



IPPF Medical Bulletin

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Tools for assessment of STI risk in family planning settings

Willard Cates Jr, Michael J Welsh

Assessment of the risk of sexually transmitted infection (STI) has long been part of disease control programmes.¹ In addition, it can be of help to family planning (FP) workers, since risk of STI/HIV is relevant to the choice of contraception.² What exactly is STI risk assessment? Quite simply, it is the use of demographic, behavioural, and clinical factors (other than the laboratory) to assess the likelihood that a person is either currently infected or at high risk of future infection.³ These factors can be aggregated into graduated scales of increasing risk called clinical algorithms. The derived models can then be used as aids to both STI management and FP counselling. This article focuses on the latter goal.

STI risk assessment for contraceptive management

Although clinical algorithms are based on predictions at population level, the profile that emerges can be helpful to individual clients by opening up the subject of STI and its implications for contraceptive choice. A key concept is the test statistic of *negative predictive value*, which yields the percentage of clients found negative by the algorithm who are actually uninfected. By identifying those clients most likely to be free of an STI, a risk assessment algorithm with a high negative predictive value will be a useful tool for FP service providers.³

A conceptual model

Imagine a real-world population curve, with a bell-shaped distribution according to the probability of being infected

(Figure 1). This population would range from those who were definitely uninfected (score 0) to those who were definitely infected (score 10). The location of this curve would be skewed on the scale according to the population being served. For example, populations attending STI clinics would have a curve distributed to higher scores, the general population would have low scores, and those attending FP clinics would be somewhere in between. The scores are based on interacting behavioural/clinical/demographic/epidemiological factors. Clients who are sexually inactive, have no symptoms or signs, are older married persons, and reside in low-prevalence regions will have the lowest score; those who have had recent unprotected sex with an infected partner, who are young and unmarried, and who live in high-prevalence regions would have higher scores; and those who have symptoms or signs would have the highest scores and should be referred for presumptive treatment.

These risk assessment scores would then be used to guide clinical contraceptive management. Clients with the lowest scores would be good candidates for intrauterine devices; those with the highest scores would be encouraged to use, and be provided with, barrier methods. Persons in the intermediate category could be referred for laboratory testing (if available) before a particular contraceptive method was recommended. While the risk assessment tool does not predict the risk of any individual client, it allows a provider to view the client in the context of populations with similar attributes.

Need for empirical data

Many FP professionals are already operating their clinics implicitly, though not explicitly, according to these principles. What is needed, for each population, is a set of objective criteria that translate into an aggregate score for use in contraceptive management. One such effort has been reported by researchers from Family Health International.⁴ They used data from six countries to develop and validate a categorical algorithm targeted to insertion of intrauterine devices (IUDs). They found that an algorithm based on demographic and historical variables (age less than 25, not living with partner, low education, bleeding between periods, no/some condom use with one or more sex partners) usefully discriminated those women best suited for immediate IUD insertion. Clinical data added little to its value. A crucial measure, for such an algorithm to work well, is the prevalence of STI in the community.⁵ However, even in settings of moderate or high STI prevalence, the risk of pelvic inflammatory disease after IUD insertion can be kept low by use of an algorithm.⁶

FIGURE 1 DISTRIBUTIONS OF STI/HIV RISK IN THREE POPULATIONS

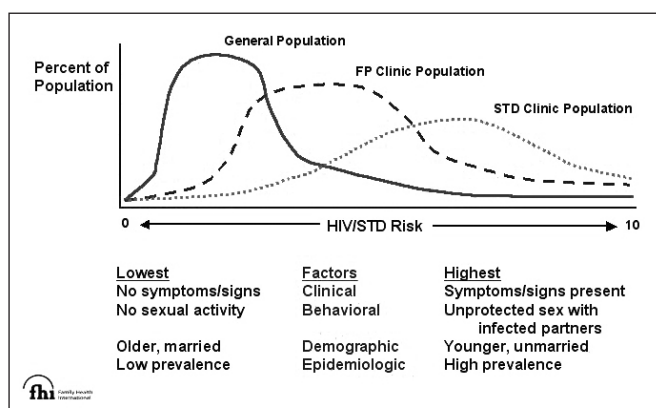
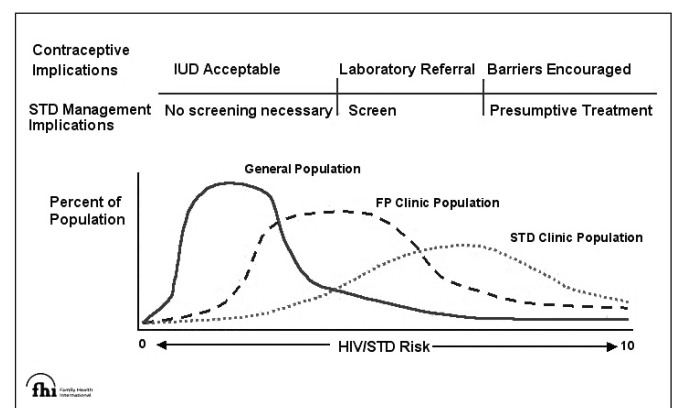


FIGURE 2 LEVELS OF STI/HIV RISK – EFFECT ON CONTRACEPTIVE AND STI MANAGEMENT



Current versus future infection risks

While the above example has concentrated on the risk of *current* STI, the same concept can be used to assess the likelihood of *future* infection. Unfortunately, fewer data on the risk of becoming infected are available to provide a foundation for assessing the thresholds to guide counselling. If a person is currently infected, he/she is at excess risk of becoming reinfected in the future, and the same combination of demographic, behavioural, and clinical factors applies.

The dynamic nature of many sexual relationships, as well as the multiple stages of a woman's reproductive life,⁷ means that this model should not be viewed as static. Contraceptive needs will vary with changes in a person's sexual behaviour, and resultant STI risk. A woman who now seems an excellent candidate for an IUD may need to use barrier methods in the future, either as her primary contraceptive method or as a second method to provide STI protection with new partners.

Partner's risk versus client's risk

Another challenge for risk assessment in FP programmes is the need for better ways to assess risk of infection of a client's partner,⁸ which may be a stronger predictor of risk than the indices from the client herself.⁹⁻¹¹ Indeed, an algorithm built on a male partner's risk profile may be an effective means of assessing a client's actual risk. Creation of algorithms of this kind demands more effective ways of talking about sex and sexuality with clients. Couple counselling, which seems feasible in some cultures, may offer a means of independently assessing the risk of infection in both partners.

From research to practice

The rationale for more effective risk assessment tools is clear. Emerging research⁴ indicates that the use of historical data (age, education, behavioural risk) can provide insights into the true risk profile of clients seeking FP services. However, the algorithms rely greatly on estimates of STI prevalence in the community, and at present we are not collecting the information on common infections that would allow estimation of risk in clinic catchment areas.

Moreover, sexual behaviour is intimately bound to culture. Factors that predict in one culture may be less useful in another.

Acceptability of amenorrhoea associated with contraception

Anna Glasier

Of all the reversible methods of contraception only barrier methods are without effects on menstruation. Copper intrauterine devices tend to make women's periods longer and heavier. The combined pill, the contraceptive patch, and the combined injectable all confer a regular but artificial withdrawal bleed and are often associated with breakthrough bleeding. Low-dose progestogen-only contraceptives (pills, implants, and the intrauterine system) all disrupt the normal vaginal bleeding pattern in most users. Depot medroxyprogesterone and norethisterone oenanthate are commonly associated with amenorrhoea.

Disturbance of menstrual bleeding patterns is the commonest reason for discontinuation of hormonal methods of contraception and IUDs, and there has long been a belief that amenorrhoea in association with contraception is unacceptable to most women, especially in developing countries. This belief arises from surveys undertaken in the 1970s and 1980s which suggested that women like to have regular periods because menstruation indicates femininity and normality (including potential fertility) as well as offering reassurance to the woman that she is not pregnant. In fact regular menstruation is not 'natural': before modern contraception women spent much of their reproductive lives amenorrhoeic as a consequence of either pregnancy or breastfeeding.

In Europe in recent years amenorrhoea has become much more popular and indeed several published reports have suggested that women would be glad if they had periods less

No tool will ever replace a clinician's subjective client assessment skills, but a risk assessment algorithm based on sound local prevalence data could be of great help to busy clinicians in discussion of sensitive sexual matters. There is a pressing need for such tools that will improve the effectiveness of counselling services and permit more informed contraceptive choice in the context of STI/HIV.

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References

1. Curtis JR, Holmes, KK. Individual-level risk assessment for STD/HIV infections. In: Holmes KK, et al. Sexually Transmitted Diseases, 3rd edn. New York: McGraw Hill, 1999:669-83
2. Cates W Jr. Reproductive tract infections. In: Hatcher RA, et al., eds. Contraceptive Technology, 17th edn. New York: Ardent Media, 1998:179-210.
3. Cates W Jr. A risk assessment tool for integrated reproductive health services. *Fam Plann Perspect* 1997;**29**:41-3
4. Morrison C, Kwok C, Weiner D. Identifying appropriate candidates for IUD insertion in moderate to high STI settings: The IUD Algorithm Project. Research Triangle Park, North Carolina: Family Health International, 2003
5. Miller WC. Screening for chlamydial infection: a model program based on prevalence. *Sex Transm Dis* 1998;**25**:201-10
6. Shelton JD. Risk of clinical pelvic inflammatory disease attributable to an intrauterine device. *Lancet* 2001;**357**:443
7. Forrest JD. Timing of reproductive life stages. *Obstet Gynecol* 1993;**82**:105-11
8. Welsh M, Feldblum PJ, Chen S. Sexually transmitted disease risk assessment used among low risk populations in East/Central Africa: a review. *E Afr Med J* 1997;**74**:764-70
9. Hunter DJ, Maggwa BN, Mati JKG, Tukei PM, Mbugua S. Sexual behavior, sexually transmitted diseases, male circumcision and risks of HIV infection among women in Nairobi, Kenya. *AIDS* 1994;**8**:93-9
10. Allen S, Lindan C, Serufilira A, et al. Human immunodeficiency virus infection in urban Rwanda. Demographic and behavioral correlates in a representative sample of childbearing women. *JAMA* 1991;**266**:1657-63
11. Kapiga SH, Shao JF, Lwihula GK, Hunter DJ. Risk factors for HIV infection among women in Dar-es-Salaam, Tanzania. *J Acquir Immune Defic Syndr* 1994;**7**:301-9

often. A study from the Netherlands¹ indicated that 26% of women aged 15-19 and 31% of women aged 25-34 would prefer never to menstruate at all. If they had the opportunity to design their own bleeding patterns, another one-third of young women would choose to bleed only once every three months.

In a recently published survey² of 1000 women attending family planning clinics and 290 contraceptive providers in China, South Africa, Nigeria, and Scotland, black women in Africa were the only group in which the majority liked having periods. In all centres except Shanghai and Hong Kong the majority of women - over 60% in Scotland and South Africa and over 70% in Nigeria - were willing to consider a method of contraception which stopped their periods. Even in the two Chinese centres more than one-third of women would be prepared to try a contraceptive method which induced amenorrhoea.

Providers have a very powerful influence on the method of contraception which women ultimately choose to use. In all centres in this international study, over 80% of providers thought that regular menstruation during contraceptive use was either quite important or very important to their clients. The biggest contrast between providers' views and those of their clients was in Nigeria where 48% of providers would not recommend a method of contraception which caused amenorrhoea to the clients but 73% of the women themselves said they would consider using such a method.

The widespread belief among agencies involved in contraceptive development that amenorrhoea is unacceptable has deterred them from developing new methods of contraception which stop menstruation. It is clear from the recent research that women's attitudes to amenorrhoea are

changing. In Western Europe women are actively choosing depot medroxyprogesterone and the levonorgestrel-releasing intrauterine system *because* they wish to avoid bleeding, and increasing numbers of women manipulate use of the combined pill for the same purpose. In the USA a new combined oral contraceptive, Seasonale, is to be taken for 84 days continuously before a 7-day interruption for withdrawal bleeding. In the developing world it seems that women are likewise beginning to accept that menstruation is not inevitable. Contraceptive providers need to catch up with the changing views of their clients.

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References

1. Den Tonkelaar I, Oddens BJ. Preferred frequency and characteristics of menstrual bleeding in relation to reproductive status, oral contraceptive use and hormone replacement therapy use. *Contraception* 1999; **59**: 357–62
2. Glasier AF, Smith KB, Van der Spuy ZM, et al. Amenorrhea associated with contraception – an international study on acceptability. *Contraception* 2003; **67**:1–8

Progestogen-only emergency contraception and risk of ectopic pregnancy

Susan Brechin

Progestogen-only emergency contraception (POEC) is an effective method of preventing pregnancy following unprotected sex or potential contraceptive failure.^{1–3} A UK report draws attention to the possibility of ectopic pregnancy when POEC is unsuccessful.⁴ The limited evidence regarding ectopic risk following POEC is summarised here.

Mode of action

The mode of action of POEC is incompletely understood but ovulation is inhibited in up to 80% of women if it is used before the luteinising hormone surge.⁵ There is little evidence for an anti-implantation effect.⁶ Routine progestogen-only contraceptive pills (POPs) work by thickening cervical mucus, delaying ovum transport, inhibiting ovulation, and providing an endometrium hostile to implantation.⁷ The potential delay in ovum transport with POPs raises concerns of ectopic pregnancy if POPs fail but this should not be confused with the use of POEC. One in ten pregnancies occurring due to POP failure is likely to be ectopic but the contraceptive efficacy of POP means that the overall risk of ectopic pregnancy is no higher than that in women not using contraception.⁷

Risk of ectopic pregnancy

Of 201 unintended pregnancies following POEC use that were reported to the UK Committee on Safety of Medicines, 12 (6%) were ectopic. The reports were spontaneous, and there might have been a bias towards reporting of ectopic pregnancies. A large randomised trial² identified a lower rate. In this trial, 44 pregnancies were reported following POEC use by 2712 women, but only one was ectopic. In its *Medical Eligibility Criteria for Contraceptive Use*, the World Health Organization recommends that POEC may be used in women who have already had an ectopic pregnancy.⁸

Improving efficacy of progestogen-only emergency contraception

Failure rates for POEC increase with time since unprotected sex or potential contraceptive failure.¹ In a randomised trial the proportion of expected pregnancies prevented was 95% when the method was used less than 24 hours after unprotected sex. This fell to 85% at 25–48 hours, and 58% at 49–72 hours. One way to reduce failure rates (both intrauterine and extrauterine) is therefore to improve access and compliance. This may be achieved by: education and advanced supply; patient group directions for nurse supply and administration; or pharmacy supply. Randomised trials have shown that advanced provision of emergency contraception is safe and may reduce unintended pregnancies.^{9,10} When women have advanced supplies the uptake of regular contraception is unchanged⁹ and there is no increase in unprotected sex.¹⁰ Advanced provision allows

health professionals to offer education and counselling on emergency methods, ongoing contraception, and other matters relating to reproductive and sexual health. Nurse and pharmacist supply can facilitate access to POEC. In the UK, women are able to purchase progestogen-only emergency contraception from pharmacies without a medical prescription, but the high price may limit access. Compliance with treatment might increase if the pills could be given in a single dose rather than two doses of 0.75 mg with an interval of 12–16 hours. Evidence from a randomised controlled trial² suggests that a single dose of 1.5 mg is no less effective, but the UK product licence does not yet cover this regimen.

Evidence-based recommendations

In the UK, the Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit has recently published evidence-based graded recommendations, and good practice points where no evidence exists, to help professionals and their clients to make decisions on use of emergency contraception.¹¹ Panel 1 lists recommendations relevant to POEC and ectopic pregnancy. Women should be advised of other methods of emergency contraception, such as the copper-bearing intrauterine contraceptive device, which may be more effective. Information on how and when to seek help should be provided to all women receiving POEC.

At present there is insufficient evidence to state the true rate of ectopic pregnancy following the use of POEC but women should be reassured that the risk is slight. The risk of any pregnancy is lowest when POEC is used early.

PANEL 1: UK RECOMMENDATIONS FOR USE OF PROGESTOGEN-ONLY EMERGENCY CONTRACEPTION¹¹

Improve efficacy

POEC should be started as soon as possible and within 72 hours of unprotected sex or potential contraceptive failure. In routine practice, one tablet containing 0.75 mg levonorgestrel should be given and repeated 12–16 hours later.

To facilitate early use, advanced provision of POEC and instructions on use can be offered to those attending family planning and sexual health services.

Improve compliance

In situations where patient compliance is likely to be poor, POEC may be given as a single dose of 1.5 mg levonorgestrel.

Follow-up

Women should be asked to return for a pregnancy test if their expected menstruation is more than seven days late, or lighter than usual.

The possibility of an ectopic pregnancy should be considered if POEC has failed or where an abnormal bleeding pattern follows its use (*good practice point*).

Women should be provided with written information on how to access help and advice should any side effects occur (*good practice point*).

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References

1. Task Force on Postovulatory Methods of Fertility Regulation. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet* 1998;**352**:428–33
2. von Hertzen H, Piaggio G, Ding J, et al. Low dose mifepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicentre randomised trial. *Lancet* 2002;**360**:1803–10
3. Turner AN, Ellertson C. How safe is emergency contraception? *Drug Safety* 2002;**25**:695–706
4. Chief Medical Officer. Levonelle/Levonelle-2 emergency contraception: new advice. 35, 2003

IMAP recommendation on single-dose levonorgestrel for emergency contraception

At its latest meeting IPPF's International Medical Advisory Panel (IMAP) reviewed the results of a WHO randomised trial (*Lancet* 2002; **360**: 1803–10) which provides evidence that a single 1.5 mg dose of levonorgestrel is as effective as two 0.75 mg doses taken 12 hours apart. In addition the trial shows that, although levonorgestrel for emergency contraception is most effective when taken within 72 hours after intercourse, the method still provides some protection when it is used on the 4th and 5th days. In the light of these findings, IMAP recommends that a single dose of levonorgestrel should be an alternative to two doses. This recommendation for a single dose applies only to the levonorgestrel method, not to the combined method (Yuzpe). The Yuzpe method should remain

5. Durand M, del Carmen Cravioto M, et al. On the mechanisms of short-term levonorgestrel administration in emergency contraception. *Contraception* 2001;**64**:227–34
6. Croxatto MB. Emergency contraception pills: how do they work? *IPPF Med Bull* 2002; **36**(6): 1–2
7. McCann MF, Potter LS. Progestin-only oral contraception: a comprehensive review. *Contraception* 1994; **50** (suppl): S9–195
8. World Health Organization. *Improving Access to Quality Care in Family Planning. Medical Eligibility Criteria for Contraceptive Use*. Geneva: WHO, 2000
9. Glasier A, Baird D. The effects of self-administering emergency contraception. *N Engl J Med* 1998;**339**:1–4
10. Ellertson C, Ambardekar S, Hedley A, Coyaji K, Trussell J, Blanchard K. Emergency contraception: randomized comparison of advance provision and information only. *Obstet Gynecol* 2001;**98**:570–5
11. FFPRHC Guidance. Emergency contraception. *J Fam Planning Reprod Healthcare* 2003; **29**(2): 9–16

an option, because it is a good alternative and less costly in many countries. IMAP reminds providers of the high effectiveness of intrauterine devices (IUDs) as emergency contraception in women who are eligible. Prompt and easy access to emergency contraception is crucial. IMAP recommends the following strategy, based on effectiveness, for the 5 days after unprotected intercourse:

Days 1–3

First choice: single oral dose of 1.5 mg levonorgestrel *or* two oral doses of 0.75 mg levonorgestrel 12 h apart

Second choice: IUD *or* two doses of combined pills (Yuzpe regimen)

Days 4–5

First choice: IUD

Second choice: single dose of 1.5 mg levonorgestrel *or* two doses of 0.75 mg levonorgestrel 12 h apart

News

Sexual networks in HIV-positive women

In their article at the beginning of this *Bulletin*, on assessment of STI/HIV risk, Dr Cates and Dr Welsh indicate that data from a woman's partner may be more informative than data from the woman herself. This is borne out by a study of sexual networks in women attending a maternity hospital in Lima, Peru. Johnson and co-workers¹ interviewed 75 HIV-positive women, 41 of their most recent partners, and two control groups totalling 137 uninfected pregnant women and 70 of their most recent male partners. Each woman's sexual network size was estimated through second and third generation partners over the past year, and lifetime. Few of the HIV-positive women reported behavioural factors for HIV infection, but 79% of their partners were infected. The mean 5-year sexual network sizes through the second generation (8.4 persons for HIV-positive women, 2.5 and 1.9 in the two control groups, predicted HIV in the woman independently of her own number of partners. Johnson et al. conclude, "HIV infection risk among pregnant women in Lima depends largely on their male partners' risk behaviors. Even monogamous women had very large sexual networks."

Reference

1. Johnson KM, Alarcon J, Watts DM, et al. Sexual networks of pregnant women with and without HIV infection. *AIDS* 2003; **17**:605–12

Hormonal contraceptives and risk of cervical cancer

A year ago, Dr Olav Meirik reviewed research indicating that cervical cancer occurs almost exclusively in women who have persistent cervical infection with oncogenic human papillomavirus (HPV), and that the risk of such cancers is modestly increased among users of combined oral contraceptives.¹ The World Health Organization had recommended no immediate action in response to the new finding, pending further research: the number of cervical cancers resulting from oral contraceptive use was likely to be small, especially in countries with screening programmes. A systematic review of 28 relevant studies now confirms this conclusion, though with generally lower estimates of excess risk.² The paper indicates that, among HPV-positive women, relative risks for users of oral contraceptives (compared with never users) are 0.9 at <5 years, 1.3 at 5–9 years, and 2.5 at 10 or more years. The authors say, "Although long duration use of hormonal contraceptives is associated with an increased risk of cervical cancer, the public health implications of these findings depend largely on the extent to which the observed associations remain long after use of hormonal contraceptives has ceased, and this cannot be evaluated properly from published data." So again, more research is needed.

References

1. Meirik O. Combined oral contraceptives, human papillomavirus, and cervical cancer. *IPPF Med Bull* 2002; **36** (no. 4): 2–3
2. Smith JS, Green J, Berrington de Gonzalez A, et al. Cervical cancer and use of hormonal contraceptives: a systematic review. *Lancet* 2003; **361**: 1159–67

