Reviewer No.2 Commentary: contraceptive medicines: does choice make a difference?

The detailed review by Andrew Gray and colleagues (Systematic review of contraceptive medicines: does choice make a difference? October 2006) seeks to determine if increasing the choice of contraceptive methods improves acceptance, wellbeing, and contraceptive efficacy. Despite an extensive search of the literature, the Review did not find sufficiently robust evidence to draw firm conclusions or make specific recommendations. It points out that the choice of a contraception method is dictated by a range of factors other than just contraceptive efficacy.

1. Remit of the Review

The reviewers have understandably confined themselves to the primary remit which was to Review ‘evidence supporting the value of the choice philosophy’ (Section 3). A commentary on the appropriateness of interventions actually included in the March 2005 Model List of Essential Medicines might have been valuable; it would have helped to identify important gaps in the choice offered currently.

2. Scope of review: methods available

It might have been helpful to have stated, at the outset of the review, all the contraceptive methods available and to have enumerated the ones that are already included in the Model List. The following are the major methods of fertility control:

**Periodic abstinence**
- Calendar
- Ovulation method
- Sympto-thermal
- Post-ovulation

**Sterilization**
- Male
- Female

**Spermicides [deleted 2003]**

**Barrier (possibly with spermicide)**
- Sponge
- Diaphragm
- Female condom
- Pessary
- Male condom

**Intra-uterine devices**
- Copper intra-uterine devices

**Hormonal contraception**
- Oral
  - Combined (oestrogen + progestogen) oral contraceptive
  - Progestogen-only contraceptive
- Transdermal patches
- Injection (depot)
  - Progestogen only
  - Combined oestrogen + progestogen [Application under consideration]
- Progestogen subcutaneous implant [Application under consideration]
- Progestogen-containing intra-uterine devices [rejected 2005]
- Vaginal rings
Given that the Review favours greater choice, one needs to determine what could be added to the Model List. The general thrust of the Review does not suggest that any method currently on the list should be removed!

In the list above, periodic abstinence and sterilization do not fall within the scope of Essential Medicines. In 2003, the Committee recommended’ removal of the spermicide nonoxynol from the Model List because of evidence indicating increased risk of HIV transmission; at the time there was insufficient evidence to suggest an alternative spermicide.

In 2005, the Committee considered an application for the addition of levonorgestrel-releasing intra-uterine device. The method was considered as effective as copper-containing intra-uterine devices (with a surface area of greater than 250 mm$^2$). However the application was unsuccessful because, compared to the intra-uterine device already on the list, the levonorgestrel device was no more effective, it had a greater discontinuation rate, and it was more expensive.

The methods shown in **bold** are already available in the WHO Model List of Essential Medicines; the two shown in *italic* are to be considered by the Expert Committee in March 2007.

Thus the contraception methods that might be considered for inclusion in section 18.3 of the Model List are:

- **Barrier methods:** sponge, female condom, and pessary
- **Hormonal methods:** progestogen-containing intra-uterine devices, transdermal patches, and vaginal rings

The Review provides little direct support for the introduction of these specific methods. The contraceptive effectiveness of the *sponge* and *female condom* is relatively poor (typical failure rates of 5–20% with ‘perfect’ use compared to failure rates of less than 1% with oral hormonal contraceptives and copper intra-uterine devices). No evidence on the use of *pessaries* is considered by the review.

The evidence reviewed on *levonorgestrel intra-uterine system* (p. 26 of the review) accords well with the background considered in 2005 by the Committee and provides no reason to reconsider its inclusion.

**Transdermal patches** are as effective as combined oral contraceptives but they are more often associated with breast pain (p. 27 of the review). While self-reported adherence was reported to be better than combined oral contraceptives, at least one study suggested a high discontinuation rate with transdermal patches. In some markets, the cost of contraception with transdermal patches is 10-fold greater than with combined oral contraceptives and the same precautions and contra-indications are likely to apply to both methods.

The Review has found evidence of good contraceptive efficacy with *vaginal rings* (the vaginal rings available in Europe release etonogestrel 120 µg and ethinylestradiol 15 µg
daily) and it compared well with other effective methods in terms of satisfaction and adherence (p. 30).

3. Interpretation of the evidence presented

While the evidence identified by the Review indicates that increasing the choice of available methods could improve relevant outcomes (from acceptance and wellbeing to a reduction in the rate of unintended pregnancy), a thorough analysis of the evidence is hampered by the following:

- Lack of definition of ‘limited choice’ versus ‘wide choice’ of contraceptive methods. Without proper definitions, these terms are used variably.
- Difficulty in determining what methods are included by the studies for quantifying the range of available methods—do all the studies count periodic abstinence (see above), sterilization, and use of spermicides or barriers among the choice of contraceptive methods?
- Variability of the classification of contraceptive methods—for example, are variants of injectable methods (say, medroxyprogesterone acetate and norethisterone enantate) regarded as one type of method (injectable progestogen) or two?
- Many of the studies report relatively ‘soft’ outcomes (acceptance, perseverance, satisfaction) rather than the ‘hard’ outcome of a reduction in pregnancy rate (described as the ‘ultimate’ outcome in the review); it goes without saying that wellbeing and freedom from unwanted effects are very important but they are less useful for measuring contraceptive efficiency.
- Some studies were conducted in very special populations and it might not be appropriate to generalise the conclusions of these studies to the entire population seeking contraception.

The reviewers have identified and processed a very considerable body of research on contraceptive methods, paying particular heed to the remit of the review. However, it is possible that some important studies that compare different contraceptive methods and comment on the cost-effectiveness of contraceptives might have been missed.

In 1995, Trussell and colleagues published a study comparing the costs and clinical outcomes of 15 different contraceptive methods. Although the study uses American costs, the economic analysis is of considerable interest.

Another informative study also focussed on cost-effectiveness; it studied reproductive and non-reproductive effects as well as favourable and detrimental effects (including the probability of acquiring sexually transmitted infections including HIV) of 13 contraceptive methods. The societal perspective of this study makes it particularly valuable.

The choice of contraceptive by the same women as they grow older is explored by a Swedish study. Questionnaire responses from 430 women provide some insight into how the methods change over a decade and also how outcomes (pregnancy and adverse effects) change.
It is possible that the above studies were not specifically mentioned in the Review because the results were incorporated in some of the systematic reviews considered.

4. Criteria for inclusion of contraceptive methods on the Model List

The review’s executive summary states that expansion of the choice of methods for contraception is ‘consistent with a human rights and Essential Medicines approach’. However, it acknowledges a possible tension between on the one hand, ‘a rights-based approach’ which favours wide choice and on the other, the approach used for identifying medicines considered essential for the purpose of the Model List. The Review argues that in fact these two approaches are consistent (p. 12).

No persuasive argument is presented to show that while it is appropriate to be highly selective in respect of medicines used for therapeutic purposes, such an approach should be abandoned for considering contraceptive methods. Essential medicines are selected with due regard to disease prevalence, evidence on efficacy and safety, and comparative cost-effectiveness. The drivers for selecting a list of few but highly cost-effective medicines must surely also apply to contraceptive methods.

While the principles of the Model List of Essential Medicines should be applied to contraceptives, it is nevertheless important to recognise and address the diverse needs that contraceptive methods are required to meet, as identified in the review; the more important of these are:

- contraceptive efficacy;
- reversibility;
- contraceptive duration;
- type of individual most suitable for (age, lifestyle, fertility history, changing motivation for practising contraception);
- compelling contra-indications;
- compelling indications (or non-contraceptive advantages); and
- clinical support available for initiation and continued use

In contrast to other medicines used for chronic conditions or prophylaxis, for contraceptive methods, special attention also needs to be paid to:

- local custom and religious beliefs;
- societal pressures;
- individuals’ understanding of reproductive processes and acceptance of changes to ‘normal’ functioning; and
- sensitivity to potentially different attitudes and expectations between partners.

These last points in particular call for considerable local input into the range and types of contraceptive methods available; it would be inappropriate to address these issues by means of global policies.
5. Conclusions

While the Review makes a good case for ensuring that a sufficient number of appropriate methods should be available, in order to inform changes to the current list, the Committee needs to be provided with evidence to help it decide:

- What the most pressing needs are for individuals seeking contraception
- Which of these needs are not met by the methods already on the Model List
- What methods need to be introduced in order to meet the priority needs

6. Recommendations

In the light of the Review it is recommended that the Committee should:

1. Make no immediate change to the Model List (except in relation to the applications being considered)
2. Consider inviting an application for the introduction of hormone-releasing vaginal ring
3. Commission a further review that takes into account priority needs and cost-effectiveness; opportunity should be taken to consider the need for continuing to include two progestogen-only depot injections. The review should take into account cost-effectiveness research of the type identified,\(^3\,^5\) as well as evidence-based national and international guidelines.

January 2007

References

1. WHO Technical Report Series 920, section 4.2.2
2. WHO Technical Report Series 933, section 4.2.10