LARC proved to be more cost-effective than the COC even in the

short run; this result was driven by the significantly lower failure rates of LARC compared to those reflecting typical use of the COC. Although the effectiveness of the COC at perfect use (efficacy) is comparable to that of LARC, this is greatly reduced at typical use of COC, due to reduced compliance. In contrast, because LARC effectiveness is independent of user compliance, typical and perfect use are characterised by virtually the same failure rates. Cost-effectiveness of LARC compared to COC was robust to increases in LARC discontinuation rates.

Female sterilisation dominated all LARC for periods of contraceptive protection equal to 7 years or above, mainly due to the high rates of discontinuation characterising LARC use. Sensitivity analysis showed that as LARC discontinuation rates declined, their cost-effectiveness relative to female sterilisation improved. At the extreme situation of zero discontinuation, most LARC dominated female sterilisation for the majority of time frames examined (IUS in particular dominated female sterilisation even when the full duration of effect -15 years- was assumed for the latter).

Among LARC, the injectable was constantly dominated by the rest methods (except at 1 year of use), while the IUS was constantly dominated by absolute or extended dominance. The implant was the most effective and the IUD was the cheapest option. The ICER of the implant versus the IUD varied greatly depending on the duration of intended use, generally decreasing as duration of use increased. With the exception of the injectable, cost-effectiveness across LARC was vastly influenced by even small changes in their discontinuation rates.

The economic model did not incorporate the incidence of side effects following contraceptive use. Besides causing distress to the user, some side effects may require additional healthcare resource use for their management, which incurs further costs. Non-contraceptive beneficial effects and associated cost savings were also not considered in the analysis. These omissions are acknowledged as limitations of the study.

The value of an unintended pregnancy prevented by contraceptive use is difficult to determine; in order to make an estimate, one needs to consider the psychological distress to the woman and her family following an unintended pregnancy, the value of a life foregone due to contraceptive use (or of a life resulting from contraceptive failure), and also the long-term costs and benefits (both financial and intangible) to society associated with an unintended pregnancy (either occurring

or averted). Currently, there are no research data to indicate this value. Consequently, clear conclusions on the relative cost-effectiveness of LARC cannot be reached, apart from cases of dominance.

Nevertheless, the aim of this study was not to accurately determine the relative cost-effectiveness of LARC, but rather to explore in what degree this is affected by discontinuation. The analysis demonstrated that discontinuation is a key driver of the relative cost-effectiveness between LARC, at least in the case of the implant, the IUD and the IUS. Discontinuation affects modestly the cost-effectiveness of LARC versus female sterilisation, and has no impact on the cost-effectiveness of LARC compared with the COC.

Other studies that considered discontinuation at the estimation of costs and benefits associated with contraceptive use did not investigate whether and/or how the level of discontinuation affects the relative cost-effectiveness of LARC: in two studies the impact of discontinuation was not even tested in a sensitivity analysis[9,12]; another study explored the impact of discontinuation on cost-effectiveness of LARC, but it did not provide an incremental analysis to demonstrate the changes in relative cost-effectiveness between methods following changes in discontinuation rates[13]. Finally, one study incorporated ranges of discontinuation rates in a Monte-Carlo simulation performed for a probabilistic analysis, but it did not consider the aspect of discontinuation separately, to examine how this affected the study base-case results[14].

It has been demonstrated that the risk of discontinuation associated with the injectable is reduced if, before initiation of the method, women are provided with detailed, structured information on the efficacy, changes in bleeding patterns and side-effects of the method, and are encouraged to return to the clinic if they experience any side effects[40-42]. With respect to the rest LARC methods, it has also been suggested that counselling explicitly about side-effects before insertion, combined with regular counselling and management of side-effects that may occur during contraceptive use, is likely to increase user satisfaction and tolerance of side effects and, consequently, prevent discontinuation[43-47]. Pre-initiation counselling and tailored advice according to women's preferences, acceptability and individual needs is essential to all women seeking contraception, as it enables them to make an informed choice on which method to use. In addition, regular counselling and management of side-effects should be accessible to all users of contraception. These practices are highly likely to prevent discontinuation caused by unexpected changes in menstrual bleeding and other side-

effects. Further research is required to determine other reasons that may contribute to the rather high levels of discontinuation associated with LARC use, as well as to identify practices that can improve continuation of LARC according to women's intension for contraceptive protection. Besides enhancing users' satisfaction, elimination of reasons for discontinuation has a strong impact on the relative cost-effectiveness of LARC methods, with direct resource implications for the health service.

Conclusion

Long-acting reversible contraception is a cost-effective option for the NHS; however, discontinuation is an important factor affecting its relative cost-effectiveness. Health professionals should provide women seeking contraception with sufficient information on all contraceptive methods available in the NHS and enable them choose the one that is most suitable and acceptable to them. Women should be encouraged to seek advice if they experience changes in menstrual bleeding patterns and other side-effects due to contraception. By adopting these principles of care, the risk of discontinuation of LARC is expected to decrease, leading to an improvement in the relative cost-effectiveness of LARC methods.

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Table 1 Cost data utilised in the economic model

Procedure	Baseline value	Cost components and basic assumptions	
		Component	Cost
IUD provision		Ingredient cost (T-Safe CU 380A)	£9.56 per device[22]
First year cost:	£133	Initial GP consultation, 20 min	£44.80[26]
Total 8 year cost:	£159	Consultation for insertion, 18 min	£40.32[26]
		Sterile pack for insertion	£18.20
		Follow-up consultation 3–6 weeks after insertion, 9 min	£20.16[26]
		Consultation for removal, 10 min	£22.40[26]
		Sterile pack for removal	£3.17
IUS provision		Ingredient cost (Mirena)	£83.16 per device[22]
First year cost:	£207	Initial GP consultation, 20 min	£44.80[26]
Total 5 year cost:	£232	Consultation for insertion, 18 min	£40.32[26]
		Sterile pack for insertion	£18.20
		Follow-up consultation 3–6 weeks after insertion, 9 min	£20.16[26]
		Consultation for removal, 10 min	£22.40[26]
		Sterile pack for removal	£3.17
Injectable provision		Ingredient cost (DMPA)	£5.01 per dose[22]
Annual method cost		Initial GP consultation (first year), 20 min	£44.80[26]
First year:	£144	Consultation for injection every 12 weeks, 8 min	£17.92[26]
Following years:	£99		
Implant provision		Ingredient cost (Implanon)	£90.00 per device[22]
First year cost:	£175	Initial GP consultation, 20 min	£44.80[26]
Total 3 year cost:	£230	Consultation for insertion, 16 min	£35.84[26]
		Sterile pack for insertion	£4.40
		Consultation for removal, 22 min	£49.28[26]
		Sterile pack for removal	£5.50
COC provision		Weighted average ingredient cost	£1.37 per month[22,23]
Annual method cost		Initial GP consultation (first year), 20 min	£44.80[26]
First year:	£106	Two routine consultations per year, 10 min each	£44.80[26]
Following years:	£61		
Female sterilisation	£712	Average NHS reference cost for upper genital tract intermediate procedures (day cases)[20], adding an initial 20 min GP consultation cost. In case of contraceptive failure, repeat of the procedure was considered.	
Average contraceptive method		Weighted cost based on contraceptive usage rates in the UK for women 'at risk of pregnancy'[1]. Incidence rates rather than prevalence were used for female sterilisation[24]. An initial 20 min GP consultation was assumed. Annual cost of female sterilisation derived by dividing total cost by 15 years (average duration of effect-GDG opinion). Male condom ingredient cost based on market retail prices.	
Average annual cost:	£38		
Initiation:	£45		
Total maternity cost	£2,137	Including cost of antenatal care, birth, care of unhealthy neonates & NICU Total NHS reference costs of antenatal clinics, outpatient obstetrics and community midwifery visits were divided by the number of births reported in the document in order to estimate the cost of antenatal care per live birth[20]. Cost of live birth was estimated as weighted average NHS reference cost of normal deliveries, assisted deliveries and caesarean sections, treated as elective, non-elective and day cases or in community services[20]. Total NHS reference costs of unhealthy neonates were added to the total NHS reference costs of NICU levels 1 and 2; the sum was divided by the number of births provided in the document in order to estimate the cost of additional neonatal care of unhealthy infants[20].	
Miscarriage	£321	Cost calculated by combining the weighted average NHS reference cost (elective, non-elective and day cases)[20] and the GP fee for miscarriage[21], assuming that 30% of the miscarriages are treated by GPs (GDG opinion).	
Abortion	£497	Weighted average NHS reference cost (surgical or medical termination of pregnancy treated as elective, non-elective or day case)[20].	
Ectopic pregnancy	£1,398	Weighted average NHS reference cost (elective, non-elective and day cases) for upper genital tract intermediate procedures, upper genital tract major procedures, and non-surgical treatment of ovaries, tube, pelvis disorders (reflecting laparoscopy, laparotomy and medical treatment respectively)[20]. It was assumed that management of ectopic pregnancy involved 58% laparoscopy, 35% laparotomy, and 7% medical management[25].	

Table 2 Effectiveness data and other input parameters utilised in the economic model

Input parameter	Baseline value (%)	Comments
Annual failure rate		
IUD		
Year 1:	0.5	Annual failure rates based on 1- and 8-year cumulative failure rates reported in the guideline[19]. The annual failure rate at 2–8 years was assumed to be stable. After reinsertion, the annual failure rate was assumed to be equal to that at 2-8 years.
Years 2–8:	0.246	
Years 9–15:	0.246	
IUS		
Year 1–5:	0.1	Annual failure rates based on the 5-year cumulative failure rates reported in the guideline[19]. The annual failure rate at 1-5 years was assumed to be stable. After reinsertion, the annual failure rate was assumed to be equal to that in previous years.
Years 6–15:	0.1	
Injectable		
Year 1:	0.1	Annual failure rates based on cumulative failure rates for the first 2 years of use reported in the guideline[19]. It was assumed that after the second year of use, the annual failure rate was stable over time and equal to that of year 1.
Year 2:	0.3	
Years 3–15:	0.1	
Implant		
Years 1–15:	0.005	Annual failure rate based on GDG expert opinion. All studies included in the LARC guideline[19] reported no pregnancies following use of the implant.
COC		
Years 1–15:	8	Failure rate for typical use, based on a published review[5].
Female sterilisation		
Year 1:	0.5	Failure rate for year 1 based on a published review[5]. Annual failure rates for years 2-10 based on the cumulative 10-year rate of the CREST study reported in the RCOG guideline on sterilisation[27] after taking into account the year 1 failure rate. The annual failure rate at 2–10 years was assumed to be stable over time. For years 11-15, the annual failure rate was assumed to be equal to that in year 10.
Years 2–10:	0.129	
Years 11–15:	0.129	
Average contraceptive method		
Years 1–15:	12.81	Weighted average failure rate based on contraceptive usage rates in the UK for women 'at risk of pregnancy'[1]
Annual discontinuation rate		
IUD		
Year 1:	21.6	Discontinuation rates for years 1-5 represent mean values of rates reported in a European multicentre RCT[28] and a UK community-based study, reflecting routine use[15]. The rates refer to the initial hypothetical cohort of women. Discontinuation rate for following years based on GDG opinion and applied to the subgroup of women remaining in the cohort each year.
Year 2:	13.4	
Year 3:	11.8	
Year 4:	9.05	
Year 5:	5.65	
Following years:	1	
IUS		
Year 1:	25.25	Discontinuation rates for years 1-5 represent mean values of rates reported in a European multicentre RCT[28] and a UK community-based study, reflecting routine use[16]. The rates refer to the initial hypothetical cohort of women. Discontinuation rate for following years based on GDG opinion and applied to the subgroup of women remaining in the cohort each year.
Year 2:	13.25	
Year 3:	8.4	
Year 4:	5.95	
Year 5:	3.9	
Following years:	1	
Injectable		
Year 1:	50	Discontinuation rate for year 1 was based on the summary of evidence reported in the LARC guideline[19]. Discontinuation rate for following years based on GDG opinion and applied to the subgroup of women remaining in the cohort each year.
Following years:	5	
Implant		
Year 1:	22.5	Discontinuation rates for years 1-4 (including reinsertion) represent mean values of rates reported in an international multicentre RCT[18] and a Scottish community-based study, reflecting routine use[29]. The rates refer to the initial hypothetical cohort of women. Discontinuation rate for following years based on GDG opinion and applied to the subgroup of women remaining in the cohort each year.
Year 2:	14.5	
Year 3:	9	
Year 4 (reinsertion):	5	
Following years:	1	
COC		
Year 1:	45	GDG expert opinion. Discontinuation rate for following years applied to the subgroup of women remaining in the cohort each year.
Following years:	10	
Female sterilisation	-	It was assumed that no discontinuations (and subsequent reversals) occurred. In case of contraceptive failure, repeat of the procedure was considered.

Table 2 Effectiveness data and other input parameters utilised in the economic model (continued)

Input parameter	Baseline value (%)	Comments
Relative probabilities of ectopic pregnancy		
IUD	6	Based on FFPRHC guidance[30]
IUS	25	Based on data from a survey on 17,360 IUS users[31]
Female sterilisation	33	Based on summary of data reported in a clinical guideline on sterilisation[27]
Injectable	1.15	
Implant	1.15	
COC	1.15	Incidence of ectopic pregnancy among pregnancies in the UK general population[32]
Average contraceptive method	1.15	
Probabilities of outcomes following unintended pregnancy		
Birth	46.4	Estimates account for outcomes resulting from *unintended* pregnancies, based on national statistics[33,34], a literature review on unintended pregnancy[35-38] and additional assumptions agreed with the GDG.
Abortion	13	
Miscarriage	40.6	
Discount rate	3.5	NICE guidance[39]

Table 3: Average annual costs and number of unintended pregnancies due to contraceptive failure per 1,000 women for 1 to 15 years of intended contraceptive use

Method	1 year		Method	2 years		Method	3 years	
	Pregnancies	Costs (£)		Pregnancies	Costs (£)		Pregnancies	Costs (£)
F sterilisation	5	722,004	F sterilisation	3	362,249	F sterilisation	2	242,302
Implant	14	262,117	Implant	26	161,470	Implant	34	133,649
IUS	17	270,749	IUD	28	128,286	IUD	35	112,402
IUD	18	195,442	IUS	29	168,546	IUS	36	139,539
Injectable	33	190,534	Injectable	50	169,188	Injectable	56	160,726
COC	91	232,932	COC	95	203,183	COC	96	191,773
Method	**4 years**		**Method**	**5 years**		**Method**	**6 years**	
	Pregnancies	Costs (£)		Pregnancies	Costs (£)		Pregnancies	Costs (£)
F sterilisation	2	182,309	F sterilisation	2	146,297	F sterilisation	2	122,276
Implant	39	145,111	Implant	43	133,363	Implant	45	125,200
IUD	41	108,004	IUS	46	120,707	IUS	48	127,956
IUS	42	127,217	IUD	46	106,911	IUD	50	106,109
Injectable	59	155,734	Injectable	60	152,120	Injectable	62	149,190
COC	96	184,941	COC	96	179,939	COC	96	175,855
Method	**7 years**		**Method**	**8 years**		**Method**	**9 years**	
	Pregnancies	Costs (£)		Pregnancies	Costs (£)		Pregnancies	Costs (£)
F sterilisation	2	105,108	F sterilisation	2	92,223	F sterilisation	2	82,194
Implant	46	129,727	Implant	47	123,549	Implant	48	118,521
IUS	50	122,740	IUS	51	118,523	IUS	52	114,978
IUD	52	105,146	IUD	54	104,079	IUD	55	106,537
Injectable	62	146,648	Injectable	63	144,348	Injectable	63	142,208
COC	95	172,300	COC	95	169,082	COC	94	166,095

Table 3: Average annual costs and number of unintended pregnancies due to contraceptive failure per 1,000 women for 1 to 15 years of intended contraceptive use (continued)

Method	10 years		Method	11 years		Method	12 years	
	Pregnancies	Costs (£)		Pregnancies	Costs (£)		Pregnancies	Costs (£)
F sterilisation	1	74,164	F sterilisation	1	67,588	F sterilisation	1	62,103
Implant	48	120,822	Implant	48	116,603	Implant	48	112,929
IUD	52	111,908	IUS	52	114,270	IUS	52	111,403
IUS	55	105,042	IUD	55	103,567	IUD	56	102,125
Injectable	64	140,182	Injectable	64	138,240	Injectable	64	136,363
COC	93	163,276	COC	92	160,587	COC	91	158,003
Method	**13 years**		**Method**	**14 years**		**Method**	**15 years**	
	Pregnancies	Costs (£)		Pregnancies	Costs (£)		Pregnancies	Costs (£)
F sterilisation	1	57,457	F sterilisation	1	53,471	F sterilisation	1	50,013
Implant	48	114,063	Implant	48	110,834	Implant	48	107,916
IUS	52	108,810	IUS	52	106,434	IUS	52	104,237
IUD	56	100,715	IUD	55	99,335	IUD	55	97,984
Injectable	64	134,539	Injectable	63	132,758	Injectable	63	131,015
COC	91	155,505	COC	90	153,082	COC	89	150,725

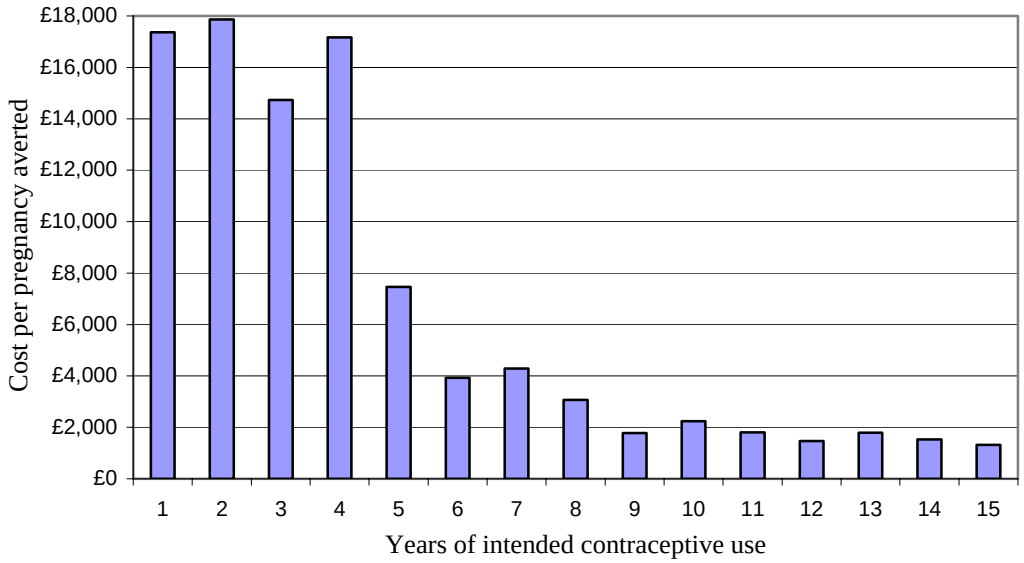
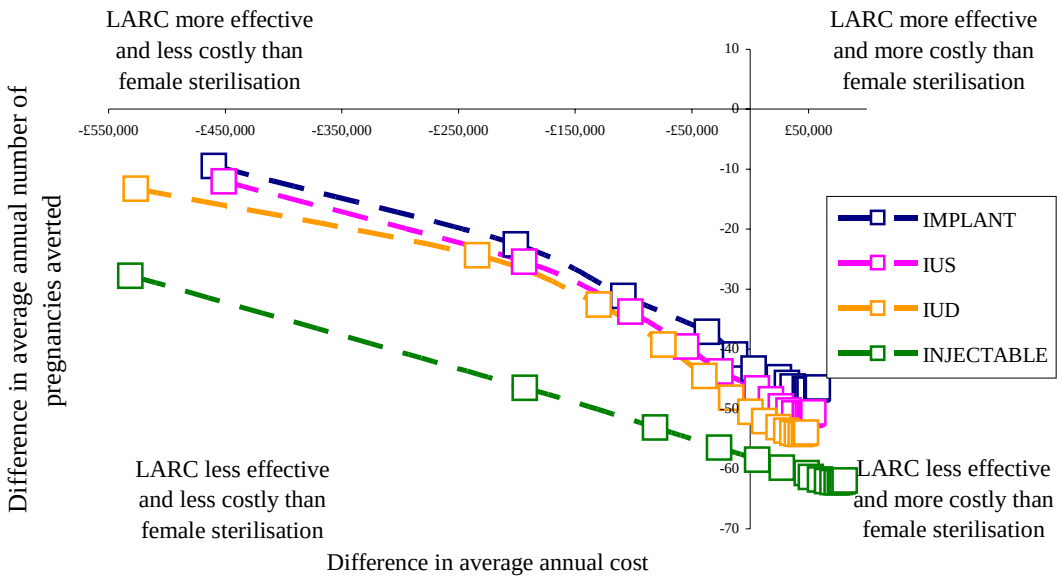
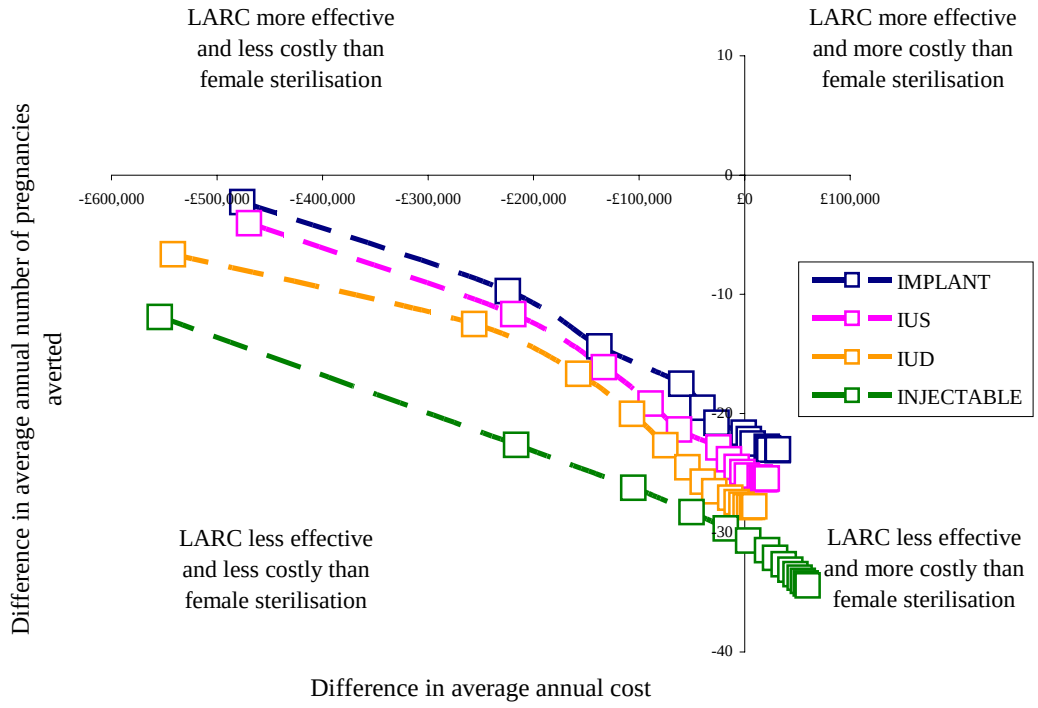


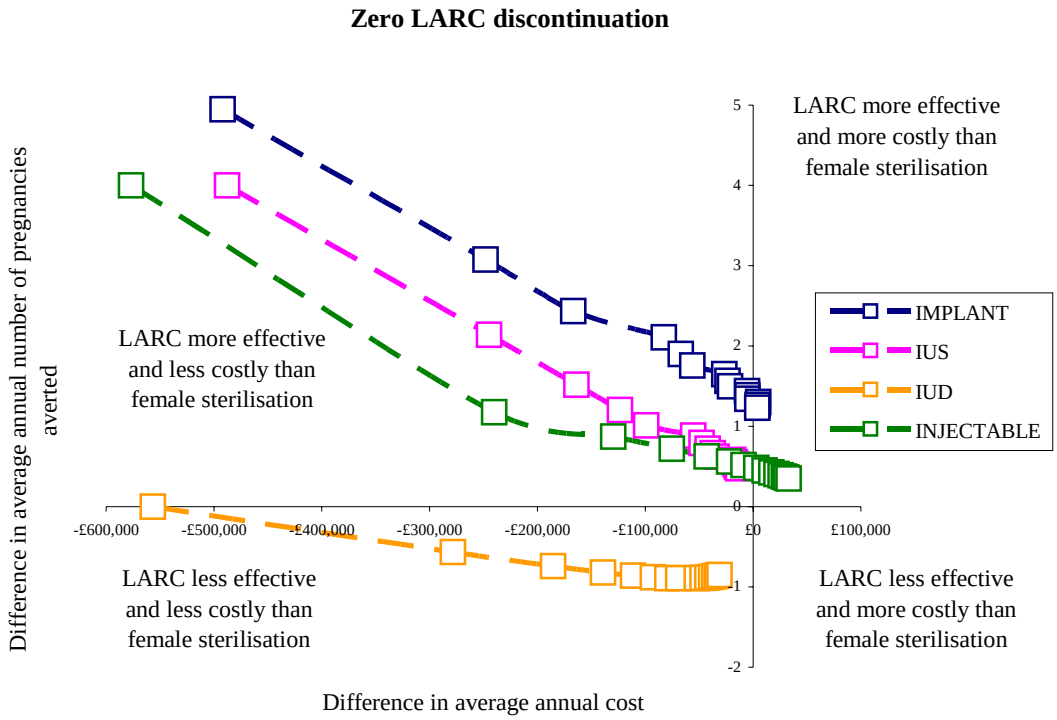
Figure 1: Variation of the ICER of the implant versus the IUD from 1 to 15 years of intended contraceptive use

LARC discontinuation rates: base-case values



LARC discontinuation rates: 50% reduction in the base-case values





<u>Figure 2:</u> Comparison between LARC and female sterilisation at various levels of LARC discontinuation rates using cost-effectiveness planes. Results presented per 1,000 women for 1-15 years of contraceptive protection. (Note that different scales in vertical and horizontal axes have been used, depending on the rate of discontinuation)