Long-acting reversible contraception

the effective and appropriate use of long-acting reversible contraception

National Collaborating Centre for Women's and Children's Health

Commissioned by the National Institute for Health and Clinical Excellence

October 2005

RCOG Press

Update information 2019

In March 2019 we revised our decision on how to implement the recommendations of our October 2017 review. Although no new evidence was identified, we noted significant changes in how we commission and provide contraceptive services in England. We have removed the recommendations in the short version of the guideline that no longer fit with current practice, and have deleted or redacted the content related to those removed recommendations in this guideline. There are also many new LARC products now available. See our Long-acting reversible contraception: implementation resource summary for links to the latest information, which is available in the short version of the guideline (along with links to the October 2017 review) at: http://www.nice.org.uk/cg30

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Addenbrookes NHS Trust
Amber Valley Primary Care Trust
Anglesey Local Health Board
Ashfield and Mansfield District Primary Care Trust
Association of British Healthcare Industries
Association of Surgeons of Great Britain and Ireland
Association of the British Pharmaceuticals Industry (ABPI)
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National Patient Safety Agency
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NHS Direct
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The Survivors Trust
Trafford Primary Care Trusts
University College London Hospitals NHS Trust
Vale of Aylesbury Primary Care Trust
Welsh Assembly Government (formerly National Assembly for Wales)

Abbreviations

ALOs	*Actinomyces*-like organisms
BMD	bone mineral density
BMI	body mass index
BNF	British National Formulary
BTB	breakthrough bleeding
CHC	combined hormonal contraceptive
CI	confidence interval
COC	combined oral contraceptive
CVD	cardiovascular disease
DFFP	Diploma of the Faculty of Family Planning and Reproductive Health Care
DH	Department of Health
DMPA	depot medroxyprogesterone acetate
*e*MC	Electronic Medicines Compendium
ENG	etonogestrel
FPC	family planning clinic
FFPRHC	Faculty of Family Planning and Reproductive Health Care
GDG	Guideline Development Group
GP	general practitioner
GPP	good practice point
GU	genitourinary
HDL	high-density lipoprotein
HIV	human immunodeficiency virus
HRT	hormone replacement therapy
HTA	Health Technology Assessment
IUS	intrauterine system
ICER	incremental cost effectiveness ratio
IUD	intrauterine device
LARC	long-acting reversible contraception
LDL	low-density lipoprotein
LNG	levonorgestrel
LoC	letter of competence
LSHTM	London School of Hygiene and Tropical Medicine
MBL	menstrual blood loss
MHRA	Medicines and Healthcare products Regulatory Agency
MI	myocardial infarction
MPA	medroxyprogesterone acetate
NCC-MH	National Collaborating Centre for Mental Health
NCC-WCH	National Collaborating Centre for Women's and Children's Health
NET-EN	norethisterone enantate
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NICU	neonatal intensive care unit
NMC	Nursing and Midwifery Council
NSAID	non-steroidal anti-inflammatory drug
OC	oral contraceptive pill
OR	odds ratio
PCT	primary care trust
PID	pelvic inflammatory disease
POC	progestogen-only oral contraceptive
POICs	progestogen-only injectable contraceptives
POSDIs	progestogen-only subdermal implants

QALY	quality adjusted life year
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	randomised controlled trial
RR	risk ratio
SD	standard deviation
SPC	Summary of Product Characteristics
STI	sexually transmitted infection
STIF	sexually transmitted infections foundation course
TTP	time to pregnancy
UKSPR	UK Selected Practice Recommendations for Contraceptive Use
VTE	venous thromboembolism
WHO	World Health Organization
WHO-MEC	World Health Organization Medical Eligibility Criteria for Contraceptive Use
WHOSPR	World Health Organization Selected Practice Recommendations for Contraceptive Use
WMD	weighted mean difference

Glossary of terms

Bias

Influences on a study that can lead to invalid conclusions about a treatment or intervention. Bias in research can make a treatment look better or worse than it really is. Bias can even make it look as if the treatment works when it does not. Bias can occur by chance or as a result of systematic errors in the design and execution of a study. Bias can occur at various stages in the research process, for example, in the randomisation, collection, analysis, interpretation, publication or review of research data.

Blinding or masking

The practice of keeping the investigators or subjects of a study ignorant of the group to which a subject has been assigned. For example, a clinical trial in which the participating patients or their doctors are unaware of whether they (the patients) are taking the experimental drug or a placebo (dummy treatment). The purpose of 'blinding' or 'masking' is to protect against bias. See also **double blind study**.

Case–control study

A study that starts with the identification of a group of individuals sharing the same characteristics (for example, people with a particular disease) and a suitable comparison (control) group (for example, people without the disease). All subjects are then assessed with respect to things that happened to them in the past, for example, things that might be related to getting the disease under investigation. Such studies are also called retrospective as they look back in time from the outcome to the possible causes.

Case report (or case study)

Detailed report on one patient (or case), usually covering the course of that person's disease and their response to treatment.

Case series

Description of several cases of a given disease, usually covering the course of the disease and the response to treatment. There is no comparison (control) group of patients.

Clinical trial

A research study conducted with patients which tests out a drug or other intervention to assess its effectiveness and safety. Each trial is designed to answer scientific questions and to find better ways to treat individuals with a specific disease. This general term encompasses **controlled clinical trials** and **randomised controlled trials**.

Cohort

A group of people sharing some common characteristic (for example, patients with the same disease), followed up in a research study for a specified period of time.

Cohort study

An observational study that takes a group (cohort) of patients and follows their progress over time in order to measure outcomes such as disease or mortality rates and make comparisons according to the treatments or interventions that patients received. Thus, within the study group, subgroups of patients are identified (from information collected about patients) and these groups are compared with respect to outcome, for example, comparing mortality between one group that received a specific treatment and one group that did not (or between two groups that received different levels of treatment). Cohorts can be assembled in the present and followed into the future (a 'concurrent' or 'prospective' cohort study) or identified from past

records and followed forward from that time up to the present (a 'historical' or 'retrospective' cohort study). Because patients are not randomly allocated to subgroups, these subgroups may be quite different in their characteristics and some adjustment must be made when analysing the results to ensure that the comparison between groups is as fair as possible.

Confidence interval

A way of expressing certainty about the findings from a study or group of studies, using statistical techniques. A confidence interval describes a range of possible effects (of a treatment or intervention) that is consistent with the results of a study or group of studies. A wide confidence interval indicates a lack of certainty or precision about the true size of the clinical effect and is seen in studies with too few patients. Where confidence intervals are narrow they indicate more precise estimates of effects and a larger sample of patients studied. It is usual to interpret a '95%' confidence interval as the range of effects within which there is 95% confidence that the true effect lies.

Control group

A group of patients recruited into a study that receives no treatment, a treatment of known effect, or a placebo (dummy treatment), in order to provide a comparison for a group receiving an experimental treatment, such as a new drug.

Controlled clinical trial

A study testing a specific drug or other treatment involving two (or more) groups of patients with the same disease. One (the experimental group) receives the treatment that is being tested, and the other (the comparison or control group) receives an alternative treatment, a placebo (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. A controlled clinical trial where patients are randomly allocated to treatment and comparison groups is called a **randomised controlled trial**.

Cost effectiveness analysis

A type of economic evaluation where outcomes are expressed in natural units, for example, number of cases cured, number of lives saved, etc.

Crossover study design

A study comparing two or more interventions in which the participants, upon completion of the course of one treatment, are switched to another. For example, for a comparison of treatments A and B, half the participants are randomly allocated to receive them in the order A, B and half to receive them in the order B, A. A problem with this study design is that the effects of the first treatment may carry over into the period when the second is given. Therefore a crossover study should include an adequate 'wash-out' period, which means allowing sufficient time between stopping one treatment and starting another so that the first treatment has time to wash out of the patient's system.

Cross-sectional study

The observation of a defined set of people at a single point in time or time period – a snapshot. (This type of study contrasts with a **longitudinal study**, which follows a set of people over a period of time.)

Decision-analytic model

A mathematical simulation of the real world, where cost and outcome data derived from various sources are incorporated, resulting in the estimation of the relative cost effectiveness between two or more interventions; it enables economic evaluation of alternative courses of action, therefore contributing to decision making.

Dominance

A possible result of comparison between two alternatives in economic evaluation; one intervention is said to dominate its comparator when it is both more effective and less costly.

Double blind study
A study in which neither the subject (patient) nor the observer (investigator or clinician) is aware of which treatment or intervention the subject is receiving. The purpose of blinding is to protect against bias.

Dysmenorrhoea
Painful menstrual bleeding.

Economic evaluation
The comparative analysis between two or more interventions, in terms of both their costs and outcomes.

Evidence-based clinical practice
Evidence-based clinical practice involves making decisions about the care of individual patients based on the best research evidence available rather than basing decisions on personal opinions or common practice (which may not always be evidence based). Evidence-based clinical practice therefore involves integrating individual clinical expertise and patient preferences with the best available evidence from research.

Evidence table
A table summarising the results of a collection of studies which, taken together, represent the body of evidence supporting a particular recommendation or series of recommendations in a guideline.

Exclusion criteria
See **selection criteria**.

Experimental study
A research study designed to test whether a treatment or intervention has an effect on the course or outcome of a condition or disease, where the conditions of testing are to some extent under the control of the investigator. **Controlled clinical trial and randomised controlled trial** are examples of experimental studies.

Extrapolation
The projection or extension of directly established knowledge to an area not currently open to observation on the basis of known data.

Fraser guidelines
A set of criteria which must be applied when medical practitioners are offering contraceptive services to under-16s without parental knowledge or permission. These guidelines stem from the legal challenge by Victoria Gillick in the early 1980s to medical practitioners' right to provide children under 16 years of age treatment or contraceptive services without parental permission. On occasion practitioners may refer to assessing whether a young person is Gillick competent.

Gillick competence
See **Fraser guidelines**.

Gold standard
A method, procedure or measurement that is widely accepted as being the best available.

Hazard ratio
In survival analysis, a summary of the difference between two survival curves, representing the reduction in the risk of death on treatment compared with control, over the period of follow-up.

Health economics
A field of conventional economics which examines the benefits of healthcare interventions (for example, medicines) compared with their financial costs.

Heterogeneity
Or lack of **homogeneity**. The term is used in **meta-analysis** and **systematic review** when the results or estimates of effects of treatment from separate studies seem to be very different, in terms of the size of treatment effects, or even to the extent that some indicate beneficial and others suggest adverse treatment effects. Such results may occur as a result of differences between studies in terms of patient populations, outcome measures, definition of **variables** or duration of follow-up.

Homogeneity
This means that the results of studies included in a **systematic review** or **meta-analysis** are similar and there is no evidence of **heterogeneity**. Results are usually regarded as homogeneous when

	differences between studies could reasonably be expected to occur by chance.
Incidence	The rate of occurrence of new cases of a particular disease in a population being studied.
Inclusion criteria	See **selection criteria**.
Incremental cost effectiveness ratio	A method of presentation of results of an economic evaluation; it expresses the additional (incremental) cost incurred for an additional unit of benefit gained, by adopting an intervention over its comparator.
Intervention	Healthcare action intended to benefit the patient, for example, with drug treatment, surgical procedure or psychological therapy.
Kaplan–Meier method	A nonparametric technique for estimating time-related events (the survivorship function). Ordinarily it is used to analyse death as an outcome. It may be used effectively to analyse time to an endpoint, such as remission.
Level one service	Minimum level of provision within primary care sexual health services.
Longitudinal study	A study of the same group of people at more than one point in time. (This type of study contrasts with a **cross-sectional study**, which observes a defined set of people at a single point in time.)
Masking	See **blinding**.
Menarche	The beginning of the menstrual function, particularly the first menstrual period of a female.
Menopause	The period of natural cessation of menstruation, usually occurring between the ages of 45 and 50 years, signalling the end of a woman's reproductive capacity.
Menorrhagia	Excessive or prolonged menstrual bleeding.
Metromenorrhagia	Uterine bleeding between menstrual periods and increased flow of bleeding during menstrual periods.
Meta-analysis	Results from a collection of independent studies (investigating the same treatment) are pooled, using statistical techniques to synthesise their findings into a single estimate of a treatment effect. Where studies are not compatible, for example, because of differences in the study populations or in the outcomes measured, it may be inappropriate or even misleading to statistically pool results in this way. See also **systematic review** and **heterogeneity**.
Non-experimental study	A study based on subjects selected on the basis of their availability, with no attempt having been made to avoid problems of bias.
Nulliparity	Having never given birth to a viable infant.
Observational study	In research about diseases or treatments, this refers to a study in which nature is allowed to take its course. Changes or differences in one characteristic (for example, whether or not people received a specific treatment or intervention) are studied in relation to changes or differences in other(s) (for example, whether or not they died), without the intervention of the investigator. There is a greater risk of selection bias than in experimental studies.
Odds ratio	Odds are a way of representing probability, especially familiar for betting. In recent years odds ratios have become widely used in reports of clinical studies. They provide an estimate (usually with a **confidence interval**) for the effect of a treatment. Odds are used to convey the idea of 'risk' and an odds ratio of one between two

	treatment groups would imply that the risks of an adverse outcome were the same in each group. For rare events the odds ratio and the **relative risk** (which uses actual risks and not odds) will be very similar. See also **relative risk** and **risk ratio**.
Oligomenorrhoea	Reduction in the frequency of menstrual bleeding.
Osteopenia	Decreased calcification or density of bone.
Osteoporosis	A reduction in the amount of bone mass that can lead to fractures after minimal trauma.
Peer review	Review of a study, service or recommendations by those with similar interests and expertise to the people who produced the study findings or recommendations. Peer reviewers can include professional, patient and carer representatives.
Perimenopausal	The time leading up to menopause when oestrogen levels begin to drop.
Placebo	Placebos are fake or inactive treatments received by participants allocated to the **control group** in a **clinical trial**, which are indistinguishable from the active treatments being given in the experimental group. They are used so that participants and investigators are ignorant of their treatment allocation in order to be able to quantify the effect of the experimental treatment over and above any placebo effect due to receiving care or attention.
Placebo effect	A beneficial (or adverse) effect produced by a placebo and not due to any property of the placebo itself.
Postpartum	Occuring in or being the period following childbirth.
Power	See **statistical power**.
Premenstrual syndrome	Symptoms manifested by some women prior to menstruation including irritability, insomnia, fatigue, headache and abdominal pain.
Prevalence	The number of cases of disease or other eventualities which occur in a population at or during a given time.
Prospective study	A study in which people are entered into the research and then followed up over a period of time with future events recorded as they happen. This contrasts with studies that are **retrospective**.
p value	If a study is done to compare two treatments then the p value is the probability of obtaining the results of that study, or something more extreme, if there really was no difference between treatments. (The assumption that there really is no difference between treatments is called the 'null hypothesis'.) Suppose the p value was 0.03. What this means is that, if there really was no difference between treatments, there would only be a 3% chance of getting the kind of results obtained. Since this chance seems quite low we should question the validity of the assumption that there really is no difference between treatments. We would conclude that there probably is a difference between treatments. By convention, where the value of p is below 0.05 (that is, less than 5%) the result is seen as statistically significant. Where the value of p is 0.001 or less, the result is seen as highly significant. P values just tell us whether an effect can be regarded as statistically significant or not. In no way do they relate to how big the effect might be, for which we need the **confidence interval**.
Qualitative research	Qualitative research is used to explore and understand people's beliefs, experiences, attitudes, behaviour and interactions. It generates non-numerical data, for example, a patient's description of

their pain rather than a measure of pain. In health care, qualitative techniques have been commonly used in research documenting the experience of chronic illness and in studies about the functioning of organisations. Qualitative research techniques such as focus groups and in-depth interviews have been used in one-off projects commissioned by guideline development groups to find out more about the views and experiences of patients and carers.

Quantitative research

Research that generates numerical data or data that can be converted into numbers, for example, clinical trials or the National Census, which counts people and households.

Random allocation or randomisation

A method that uses the play of chance to assign participants to comparison groups in a research study, for example, by using a random numbers table or a computer-generated random sequence. Random allocation implies that each individual (or each unit in the case of cluster randomisation) being entered into a study has the same chance of receiving each of the possible interventions.

Randomised controlled trial

A study to test a specific drug or other treatment in which people are randomly assigned to two (or more) groups: one (the experimental group) receiving the treatment that is being tested, and the other (the comparison or **control group)** receiving an alternative treatment, a **placebo** (dummy treatment) or no treatment. The two groups are followed up to compare differences in outcomes to see how effective the experimental treatment was. (Through randomisation, the groups should be similar in all aspects apart from the treatment they receive during the study.)

Relative risk

A summary measure which represents the ratio of the risk of a given event or outcome (for example, an adverse reaction to the drug being tested) in one group of subjects compared with another group. When the 'risk' of the event is the same in the two groups the relative risk is one. In a study comparing two treatments, a relative risk of two would indicate that patients receiving one of the treatments had twice the risk of an undesirable outcome than those receiving the other treatment.

Reliability

Reliability refers to a method of measurement that consistently gives the same results. For example, someone who has a high score on one occasion tends to have a high score if measured on another occasion very soon afterwards. With physical assessments it is possible for different clinicians to make independent assessments in quick succession and if their assessments tend to agree then the method of assessment is said to be reliable.

Retrospective study

A retrospective study deals with the present and past and does not involve studying future events. This contrasts with studies that are **prospective**.

Risk ratio

Ratio of the risk of an undesirable event or outcome occurring in a group of patients receiving experimental treatment compared with a comparison (**control**) **group**.

Sample

A part of the study's target population from which the subjects of the study will be recruited. If subjects are drawn in an unbiased way from a particular population, the results can be generalised from the sample to the population as a whole.

Screening

The presumptive identification of an unrecognised disease or defect by means of tests, examinations or other procedures that can be applied rapidly. Screening tests differentiate apparently well people who may have a disease from those who probably do not. A screening

	test is not intended to be diagnostic but should be sufficiently sensitive and specific to reduce the proportion of false results, positive or negative, to acceptable levels. People with positive or suspicious findings must be referred to the appropriate healthcare provider for diagnosis and necessary treatment.
Selection criteria	Explicit standards used by guideline development groups to decide which studies should be included and excluded from consideration as potential sources of evidence.
Sensitivity analysis	A technique used in economic evaluation in order to test the robustness of the results under the uncertainty/imprecision in the estimates of costs and outcomes, or under methodological controversy.
Statistical power	The ability of a study to demonstrate an association or causal relationship between two **variables**, given that an association exists. For example, 80% power in a clinical trial means that the study has an 80% chance of ending up with a **p value** of less than 5% in a statistical test (that is, a statistically significant treatment effect) if there really was an important difference (for example, 10% versus 5% mortality) between treatments. If the statistical power of a study is low, the study results will be questionable (the study might have been too small to detect any differences). By convention, 80% is an acceptable level of power. See also **p value**.
Sterilisation – female	Surgical contraceptive methods, whereby the fallopian tubes undergo bilateral ligation or interruption.
Sterilisation – male	Surgical contraceptive method, whereby the vas deferens undergoes bilateral ligation or interruption.
Systematic review	A review in which evidence from scientific studies is identified, appraised and synthesised in a methodical way according to predetermined criteria. May or may not include a **meta-analysis**.
Validity	Assessment of how well a tool or instrument measures what it is intended to measure.
Variable	A measurement that can vary within a study, for example, the age of participants. Variability is present when differences can be seen between different people or within the same person over time, with respect to any characteristic or feature that can be assessed or measured.

1. Introduction

Contraception can be divided into two broad categories: hormonal and nonhormonal. There are two categories of hormonal contraception: combined oestrogen and progestogen and progestogen-only. Long-acting reversible contraception (LARC) is defined in this guideline as methods that require administering less than once per cycle or month.

Included in the category of LARC are the copper intrauterine devices (nonhormonal) and three progestogen-only methods of contraception (intrauterine system, injectables and the implants). The combined vaginal ring is not licensed in the UK and is therefore excluded from this guideline.

In 2003/04, about 8% of women aged 16–49 years in Great Britain used LARC as a method of contraception.[1] [EL = 3]

1.1 Aim of the guideline

Clinical guidelines have been defined as 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'.[2] The guideline has been developed with the aim of providing guidance on LARC. The effectiveness of barrier and oral contraceptive pills is dependent on their correct and consistent use. In contrast, long-acting reversible methods have effectiveness that does not depend on daily adherence. Currently there is a very low uptake of LARC (around 8% of contraceptive usage in 2003/04).[1] A number of factors contribute to this. Issues for providers include the initial cost, which may be thought of as too high, particularly if the methods may not be used or required for the intended duration, the need for specific clinical skills (including awareness of current best practice, insertion practice and ability to give information or advice on the methods available) and facilities. Expert clinical opinion is that LARC methods may have a wider role and an increase in their use could help to reduce unintended pregnancy. The current very low uptake suggests that healthcare professionals need better guidance and training so that they can help women to make an informed choice from a full range of contraceptive methods. Enabling women to make an informed choice about LARC and addressing consumer preferences is an important objective of this guideline.

There are no current formal professional or NHS guidelines covering this topic that are widely used or tailored to cover UK practice. This guideline offers best practice advice for all women of reproductive age who may wish to regulate their fertility through the use of long-acting reversible contraceptive methods and considers specific issues for the use of these methods in women during the menarche and before the menopause. The guideline also identifies specific issues that may be relevant to particular groups, including women with HIV, learning disabilities and physical disabilities, and under-16s.

1.2 Areas outside the remit of the guideline

The guideline does not include any contraception for men because there are currently no long-acting reversible methods. The guideline does not cover methods of contraception that are intended to result in permanent sterilisation. Contraceptive methods that are related to coitus or that require frequent (more than once per cycle (month) for women) repeat administration – for example, the combined oral contraceptive (COC) pill or progestogen-only pills – are also not included. Post-coital or emergency contraceptive methods including intrauterine device (IUD) insertion for that use are also not covered. The use of these technologies for non-contraceptive reasons (such as heavy menstrual bleeding or hormone replacement therapy) is outside the scope of this guideline.

1.3 For whom is the guideline intended?

This guideline is of relevance to those who work in or use the National Health Service in England and Wales. In particular:

- professional groups who are involved in the care of women seeking advice on contraception (including general practitioners, gynaecologists, nurses, and practitioners in community contraceptive clinics, sexual health clinics and hospital services)
- those responsible for commissioning and planning healthcare services, including primary care trust commissioners, Health Commission Wales commissioners, and public health and trust managers
- women seeking advice on contraception, their families and other carers.

A version of this guideline for women seeking contraceptive advice, their families and the public is available, entitled *Long-acting reversible contraception – understanding NICE guidance.* It can be downloaded from the NICE website (www.nice.org.uk/CG030) or ordered via the NHS Response Line (0870 1555 455) and quote reference number NO916.

1.4 Who has developed the guideline?

The guideline was developed by a multi-professional and lay working group (the Guideline Development Group or GDG) convened by the National Collaborating Centre for Women's and Children's Health (NCC-WCH). Membership included: two consumers, two general practitioners, two family planning nurses, three specialist family planning doctors and one genitourinary medicine physician.

Staff from the NCC-WCH provided methodological support for the guideline development process, undertook systematic searches, retrieval and appraisal of the evidence, and wrote successive drafts of the guideline.

All GDG members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, shareholdings, fellowships, and support from the healthcare industry in accordance with guidance from the National Institute for Health and Clinical Excellence (NICE).

1.5 Other relevant documents

This guideline is intended to complement other existing and proposed works of relevance, including *A Strategic Framework for Promoting Sexual Health in Wales* (January 2000),[3] *The National Strategy for Sexual Health and HIV* (in England; July 2001),[4] and the subsequent implementation plan (June 2002).[5] Improving access to contraception, and to the range of methods available as an integral part of broader sexual health services, is an essential element in achieving this aim.

1.6 Guideline development methodology

This guideline was commissioned by NICE and developed in accordance with the guideline development process outlined in *The Guideline Development Process – Information for National Collaborating Centres and Guideline Development Groups* (available at www.nice.org.uk/page.aspx?o=201982).[6]

Literature search strategy

The aim of the literature review was to identify and synthesise relevant published evidence. However, evidence submitted by stakeholder organisations was considered and, if relevant to the clinical questions and of equivalent or better quality than evidence identified in the literature searches, was also included. Relevant guidelines produced by other development groups were identified using internet resources, including the National Guideline Clearinghouse, Scottish Intercollegiate Guideline Network (SIGN) and Turning Research into Practice (TRIP). The reference lists in these guidelines were checked against subsequent searches to identify missing evidence.

Evidence to answer the clinical questions formulated and agreed by the GDG was identified using biomedical databases via the OVID platform. Searches were performed using relevant medical subject headings and free-text terms. No language restrictions were applied to the searches. Both generic and specially developed search filters were employed when necessary. Databases searched were MEDLINE (1966 onwards), EMBASE (1980 onwards), Cochrane Central Register of Controlled Trials (4th Quarter 2004), Cochrane Database of Systematic Reviews (4th Quarter 2004), Database of Abstracts of Review of Effects (4th Quarter 2004), and Cumulative Index to Nursing & Allied Health Literature (1982 onwards). POPLINE®, a specialist reproduction database maintained by Johns Hopkins Bloomberg School of Public Health/Center for Communication Programs, was also utilised.

Searches to identify economic studies were undertaken using the above databases, as well as the Health Economic Evaluations Database and the National Health Service Economic Evaluations Database.

There was no systematic attempt to search grey literature (conferences, abstracts, theses and unpublished trials). Hand searching of journals not indexed on the biomedical databases was not carried out.

A preliminary scrutiny of titles and abstracts was undertaken and full copies of publications that addressed the clinical questions were obtained. Following a critical appraisal of each publication, studies that did not report relevant outcomes or were not relevant to a particular clinical question were excluded.

Searches were rerun at the end of the guideline development process, thereby including evidence published and included in the literature databases up to 1 February 2005. Any evidence published after this date was not considered for inclusion. This date should be considered for the starting point for searching for new evidence for future updates to this guideline.

Further details of literature searches can be obtained from the NCC-WCH.

Synthesis of clinical effectiveness evidence

Evidence relating to clinical effectiveness was reviewed using established guides[7–13] and classified using the established hierarchical system shown in Table 1.1.[13] This system reflects the susceptibility to bias that is inherent in particular study designs.

The type of clinical question dictates the highest level of evidence that may be sought. In assessing the quality of the evidence, each paper receives a quality rating coded as '++', '+' or '–'. For issues of therapy or treatment, the highest possible level of evidence (EL) is a well-conducted systematic review or meta-analysis of RCTs (EL = 1++) or an individual RCT (EL = 1+). Studies of poor quality are rated as '–'. Usually, studies rated as '–' should not be used as a basis for making a recommendation, but they can be used to inform recommendations. For issues of prognosis, the highest possible level of evidence is a cohort study (EL = 2–).

Table 1.1 Levels of evidence for intervention studies[13]

Level	Source of evidence
1++	• High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	• Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1–	• Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	• High-quality systematic reviews of case–control or cohort studies • High-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	• Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2–	• Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	• Non-analytical studies (for example, case reports, case series)
4	• Expert opinion, formal consensus

For each clinical question, the highest available level of evidence was selected. Where appropriate, for example, if a systematic review, meta-analysis or RCT existed in relation to a question, studies of a weaker design were not included. Where systematic reviews, meta-analyses and RCTs did not exist, other appropriate experimental or observational studies were sought. For diagnostic tests, test evaluation studies examining the performance of the test were used if the efficacy of the test was required, but where an evaluation of the effectiveness of the test in the clinical management of patients and the outcome of disease was required, evidence from RCTs or cohort studies was used.

In contraception research, investigators have not attempted to directly measure the true efficacy of a contraceptive method, compared with a control group using no method, because ethical concerns do not permit the withholding of contraception.[14,15] For this guideline, the selection criteria for including studies as a source of evidence were based on the comparability of the study population and contraceptive devices to that of the UK, as determined to be appropriate by the Guideline Development Group.

Evidence was synthesised qualitatively by summarising the content of identified papers in evidence tables and agreeing brief statements that accurately reflected the evidence. Quantitative synthesis (meta-analysis) was performed where appropriate.

Summary results and data are presented in the guideline text. More detailed results and data are presented in the accompanying evidence tables. Where possible, dichotomous outcomes are presented as relative risks (RRs) with 95% confidence intervals (CIs), and continuous outcomes are presented as mean differences with 95% CIs or standard deviations (SDs). Meta-analyses based on dichotomous outcomes are presented as pooled odds ratios (ORs) with 95% CIs, and meta-analyses based on continuous outcomes are presented as weighted mean differences (WMDs) with 95% CIs.

Health economics

The aim of the economic input to the guideline was to inform the GDG of potential economic issues related to long-acting reversible contraception. The objective was to assess the relative cost effectiveness between LARC methods and other contraceptive methods that were considered as relevant comparators by the GDG. For this purpose, a systematic review of the economic literature was undertaken, together with a cost effectiveness analysis based on a decision-analytic economic model that was developed for this guideline.

The search strategies adopted for the systematic review were designed to identify any economic study related to LARC. Abstracts of all papers identified were reviewed by the health economists and were excluded if they did not relate to the economic questions being considered in the guideline. The relevant papers were retrieved and critically appraised. Potentially relevant references in the bibliographies of the reviewed papers were also identified and reviewed. All papers reviewed were assessed by the health economists against standard quality criteria for economic evaluation.

The decision-analytic model was developed by the health economists with the support of the GDG, who provided guidance on the data needed to populate the model and on the assumptions required to make appropriate comparisons. Full details on the methodology, the structure of the model and the underlying assumptions, the data used (clinical effectiveness and UK-based cost data), the range of values used in the sensitivity analysis, as well as the full results of the economic analysis are also presented in Chapter 8.

Forming and grading recommendations

For each clinical question, recommendations were derived using, and explicitly linked to, the evidence that supported them. Initially guideline recommendations were based on an informal consensus. Consensus was achieved at formal GDG meetings to finalise the agreement of recommendations and audit criteria.

Each recommendation was graded according to the level of evidence upon which it was based using the established system shown in Table 1.2.[13] For issues of therapy or treatment, the best possible level of evidence (a systematic review or meta-analysis or an individual RCT) would

Table 1.2 Classification of recommendations[13]

Class	Evidence
A	• At least one meta-analysis, systematic review, or randomised controlled trial (RCT) that is rated as 1++, and is directly applicable to the target population, or • A systematic review of RCTs or a body of evidence that consists principally of studies rated as 1+, is directly applicable to the target population and demonstrates overall consistency of results, or • Evidence drawn from a NICE technology appraisal
B	• A body of evidence that includes studies rated as 2++, is directly applicable to the target population and demonstrates overall consistency of results, or • Extrapolated evidence from studies rated as 1++ or 1+
C	• A body of evidence that includes studies rated as 2+, is directly applicable to the target population and demonstrates overall consistency of results, or • Extrapolated evidence from studies rated as 2++
D	• Evidence level 3 or 4, or • Extrapolated evidence from studies rated as 2+, or • Formal consensus
D(GPP)	• A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group

equate to a grade A recommendation. For issues of prognosis, the best possible level of evidence (a cohort study) would equate to a grade B recommendation. However, this should not be interpreted as an inferior grade of recommendation because it represents the highest level of relevant evidence. Indirect evidence on contraceptive devices not licensed in the UK was extrapolated to form recommendations reflecting a lower grading.

External review

The guideline has been developed in accordance with the NICE guideline development process. This has included giving registered stakeholders the opportunity to comment on the scope of the guideline at the initial stage of development and on the evidence and recommendations at the concluding stage. The developers have carefully considered all of the comments during the two stages of consultation by registered stakeholders and validation by the Institute. After the second consultation, changes were made to the final document. A summary of these changes is presented in Appendix A.

Outcome measures used in the guideline

For this guideline, the effectiveness of contraceptive methods has been assessed against a number of outcomes which were agreed by the GDG on the basis of their relevance to patients and professionals. These outcomes are contraceptive effectiveness (measured by failure rates, i.e. pregnancy per 100 women-years); impact on menstrual bleeding; discontinuation and acceptability of method; and impact on longer-term reproductive health. Side effects from methods include hormonal effects – menstrual disturbances, skin effects, bone mineral density, mood (premenstrual symptoms and depression) – and risks of thromboembolic disease. Specific consideration was given to the effectiveness and use of these methods in specific groups of women, such as women who are breastfeeding, teenagers, women at risk of sexually transmitted infection and HIV, women aged over 35 years and women with other conditions such as diabetes, epilepsy and HIV which may impact on their contraceptive choices.

2. Summary of recommendations and practice algorithm

2.1 Summary of recommendations

Chapter 3 Contraceptive use and principles of care

Contraceptive provision

Women requiring contraception should be given information about and offered a choice of all methods, including long-acting reversible contraception (LARC) methods. (Chapter 3.2) — D(GPP)

Women should be provided with the method of contraception that is most acceptable to them provided it is not contraindicated. (Chapter 3.8) — D(GPP)

Contraceptive service providers should be aware that — C

- all currently available LARC methods (intrauterine devices [IUDs], the intrauterine system [IUS], injectable contraceptives and implants) are more cost effective than the combined oral contraceptive pill even at 1 year of use
- IUDs, the IUS and implants are more cost effective than the injectable contraceptives
- increasing the uptake of LARC methods will reduce the number of unintended pregnancies. (Chapter 8.6)

Provision of information and informed choice

Women considering LARC methods should receive detailed information – both verbal and written – that will enable them to choose a method and use it effectively. This information should take into consideration their individual needs and should include: (Chapter 3.5) — D(GPP)

- contraceptive efficacy
- duration of use
- risks and possible side effects
- non-contraceptive benefits
- the procedure for initiation and removal/discontinuation
- when to seek help while using the method.

Counselling about contraception should be sensitive to cultural differences and religious beliefs. (Chapter 3.5) — D(GPP)

Healthcare professionals should have access to trained interpreters for women who are not English speaking, and to advocates for women with sensory impairments or learning disabilities. (Chapter 3.5) — D(GPP)

Contraceptive prescribing

A medical history – including relevant family, menstrual, contraceptive and sexual history – should be taken as part of the routine assessment of medical eligibility for individual contraceptive methods. (Chapter 3.6) D(GPP)

Healthcare professionals helping women to make contraceptive choices should be familiar with nationally agreed guidance on medical eligibility and recommendations for contraceptive use. (Chapter 3.6) D(GPP)

When considering choice of LARC methods for specific groups of women and women with medical conditions, healthcare professionals should be aware of and discuss with each woman any issues that might affect her choice. (Chapter 3.5/3.6) D(GPP)

Healthcare professionals should exclude pregnancy by taking the menstrual and sexual history before initiating any contraceptive methods. (Chapter 3.6) D(GPP)

Healthcare professionals should supply an interim method of contraception at the first appointment if required. (Chapter 3.6) D(GPP)

Healthcare professionals should ensure that informed consent is obtained from the woman whenever any method of LARC is being used outside the terms of the UK Marketing Authorisation. This should be discussed and documented in the notes. (Chapter 3.6) D(GPP)

Women who have a current venous thromboembolism (VTE) and need hormonal contraception while having treatment for the VTE should be referred to a specialist in contraceptive care. (Chapter 5.7) D(GPP)

Contraception and sexually transmitted infection

Healthcare professionals providing contraceptive advice should promote safer sex. (Chapter 3.11) D(GPP)

Healthcare professionals providing contraceptive advice should be able to assess risk for sexually transmitted infections (STIs) and advise testing when appropriate. (Chapter 3.11) D(GPP)

Healthcare professionals should be able to provide information about local services for STI screening, investigation and treatment. (Chapter 3.11) D(GPP)

Contraception for special groups

Healthcare professionals should be aware of the law relating to the provision of advice and contraception for young people and for people with learning disabilities. Child protection issues and the Fraser guidelines should be considered when providing contraception for women younger than 16 years.* (Chapter 3.13) D(GPP)

Women with learning and/or physical disabilities should be supported in making their own decisions about contraception. (Chapter 3.13) D(GPP)

Contraception should be seen in terms of the needs of the individual rather than in terms of relieving the anxieties of carers or relatives. (Chapter 3.13) D(GPP)

When a woman with a learning disability is unable to understand and take responsibility for decisions about contraception, carers and other involved parties should meet to address issues around the woman's contraceptive need and to establish a care plan. (Chapter 3.13) D(GPP)

Training of healthcare professionals in contraceptive care

Healthcare professionals advising women about contraceptive choices should be competent to: (Chapter 3.14) D(GPP)

* See the Department of Health's *Best Practice Guidance for Doctors and Other Health Professionals on the Provision of Advice and Treatment to Young People under 16 on Contraception, Sexual and Reproductive Health* (July 2004), available from www.dh.gov.uk.

- help women to consider and compare the risks and benefits of all methods relevant to their individual needs
- manage common side effects and problems.

Contraceptive service providers who do not provide LARC in their practice or service should have an agreed mechanism in place for referring women for LARC. (Chapter 3.14) **D(GPP)**

Healthcare professionals providing intrauterine or subdermal contraceptives should receive training to develop and maintain the relevant skills to provide these methods. (Chapter 3.14) **D(GPP)**

IUDs and the IUS should only be fitted by trained personnel with continuing experience of inserting at least one IUD or one IUS a month. (Chapter 4.10/5.10) **C**

Contraceptive implants should be inserted and removed only by healthcare professionals trained in the procedure. (Chapter 7.9) **D(GPP)**

~~Chapter 4 Copper intrauterine devices (IUDs)~~

~~*Decision making*~~
~~Women should be given the following information.~~

~~Contraceptive efficacy~~

- ~~IUDs act by preventing fertilisation and inhibiting implantation. (Chapter 4.1)~~ **C**
- ~~The licensed duration of use for IUDs containing 380 mm^2 copper ranges from 5 to 10 years, depending on the type of device. (Chapter 4.1)~~ **D**
- ~~The pregnancy rate associated with the use of IUDs containing 380 mm^2 copper is very low (fewer than 20 in 1000 over 5 years). (Chapter 4.2)~~ **C**
- ~~There is no evidence of a delay in the return of fertility following removal or expulsion of IUDs. (Chapter 4.8)~~ **C**

~~Effect on periods~~

- ~~Heavier bleeding and/or dysmenorrhoea are likely with IUD use. (Chapter 4.5)~~ **C**

~~Risks and possible side effects~~

- ~~Up to 50% of women stop using IUDs within 5 years; the most common reasons for discontinuation are unacceptable vaginal bleeding and pain. (Chapter 4.4)~~ **C**
- ~~There is no evidence that IUD use affects weight. (Chapter 4.6)~~ **C**
- ~~Any changes in mood and libido are similar whether using IUDs or the IUS, and the changes are small. (Chapter 4.6)~~ **C**
- ~~The risk of uterine perforation at the time of IUD insertion is very low (less than 1 in 1000). (Chapter 4.7)~~ **D**
- ~~The risk of developing pelvic inflammatory disease following IUD insertion is very low (less than 1 in 100) in women who are at low risk of STIs. (Chapter 4.7)~~ **C**
- ~~IUDs may be expelled but this occurs in fewer than 1 in 20 women in 5 years. (Chapter 4.3)~~ **C**
- ~~The risk of ectopic pregnancy when using IUDs is lower than when using no contraception. (Chapter 4.7)~~ **D**
- ~~The overall risk of ectopic pregnancy when using the IUD is very low, at about 1 in 1000 in 5 years.~~ **C**
- ~~If a woman becomes pregnant with the IUD in situ, the risk of ectopic pregnancy is about 1 in 20, and she should seek advice to exclude ectopic pregnancy. (Chapter 4.7)~~ **C**

- ~~contraceptive implants are medically safe for women to use if oestrogen is contra-indicated (Chapter 7.6)~~ C
- ~~there is no evidence of an effect of Implanon use on bone mineral density. (Chapter 7.6)~~ C
- ~~Implanon is not recommended as a contraceptive method for women taking liver enzyme-inducing drugs. (Chapter 7.12)~~ D

~~*Practical details of fitting implants*~~

~~Provided that it is reasonably certain that the woman is not pregnant, Implanon may be inserted: (Chapter 7.8)~~ D(GPP)

- ~~at any time (but if the woman is amenorrhoeic or it has been more than 5 days since menstrual bleeding started, additional barrier contraception should be used for first 7 days after insertion)~~
- ~~immediately after abortion in any trimester~~
- ~~at any time postpartum.~~

~~*Advice for women at time of fitting*~~

~~Women should be informed that Implanon insertion and removal both cause some discomfort and bruising but that technical problems are unusual (less than 1 in 100). (Chapter 7.8)~~ C

~~*Follow-up and managing problems*~~

~~No routine follow-up is needed after implant insertion. However, a woman should be strongly encouraged to return at any time to discuss problems, if she wants to change her method of contraception, or if it is time to have the implant removed. (Chapter 7.13)~~ D(GPP)

~~Irregular bleeding associated with implant use can be treated with mefenamic acid or ethinylestradiol.* (Chapter 7.4)~~ B

~~There is no evidence of a teratogenic effect of Implanon use but, if a woman becomes pregnant and continues with the pregnancy, the implant should be removed. (Chapter 7.6)~~ D(GPP)

~~If an Implanon implant cannot be palpated (due to deep insertion, failed insertion or migration) it should be localised by ultrasound investigation before being removed. Deeply inserted implants often need to be removed by an expert. (Chapter 7.8)~~ D(GPP)

2.2 Future research recommendations

The scarcity of robust evidence to answer important clinical questions on the use of LARC methods by women in the UK has posed great challenges to the developers of this guideline. In the majority of cases, the guideline recommendations are based on extrapolated evidence that is indirect or of poor methodological quality. The GDG has made the following recommendations for research on the basis of its review of the evidence. The GDG regards these questions as being the most important research areas in terms of improving NICE guidance on the use of LARC, and the care of women choosing LARC, when this guideline is updated in 4 years' time.

In making these recommendations for research, the guideline developers consider it important and relevant that the research should be specific to the UK population because there are cultural differences in the response to side effects and non-contraceptive effects of hormonal contraceptives. In addition, freedom to choose any contraceptive method and the provision of a free

* The recommendation on treating irregular bleeding after insertion of a contraceptive implant has been changed (this is recommendation 1.5.4.2 in the NICE guideline). Although the evidence does show that mifepristone is effective at controlling irregular bleeding associated with implants, it is not licensed for this indication. The revised recommendation reads: 'Irregular bleeding associated with implant use can be treated with mefenamic acid or ethinylestradiol.'

contraceptive health service in the UK can influence important outcomes such as continuation rates and patterns of method switching.

Typical use of contraception

Few women use contraception perfectly (that is, exactly in accordance with the product instructions) and consistently. Pregnancy rates during typical use reflect effectiveness of a method among women who use the methods incorrectly or inconsistently. Few data are available on typical use of any contraceptive method among women in the UK. Much of the data on contraceptive effectiveness used in the guideline comes from clinical trials or surveys undertaken in other countries such as the USA. Large prospective cohort studies are required to compare the contraceptive effectiveness of LARC methods with non-LARC methods during typical use in the UK.

Patterns of LARC use

Most women will need to use contraception for more than 30 years. Patterns of contraceptive use vary with age, ethnicity, marital status, fertility intention, education and lifestyle. Large prospective cohort studies are required to identify:

- patterns of use (initiation, continuation and switching between methods) of LARC methods compared with non-LARC methods
- factors which influence the patterns of use of LARC.

Uptake and acceptance of LARC

In addition to individual circumstances and needs, a woman's choice and acceptance of LARC may be influenced by potential health disbenefits (side effects and risks) as well as non-contraceptive benefits (such as alleviation of menorrhagia) of LARC. Large population studies of appropriate design are required to determine these effects on the uptake of LARC methods and the implications for NHS resources.

Bone mineral density in women using DMPA

The effect of injectable contraceptives on bone mineral density in women who have used depot medroxyprogesterone acetate (DMPA) for longer than two years is uncertain. Adequately powered surveys or cross-sectional studies are required to examine the recovery of bone mineral density following discontinuation of DMPA after long-term and very long-term use. Studies are also required to examine the risk of bone fractures in older women.

2.3 ~~LARC selection algorithm~~

3. Contraceptive use and principles of care

3.1 Normal fertility

During sexual intercourse, spermatozoa are deposited into the vagina. They migrate through the cervix and uterine cavity to the fallopian tubes where, if they meet the egg, fertilisation can take place. The embryo then travels down the fallopian tube and enters the uterine cavity where implantation takes place. The length of a menstrual cycle varies from 21 days to 35 days. Ovulation usually takes place 12–16 days before the start of the next period. For a woman with a 28-day menstrual cycle (the first day of menstruation being day 1), ovulation takes place around day 14. After ovulation, the egg usually lives for up to 24 hours. After ejaculation, sperm can survive for up to 7 days in the genital tract.[16] [EL = 3] Most pregnancies can be attributed to sexual intercourse during a 6-day period ending on the day of ovulation,[17,18] [EL = 3] with the highest estimated conception rates associated with intercourse 2 days before ovulation.[19] [EL = 3] This information is used as the basis for methods of contraception relying on fertility awareness (periodic abstinence) and informs the advice relating to the use of emergency contraception and what action to take when oral contraceptive pills are missed. Misunderstandings about inherent fertility and about the time in the cycle when pregnancy is most likely to occur lead to incorrect and inconsistent use of barrier methods and oral contraceptives.

In the general population it is estimated that 84% of women would conceive within 1 year of regular unprotected sexual intercourse. This rises cumulatively to 92% after 2 years and 93% after 3 years.[20,21]

The conception rate per menstrual cycle is known as fecundability. Natural female fertility declines with age.[22] [EL = 3] The decline with age in rates of conception is seen after 30 years of age and is more marked after age 35 years.[23,24] [EL = 3]

3.2 Contraceptive provision

In 1994 at the International Conference on Population and Development (ICPD) in Cairo, Egypt, government delegations from 179 countries, including the UK, agreed a Programme of Action to stabilise the world's population. The Programme of Action defined reproductive rights and stated that people should have the freedom to decide if, when, and how often to have children. ICPD further called for universal access to a full range of high-quality, affordable, accessible and convenient sexual and reproductive health services.[25]

Since 1974 contraception has been provided free of prescription charges in the UK. It is provided by general practitioners (GPs), community (NHS) family planning clinics (FPCs) and, increasingly, in some not-for-profit charitable clinics such as Brook (usually limited to young people under 25 years). Contraception is also provided in sexual health clinics, NHS walk-in centres and some genitourinary medicine clinics. Some pharmacies provide emergency contraception free through specific NHS protocols. In Great Britain in 2003/04 almost 57% of women aged 16–49 years had used at least one service in the previous 5 years.[1] Most (81%) had visited their GP surgery but 32% had used a community FPC. Not all settings provide all methods of contraception, and not all doctors are competent to fit intrauterine devices (IUDs) or systems (IUS) or contraceptive implants (refer to Medical Foundation for AIDS and Sexual Health (MedFASH) Sexual Health Standards at www.medfash.org.uk/). Women attending FPCs are more

likely to use a long-acting method of contraception, particularly implants and IUD/IUS, than those consulting their GP.

In the UK, because contraceptives are provided free of charge, cost plays no part in determining an individual's choice of method and does not influence continuation rates or method switching. In countries where contraceptives are not free and where the consultation and procedure may also be charged to the user, cost plays a much bigger part in uptake and continuation and data from these countries must be extrapolated to the UK with caution. In one state in the USA in the early 1990s women were offered a payment of $500 if they had Norplant® inserted and further annual payments of $50 for each year they kept it.[26] Cost, however, is relevant to the service provider and may determine the choice of methods available in some settings. Some local formulary committees withhold approval of the newer, more expensive contraceptive methods (such as the contraceptive patch and newer brands of oral contraceptive pill) arguing that there is no evidence of superiority over existing cheaper methods. Providers' attitudes towards, knowledge of, and preferences for particular methods of contraception influence the choices made by the users.[27] If women/couples are not informed about all available methods of contraception, their choices are restricted.

RECOMMENDATION

Women requiring contraception should be given information about and offered a choice of all methods, including long-acting reversible contraception (LARC) methods. **D(GPP)**

3.3 Contraceptive prevalence

Almost everyone in the UK uses contraception at some time in their lives. Contraceptive prevalence has increased dramatically in the last 30 years. In Great Britain in 2003/04, 52% of all women aged 16–49 years were using a reversible method of contraception and just under a quarter had either been sterilised (11%) or had a partner who was sterilised (12%).[1] Of women 'at risk' of pregnancy (i.e. in a heterosexual relationship, presumed fertile and not actively trying to become pregnant) only 2% were not using any method of contraception.[1]

The pattern of contraceptive use varies with age, ethnicity and race, marital status, fertility intentions and education.[28] In Great Britain in 2003/04, the oral contraceptive pill was the most popular method of contraception among women aged 16–49 years (25% of women use it) while the next most popular method was the male condom (23% of women)[1] (Table 3.1). Long-acting methods of contraception (injectables, implants, IUDs and IUS) were used by 8% of women. In general, the IUD/IUS tends to be adopted by older, parous women while injectable contraceptives such as Depo-Provera® and contraceptive implants such as Implanon® are more commonly used by younger women and women without children. Most hormonal methods of contraception have an effect on vaginal bleeding patterns.[29] For women with certain religious beliefs, methods which cause irregular bleeding can be a major inconvenience. Not all methods are available in all countries and not all available methods are marketed in the UK. Women coming to the UK from elsewhere may be using a method which is unavailable or (e.g. norethisterone enantate, NET-EN) only licensed for short-term use in the UK.

The average age of first intercourse in the UK has stabilised for both men and women at 16 years[30] and the average age of first childbirth has risen to almost 30 years. Since the mean age of menopause is 51 years and the total fertility rate in the UK in 2004 was 1.7, most women/couples will need to use contraception for more than 30 years.[31]

Unintended pregnancy

Despite the widespread use of contraception, unintended pregnancy is common. In England and Wales the abortion rate for the quarter January–March 2004 was 18.6 per 1000 women of reproductive age. The abortion rates were 33.6 per 1000 for women in the 20–24 year age group, 28.1 per 1000 women for women in the 16–19 years age group and 3.9 per 1000 women in women under 16 years of age.[32] [EL = 3] Not all unintended pregnancies end in abortion. It has been suggested that as many as 30% of pregnancies which end in childbirth are unplanned when they are conceived.[33] A UK questionnaire survey of pregnant women (n = 12 106) designed to investigate the association of duration of OC usage with time to conception reported that

Table 3.1 Current use of contraception by age in Great Britain (women aged 16–49 years); data from the Office for National Statistics

Current use of contraception	Use by each age range (%)								Use by all ages the during the indicated period (%)						
	16 –17	18 –19	20 –24	25 –29	30 –34	35 –39	40 –44	45 –49	2003/ 04	2002/ 03	2001/ 02	2000/ 01	1999/ 2000	1998/ 99	1997/ 98
Nonsurgical															
Pills[a]	26	58	49	40	31	15	12	5	25	25	28	25	26	26	26
Minipill	1	14	9	6	4	4	5	2	5	5	5	5	5	5	5
Combined pill	20	29	31	31	24	10	6	2	17	18	21	17	18	19	19
Male condom	33	36	37	24	24	22	15	14	23	20	21	21	23	21	21
Withdrawal	3	–	1	3	5	5	1	1	3	3	4	3	5	6	4
IUD	2	–	1	3	5	5	5	4	4	5	3	5	4	4	4
Injection/implant	3	2	6	5	4	3	1	1	3	3	3	3	3	2	
Safe period/rhythm method/Persona	–	–	1	1	2	1	1	0	1	1	2	1	2	2	2
Cap/diaphragm	–	1	0	0	1	1	1	2	1	1	1	1	1	1	2
Foam/gels	–	–	–	–	0	0	–	1	0	0	0	0	0	1	0
Hormonal IUS	–	–	0	1	1	1	1	1	1	1	1	1	1	0	0
Female condom	–	–	–	–	0	0	–	–	0	0	0	0	0	0	0
Emergency contraception[b]	5	4	2	0	0	0	–	–	1	1	1	1			
Total using at least one non-surgical method	50	70	75	66	63	48	35	28	52	51	53	51	54	50	52
Surgical															
Sterilised	–	1	2	3	5	17	17	25	11	11	10	11	12	12	11
Partner sterilised	–	–	1	4	9	15	25	20	12	12	12	11	11	12	10
Total using at least one method	50	71	78	73	77	80	77	73	75	74	75	73	76	75	74
Total not using any method	50	29	22	27	23	20	23	27	25	26	25	27	24	25	26

[a] Includes women who did not know the type of pill used.
[b] Category included for the first time in the 2000/01 questionnaire.

29.4% of the pregnancies were unintentional.[34] [EL = 3] Most data suggest that true method failure accounts for fewer than 10% of unintended pregnancies, the rest arising either because no method was used at the time conception occurred (30–50%) or because the method was used inconsistently or incorrectly.[35–37] Failure due to inconsistent use of oral contraception and condoms was reported to be the main cause of pregnancy among women undergoing termination.[38,39] [EL = 3]

It is important for repeat unwanted pregnancies to be prevented rather than aborted. Repeat abortions are common, estimated to be between 27% to 48% of all induced abortions.[40–44] [EL = 3]

Teenage pregnancy

In 2001, 7.4% of all births in England and Wales were to women aged under 20.[45] [EL = 3] In 2003, the under-18 years conception rate was 42.3 per 1000 women (aged 15–17 years) and 46% of these conceptions resulted in legal abortions. In 2002, the under-16 conception rate was 7.9 per 1000 women (aged 13–15 years) and 55.7% of these conceptions led to abortions.[46] [EL = 3] In 2003, the age-standardised abortion rate was 17.5 per 1000 resident women aged 15–44 years (17.0 in 2002). The abortion rate was the highest at 31.4 per 1000, for women in the 20–24 year age group (30.7 in 2002). The under-16 years abortion rate was 3.9 in 2003 compared with 3.7 per 1000 in 2002. Infant mortality rates for children born to teenage mothers are 1.3-fold higher than that for total births, due mainly to low birth weight and congenital anomalies.[47] [EL = 3]

Based on a report by the Social Exclusion Unit (SEU) on teenage pregnancy in 1999,[48] the Department of Health has developed a national strategy to:

- reduce the rate of teenage conceptions, with the specific aim of halving the rate of conceptions among under-18s by 2010, with an interim reduction of 15% by 2004
- set a firmly established downward trend in the under-16 years conception rate by 2010
- increase the participation of teenage parents in education and work, to reduce their risk of long-term social exclusion.[49] [EL = 4]

3.4 Efficacy and effectiveness of contraception

The effectiveness of a method of contraception is judged by the failure rates associated with its use. Table 3.2 shows failure rates for typical use of methods currently available in the USA.[50] The rates are estimated from US studies, including the National Survey of Family Growth, and show the percentage of couples who experience an accidental pregnancy during the first year of use of each method.[51] Similarly collected data are not available for effectiveness of contraceptives in UK use. Effectiveness rates for LARC from a variety of sources are shown in the individual method chapters in this guideline. The effectiveness of a contraceptive depends on its mode of action and how easy it is to use.[52] Pregnancy rates during perfect use of a method reflect its efficacy. If a method prevents ovulation in every cycle in every woman, it should have an efficacy of 100%, since if there is no egg there can be no conception. Only if a mistake is made, or if the method is used inconsistently, will a pregnancy occur. Imperfect use with long-acting methods of contraception is usually due to provider error – undetected uterine perforation during IUD insertion, for example.

The contraceptive implant Implanon® inhibits ovulation for 3 years and is extremely effective as the user has to take no action once the implant is inserted.[53] The combined pill is probably as effective at preventing ovulation and pregnancy; failure rates for perfect use are only 0.1 in 100 within the first year of use. True pill failures are due to incomplete inhibition of ovulation mainly among women who metabolise the pill rapidly. Inhibition of ovulation, however, depends on the pill being taken perfectly. With imperfect use ovulation can occur and typical-use failure rates are 8 in 100 within the first year of use (Table 3.2).[50]

LARC methods are more effective than barrier methods or oral contraceptives because they demand much less – or are independent of the need for – adherence. Failure rates associated with typical use are virtually the same as those associated with perfect use. Active steps must be taken if a woman wishes to stop using an IUD, IUS or implant while discontinuation of other

Table 3.2 Percentage of women experiencing an unintended pregnancy during the first year of typical use, and the first year of perfect use of contraception (United States); adapted with permission from Trussell[435]

Method	Women experiencing an unintended pregnancy within the first year of use (%)	
	Typical use[a]	Perfect use[b]
No method[c]	85	85
Spermicides[d]	29	15
Withdrawal	27	4
Periodic abstinence	25	
Calendar		9
Ovulation method		3
Sympto-thermal[e]		2
Post-ovulation		1
Cap[f]		
Parous women	32	26
Nulliparous women	16	9
Sponge		
Parous women	32	20
Nulliparous women	16	9
Diaphragm[f]	16	6
Condom[g]		
Female (Reality)	21	5
Male	15	2
Combined pill and minipill	8	0.3
Evra patch	8	0.3
NuvaRing	8	0.3
Depo-Provera	3	0.3
Lunelle	3	0.05
IUD		
Progestasert (progesterone T)	2	1.5
ParaGard (copper T)	0.8	0.6
Mirena (LNG-IUS)	0.1	0.1
Norplant and Norplant-2	0.05	0.05
Female sterilisation	0.5	0.5
Male sterilisation	0.15	0.10

[a] Among typical couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason. Estimates of the probability of pregnancy during the first year of typical use for spermicides, withdrawal, periodic abstinence, the diaphragm, the male condom, the pill and Depo-Provera are taken from the 1995 National Survey of Family Growth corrected for underreporting of abortion.

[b] Among couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently and correctly), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

[c] The percentages becoming pregnant are based on data from populations where contraception is not used and from women who cease using contraception in order to become pregnant. Among such populations, about 89% become pregnant within 1 year. This estimate was lowered slightly (to 85%) to represent the percentage who would become pregnant within 1 year among women now relying on reversible methods of contraception if they abandoned contraception altogether.

[d] Foams, creams, gels, vaginal suppositories and vaginal film.

[e] Cervical mucus (ovulation) method supplemented by calendar in the pre-ovulatory and basal body temperature in the post-ovulatory phases.

[f] With spermicidal cream or jelly.

[g] Without spermicides.

NB. Some of the methods listed in this table are not available in the UK and some of the methods available in the UK are not available in the USA and therefore are not listed here. This table does not include any data on Implanon. ParaGard® is the TCu 380A IUD.

methods (including injectables) is passive. In a cohort study of US teenagers using Norplant (n = 200), pills (n = 100) or condoms (n = 99), there were no pregnancies among Norplant users while one-third of teenagers using pills or condoms had conceived.[54]

Pregnancy rates are still often described by the Pearl Index (PI) – the number of unintended pregnancies divided by the number of women-years of exposure to the risk of pregnancy while using the method. The PI is expressed as the pregnancy rate per 100 woman-years (a woman-year is defined as 13 menstrual cycles).[55] If, out of 100 women using a contraceptive method for 13 cycles, one becomes pregnant the PI is 1.0.

Failure rates of most methods decrease with time since women most prone to failure will become pregnant soon after starting a method.[51] Over time, a cohort of couples still using a method increasingly comprises couples in which the woman is unlikely to become pregnant (because they are good at using the method, highly motivated to avoid pregnancy, or are infertile). So, the longer a contraceptive trial lasts, the lower the pregnancy rate is likely to be. Furthermore, failure rates in most clinical trials are often underestimated because all of the months of use of the method are taken into account when calculating failure rates, regardless of whether or not intercourse has occurred during that cycle. For long-acting methods of contraception such as IUDs and implants, the pregnancy rate with time (cumulative pregnancy rate) is more informative and is presented as the standard measure of contraceptive effectiveness in this guideline.

The effectiveness of all methods of contraception is likely to be higher in clinical trials than in real life[56] since trial participants are not representative of the general population of contraceptive users and the routine daily recording of contraceptive use (mandatory in trials) enhances adherence. Randomised placebo-controlled trials are widely regarded as the gold standard for determining effectiveness of drugs and other therapeutic interventions. However, use of a placebo is unethical in trials of a contraceptive method since all contraceptive users wish to avoid pregnancy. While RCTs between like methods (one type of copper IUD versus another, or one brand of combined pill versus another) are possible, it is extremely difficult to recruit people willing to participate in RCTs comparing different types of contraceptive. In developed countries most women are well informed about contraceptive choice and have strong views about methods they do – and particularly do not – want to use.[57,58]

The effectiveness of some hormonal methods of contraception is affected by the body weight of the user. Women of a high body weight have higher failure rates with pills,[59] Norplant[60,61] and patches.[62] Body weight may also influence bleeding patterns; women with a low body weight are more likely to experience amenorrhoea while using Norplant.[63] Trials of effectiveness in populations of women with a much lower body weight than that of the average UK female population (such as women from Thailand or Indonesia) may underestimate failure rates and the side effects profile.

3.5 Provision of information and informed choice

Accurate, up-to date information is essential to enable users to make an informed and voluntary choice of a contraceptive method. User satisfaction and successful use of contraception depend on adequate knowledge and accurate perceptions of the method. Counselling is a face-to-face communication in which one person helps another make decisions and act on them.[64] The ultimate goal of contraceptive counselling is to allow women to choose a method they feel most comfortable with and will continue using, taking into account their lifestyle preferences and concerns. Contraceptive counselling helps women to learn more about contraception and combats misinformation about contraceptive methods. In addition, counselling can provide the basis for informed consent and set the stage for increased user satisfaction with the method chosen. Informed choice is facilitated by promoting understanding of the relative effectiveness of the method, how it works, insertion and removal procedures, correct use, common side effects, health risks and benefits, when to seek medical advice, information on return to fertility after discontinuation, and advice on STI protection and sexual health.

A UK questionnaire survey of family planning physicians at six centres on counselling Norplant users (n = 521) reported that patient counselling contributed to increasing patient acceptance of

Norplant. Eighty-two percent of women accepted the implants despite an overall rate of menstrual bleeding irregularities of 13%. Pre-insertion counselling occurred 100% of the time at these centres and physicians and nurses were responsible for counselling 78% and 39% of the time, respectively.[65] [EL = 3]

Knowledge and concerns about contraceptive methods

Using a series of semi-structured focus groups, a UK study assessed women's knowledge of the effectiveness of various contraceptive methods and of the risks of thrombosis associated with hormonal contraceptives. Women (n = 45) tended to underestimate the effectiveness of hormonal contraceptives, particularly implants, and to overestimate the risk of thrombosis associated with hormonal contraceptives.[66] [EL = 3] Many were more concerned about the adverse effects (especially bleeding irregularities and weight gain) than about effectiveness.

A US questionnaire survey (n = 249, aged 12–20 years) reported that knowledge of Norplant among the general adolescent population was poor. However, young women who were using Norplant were 11 times more likely than those using other types of contraceptive methods to be more knowledgeable about Norplant, having received additional counselling from healthcare providers.[67] [EL = 3]

Source of information

An audit in the UK undertaken to develop informational materials about new contraceptive products reported that women received information about a broad range of contraception available, but that 33% of women came with their 'own agenda' and were sure before the visit about which method they wanted.[57] [EL = 3]

One survey (n = 4500) in the Netherlands reported that women were well informed about all aspects of contraception as a result of formal and informal education at school, from their families, and by the media. Most of these women (86%) viewed their contraceptive choices as their own. The GP was regarded as the most important and reliable source of information (73%).[58] [EL = 3]

Effect of information on satisfaction and continuation

A Finnish survey of LNG-IUS users (n = 17 360) evaluated the impact of advance information on user satisfaction with the method. User satisfaction was associated with information (on menstrual disturbances, pelvic inflammatory disease (PID), greasiness of hair or skin, and the possibility of pregnancy) given at the time the LNG-IUS was inserted. Women who received information about the possibility of amenorrhoea were more satisfied when compared with the women who were less well informed (OR 5.0, 95% CI 4.1 to 5.9).[68] [EL = 3]

A survey of new DMPA users in Bolivia (n = 352) reported that women who received information on the efficacy, side effects and amenorrhoea of DMPA had higher continuation rates than those who did not receive such information. Women advised to return to the clinic if experiencing problems were 2.7 times more likely to continue DMPA at 1 year, and those advised of amenorrhoea were 2.5 times more likely to return for a second injection of DMPA compared with women who did not receive such information from the provider.[69] [EL = 3] Similar findings were reported from a study of 350 new DMPA users in Mexico where detailed, structured, pre-treatment counselling resulted in fewer method discontinuations at 12 months compared with routine contraceptive counselling (15% versus 39% overall and 9 % versus 32% for menstrual disturbance including amenorrhoea).[70] [EL = 1+]

One RCT (n = 636) in the UK assessed the effectiveness of providing educational leaflets versus verbal information in improving knowledge of contraception in women taking the combined pill. Baseline knowledge of contraception in the control group was poor. Written information had a significant effect on knowledge of factors associated with pill failure. Improvement in knowledge occurred with the provision of summary leaflets (adjusted OR 4.04, 95% CI 1.68 to 9.75), the Family Planning Association's leaflet (OR 3.43, 95%CI 1.45 to 8.09) and asking questions (OR 3.03, 95% CI 1.30 to 7.00). This study suggested that provision of educational leaflets on contraception and/or asking women relevant questions, though time-consuming, may help improve women's knowledge of contraception.[71] [EL = 1+]

Method of information giving

The provision of written information may enhance understanding. One RCT (n = 461) in the USA evaluated three different approaches to increase women's understanding of risk of pregnancy associated with various contraceptive methods. A table with categories of contraceptives communicated relative contraceptive effectiveness better than the tables with numbers. However, without the presentation of the numbers, women grossly overestimated the absolute risk of pregnancy while using contraception. A table, developed by the World Health Organization (WHO), presenting a combination of categories of contraceptives and a general range of risk for each category may provide the most accurate understanding of both relative and absolute pregnancy risk.[72] [EL = 1–]

A survey (n = 211) in the USA reported that women relied heavily on their own experiences in assessing the risks and benefits of oral contraceptives. Written information was cited more frequently than medical personnel as a major source of information on cardiovascular and cancer risks and the benefits of OCs. The internet played a minimal, if any, role in educating women about OCs.[73] [EL = 3]

RECOMMENDATIONS

Women considering LARC methods should receive detailed information – both verbal and written – that will enable them to choose a method and use it effectively. This information should take into consideration their individual needs and should include: D(GPP)

- contraceptive efficacy
- duration of use
- risks and possible side effects
- non-contraceptive benefits
- the procedure for initiation and removal/discontinuation
- when to seek help while using the method.

Specific groups

One survey (n = 406) in the USA which examined the relationship between reading ability and knowledge of family planning reported that women with low reading skills were 2.2 times more likely to want to know more about birth control methods (95% CI 1.1 to 4.4). They were 4.4 times more likely to have incorrect knowledge about when they were most likely to become pregnant (95% CI 2.1 to 9.0) than women with good reading skills. This raised additional questions of whether women with low reading skills understand the concept of informed consent prior to accepting contraceptive use.[74] [EL = 3]

An interview survey (n = 32) of Somalian women attending a UK well-woman clinic reported that effective contraceptive care and service provision needed to take into account the cultural interpretation of reproduction and family planning within a wider social and religious context in order to meet the needs of these women.[75] [EL = 3]

RECOMMENDATIONS

Counselling about contraception should be sensitive to cultural differences and religious beliefs. D(GPP)

Healthcare professionals should be able to provide information that is in a format appropriate for all women with special needs. D(GPP)

For women whose first language is not English, written information about contraceptive methods should be available in their preferred language. D(GPP)

Healthcare professionals should have access to trained interpreters for women who are not English speaking, and to advocates for women with sensory impairments or learning disabilities. D(GPP)

3.6 Contraceptive prescribing

Most contraceptive users are medically fit and can use all available methods safely. However, a few medical conditions are associated with theoretical increased health risks with certain contraceptives, either because the method adversely affects the condition (for example, combined hormonal contraceptives may increase the risk of a woman with diabetes developing cardiovascular complications), or because the condition or its treatment affects the contraceptive (some anti-epileptic drugs interfere with the efficacy of hormonal methods). Since most trials of new contraceptive methods deliberately exclude subjects with serious medical conditions, there is little direct evidence on which to base sound prescribing advice. In an attempt to produce a set of international norms for providing contraception to women and men with a range of medical conditions which may contraindicate one or more contraceptive methods, the WHO has developed a system to address medical eligibility criteria for contraceptive use (WHO-MEC).[76] Using evidence-based systematic reviews,[77] the document classifies conditions into one of four categories. Category 1 includes conditions for which there is no restriction for the use of the method while category 4 includes conditions which represent an unacceptable health risk if the contraceptive method is used (absolutely contraindicated). Classification of a condition into category 2 indicates that the method may generally be used but that more careful follow-up is required. Category 3 conditions are those for which the risks of the method generally outweigh the benefits (relatively contraindicated). Provision of a method to a woman with a category 3 condition requires careful clinical judgement since use of that method is not recommended unless there is no acceptable alternative. The WHO-MEC document is available on the internet[63] and a system is in place to incorporate new data into the guidelines as they become available. A UK version of the WHO-MEC document is currently under development by the FFPRHC and will be published by the end of 2005.

In an attempt to provide evidence-based guidance on safe and effective contraception, the WHO produced the *Selected Practice Recommendations for Contraceptive Use* (WHOSPR).[77,78] The UK Selected Practice Recommendations for Contraceptive Use (UKSPR), a document adapted by the FFPRHC for use in the UK, provides guidance on assessment before providing contraceptives, including when to start a method, history taking, follow-up, and the management of common side effects.[79]

The vast majority of women who use hormonal contraception do not have any medical problems and they are young. Providers need to recognise the very few who may be at risk of the rare but serious complications of hormonal contraception. Taking a careful history (including family history) and observing obvious physical characteristics (such as obesity) provides a lot of useful information. The WHO distinguishes between examinations and investigations which are essential for safe prescribing of contraception and those which 'do not contribute substantially to safe and effective use of the contraceptive method' but which are commonly done.[77] Routine breast and pelvic examination, cervical smears and blood tests such as the measurement of serum cholesterol fall into the latter category. The only tests considered mandatory in the UK are the measurement of blood pressure before starting combined hormonal contraception, and pelvic examination before IUD/IUS insertion.

When prescribing contraceptives beyond the duration of product licence, healthcare professionals need to inform the woman and discuss with her the evidence supporting use outside licence, document all this information in case records and obtain her consent.[80] [EL = 1–4]

The UKSPR, in agreement with the WHOSPR, recommends the ideal time in the cycle when a particular method of contraception should be initiated and how best to switch methods. Recognising that this may not always be the most convenient time, the UKSPR further recommends that all methods can be started at any time in the cycle provided it is reasonably certain that the woman is not pregnant. It is not necessary to undertake pregnancy testing before a method is started, even later in the cycle. Pregnancy can be excluded by taking a menstrual and contraceptive history and asking about sexual activity. A test is indicated only if the history suggests that there is a risk that the woman might be pregnant.

RECOMMENDATIONS

A medical history – including relevant family, menstrual, contraceptive and sexual history – should be taken as part of the routine assessment of medical eligibility for individual contraceptive methods. D(GPP)

Healthcare professionals helping women to make contraceptive choices should be familiar with nationally agreed guidance on medical eligibility and recommendations for contraceptive use. D(GPP)

Healthcare professionals should exclude pregnancy by taking the menstrual and sexual history before initiating any contraceptive method. D(GPP)

Healthcare professionals should supply an interim method of contraception at the first appointment if required. D(GPP)

Healthcare professionals should ensure that informed consent is obtained from the woman whenever any method of LARC is being used outside the terms of the UK Marketing Authorisation.* This should be discussed and documented in the notes. D(GPP)

3.7 Health benefits of contraception

The non-contraceptive health benefits of LARC influence the uptake and continuation of the methods. They are summarised below. It is not possible to quantify the potential savings to the NHS that these additional health benefits might make (for example, the LNG-IUS is also licensed for the management of menorrhagia; women who use the method for contraception may be much less likely to report menorrhagia than women who are sterilised). The non-contraceptive benefits have, therefore, not been included in the cost effectiveness models.

Most couples use contraception for over 30 years. Additional health benefits beyond pregnancy prevention offer significant advantages and influence acceptability. In a nationwide sample of 943 US women, satisfaction with oral contraception was most likely among women aware of the non-contraceptive benefits of the pill and who experienced few side effects.[69]

Existing combined hormonal methods improve menstrual bleeding patterns, alleviate dysmenorrhoea, acne and sometimes pre-menstrual syndrome and reduce the risk of ovarian and endometrial cancer. Increasing numbers of women choose the LNG-IUS and DMPA because of the amenorrhoea they confer. One non-comparative study (n = 165) in Austria assessed long-term acceptability of LNG-IUS and reported that cessation of menstruation occurred in 47% of women at 3 years, over 80% of whom considered this to be a positive change.[81] [EL = 3] Perimenopausal women appreciate the facility to continue using the LNG-IUS into the menopause when it can be used to deliver the progestogen component of HRT.

The non-contraceptive benefits can influence continuation rates of contraception. One study in the USA demonstrated that women who experienced troublesome dysmenorrhoea prior to using the COC were 8 times more likely to continue using the pill than women who did not report dysmenorrhoea.[82]

3.8 Acceptability

Continuation rates are often regarded as a surrogate for acceptability of a method. This is simplistic. Many factors determine acceptability and continuation of a method may only reflect that it is the best of a bad lot. In recent years clinical trials have routinely included questions on acceptability at regular follow-up intervals but this is at best a crude measure of what is a complex issue. There is evidence to demonstrate that the acceptability of a contraceptive method (and continuation rate) is increased when users are well informed about the side effects and risks.[69]

* Check the Summary of Product Characteristics of individual devices for current licensed indications.

The current uptake of LARC in Great Britain is low (8% of contraceptive usage in 2003/04).[1] In a national survey of 1688 US women (where fewer than 2% used contraceptive implants and under 3% used injectables), women gave three major reasons for not using LARC: lack of knowledge, fear of side effects/risks, and satisfaction with the method they were currently using. Women aged 30 years or older and those with a college education were half as likely as younger women and those without college education to mention fear of side effects as their main reason for not using implants.[83] [EL = 3] Important reasons for choosing a contraceptive included: how well it works,[66,71,72] ease of use and protection against STI and HIV.[72]

Contraceptive choice is strongly influenced by the provider's views and by the advice and information that he/she gives to the potential user. Providers may hold very different views from users. In a study of the acceptability of methods of contraception which confer amenorrhoea,[84] providers thought that having a regular period was important to their clients while women themselves did not feel that it was important. The methods which a provider is able to offer also influence contraceptive choice. If a provider is unable to insert contraceptive implants, he/she is less likely to offer the method or, indeed, to be sufficiently well informed to give good information. Women may settle for a method which is easily available from their GP rather than have to travel to another service to obtain something different.

Acceptability of the chosen method is likely to be fundamental to correct and consistent use and to continuation. If a woman is unhappy with her method, for whatever reason, she is likely to discontinue it. If choice determines effective use and continuation, it can be argued that it should supersede considerations of cost.

RECOMMENDATION

Women should be provided with the method of contraception that is most acceptable to them provided it is not contraindicated. **D(GPP)**

3.9 Adherence

Many couples use contraception inconsistently and/or incorrectly. Inconsistent or incorrect use accounts for the difference between perfect use and typical use failure rates. Some methods are easier to use than others. The IUD/IUS and implants are inserted and removed by a healthcare professional and are completely independent of adherence for efficacy. Their failure rates are accordingly very low (Table 3.2)[85] and typical and perfect use rates are almost the same. Progestogen-only injectables last 8 to 12 weeks, but still demand the motivation and organisational skills required to attend for repeat doses. Adherence to oral contraception is not easy. In one US study, 47% of women reported missing one or more pills per cycle and 22% reported missing two or more pills per cycle.[27] In a study using electronic diaries to record adherence, 63% of women missed one or more pills in the first cycle of use, and 74% in the second cycle.[52] Typical use failure rates are even higher with methods of contraception (condoms, diaphragms, withdrawal and natural family planning) which rely on correct use with every act of intercourse.

A descriptive review assessed the impact of health concerns on adherence to hormonal contraceptives. It reported that contraceptive-related knowledge among sexually active adolescents was poor and the general public had many concerns about the safety of hormonal contraception. The development of side effects, especially those related to menstruation, caused adolescents and young women to feel that their general and reproductive health was being threatened. Counselling tailored to address specific reasons for non-adherence in this population may be beneficial.[86] [EL = 3]

3.10 Discontinuation

In an international review of discontinuation rates after 1 year of use of hormonal contraception, rates varied from 19% (for Norplant) to 62% (the combined pill).[87] Many of these data come from clinical trials in which continuation rates are almost always higher than in 'real life'. Data

specific to the UK are lacking. Discontinuation rates are higher for methods which do not require removal by a healthcare professional, as is clear from Table 3.3 (note that this table does not include any data on Implanon),[85] which shows the percentage of couples in the USA still using each method at the end of 1 year. Reasons for discontinuation are often associated with perceived risks and with real or perceived side effects. In a US study of 1657 women initiating or changing to use a new contraceptive pill, 32% of new starts and 16% of switchers had discontinued the method within six months. Of those who discontinued, 46% did so because of side effects (most of which they did not discuss with a healthcare professional and most of which would have resolved themselves within weeks).[27] In Sweden a common reason for discontinuation of the oral contraceptive pill is weight gain (perceived to be caused by the pill) and fear of health risks such as breast cancer.[29]

Discontinuation rates from countries where access to contraception is limited and/or expensive may differ from those in the UK, for example, in developing countries. Similarly, data from countries where women are characteristically of significant lower body weight (such as Indonesia or Thailand) than women in the UK may overestimate the effectiveness of hormonal methods of contraception and the side effect profile.

Continuation rates influence the effectiveness of contraception, since women often change to a less effective method or spend some weeks or months using no method while they decide what to use next. More than four-fifths of women in the US study who stopped the pill, despite being at risk of pregnancy, either failed to adopt another method or changed to a less effective one.[88]

Data from the US National Survey of Family Growth demonstrate high rates of method switching (61% of unmarried women will change their method over a period of 2 years).[89] Switching to a less effective method is common.[90] However, data specific to the UK are lacking.

Continuation rates of LARC are also fundamental to cost effectiveness. A method which costs £100 works out at £1.66/month if used for 5 years; discontinued after only 1 year of use the cost is £8.33/month.

3.11 Contraception and sexually transmitted infection

Sexual activity not only risks pregnancy but also sexually transmitted infection (STI) including HIV. Whilst methods of contraception are not designed to protect against STI, men and women who wish to protect themselves from STI should use a condom with every act of intercourse. Only the male condom has been shown to prevent some STIs including HIV. The sexual behaviour of potential users of contraception has relevance to method choice. For example, the IUD is relatively contraindicated for a woman with multiple partners.

LARC is not protective against STIs and HIV. There is some concern that use of hormonal methods of contraception may increase the risk of STIs including HIV.[91] (For more information see relevant chapters.)

WHO-MEC advises that for women at risk of STI including HIV, correct and consistent use of condoms is recommended, either alone or with another contraceptive method.

RECOMMENDATIONS

Healthcare professionals providing contraceptive advice should promote safer sex. **D(GPP)**

Healthcare professionals providing contraceptive advice should be able to assess risk for sexually transmitted infections (STIs) and advise testing when appropriate. **D(GPP)**

Healthcare professionals should be able to provide information about local services for STI screening, investigation and treatment. **D(GPP)**

Table 3.3 Percentage of women continuing use at the end of the first year (United States); adapted with permission from Trussell[435]

Method	Women continuing use at one year(%)[a]
No method[b]	
Spermicides[b]	42
Withdrawal	43
Periodic abstinence	51
Calendar	
Ovulation method	
Sympto-thermal[d]	
Post-ovulation	
Cap[e]	
Parous women	46
Nulliparous women	57
Sponge	
Parous women	46
Nulliparous women	57
Diaphragm[e]	57
Condom[f]	
Female (Reality)	49
Male 53	
Combined pill and minipill	68
Evra patch	68
NuvaRing	68
Depo-Provera	56
Lunelle	56
IUD	
Progestasert (progesterone T)	81
ParaGard (copper T)	78
Mirena (LNG-IUS)	81
Norplant and Norplant-2	84
Female sterilisation	100
Male sterilisation	100

Emergency contraceptive pills: treatment initiated within 72 hours after unprotected intercourse reduces the risk of pregnancy by at least 75%.[g]
Lactational amenorrhea method: LAM is a highly effective, *temporary* method of contraception.[h]

[a] Among couples attempting to avoid pregnancy, the percentage who continue to use a method for 1 year.

[b] The percentages becoming pregnant are based on data from populations where contraception is not used and from women who cease using contraception in order to become pregnant. Among such populations, about 89% become pregnant within 1 year. This estimate was lowered slightly (to 85%) to represent the percentage who would become pregnant within 1 year among women now relying on reversible methods of contraception if they abandoned contraception altogether.

[c] Foams, creams, gels, vaginal suppositories and vaginal film.

[d] Cervical mucus (ovulation) method supplemented by calendar in the pre-ovulatory and basal body temperature in the post-ovulatory phases.

[e] With spermicidal cream or jelly.

[f] Without spermicides.

[g] The treatment schedule is one dose within 120 hours after unprotected intercourse, and a second dose 12 hours after the first dose.

[h] However, to maintain effective protection against pregnancy, another method of contraception must be used as soon as menstruation resumes, the frequency or duration of breastfeeds is reduced, bottle feeds are introduced, or the baby reaches 6 months of age.

NB. Some of the methods listed in this table are not available in the UK and some of the methods available in the UK are not available in the USA and therefore are not listed here. This table does not include any data on Implanon. ParaGard® is the TCu 380A IUD.

3.12 User autonomy and consent

The law and policy governing access to contraception is well developed in the UK, in that all women have had access to free contraception since 1974 via a number of providers.[92] [EL = 4] Not all methods are available to all women equally as a result of regional variation.

Globally, reproductive rights are not always recognised, leading to statements such as: 'Reproductive rights rest on the recognition of basic rights of couples and individuals to decide freely and responsibly the number and spacing and timing of their children and to have the information to do so, and the right to attain the highest standard of sexual and reproductive health.' (para 95, Beijing Platform for Action, 1995)[93]

Reproductive and sexual health care including family planning services and information is recognised as a key intervention for improving the health of women and children, but also as a human right. Right to access, choice and benefit of scientific progress (evidence-based information) are considered important in making an informed choice of contraceptive methods.[63]

For the process of seeking consent to be meaningful, refusal of treatment needs to be one of the patient's options. Competent adults are entitled to refuse treatment even when the treatment would clearly benefit their health. Ethical guidance for obtaining consent, points of law and model documentation are available.[94–97] [EL = 4]

3.13 Contraception for special groups

Adolescents

Young people aged 16 and 17 are generally presumed to have the ability to consent to their own medical treatment, including contraceptive treatment. Healthcare professionals can provide contraceptive advice and treatment to a young person under the age of 16 years without parental involvement if the young person is judged to understand the advice provided and its implications, and her/his physical or mental health would otherwise be likely to suffer, and so provision of advice or treatment is in their best interests.[98]

It is considered to be good practice to follow the criteria outlined by Lord Justice Fraser in the case of Gillick versus West Norfolk and Wisbech Area Health Authority (AHA) and the Department of Health and Social Services (DHSS) when deciding whether a patient under 16 years is competent to consent to treatment. These criteria (known as the Fraser guidelines or 'Gillick competence') are that:

- the young person will understand the professional's advice
- the young person cannot be persuaded to inform their parents
- the young person is likely to begin, or to continue having, sexual intercourse with or without contraceptive treatment
- unless the young person receives contraceptive treatment, their physical or mental health, or both, are likely to suffer
- the young person's best interests require them to receive contraceptive advice or treatment with or without parental consent.

The consent of a competent young person cannot be overruled by a parent. If a person under the age of 18 years refuses to consent to treatment, it is possible in some cases for their parents to overrule their decision, though this is generally very rare. This right can only be exercised on the basis that the welfare of the young person is paramount. In this context welfare does not simply mean their physical health. The psychological effect of having the decision overruled would have to be taken into account and this option would normally only be pursued when the young person was thought likely to suffer 'grave and irreversible mental or physical harm' as a result of their refusal to consent to treatment.[99]

Young people under the age of 16 years have as great a right to confidentiality as any other patient. If someone under 16 is not judged mature enough to consent to treatment, the consultation itself can still remain confidential unless there are exceptional circumstances which suggest that the young person's health, safety or welfare is at risk. In this case local child protection procedures should be followed.[100] (www.dh.gov.uk/assetRoot/04/06/72/04/04067204.pdf)

The FFPRHC provides guidance on contraceptive choices for young people,[101] and DH provides guidance for healthcare professionals on the provision of contraceptive services for under-16s.[102]

People with learning disabilities

People over the age of 16 years are usually regarded as competent to decide their own treatment unless demonstrated otherwise. This applies to people with learning disabilities as much as any other person. It should not be assumed that adults or children are unable to make decisions about their own treatment simply because they have a learning disability. A key factor in assessing a person's ability to give consent is whether she/he can understand and weigh up the information needed to make the decision about contraceptive treatment. If information is presented in an appropriate way (for instance using simple language or pictorial aids) many people with learning disabilities will be able to consent to their own treatment. The involvement of specialists from learning disability teams or speech or language therapists can be helpful in assessing the individual's capacity to give consent to treatment though the patient's right to confidentiality should be borne in mind before involving anyone else.[98,103]

Currently no one else can give consent on behalf of an adult who is not judged to have the capacity to make a decision on their own behalf. However, healthcare professionals may treat the person if it would be in their best interests to do so. The High Court has ruled that 'best interests' go further than the medical interests of the person to include factors such as their general wellbeing and quality of life, their relationships with people close to them, and their religious or spiritual beliefs. Although the healthcare professional is legally responsible for deciding what is in the patient's 'best interests', any decision should ideally reflect the views of the individual's family, carers or friends. Any decision must be guided by what is genuinely in the best interests of the individual and not what would make life easier for their family or carers. Where there is serious disagreement between healthcare professionals and a patient's family that cannot be resolved, an application may be made to the High Court.[104] (www.dh.gov.uk/assetRoot/04/01/91/59/04019159.pdf)

The Mental Capacity Act 2005, which is expected to be implemented in 2007, will define what is meant by capacity and clarify the law on who can make decisions on behalf of people judged to lack capacity.

People with physical disabilities

There is a tendency to assume incorrectly that men and women with physical disabilities are not sexually active and have no need of contraception.

People with learning and physical disabilities have the same right to information and help with contraception as non-disabled people. Physical disabilities may influence the acceptability, safety and appropriateness of certain methods of contraception. A woman with a disability which makes dealing with monthly menstruation and sanitary protection difficult may appreciate a method which is associated with amenorrhoea. Combined hormonal contraception (CHC) may be less safe for a woman confined to a wheelchair, since immobilisation is associated with an increased risk of venous thromboembolism and so is CHC. Insertion of an IUD, and the need to check the threads regularly, may prove difficult for some women with a disability. These factors need to be taken into consideration when discussing contraception with women with disabilities.

RECOMMENDATIONS

Healthcare professionals should be aware of the law relating to the provision of advice and contraception for young people and for people with learning disabilities. Child protection issues and the Fraser Guidelines should be considered when providing contraception for women younger than 16 years.* D(GPP)

Women with learning and/or physical disabilities should be supported in making their own decisions about contraception. D(GPP)

Contraception should be seen in terms of the needs of the individual rather than in terms of relieving the anxieties of carers or relatives. D(GPP)

Where a woman with a learning disability is unable to understand and take responsibility for decisions about contraception, carers and other involved parties should meet to address issues around the woman's contraceptive need and to establish a care plan. D(GPP)

3.14 Training of healthcare professionals in contraceptive care

Medical and nurse training are, for the most part, delivered separately. The gold standard basic competency-based training for doctors in the provision of basic sexual and reproductive healthcare, which includes contraception, is the Diploma of the Faculty of Family Planning and Reproductive Health Care (DFFP). The DFFP includes the provision of some of the long-acting methods of contraception and is currently held by approximately 10 000 doctors in the UK, many working in general practice. Additional competency-based training is required to obtain the qualifications for the provision of intrauterine methods (IUD and IUS) and for subdermal methods of contraception. These qualifications are also awarded by the Faculty of Family Planning and Reproductive Health Care and are known as letters of competence (LoC) in intrauterine techniques and in subdermal techniques, respectively. All Faculty qualifications are recertifiable on a five-yearly cycle. The Membership of the Faculty of Family Planning and Reproductive Health Care (MFFP) is specific to the field of sexual and reproductive health and is obtained through examination similar to other College memberships.

The structure of nurse education has changed and many of the old, validated courses are about to or have now expired. In the past, the national boards had responsibility for standards and curricula for training and though these were variable there was some standardisation and recognition within family planning and contraception. In the ensuing reorganisation, Scotland, Wales and Northern Ireland replaced their national boards but England did not. Standards are now the remit of the Nursing and Midwifery Council (NMC), but curricula and course structure is delegated to individual higher education institutes. This has meant that training in family planning and contraception has been addressed in different ways according to the set-up within individual universities. For example, it may be part of degrees in general practice, sexual health or women's health or as stand-alone modules in contraception, reproductive or women's health. In 2004 the Royal College of Nursing (RCN) published a Sexual Health Competency framework which was developed in partnership with a number of organisations. This framework is designed to act as a template which reflects the levels of competency expected from registered practitioner through to consultant practitioner levels, and should help to underpin training in the future.[105] The RCN recommends that all nurses working in general practice, family planning, contraception and genitourinary (GU) clinics should undertake a two-day Sexually Transmitted Infections Foundation course (STIF details are available at www.bashh.org), and that family planning and GU-trained nurses should regularly update their knowledge and skills to maintain their competence to practise. Training guidance is available from the RCN for nurses working in this field in the following areas: contraception and sexual health in primary care,[106] inserting intrauterine devices,[107] and inserting and/or removing subdermal implants.[108] Details of these are

* See the Department of Health's *Best Practice Guidance for Doctors and Other Health Professionals on the Provision of Advice and Treatment to Young People under 16 on Contraception, Sexual and Reproductive Health* (July 2004), available from www.dh.gov.uk.

available from www.rcn.org.uk. An RCN-accredited Sexual Health Skills distance-learning programme has recently been developed. It is aimed at nurses who want a holistic foundation in sexual health but who may not specialise in this field. The course is validated by the University of Greenwich.

A survey undertaken by the Contraceptive Education Service run by the Family Planning Association and the Health Education Authority identified that 88% of GPs had some training in family planning but two-thirds had family planning qualifications issued in the 1970s.[109] Just 12% had recent training, with practice nurses more likely to have attended update training courses. There are no training data available for healthcare professionals working in community contraceptive services. However, job descriptions for staff grade, associate specialist and consultants specify that candidates should hold either the diploma or membership of the Faculty of Family Planning and Reproductive Health Care or an equivalent qualification with evidence of recertification if appropriate.

For nurses working within community contraceptive services, a recognised family planning qualification or equivalent is required. Training for both nurses and doctors involves a theoretical component and practical placement. Doctors training in GU medicine now need to obtain the DFFP as part of their specialist registrar training but there is no requirement by the RCOG for specialist registrars to attend a DFFP theory course and the level of contraceptive knowledge amongst trainees could benefit from improvement.

Most of the practical, hands-on training takes place in community contraceptive services. The issues of adequate funding to support training need to be discussed locally, regionally and nationally so that the future workforce is adequately equipped to provide level one services in primary care and accurate contraceptive advice in secondary care.

RECOMMENDATIONS

Healthcare professionals advising women about contraceptive choices should be competent to: **D(GPP)**

- help women to consider and compare the risks and benefits of all methods relevant to their individual needs
- manage common side effects and problems.

Contraceptive service providers who do not provide LARC within their own practice or service should have an agreed mechanism in place for referring women for LARC. **D(GPP)**

Healthcare professionals providing intrauterine or subdermal contraceptives should receive training to develop and maintain the relevant skills to provide these methods. **D(GPP)**

3.15 Cost effectiveness of LARC methods versus other reversible contraceptive methods

The economic analysis undertaken for this guideline demonstrated that all LARC methods avert a higher number of pregnancies compared with COC and male condom, for all time frames considered in the economic model, i.e. up to 15 years of contraceptive use. For 1 year of use, two of the LARC methods, the IUD and the injectable, dominate both COC and male condom. For periods of contraceptive use equal to 2 years and above, all LARC methods dominate COC and male condom (i.e. they are not only more effective but also less costly than COC and male condom). Results of the economic analysis are reported in Chapter 8.

3.16 Brief overview of features common to progestogen-only methods

This guideline discusses four methods of LARC, the copper IUD and the three progestogen-only contraceptive methods. Common features of POC regardless of dose and route of administration are described here.

Contraception can be divided into two broad categories, hormonal and nonhormonal. There are two categories of hormonal contraception, combined (oestrogen plus progestogen) and progestogen-only. Included in the category of LARC are the copper intrauterine device and three progestogen-only methods of contraception (injectables, implants and the intrauterine system).

Long-acting delivery systems have the theoretical advantage of providing very constant release rates of steroid hormone (compared with daily administration) and also avoid the first-pass effect through the liver, enabling lower doses of steroids to be used. However, the injectable preparations deliver a higher dose of hormone, while the oral preparation, implants and intrauterine systems deliver much lower doses.

Mode of action

The mode of action depends on the dose of hormone. Higher doses (injectables) inhibit follicle development and ovulation completely, alter the characteristics of cervical mucus interfering with sperm transport, and cause endometrial changes including atrophy. Intermediate doses (the subdermal implant Implanon) inhibit ovulation but allow follicular development, while very low doses (intrauterine delivery systems and the Norplant implant) inhibit ovulation only inconsistently and rely mainly on their effect on cervical mucus. In addition to the effect on the ovary and cervical mucus, all methods have an effect on the endometrium. The intrauterine system has a very marked effect, causing endometrial atrophy and inhibiting implantation.

Side effects

Bleeding disturbances

Progestogen-only methods disrupt regular menstrual cycles and the resulting 'bleeding disturbance' is the most common cause for discontinuation of the method. The mechanism of action of the method determines the predominant bleeding pattern. Bleeding patterns depend on the degree of suppression of ovarian activity. If normal ovulation occurs consistently a woman will experience menstrual bleeds at a frequency characteristic of her normal cycle. If both ovulation and follicle development are completely suppressed, amenorrhoea will result and many women do experience amenorrhoea while using Depo-Provera. If ovulation or follicular development sufficient to stimulate endometrial growth occur irregularly, bleeding will be erratic and unpredictable (implants) unless there is endometrial atrophy (LNG-IUS) when, regardless of the effect on ovarian activity, amenorrhoea is common. A local effect on the endometrium of the continuous administration of progestogens also probably contributes to the bleeding patterns.

Ovarian cysts

The incomplete suppression of ovarian activity is a recipe not only for erratic bleeding, but also for the development of ovarian follicular cysts. These occur in 20% of women using the LNG-IUS. They are almost always asymptomatic.

Metabolic side effects of progestogens

These are said to be associated with a range of common minor symptoms including acne, hirsutism, headache, mood change and weight gain or bloating. All are common complaints among women not using contraception. Depo-Provera may be associated with more significant weight increase than other POC.

Ectopic pregnancy

Ectopic pregnancy is regarded as a side effect of the POC due to the theoretical effect of progestogens on tubal motility. The best data are for Norplant, and show no increased risk compared with women not using contraception. Ectopic pregnancy is discussed in more detail in subsequent chapters.

Cancer

In the large meta-analysis reporting a relative risk of 1.24 for use of the COC,[110] an increased relative risk of breast cancer for both oral and injectable progestogen-only methods of contraception (RR 1.17 for both) was demonstrated, although for injectables this was not statistically significant. In a review of other pooled analyses[111] no significant associations were found. There

are much fewer data for POC than for COC and women with risk factors for breast cancer may be preferentially prescribed POC. Recent anxieties about the contribution of progestogens to the increased risk of breast cancer associated with HRT have not yet spread to POC. There is no evidence for any increased risk of other cancers and indeed some evidence to suggest a reduction in the risk of endometrial cancer.

Cardiovascular disease including venous thromboembolism

There is no evidence for an increase in the risk of stroke, myocardial infarction or VTE in association with POC.[112] An association between VTE and progestogen used for the treatment of gynaecological conditions such as anovulatory dysfunctional uterine bleeding[113] is likely to be due to prescriber bias since the COC – often the method of choice – is contraindicated in women with known risk factors for VTE. A very weak association between use of Norplant and hypertension[114] may be due to observer bias.

A systematic review of three cohort studies and one cross-sectional study reported no significant association of high blood pressure with the use of progestogen-only pills for up to 2–3 years of follow-up.[115] [EL = 3]

Gall bladder disease

A weak association between use of Norplant and gall bladder disease[114] has been described but there is no evidence of any association with other POC.

Bone mineral density

No study has demonstrated any adverse effect of progestogen-only implants on bone mineral density. It is unlikely therefore that use of oral or intrauterine POC would be harmful. Injectable methods, however, deliver higher doses of progestogen suppressing ovarian activity and causing hypoestrogenism and loss of bone mineral density and there are concerns that their use may increase the risk of osteoporosis.[116] (Refer to the forthcoming NICE clinical guideline *Osteoporosis: assessment of fracture risk and the prevention of osteoporotic fractures in individuals at high risk* – www.nice.org.uk/page.aspx?o=33923.)

Return to fertility

Mean time to pregnancy (TTP) after stopping contraception varied with the preceding contraceptive method and with its duration of use. Return to fertility occurs within days of cessation of all POC methods except injectables. The delay following discontinuation of DMPA is well recognised but pregnancy rates eventually reach those associated with cessation of other methods.

The methods described in the following chapters do not represent an order of recommended priority.

References

1. Dawe F, Rainsbury P. *Contraception and Sexual Health, 2003*. London: HMSO; 2004.
2. NHS Executive. *Clinical Guidelines: Using Clinical Guidelines to Improve Patient Care Within the NHS*. London: HMSO; 1996.
3. National Assembly for Wales. *A Strategic Framework for Promoting Sexual Health in Wales*. Cardiff: Health Promotion Division; 2000.
4. Department of Health. *The National Strategy for Sexual Health and HIV*. London: Department of Health; 2001.
5. Department of Health. *The National Strategy for Sexual Health and HIV: Implementation Action Plan.* London: Department of Health Publications; 2002.
6. National Institute for Clinical Excellence. *Information for National Collaborating Centres and Guideline Development Groups. No. 3*. London: Oaktree Press; 2001.
7. Oxman AD, Sackett DL, Guyatt GH. Users' guides to the medical literature. I. How to get started. The Evidence-Based Medicine Working Group. *JAMA* 1993;270:2093–5.
8. Guyatt GH, Sackett DL, Cook DJ. Users' guides to the medical literature. II. How to use an article about therapy or prevention. A. Are the results of the study valid? Evidence-Based Medicine Working Group. *JAMA* 1993;270:2598–601.
9. Guyatt GH, Sackett DL, Cook DJ. Users' guides to the medical literature. II. How to use an article about therapy or prevention. B. What were the results and will they help me in caring for my patients? Evidence-Based Medicine Working Group. *JAMA* 1994;271:59–63.
10. Jaeschke R, Guyatt G, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? Evidence-Based Medicine Working Group. *JAMA* 1994;271:389–91.
11. Jaeschke R, Guyatt GH, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-Based Medicine Working Group. *JAMA* 1994;271:703–7.
12. Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. *Evidence-based Medicine. How to Practice and Teach EBM*. 2nd ed. Edinburgh: Churchill Livingstone; 2000.
13. Scottish Intercollegiate Guidelines Network. *SIGN 50: A Guideline Developers' Handbook. No. 50.* Edinburgh: Scottish Intercollegiate Guideline Network; 2001.
14. Steiner MJ, Hertz-Picciotto I, Schulz KF, Sangi-Haghpeykar H, Earle BB, Trussell J. Measuring true contraceptive efficacy. A randomized approach–condom vs. spermicide vs. no method. *Contraception* 1998;58:375–8.
15. Trussell J. Methodological pitfalls in the analysis of contraceptive failure. *Stat Med* 1991;10:201–20.
16. Ferreira-Poblete A. The probability of conception on different days of the cycle with respect to ovulation: an overview. *Adv Contracept* 1997;13:83-95.
17. Wilcox AJ, Weinberg CR, Baird DD. Timing of sexual intercourse in relation to ovulation. Effects on the probability of conception, survival of the pregnancy, and sex of the baby. *N Engl J Med* 1995;333:1517–21.
18. Wilcox AJ, Dunson D, Baird DD. The timing of the "fertile window" in the menstrual cycle: day specific estimates from a prospective study. *BMJ* 2000;321:1259–62.
19. Dunson DB, Baird DD, Wilcox AJ, Weinberg CR. Day-specific probabilities of clinical pregnancy based on two studies with imperfect measures of ovulation. *Hum Reprod* 1999;14:1835–9.
20. te Velde ER, Eijkemans R, Habbema HDF. Variation in couple fecundity and time to pregnancy, an essential concept in human reproduction. *Lancet* 2000;355:1928–9.
21. Bongaarts J. A method for the estimation of fecundability. *Demography* 1975;12:645–60.
22. Wood JW. Fecundity and natural fertility in humans. *Oxf Rev Reprod Biol* 1989;11:61–109.
23. Schwartz D, Mayaux MJ. Female fecundity as a function of age: results of artificial insemination in 2193 nulliparous women with azoospermic husbands. *N Engl J Med* 1982;306:404–6.
24. van Noord-Zaadstra BM, Looman CWN, Alsbach H, Habbema JDF, te Velde ER, Karbaat J. Delaying childbearing: effect of age on fecundity and outcome of pregnancy. *BMJ* 1991;302:1361–5.
25. United National Population Information Network. Report of the International Conference on Population and Development. Cairo, 5–13 September 1994. [www.un.org/popin/icpd/conference/offeng/poa.html] Accessed 10 September 2005.
26. Forrest JD, Kaeser L. Questions of balance: issues emerging from the introduction of the hormonal implant. *Fam Plann Perspect* 1993;25:127–32.
27. Rosenberg MJ, Waugh MS, Burnhill MS. Compliance, counseling and satisfaction with oral contraceptives: a prospective evaluation. *Fam Plann Perspect* 1998;30:89–92.
28. Trussell J, Vaughan B. Contraceptive failure, method-related discontinuation and resumption of use: results from the 1995 National Survey of Family Growth. *Fam Plann Perspect* 1999;31:64–72,93.
29. Alexander N and d'Arcangues C. *Steroid Hormones and Uterine Bleeding*. Washington: AAAS Press; 1992.
30. Wellings K, Nanchahal K, Macdowall W, McManus S, Erens B, Mercer CH, *et al.* Sexual behaviour in Britain: early heterosexual experience. *Lancet* 2001;358:1843–50.

31. National Statistics Online. *Fertility: slight rise to 1.77 children per woman in 2004*. [www.statistics.gov.uk/cci/nugget.asp?id=951] Accessed 10 September 2005.
32. National Statistics. *Health Statistics Quarterly 25*. London: National Statistics; 2005.
33. Fleissig A. Unintended pregnancies and the use of contraception: changes from 1984 to 1989. *BMJ* 1991;302:147.
34. Farrow A, Hull MG, Northstone K, Taylor H, Ford WC, Golding J. Prolonged use of oral contraception before a planned pregnancy is associated with a decreased risk of delayed conception. *Hum Reprod* 2002;17:2754–61.
35. Duncan G, Harper C, Ashwell E, Mant D, Buchan H, Jones L. Termination of pregnancy: lessons for prevention. *Br J Fam Plann* 1990;15:112–7.
36. Mahmood TA, Lim BH, Lees DA. The characteristics of and the contraceptive practice among women seeking therapeutic termination of pregnancy in the Scottish Highlands. *Health Bull (Edinb)* 1988;46:330–6.
37. Jones RK, Darroch JE, Henshaw SK. Contraceptive use among U. S. women having abortions in 2000-2001. *Perspect Sex Reprod Health* 2002;34:294–303.
38. Jones RK, Darroch JE, Henshaw SK. Contraceptive use among U. S. women having abortions in 2000–2001. *Perspect Sex Reprod Health* 2002;34:294–303.
39. Garg M, Singh M, Mansour D. Peri-abortion contraceptive care: can we reduce the incidence of repeat abortions? *J Fam Plann Reprod Health Care* 2001;27:77–80.
40. Berger C, Gold D, Andres D, Gillett P, Kinch R. Repeat abortion: is it a problem? *Fam Plann Perspect* 1984;16:70–5.
41. Holmgren K. Repeat abortion and contraceptive use. Report from an interview study in Stockholm. *Gynecol Obstet Invest* 1994;37:254–9.
42. Westfall JM, Kallail KJ. Repeat abortion and use of primary care health services. *Fam Plann Perspect* 1995;27:162–5.
43. Lewis C, Wood C, Randall S. Unplanned pregnancy: is contraceptive failure predictable? *Br J Fam Plann* 1996;22:16–9.
44. Fisher WA, Singh SS, Shuper PA, Carey M, Otchet F, MacLean-Brine D, *et al*. Characteristics of women undergoing repeat induced abortion. *CMAJ* 2005;172:637–41.
45. National Statistics Online. *Births 2001: age of mother and area of usual residence*. [www.statistics.gov.uk/StatBase/xsdataset.asp?More=Y&vlnk=5672&All=Y&B2.x=85&B2.y=8] Accessed 17 September 2005.
46. Department of Health. *Teenage pregnancy*. 2005. [www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/TeenagePregnancy/fs/en] Accessed 10 September 2005.
47. National Statistics. *Population Trends: Autumn*. London: National Statistics; 1998.
48. Social Exclusion Unit. *Teenage Pregnancy*. London: Social Exclusion Unit; 1999.
49. Department of Health. *Government Response to the First Annual Report of the Independent Advisory Group on Teenage Pregnancy*. London: Department of Health; 2002.
50. Trussell J. Contraceptive efficacy. 14 September 1999. [Unpublished].
51. Hatcher RA. *Contraceptive Technology*. 17th ed. New York: Irvington Publishers; 1998.
52. Potter LS. How effective are contraceptives? The determination and measurement of pregnancy rates. *Obstet Gynecol* 1996;88(3 Suppl);13S–23S.
53. Croxatto HB, Urbancsek J, Massai R, Coelingh Bennink HJ, van Beek A. A multicentre efficacy and safety study of the single contraceptive implant Implanon. Implanon Study Group. *Hum Reprod* 1999;14:976–81.
54. Darney PD, Callegari LS, Swift A, Atkinson ES, Robert AM. Condom practices of urban teens using Norplant contraceptive implants, oral contraceptives, and condoms for contraception. *Am J Obstet Gynecol* 1999;180:929–37.
55. Pearl R. Factors in human fertility and their statistical evaluation. *Lancet* 1933;ii:609–11.
56. Steiner M, Dominik R, Trussell J, Hertz-Picciotto I. Measuring contraceptive effectiveness: A conceptual framework. *Obstet Gynecol* 1996;88(3);S24–30.
57. Murty J, Barron A, Searle ES. Auditing the introduction of a new product to a family planning service. *Br J Fam Plann* 1998;24:24–5.
58. van Lunsen RH, Arnolds HT, van Maris MG. Choices and changes in contraceptive behaviour; the role of information sources. *Patient Educ Couns* 1994;23:197–202.
59. Holt VL, Scholes D, Wicklund KG, Cushing-Haugen KL, Daling JR. Body mass index, weight, and oral contraceptive failure risk. *Obstet Gynecol* 2005;105:46–52.
60. Sivin I, Mishell DR, Jr., Darney P, Wan L, Christ M. Levonorgestrel capsule implants in the United States: a 5-year study. *Obstet Gynecol* 1998;92:337–44.
61. Hickey M and d'Arcangues C. Vaginal bleeding disturbances and implantable contraceptives. *Contraception* 2002;65:75–84.
62. Zieman M, Guillebaud J, Weisberg E, Shangold GA, Fisher AC, Creasy GW. Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: the analysis of pooled data. *Fertil Steril* 2002;77(2 Suppl 2):S13–18.
63. WHO. *Medical Eligibility Criteria for Contraceptive Use*. Geneva: World Health Organization; 2004 [www.who.int/reproductive-health/pages_resources/listing_family_planning.htm] Accessed 15 September 2005.
64. Counseling makes a difference. *Population Reports – Series J: Family Planning Programs* 1987;(35):1–31 [ocw.jhsph.edu/courses/FamilyPlanning/PDFs/Session7Notes.pdf] Accessed 17 September 2005.
65. Davie JE, Walling MR, Mansour DJ, Bromham D, Kishen M, Fowler P. Impact of patient counseling on acceptance of the levonorgestrel implant contraceptive in the United Kingdom. *Clin Ther* 1996;18:150–9.
66. Edwards JE, Oldman A, Smith L, McQuay HJ, Moore RA. Women's knowledge of, and attitudes to, contraceptive effectiveness and adverse health effects. *Br J Fam Plann* 2000;26:73–80.
67. Kozlowski KJ, Ohlhausen WW, Warren AM, Hendon A, Davis P, Rickert VI. Knowledge and attitudes of Norplant among adolescent females. *Adolesc Pediatr Gynecol* 1994;7:69–75.

68. Backman T, Huhtala S, Luoto R, Tuominen J, Rauramo I, Koskenvuo M. Advance information improves user satisfaction with the levonorgestrel intrauterine system. *Obstet Gynecol* 2002;99:608–13.
69. Hubacher D, Goco N, Gonzalez B, Taylor D. Factors affecting continuation rates of DMPA. *Contraception* 2000;60:345–51.
70. Canto De Cetina TE, Canto P, Ordonez LM. Effect of counseling to improve compliance in Mexican women receiving depot-medroxyprogesterone acetate. *Contraception* 2001;63:143–6.
71. Little P, Griffin S, Kelly J, Dickson N, Sadler C. Effect of educational leaflets and questions on knowledge of contraception in women taking the combined contraceptive pill: randomised controlled trial. *BMJ* 1998;316:1948–52.
72. Steiner MJ, Dalebout S, Condon S, Dominik R, Trussell J. Understanding risk: A randomized controlled trial of communicating contraceptive effectiveness. *Obstet Gynecol* 2003;102:709–17.
73. Picardo CM, Nichols M, Edelman A, Jensen JT. Women's knowledge and sources of information on the risks and benefits of oral contraception. *J Am Med Womens Assoc* 2003;58:112–6.
74. Gazmararian JA, Parker RM, Baker DW. Reading skills and family planning knowledge and practices in a low-income managed-care population. *Obstet Gynecol* 1999;93:239–44.
75. Comerasamy H, Read B, Francis C, Cullings S, Gordon H. The acceptability and use of contraception: a prospective study of Somalian women's attitude. *J Obstet Gynaecol* 2003;23:412–5.
76. Curtis KM, Chrisman CE, Peterson HB, WHO Programme for Mapping Best Practices in Reproductive Health. Contraception for women in selected circumstances. *Obstet Gynecol* 2002;99:1100–12.
77. World Health Organization. *Selected Practice Recommendations for Contraceptive Use*. Geneva: World Health Organization; 2002.
78. World Health Organization. *Selected Practice Recommendations for Contraceptive Use.* 2nd ed. Geneva: World Health Organization; 2005.
79. Faculty of Family Planning and Reproductive Health Care, Royal College of Obstetricians and Gynaecologists. *UK Selected Practice Recommendations for Contraceptive Use*. London: FFPRHC and RCOG; 2003.
80. Penney G, Brechin S, Allerton L; the Clinical Effectiveness Unit (CEU) of the Faculty of Family Planning and Reproductive Health Care (FFPRHC). FFPRHC Guidance (July 2005): The use of contraception outside the terms of the product licence. *J Fam Plann Reprod Health Care* 2005;31:225–42.
81. Baldaszti E, Wimmer-Puchinger B, Loschke K. Acceptability of the long-term contraceptive levonorgestrel-releasing intrauterine system (Mirena): a 3-year follow-up study. *Contraception* 2003;67:87–91.
82. Robinson JC, Plichta S, Weisman CS, Nathanson CA, Ensminger M. Dysmenorrhea and use of oral contraceptives in adolescent women attending a family planning clinic. *Am J Obstet Gynecol* 1992;166:578–83.
83. Tanfer K, Wierzbicki S, Payn B. Why are US women not using long-acting contraceptives? *Fam Plann Perspect* 2000;32:176–83.
84. Glasier AF, Smith KB, Cheng L, Ho PC, van der Spuy Z, Baird DT. An international study on the acceptability of a once-a-month pill. *Hum Reprod* 1999;14:3018–22.
85. Trussell J. Contraceptive failure in the United States. *Contraception* 2004;70:89–96.
86. Clark LR. Will the pill make me sterile? Addressing reproductive health concerns and strategies to improve adherence to hormonal contraceptive regimens in adolescent girls. *J Pediatr Adolesc Gynecol* 2001;14:153–62.
87. Meirik O, Fraser IS, d'Arcangues C, Affandi B, Branche V, Chikamata D, *et al.* Implantable contraceptives for women. *Hum Reprod Update* 2003;9:49–59.
88. Rosenberg MJ, Waugh MS. Oral contraceptive discontinuation: a prospective evaluation of frequency and reasons. *Am J Obstet Gynecol* 1998;179(3 Pt 1):577–82.
89. Grady WR, Billy JO, Klepinger DH. Contraceptive method switching in the United States. *Perspect Sex Reprod Health* 2002;34:135–45.
90. Piccinino LJ, Mosher WD. Trends in contraceptive use in the United States: 1982–1995. *Fam Plann Perspect* 1998;30:4–10.
91. Morrison CS, Bright P, Wong EL, Kwok C, Yacobson I, Gaydos CA, *et al.* Hormonal contraceptive use, cervical ectopy, and the acquisition of cervical infections. *Sex Transm Dis* 2004;31:561–7.
92. The National Health Service (General Medical Services Contracts) Regulations 2004. 2004 No. 291. TSO Ltd; 2004.
93. United Nations. *Platform For Action and the Beijing Declaration – 4th World Conference on Women, Beijing, China 4–15 September 1995*. New York: Dept of Public Information, United Nations; 1996.
94. Department of Health. *Good Practice in Consent Implementation Guide: Consent to Examination or Treatment*. No. 25751. London: Department of Health Publications; 2001.
95. British Medical Association. *Consent Tool Kit*. London: BMA; 2003.
96. General Medical Council. *Duties of a Doctor. Guidance from the General Medical Council*. London: General Medical Council; 1995.
97. American College of Obstetricians and Gynecologists. ACOG Committee Opinion. Surgery and patient choice: the ethics of decision making. *Obstet Gynecol* 2003;102 (5 Pt 1):1101–6.
98. Family Law Reform Act 1969.
99. Department of Health. *Best Practice Guidance for Doctors and Other Sexual Health Professionals on the Provision of Advice and Treatment to Young People under 16 on Contraception, Sexual and Reproductive Health. 1–5*. London: Department of Health; 2004.
100. Department of Health. *Seeking Consent: Working with Children. 1–27*. London: Department of Health; 2001.
101. Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. FFPRHC Guidance (October 2004): *Contraceptive Choices for Young People. J Fam Plann Reprod Health Care* 2004;30:237–50.
102. Department of Health. Publication of revised guidance for health professionals on the provision of contraceptive services for under 16s. 30-7-2004. [www.dh.gov.uk/assetRoot/04/08/69/16/04086916.pdf] Accessed 17 September 2005.

103. Department of Health. *12 Key Points on Consent: the Law in England*. London: Department of Health; 2001.
104. Department of Health. *Seeking Consent: Working with People with Learning Disabilities*. London: Department of Health; 2001.
105. Royal College of Nursing. *Sexual Health Competencies: an Integrated Career and Competency Framework for Sexual and Reproductive Health Nursing*. London: Royal College of Nursing; 2004.
106. Royal College of Nursing. *Contraception and Sexual Health in Primary Care*. London: Royal College of Nursing; 2004.
107. Royal College of Nursing. *Fitting Intrauterine Devices. Training Guidance for Nurses. 1(3)*. London: Royal College of Nursing; 2003.
108. Royal College of Nursing. *Inserting and/Or Removing Subdermal Contraceptive Implants*. London: Royal College of Nursing; 2004.
109. Family Planning Association. *Use of Family Planning Services*. London: Sexual Health Direct; 2002.
110. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996;347:1713–27.
111. Skegg DC, Noonan EA, Paul C, Spears GF, Meirik O, Thomas DB. Depot medroxyprogesterone acetate and breast cancer. A pooled analysis of the World Health Organization and New Zealand studies. *JAMA* 1995;273:799–804.
112. Debert-Ribeiro M, Medina E, Artigas J, He S, Zhong YH, De Wei Z, *et al.* Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives: Results of an international, multicenter, case–control study. *Contraception* 1998;57:315–24.
113. Vasilakis C, Jick H, Mar Melero-Montes M. Risk of idiopathic venous thromboembolism in users of progestagens alone. *Lancet* 1999;354:1610–1.
114. International Collaborative Post-Marketing Surveillance of Norplant. Post-marketing surveillance of Norplant contraceptive implants: II Non reproductive health. *Contraception* 2001;63:187–209.
115. Hussain SF. Progestogen-only pills and high blood pressure: is there an association? A literature review. *Contraception* 2004;69:89–97.
116. Westhoff C. Depot-medroxyprogesterone acetate injection (Depo-Provera): a highly effective contraceptive option with proven long-term safety. *Contraception* 2003;68:75–87.
117. Mishell DR Jr. Intrauterine devices: mechanisms of action, safety, and efficacy. *Contraception* 1998;58(3 Suppl):45S–53S.
118. Stanford JB, Mikolajczyk RT. Mechanisms of action of intrauterine devices: update and estimation of postfertilization effects. *Am J Obstet Gynecol* 2002;187:1699–708.
119. *Mechanism of Action, Safety and Efficacy of Intrauterine Devices*. Report of a WHO Scientific Group. Technical Report Series 753. Geneva: World Health Organisation; 1987.
120. Chi I. What we have learned from recent IUD studies: a researcher's perspective. *Contraception* 1993;48:81–108.
121. Gupta PK. Intrauterine contraceptive devices: vaginal cytology, pathologic changes and clinical implications. *Acta Cytol* 1982;26:571–613.
122. Joint Formulary Committee. *British National Formulary 48*. London: British Medical Association and Royal Pharmaceutical Society of Great Britain; 2004.
123. Newton J, Tacchi D. Long-term use of copper intrauterine devices. A statement from the Medical Advisory Committee of the Family Planning Association and the National Association of Family Planning Doctors. *Lancet* 1990;335:1322–3.
124. UNDP UNFPA, WHO Special Programme of Research Development and Research Training in Human Reproduction World Bank: IUD Research Group. Long-term reversible contraception. Twelve years of experience with the TCu380A and TCu220C. *Contraception* 1997;56:341–52.
125. Brechin S, Gebbie A. *Faculty Aid to Continued Professional Development Topic (FACT) on Perimenopausal Contraception*. A Self-Assessment Test. Review No 2000/01. London: Faculty of Family Planning and Reproductive Health Care of the Royal College of Obstetricians and Gynaecologists; 2000.
126. French RS, Cowan FM, Mansour DJ, Morris S, Procter T, Hughes D, *et al*. Implantable contraceptives (subdermal implants and hormonally impregnated intrauterine systems) versus other forms of reversible contraceptives: two systematic reviews to assess relative effectiveness, acceptability, tolerability and cost-effectiveness. *Health Technol Assess* 2000;4(7)i–v:1–107.
127. Arowojolu AO, Ololorin EO, Ladipo OA. Performances of copper T 380A and multiload copper 375/250 intrauterine contraceptive devices in a comparative clinical trial. *Afr J Med Med Sci* 1995;24:59–65.
128. Champion CB, Behlilovic B, Arosemena JM, Randic L, Cole LP, Wilkens LR. A three-year evaluation of TCu 380 Ag and multiload Cu 375 intrauterine devices. *Contraception* 1988;38:631–9.
129. Cole LP, Potts DM, Aranda C, Behlilovic B, Etman ES, Moreno J, *et al*. An evaluation of the TCu 380Ag and the Multiload Cu375. *Fertil Steril* 1985;43:214–7.
130. Sastrawinata S, Farr G, Prihadi SM, Hutapea H, Anwar M, Wahyudi I, *et al.* A comparative clinical trial of the TCu 380A, Lippes Loop D and Multiload Cu 375 IUDs in Indonesia. *Contraception* 1991;44:141–54.
131. UNDP/UNFPA/WHO/World Bank, Special Programme of Research, Development and Research Training in Human Reproduction: IUD Research Group. A randomized multicentre trial of the Multiload 375 and TCu380A IUDs in parous women: three-year results. *Contraception* 1994;49:543–9.
132. World Health Organization. *Annual Technical Report 2002*. Geneva: World Health Organization; 2002.
133. World Health Organization and Department of Reproductive Health and Research. *Annual Technical Report 2003*. Geneva: World Health Organization; 2004.
134. Skjeldestad FE, Rauramo I. An open randomised trial of two copper-IUDs, Nova-T 380 versus Gyne-T 380 Slimline: 3 year results. [Abstract No. 38]. 29th British Congress of Obstetrics and Gynaecology, Birmingham, 2001.
135. Cox M, Tripp J, Blacksell S, UK Family Planning and Reproductive Health Research Network. Clinical performance of the Nova T380 intrauterine device in routine use by the UK Family Planning and Reproductive Health Research Network: 5-year report. *J Fam Plann Reprod Health Care* 2002;28:69–72.

136. Batar I, Kuukankorpi A, Rauramo I, Siljander M. Two-year clinical experience with Nova-T 380, a novel copper-silver IUD. *Adv Contracept* 1999;15:37–48.

137. D'Souza RE, Masters T, Bounds W, Guillebaud J. Randomised controlled trial assessing the acceptability of GyneFix versus Gyne-T380S for emergency contraception. *J Fam Plann Reprod Health Care* 2003;29:23–9.

138. Rosenberg MJ, Foldesy R, Mishell DR Jr, Speroff L, Waugh MS, Burkman R. Performance of the TCu380A and Cu-Fix IUDs in an international randomized trial. *Contraception* 1996;53:197–203.

139. UNDP, UNFPA, and WHO Special Programme of Research, Development and Research Training in Human Reproduction, World Bank: IUD Research Group. The TCu 380A IUD and the frameless IUD "the FlexiGard": interim three-year data from an international multicenter trial. *Contraception* 1995;52:77–83.

140. Wu S, Hu J, Wildemeersch D. Performance of the frameless GyneFix and the TCu380A IUDs in a 3-year multicenter, randomized, comparative trial in parous women. *Contraception* 2000;61:91–8.

141. O'Brien PA, Marfleet C. Frameless versus classical intrauterine device for contraception. *Cochrane Database Syst Rev* 2005;(1):CD003282.

142. Sivin I, Stern J. Health during prolonged use of levonorgestrel 20 micrograms/d and the copper TCu 380Ag intrauterine contraceptive devices: a multicenter study. International Committee for Contraception Research (ICCR). *Fertil Steril* 1994;61:70–7.

143. Sivin I, Stern J, Coutinho E, Mattos CE, el Mahgoub S, Diaz S, *et al.* Prolonged intrauterine contraception: a seven-year randomized study of the levonorgestrel 20 mcg/day (LNg 20) and the Copper T380 Ag IUDS. *Contraception* 1991;44:473–80.

144. Sivin I, el Mahgoub S, McCarthy T, Mishell DR Jr, Shoupe D, Alvarez F, *et al.* Long-term contraception with the levonorgestrel 20 mcg/day (LNg 20) and the copper T 380Ag intrauterine devices: a five-year randomized study. *Contraception* 1990;42:361–78. Erratum in: *Contraception* 1991;43:100.

145. Sivin I, Alvarez F, Diaz J, Diaz S, el Mahgoub S, Coutinho E, *et al.* Intrauterine contraception with copper and with levonorgestrel: a randomized study of the TCu 380Ag and levonorgestrel 20 mcg/day devices. *Contraception* 1984;30:443–56.

146. Sivin I, Stern J, Diaz J, Diaz MM, Faundes A, el Mahgoub S, *et al.* Two years of intrauterine contraception with levonorgestrel and with copper: a randomized comparison of the TCu 380Ag and levonorgestrel 20 mcg/day devices. *Contraception* 1987;35:245–55.

147. Belhadj H, Sivin I, Diaz S, Pavez M, Tejada AS, Brache V, *et al.* Recovery of fertility after use of the levonorgestrel 20 mcg/d or Copper T 380 Ag intrauterine device. *Contraception* 1986;34:261–7.

148. Luukkainen T, Allonen H, Haukkamaa M, Lahteenmaki P, Nilsson CG, Toivonen J. Five years' experience with levonorgestrel-releasing IUDs. *Contraception* 1986;33:139–48.

149. Nilsson CG, Luukkainen T, Diaz J, Allonen H. Intrauterine contraception with levonorgestrel: a comparative randomised clinical performance study. *Lancet* 1981;1(8220 Pt 1):577–80.

150. Nilsson CG, Luukkainen T, Diaz J, Allonen H. Clinical performance of a new levonorgestrel-releasing intrauterine device. A randomized comparison with a nova-T-copper device. *Contraception* 1982;25:345–56.

151. Nilsson CG, Allonen H, Diaz J, Luukkainen T. Two years' experience with two levonorgestrel-releasing intrauterine devices and one copper-releasing intrauterine device: a randomized comparative performance study. *Fertil Steril* 1983;39:187–92.

152. Toivonen J, Luukkainen T, Allonen H. Protective effect of intrauterine release of levonorgestrel on pelvic infection: three years' comparative experience of levonorgestrel- and copper-releasing intrauterine devices. *Obstet Gynecol* 1991;77:261–4.

153. Andersson K, Odlind V, Rybo G. Levonorgestrel-releasing and copper-releasing (Nova T) IUDs during five years of use: a randomized comparative trial. *Contraception* 1994;49:56–72.

154. Luukkainen T, Allonen H, Haukkamaa M, Holma P, Pyorala T, Terho J, *et al.* Effective contraception with the levonorgestrel-releasing intrauterine device: 12-month report of a European multicenter study. *Contraception* 1987;36:169–79.

155. Andersson K, Batar I, Rybo G. Return to fertility after removal of a levonorgestrel-releasing intrauterine device and Nova-T. *Contraception* 1992;46:575–84.

156. Sekadde-Kigondu C, Mwathe EG, Ruminjo JK, Nichols D, Katz K, Jessencky K, *et al.* Acceptability and discontinuation of Depo-Provera, IUCD and combined pill in Kenya. *East Afr Med J* 1996;73:786–94.

157. Faundes A, Segal SJ, Adejuwon CA, Brache V, Leon P, Alvarez-Sanchez F. The menstrual cycle in women using an intrauterine device. *Fertil Steril* 1980;34:427–30.

158. Suvisaari J, Lahteenmaki P. Detailed analysis of menstrual bleeding patterns after postmenstrual and postabortal insertion of a copper IUD or a levonorgestrel-releasing intrauterine system. *Contraception* 1996;54:201–8.

159. Guillebaud J, Anderson AB, Turnbull AC. Reduction of mefenamic acid of increased menstrual blood loss associated with intrauterine contraception. *Br J Obstet Gynaecol* 1978;85:53–62.

160. Ylikorkala O, Viinikka L. Comparison between antifibrinolytic and antiprostaglandin treatment in the reduction of increased menstrual blood loss in women with intrauterine contraceptive devices. *Br J Obstet Gynaecol* 1983;90:78–83.

161. Roy S, Shaw ST Jr. Role of prostaglandins in IUD-associated uterine bleeding–effect of a prostaglandin synthetase inhibitor (ibuprofen). *Obstet Gynecol* 1981;58:101–6.

162. Davies AJ, Anderson AB, Turnbull AC. Reduction by naproxen of excessive menstrual bleeding in women using intrauterine devices. *Obstet Gynecol* 1981;57:74–8.

163. Faundes D, Bahamondes L, Faundes A, Petta C, Diaz J, Marchi N. No relationship between the IUD position evaluated by ultrasound and complaints of bleeding and pain. *Contraception* 1997;56:43–7.

164. Faundes D, Bahamondes L, Faundes A, Petta CA. T-shaped IUD move vertically with endometrial growth and involution during the menstrual cycle. *Contraception* 1998;57:413–5.

165. Milsom I, Rybo G, Lindstedt G. The influence of copper surface area on menstrual blood loss and iron status in women fitted with an IUD. *Contraception* 1990;41:271–81.

166. Larsson G, Milsom I, Jonasson K, Lindstedt G, Rybo G. The long-term effects of copper surface area on menstrual blood loss and iron status in women fitted with an IUD. *Contraception* 1993;48:471–80.

167. Rennie KL, Jebb SA. Prevalence of obesity in Great Britain. *Obes Rev* 2005;6:11–2.

168. Hassan DF, Petta CA, Aldrighi JM, Bahamondes L, Perrotti M. Weight variation in a cohort of women using copper IUD for contraception. *Contraception* 2003;68:27–30.

169. Spector IP, Carey MP. Incidence and prevalence of the sexual dysfunctions: a critical review of the empirical literature. *Arch Sex Behav* 1990;19:389–408.

170. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. *JAMA* 1999;281:537–44.

171. Martin-Loeches M, Orti RM, Monfort M, Ortega E, Rius J. A comparative analysis of the modification of sexual desire of users of oral hormonal contraceptives and intrauterine contraceptive devices. *Eur J Contracept Reprod Health Care* 2003;8:129–34.

172. Taneepanichskul S, Reinprayoon D, Jaisamrarn U. Effects of DMPA on weight and blood pressure in long-term acceptors. *Contraception* 1999;59:301–3.

173. Murray S, Hickey JB, Houang E. Significant bacteremia associated with replacement of intrauterine contraceptive device. *Am J Obstet Gynecol* 1987;156:698–700.

174. World Health Organization. *Improving Access to Quality Care in Family Planning. Medical Eligibility Criteria for Contraceptive Use*. 2nd ed. Geneva: World Health Organization; 2003.

175. Sivin I. Dose- and age-dependent ectopic pregnancy risks with intrauterine contraception. *Obstet Gynecol* 1991;78:291–8.

176. International Collaborative Post-Marketing Surveillance of Norplant. Post-marketing surveillance of Norplant contraceptive implants: I. Contraceptive efficacy and reproductive health. *Contraception* 2001;63:167–86.

177. The World Health Organization's Special Programme of Research, Development and Research Training in Human Reproduction: Task Force on Intrauterine Devices for Fertility Regulation. A multinational case–control study of ectopic pregnancy. *Clin Reprod Fertil* 1985;3:131–43.

178. Austoker J. Cancer prevention in primary care. Screening for cervical cancer. *BMJ* 1994;309:241–8.

179. Persson E, Holmberg K, Dahlgren S, Nilsson L. *Actinomyces israelii* in the genital tract of women with and without intra-uterine contraceptive devices. *Acta Obstet Gynecol Scand* 1983;62:563–8.

180. Fiorino AS. Intrauterine contraceptive device-associated actinomycotic abscess and Actinomyces detection on cervical smear. *Obstet Gynecol* 1996;87:142–9.

181. Persson E, Holmberg K. A longitudinal study of *Actinomyces israelii* in the female genital tract. *Acta Obstet Gynecol Scand* 1984;63:207–16.

182. Burkman RT. Intrauterine devices and pelvic inflammatory disease: evolving perspectives on the data. Obstet Gynecol *Surv* 1996;51(Suppl 12):S35–41.

183. Lippes J. Pelvic actinomycosis: a review and preliminary look at prevalence. *Am J Obstet Gynecol* 1999;180(2 Pt 1):265–9.

184. Valicenti JF Jr, Pappas AA, Graber CD, Williamson HO, Willis NF. Detection and prevalence of IUD-associated Actinomyces colonization and related morbidity. A prospective study of 69,925 cervical smears. *JAMA* 1982;247:1149–52.

185. Burkman RT, Damewood MT. Actinomyces and the intrauterine contraceptive device. In: Zatuchni GI, Goldsmith A, Sciarra JJ, editors. *Intrauterine Contraception: Advances and Future Prospects. Proceedings of an International Workshop on Intrauterine Contraception*. Philadelphia: Harper & Row; 1985. p. 427–37.

186. Curtis EM, Pine L. Actinomyces in the vaginas of women with and without intrauterine contraceptive devices. *Am J Obstet Gynecol* 1981;140:880–4.

187. Merki-Feld GS, Lebeda E, Hogg B, Keller PJ. The incidence of actinomyces-like organisms in Papanicolaou-stained smears of copper- and levonorgestrel-releasing intrauterine devices. *Contraception* 2000;61:365–8.

188. Cayley J, Fotherby K, Guillebaud J, Killick S, Kubba A, MacGregor A, *et al.* Recommendations for clinical practice: actinomyces like organisms and intrauterine contraceptives. The Clinical and Scientific Committee. *Br J Fam Plann* 1998;23:137–8.

189. Copper IUDs, infection and infertility. *Drug Ther Bull* 2002;40:67–9.

190. Macmillan S, McKenzie H, Flett G. Which women should be tested for *Chlamydia trachomatis*? *BJOG* 2000;107:1088–93.

191. Expert Advisory Group. *Summary and Conclusions of CMO's Expert Advisory Group on* Chlamydia trachomatis. London: Department of Health; 1998.

192. Gorbach SL, Ledger WJ. Reassessment of infection risk and intrauterine devices. *Infectious Diseases in Clinical Practice* 1995;4:199–205.

193. Farley TM, Rosenberg MJ, Rowe PJ, Chen JH, Meirik O. Intrauterine devices and pelvic inflammatory disease: an international perspective. *Lancet* 1992;339:785–8.

194. Grimes DA, Schulz KF. Antibiotic prophylaxis for intrauterine contraceptive device insertion. (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.

195. Walsh T, Grimes D, Frezieres R, Nelson A, Bernstein L, Coulson A, *et al.* Randomised controlled trial of prophylactic antibiotics before insertion of intrauterine devices. IUD Study Group. *Lancet* 1998;351:1005–8.

196. Zorlu CG, Aral K, Cobanoglu O, Gurler S, Gokmen O. Pelvic inflammatory disease and intrauterine devices: prophylactic antibiotics to reduce febrile complications. *Adv Contracept* 1993;9:299–302.

197. Geyoushi BE, Randall S, Stones RW. GyneFix: a UK experience. *Eur J Contracept Reprod Health Care* 2002;7:7–14.

198. Caliskan E. Analysis of risk factors associated with uterine perforation by intrauterine devices. *Eur J Contracept Reprod Health Care* 2003;8:150–5.

199. Harrison-Woolrych M, Ashton J, Coulter D. Uterine perforation on intrauterine device insertion: is the incidence higher than previously reported? *Contraception* 2003;67:53–6.

200. Chi I, Feldblum PJ, Rogers SM. IUD-related uterine perforation: an epidemiologic analysis of a rare event using an international dataset. *Contracept Deliv Syst* 1984;5:123–30.

201. Penney G, Brechin S, de Souza A, Bankowska U, Belfield T, Gormley M, *et al.*; Faculty of Family Planning and Reproductive

Health Care Clinical Effectiveness Unit. FFPRHC Guidance (January 2004). The copper intrauterine device as long-term contraception. *J Fam Plann Reprod Health Care* 2004;30:29–42. Erratum in: *J Fam Plann Reprod Health Care* 2004;30:134.

202. Treiman K, Liskin L, Kols A, Rinehart W. *IUDs: an Update*. Population Reports – Series B, No. 6. Y Baltimore: The Population Information Program, Center for Communication Programs, the Johns Hopkins School of Public Health; 1995.
203. Doll H, Vessey M, Painter R. Return of fertility in nulliparous women after discontinuation of the intrauterine device: comparison with women discontinuing other methods of contraception. *BJOG* 2001;108:304–14.
204. Grimes DA. Intrauterine devices and infertility: sifting through the evidence. *Lancet* 2001;358:6–7.
205. Guillebaud J. Intrauterine devices and infertility. *Lancet* 2001;358:1460.
206. Wilson JC. A prospective New Zealand study of fertility after removal of copper intrauterine contraceptive devices for conception and because of complications: a four-year study. *Am J Obstet Gynecol* 1989;160:391–6.
207. Hubacher D, Lara-Ricalde R, Taylor DJ, Guerra-Infante F, Guzman-Rodriguez R. Use of copper intrauterine devices and the risk of tubal infertility among nulligravid women. *N Engl J Med* 2001;345:561–7.
208. World Health Organization Special Programme of Research, Development and Research Training in Human Reproduction: Task Force on Intrauterine Devices for Fertility Regulation. Microdose intrauterine levonorgestrel for contraception. *Contraception* 1987;35:363–79.
209. Hassan MA, Killick SR. Is previous use of hormonal contraception associated with a detrimental effect on subsequent fecundity? *Hum Reprod* 2004;19:344–51.
210. Grimes D, Schulz K, Stanwood N. Immediate postabortal insertion of intrauterine devices. (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2005. Oxford: Update Software.
211. Pakarinen P, Toivonen J, Luukkainen T. Randomized comparison of levonorgestrel- and copper-releasing intrauterine systems immediately after abortion, with 5 years' follow-up. *Contraception* 2003;68:31–4.
212. Heartwell SF, Schlesselman S. Risk of uterine perforation among users of intrauterine devices. *Obstet Gynecol* 1983;61:31–6.
213. World Health Organization and Task Force on Intrauterine Devices for Fertility Regulation. IUD insertion following termination of pregnancy: a clinical trial of the TCu 220C, Lippes Loop D, and copper 7. *Stud Fam Plann* 1983;14:98–108.
214. Tuveng JM, Skjeldestad FE, Iversen T. Postabortal insertion of IUD. *Adv Contracept* 1986;2:387–92.
215. Royal College of Obstetricians and Gynaecologists. *The Care of Women Requesting Induced Abortion*. London: RCOG; 2004.
216. Grimes D, Schulz K, Van Vliet H, Stanwood N. Immediate post-partum insertion of intrauterine devices. *Cochrane Database Syst Rev* 2003;(1):CD003036.
218. Mishell DR Jr, Roy S. Copper intrauterine contraceptive device event rates following insertion 4 to 8 weeks post partum. *Am J Obstet Gynecol* 1982;143:29–35.
219. Curtis KM, Chrisman C. *Medical Eligibility Criteria for Contraceptive Use: a Review of New Evidence on Selected Topics - Draft*. Geneva: World Health Organization Division of Reproductive Health, Centers for Disease Control and Prevention National Center for Chronic Disease Prevention and Health Promotion; 2000.
220. Farr G, Rivera R, Amatya R. Non-physician insertion of IUDs: clinical outcomes among TCu380A insertions in three developing-country clinics. *Adv Contracept* 1998;14:45–57.
221. Andrews GD, French K, Wilkinson CL. Appropriately trained nurses are competent at inserting intrauterine devices: an audit of clinical practice. *Eur J Contracept Reprod Health Care* 1999;4:41–4.
222. Gupta S, Kirkman R. Intrauterine devices – update on clinical performance. *Obstetrician & Gynaecologist* 2002;4:37–43.
223. Stumpf PG, Lenker RM. Insertion technique, not design, affects expulsion rates of postpartum intrauterine device. *Contraception* 1984;30:327–30.
224. Reinprayoon D, Taneepanichskul S. Menstrual problems and side effects associated with long-term TCu 380A IUD use in perimenopausal women. *Contraception* 1998;57:417–9.
225. Goldstuck ND. First insertion of an IUD in nulliparous women over 40 years of age. *Contracept Deliv Syst* 1981;2:271–4.
226. Castro A, Abarca L, Rios M. The clinical performance of the Multiload IUD. II. The influence of age. *Adv Contracept* 1993;9:291–8.
227. Rodrigues da Cunha AC, Dorea JG, Cantuaria AA. Intrauterine device and maternal copper metabolism during lactation. *Contraception* 2001;63:37–9.
228. Bjarnadottir RI, Gottfredsdottir H, Sigurdardottir K, Geirsson RT, Dieben TO. Comparative study of the effects of a progestogen-only pill containing desogestrel and an intrauterine contraceptive device in lactating women. *BJOG* 2001;108:1174–80.
229. Rogovskaya S, Rivera R, Grimes DA, Chen PL, Pierre-Louis B, Prilepskaya V, *et al*. Effect of a levonorgestrel intrauterine system on women with type 1 diabetes: a randomized trial. *Obstet Gynecol* 2005;105:811–5.
230. Kenshole A. Contraception and the woman with diabetes. *Can J Diabetes Care* 1997;21:14–8.
231. Kjos SL, Ballagh SA, La Cour M, Xiang A, Mishell DR Jr. The copper T380A intrauterine device in women with type II diabetes mellitus. *Obstet Gynecol* 1994;84:1006–9.
232. Diab KM, Zaki MM. Contraception in diabetic women: comparative metabolic study of Norplant, depot medroxyprogesterone acetate, low dose oral contraceptive pill and CuT380A. *J Obstet Gynaecol Res* 2000;26:17–26.
233. Curtis KM, Chrisman CE, Peterson HB, World Health Organization, Programme for Mapping Best Practices in Reproductive Health. Contraception for women in selected circumstances. *Obstet Gynecol* 2002;99:1100–12.
234. Sinei SK, Morrison CS, Sekadde-Kigondu C, Allen M, Kokonya D. Complications of use of intrauterine devices among HIV-1-infected women. *Lancet* 1998;351:1238–41.
235. Morrison CS, Sekadde-Kigondu C, Sinei SK, Weiner DH, Kwok C, Kokonya D. Is the intrauterine device appropriate contraception for HIV-1-infected women? *BJOG* 2001;108:784–90.
236. Richardson BA, Morrison CS, Sekadde-Kigondu C, Sinei SK, Overbaugh J, Panteleeff DD, *et al*. Effect of intrauterine device use on cervical shedding of HIV-1 DNA. *AIDS* 1999;13:2091–7.

237. Pakarinen PI, Lahteenmaki P, Lehtonen E, Reima I. The ultrastructure of human endometrium is altered by administration of intrauterine levonorgestrel. *Hum Reprod* 1998;13:1846–53.

238. Critchley HO, Wang H, Jones RL, Kelly RW, Drudy TA, Gebbie AE, *et al.* Morphological and functional features of endometrial decidualization following long-term intrauterine levonorgestrel delivery. *Hum Reprod* 1998;13:1218–24.

239. Jones RL, Critchley HO. Morphological and functional changes in human endometrium following intrauterine levonorgestrel delivery. *Hum Reprod* 2000;15(Suppl 3):162–72.

240. Barbosa I, Bakos O, Olsson SE, Odlind V, Johansson ED. Ovarian function during use of a levonorgestrel-releasing IUD. *Contraception* 1990;42:51–66.

241. Nilsson CG, Lahteenmaki PL, Luukkainen T. Ovarian function in amenorrheic and menstruating users of a levonorgestrel-releasing intrauterine device. *Fertil Steril* 1984;41:52–5.

242. Diaz J, Faundes A, Diaz M, Marchi N. Evaluation of the clinical performance of a levonorgestrel-releasing IUD, up to seven years of use, in Campinas, Brazil. *Contraception* 1993;47:169–75.

243. Ronnerdag M, Odlind V. Health effects of long-term use of the intrauterine levonorgestrel-releasing system. A follow-up study over 12 years of continuous use. *Acta Obstet Gynecol Scand* 1999;78:716–21.

244. Cox M, Tripp J, Blacksell S. Clinical performance of the levonorgestrel intrauterine system in routine use by the UK Family Planning and Reproductive Health Research Network: 5-year report. *J Fam Plann Reprod Health Care* 2002;28:73–7.

245. Backman T, Huhtala S, Blom T, Luoto R, Rauramo I, Koskenvuo M. Length of use and symptoms associated with premature removal of the levonorgestrel intrauterine system: a nation-wide study of 17,360 users. *BJOG* 2000;107:335–9.

246. Dubuisson JB, Mugnier E. Acceptability of the levonorgestrel-releasing intrauterine system after discontinuation of previous contraception: results of a French clinical study in women aged 35 to 45 years. *Contraception* 2002;66:121–8.

247. Cohen EB, Rossen NN. Acne vulgaris in connection with the use of progestagens in a hormonal IUD or a subcutaneous implant. [Dutch]. *Ned Tijdschr Geneeskd* 2003;147:2137–9.

248. Boardman HF, Thomas E, Croft PR, Millson DS. Epidemiology of headache in an English district. *Cephalalgia* 2003;23:129–37.

249. Backman T, Rauramo I, Huhtala S, Koskenvuo M. Pregnancy during the use of levonorgestrel intrauterine system. *Am J Obstet Gynecol* 2004;190:50–4.

250. Zhou L, Harrison-Woolrych M, Coulter DM. Use of the New Zealand Intensive Medicines Monitoring Programme to study the levonorgestrel-releasing intrauterine device (Mirena). *Pharmacoepidemiol Drug Saf* 2003;12:371–7.

251. Sivin I, Stern J, Diaz S, Pavez M, Alvarez F, Brache V, *et al.* Rates and outcomes of planned pregnancy after use of Norplant capsules, Norplant II rods, or levonorgestrel-releasing or copper TCu 380Ag intrauterine contraceptive devices. *Am J Obstet Gynecol* 1992;166:1208–13.

252. Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. FFPRHC Guidance (April 2004). The levonorgestrel-releasing intrauterine system (LNG-IUS) in contraception and reproductive health. *J Fam Plann Reprod Health Care* 2004;30:99–108.

253. Suhonen S, Haukkamaa M, Jakobsson T, Rauramo I. Clinical performance of a levonorgestrel-releasing intrauterine system and oral contraceptives in young nulliparous women: a comparative study. *Contraception* 2004;69:407–12.

254. Heikkila M, Haukkamaa M, Luukkainen T. Levonorgestrel in milk and plasma of breast-feeding women with a levonorgestrel-releasing IUD. *Contraception* 1982;25:41–9.

255. Bounds W, Guillebaud J. Observational series on women using the contraceptive Mirena concurrently with anti-epileptic and other enzyme-inducing drugs. *J Fam Plann Reprod Health Care* 2002;28:78–80.

256. Crawford P. Interactions between antiepileptic drugs and hormonal contraception. *CNS Drugs* 2002;16:263–72.

257. Elder MG. Injectable contraception. *Clin Obstet Gynaecol* 1984;11:723–41.

258. Jain J, Dutton C, Nicosia A, Wajszczuk C, Bode FR, Mishell DR Jr. Pharmacokinetics, ovulation suppression and return to ovulation following a lower dose subcutaneous formulation of Depo-Provera(R). *Contraception* 2004;70:11–8.

259. International Planned Parenthood Federation (IPPF). *Statement on Injectable Contraception.* IPPF; 1999.

260. Bhathena RK. The long-acting progestogen-only contraceptive injections: an update. *BJOG* 2001;108:3–8.

261. Gold MA. Contraception update: implantable and injectable methods. Pediatr *Ann* 1995;24:203–7.

262. Fraser IS, Weisberg E. A comprehensive review of injectable contraception with special emphasis on depot medroxyprogesterone acetate. *Med J Aust* 1981;1(1 Suppl):3–19.

263. Howard G, Blair M, Fotherby K, Elder MG, Bye P. Seven years clinical experience of the injectable contraceptive, norethisterone oenanthate. *Br J Fam Plann* 1985;11:9–16.

264. Technical Guidance/Competence Working Group and World Health Organization. *Progestin-Only Injectables (DMPA and NET-EN). Recommendations for Updating Selected Practices in Contraceptive Use.* [www.reproline.jhu.edu/english/6read/6multi/tgwg/tgit__e.htm Background%20and%20Contributors] Accessed 17 September 2005.

265. Mishell DR. Long-acting contraceptive steroids. Postcoital contraceptives and antiprogestins. In: Mishell DR, Davajan V, Lobo RA, editors. *Infertility, Contraception and Reproductive Endocrinology*. Boston: Blackwell; 1991. p. 872–94.

266. Schwallie PC, Assenzo JR. The effect of depo-medroxyprogesterone acetate on pituitary and ovarian function, and the return of fertility following its discontinuation: a review. *Contraception* 1974;10:181–202.

267. Garza-Flores J, Hall PE, Perez-Palacios G. Long-acting hormonal contraceptives for women. *J Steroid Biochem Mol Biol* 1991;40:697–704.

268. Task Force on Long-Acting Agents for the Regulation of Fertility. Multinational comparative clinical trial of long-acting injectable contraceptives: norethisterone enanthate given in two dosage regimens and depot-medroxyprogesterone acetate. Final report. *Contraception* 1983;28:1–20.

269. WHO Special Programme of Research, Development and Research Training in Human Reproduction. Task Force on Long-Acting Agents for the Regulation of Fertility. Multinational comparative clinical trial of long-acting injectable contraceptives:

norethisterone enanthate given in two dosage regimens and depot-medroxyprogesterone acetate. Final Report. *Contraception* 1983;28:1–19.

270. Chinnatamby S. A comparison of the long-acting contraceptive agents norethisterone oenanthate and medroxyprogesterone acetate. *Aust N Z J Obstet Gynaecol* 1971;11:233–6.
271. O'Dell CM, Forke CM, Polaneczky MM, Sondheimer SJ, Slap GB. Depot medroxyprogesterone acetate or oral contraception in postpartum adolescents. *Obstet Gynecol* 1998;91:609–14.
272. Said S, Omar K, Koetsawang S, Kiriwat O, Srisatayapan Y, Kazi A, *et al*. A multicentered phase III comparative clinical trial of depot-medroxyprogesterone acetate given three-monthly at doses of 100 mg or 150 mg: II. The comparison of bleeding patterns. World Health Organization. Task Force on Long-Acting Systemic Agents for Fertility Regulation Special Programme of Research, Development and Research Training in Human Reproduction. *Contraception* 1987;35:591–610.
273. Potter LS, Dalberth BT, Canamar R, Betz M. Depot medroxyprogesterone acetate pioneers. A retrospective study at a North Carolina Health Department. *Contraception* 1997;56:305–12.
274. Polaneczky M, Guarnaccia M, Alon J, Wiley J. Early experience with the contraceptive use of depot medroxyprogesterone acetate in an inner-city clinic population. *Fam Plann Perspect* 1996;28:174–8.
275. Westfall JM, Main DS, Barnard L. Continuation rates among injectable contraceptive users. *Fam Plann Perspect* 1996;28:275–7.
276. Schwallie PC, Assenzo JR. Contraceptive use–efficacy study utilizing medroxyprogesterone acetate administered as an intramuscular injection once every 90 days. *Fertil Steril* 1973;24:331–9.
277. Fraser IS, Dennerstein GJ. Depo-Provera use in an Australian metropolitan practice. *Med J Aust* 1994;160:553–6.
278. Paul C, Skegg DC, Williams S. Depot medroxyprogesterone acetate. Patterns of use and reasons for discontinuation. *Contraception* 1997;56:209–14.
279. Colli E, Tong D, Penhallegon R, Parazzini F. Reasons for contraceptive discontinuation in women 20-39 years old in New Zealand. *Contraception* 1999;59:227–31.
280. Templeman CL, Cook V, Goldsmith LJ, Powell J, Hertweck SP. Postpartum contraceptive use among adolescent mothers. *Obstet Gynecol* 2000;95:770–6.
281. Harel Z, Biro FM, Kollar LM, Rauh JL. Adolescents' reasons for and experience after discontinuation of the long-acting contraceptives Depo-Provera and Norplant. *J Adolesc Health* 1996;19:118–23.
282. Said S, Sadek W, Rocca M, Koetsawang S, Kirwat O, Piya-Anant M, *et al*. Clinical evaluation of the therapeutic effectiveness of ethinyl oestradiol and oestrone sulphate on prolonged bleeding in women using depot medroxyprogesterone acetate for contraception. World Health Organization, Special Programme of Research, Development and Research Training in Human Reproduction, Task Force on Long-acting Systemic Agents for Fertility Regulation. *Hum Reprod* 1996;11(Suppl 2):1–13.
283. Tantiwattanakul P, Taneepanichskul S. Effect of mefenamic acid on controlling irregular uterine bleeding in DMPA users. *Contraception* 2004;70:277–9.
284. Jain JK, Nicosia AF, Nucatola DL, Lu JJ, Kuo J, Felix JC. Mifepristone for the prevention of breakthrough bleeding in new starters of depo-medroxyprogesterone acetate. *Steroids* 2003;68:(10–13)1115-9.
285. Sapire KE. A study of bleeding patterns with two injectable contraceptives given postpartum and the effect of two non-hormonal treatments. *Adv Contracept* 1991;7:379–87.
286. Lei ZW, Wu SC, Garceau RJ, Jiang S, Yang QZ, Wang WL, *et al*. Effect of pretreatment counseling on discontinuation rates in Chinese women given depo-medroxyprogesterone acetate for contraception. *Contraception* 1996;53:357–61.
287. Mangan SA, Larsen PG, Hudson S. Overweight teens at increased risk for weight gain while using depot medroxyprogesterone acetate. *J Pediatr Adolesc Gynecol* 2002;15:79–82.
288. Mohllajee AP, Curtis KM. *Progestogen-only Contraceptive Use in Obese Women*. World Health Organization, Division of Reproductive Health, Centers for Disease Control and Prevention, US Agency for International Development and National Institute of Child Health and Human Development; 2004.
289. Civic D, Scholes D, Ichikawa L, LaCroix AZ, Yoshida CK, Ott SM, *et al*. Depressive symptoms in users and non-users of depot medroxyprogesterone acetate. *Contraception* 2000;61:385–90.
290. Gupta N, O'Brien R, Jacobsen LJ, Davis A, Zuckerman A, Supran S, *et al*. Mood changes in adolescents using depot-medroxyprogesterone acetate for contraception: A prospective study. *J Pediatr Adolesc Gynecol* 2001;14:71–6.
291. Cromer BA, Smith RD, Blair JM, Dwyer J, Brown RT. A prospective study of adolescents who choose among levonorgestrel implant (Norplant), medroxyprogesterone acetate (Depo-Provera), or the combined oral contraceptive pill as contraception. *Pediatrics* 1994;94:687–94.
292. Westhoff C, Truman C, Kalmuss D, Cushman L, Davidson A, Rulin M, *et al*. Depressive symptoms and Depo-Provera. *Contraception* 1998;57:237–40.
293. Stathakis V, Kilkenny M, Marks R. Descriptive epidemiology of acne vulgaris in the community. *Australas J Dermatol* 1997;38:115–23.
294. Zwart JA, Dyb G, Holmen TL, Stovner LJ, Sand T. The prevalence of migraine and tension-type headaches among adolescents in Norway. The Nord-Trondelag Health Study (Head-HUNT-Youth), a large population-based epidemiological study. *Cephalalgia* 2004;24:373–9.
295. Enk L, Landgren BM, Lindberg UB, Silfverstolpe G, Crona N. A prospective, one-year study on the effects of two long acting injectable contraceptives (depot-medroxyprogesterone acetate and norethisterone oenanthate) on serum and lipoprotein lipids. *Horm Metab Res* 1992;24:85–9.
296. Anwar M, Soejono SK, Maruo T, Abdullah N. Comparative assessment of the effects of subdermal levonorgestrel implant system and long acting progestogen injection method on lipid metabolism. *Asia Oceania J Obstet Gynaecol* 1994;20:53–8.
297. Oyelola OO. Fasting plasma lipids, lipoproteins and apolipoproteins in Nigerian women using combined oral and progestin-only injectable contraceptives. *Contraception* 1993;47:445–54.
298. Curtis KM, Mohllajee AP. *Age and Progestogen-only Contraceptives*. World Health Organization, Division of Reproductive Health,

Centers for Disease Control and Prevention, US Agency for International Development and National Institute of Child Health and Human Development; 2004.

299. Petitti DB, Piaggio G, Mehta S, Cravioto MC, Meirik O. Steroid hormone contraception and bone mineral density: a cross-sectional study in an international population. *Obstet Gynecol* 2000;95:736–44.
300. Perrotti M, Bahamondes L, Petta C, Castro S. Forearm bone density in long-term users of oral combined contraceptives and depot medroxyprogesterone acetate. *Fertil Steril* 2001;76:469–73.
301. Bahamondes L, Perrotti M, Castro S, Faundes D, Petta C, Bedone A. Forearm bone density in users of Depo-Provera as a contraceptive method. *Fertil Steril* 1999;71:849–52.
302. Cundy T, Cornish J, Roberts H, Elder H, Reid IR. Spinal bone density in women using depot medroxyprogesterone contraception. *Obstet Gynecol* 1998;92(4 Pt 1):569–73.
303. Gbolade B, Ellis S, Murby B, Randall S, Kirkman R. Bone density in long term users of depot medroxyprogesterone acetate. *Br J Obstet Gynaecol* 1998;105:790–4.
304. Tang OS, Tang G, Yip P, Li B, Fan S. Long-term depot-medroxyprogesterone acetate and bone mineral density. *Contraception* 1999;59:25–9.
305. Taneepanichskul S, Intarprasert S, Theppisai U, Chaturachinda K. Bone mineral density in long-term depot medroxyprogesterone acetate acceptors. *Contraception* 1997;56:1–3.
306. Paiva LC, Pinto-Neto AM, Faundes A. Bone density among long-term users of medroxyprogesterone acetate as a contraceptive. *Contraception* 1998;58:351–5.
307. Scholes D, LaCroix AZ, Ott SM, Ichikawa LE, Barlow WE. Bone mineral density in women using depot medroxyprogesterone acetate for contraception. *Obstet Gynecol* 1999;93:233–8.
308. Banks E, Berrington A, Casabonne D. Overview of the relationship between use of progestogen-only contraceptives and bone mineral density. *BJOG* 2001;108:1214–21.
309. Scholes D, LaCroix AZ, Ichikawa LE, Barlow WE, Ott SM. Injectable hormone contraception and bone density: results from a prospective study. *Epidemiology* 2002;13:581–7.
310. Merki-Feld GS, Neff M, Keller PJ. A 2-year prospective study on the effects of depot medroxyprogesterone acetate on bone mass-response to estrogen and calcium therapy in individual users. *Contraception* 2003;67:79–86.
311. Scholes D, LaCroix AZ, Ichikawa LE, Barlow WE, Ott SM. The association between depot medroxyprogesterone acetate contraception and bone mineral density in adolescent women. *Contraception* 2004;69:99–104.
312. Scholes D, LaCroix AZ, Ichikawa LE, Barlow WE, Ott SM. Change in bone mineral density among adolescent women using and discontinuing depot medroxyprogesterone acetate contraception. *Arch Pediatr Adolesc Med* 2005;159:139–44.
313. Lara-Torre E, Edwards CP, Perlman S, Hertweck SP. Bone mineral density in adolescent females using depot medroxyprogesterone acetate. *J Pediatr Adolesc Gynecol* 2004;17:17–21.
314. Rome E, Ziegler J, Secic M, Bonny A, Stager M, Lazebnik R, *et al*. Bone biochemical markers in adolescent girls using either depot medroxyprogesterone acetate or an oral contraceptive. *J Pediatr Adolesc Gynecol* 2004;17:373–7.
315. Beksinska ME, Smit JA, Kleinschmidt I, Farley TMM, Mbatha F. Bone mineral density in women aged 40-49 years using depot-medroxyprogesterone acetate, norethisterone enanthate or combined oral contraceptives for contraception. *Contraception* 2005;71:170–5.
316. Cundy T, Cornish J, Roberts H, Reid IR. Menopausal bone loss in long-term users of depot medroxyprogesterone acetate contraception. *Am J Obstet Gynecol* 2002;186:978–83.
317. Orr-Walker BJ, Evans MC, Ames RW, Clearwater JM, Cundy T, Reid IR. The effect of past use of the injectable contraceptive depot medroxyprogesterone acetate on bone mineral density in normal post-menopausal women. Clin. *Endocrinol* 1998;49:615–8.
318. Wanichsetakul P, Kamudhamas A, Watanaruangkovit P, Siripakarn Y, Visutakul P. Bone mineral density at various anatomic bone sites in women receiving combined oral contraceptives and depot-medroxyprogesterone acetate for contraception. *Contraception* 2002;65:407–10.
319. Tharnprisarn W, Taneepanichskul S. Bone mineral density in adolescent and young Thai girls receiving oral contraceptives compared with depot medroxyprogesterone acetate: a cross-sectional study in young Thai women. *Contraception* 2002;66:101–3.
320. Cromer BA, Blair JM, Mahan JD, Zibners L, Naumovski Z. A prospective comparison of bone density in adolescent girls receiving depot medroxyprogesterone acetate (Depo-Provera), levonorgestrel (Norplant), or oral contraceptives. *J Pediatr* 1996;129:671–6.
321. Berenson AB, Radecki CM, Grady JJ, Rickert VI, Thomas A. A prospective, controlled study of the effects of hormonal contraception on bone mineral density. *Obstet Gynecol* 2001;98:576–82.
322. Berenson AB, Breitkopf CR, Grady JJ, Rickert VI, Thomas A. Effects of hormonal contraception on bone mineral density after 24 months of use. *Obstet Gynecol* 2004;103(5 Pt 1):899–906.
323. Clark MK, Sowers MR, Nichols S, Levy B. Bone mineral density changes over two years in first-time users of depot medroxyprogesterone acetate. *Fertil Steril* 2004;82:1580–6.
324. Naessen T, Olsson SE, Gudmundson J. Differential effects on bone density of progestogen-only methods for contraception in premenopausal women. *Contraception* 1995;52:35–9.
325. Ryan PJ, Singh SP, Guillebaud J. Depot medroxyprogesterone and bone mineral density. *J Fam Plann Reprod Health Care* 2002;28:12–15.
326. Duff G. *Updated Prescribing Advice on the Effect of Depo-Provera Contraception on Bones*. Medicines and Healthcare products Regulatory Agency; 2004. [www.mhra.gov.uk/news/2004/Depo-Provera_letterhealthprofs_181104.pdf] Accessed 11 September 2005.
327. Gbolade BA. Depo-Provera and bone density. *J Fam Plann Reprod Health Care* 2002;28:7–11.
328. Fotherby K, Saxena BN, Shrimanker K, Hingorani V, Takker D, Diczfalusy E, *et al*. A preliminary pharmacokinetic and pharmacodynamic evaluation of depot-medroxyprogesterone acetate and norethisterone oenanthate. *Fertil Steril* 1980;34:131–9.

329. Bassol S, Garza-Flores J, Cravioto MC, Diaz-Sanchez V, Fotherby K, Lichtenberg R, *et al*. Ovarian function following a single administration of depo-medroxyprogesterone acetate (DMPA) at different doses. *Fertil Steril* 1984;42:216–22.

330. Lan PT, Aedo AR, Landgren BM, Johannisson E, Diczfalusy E. Return of ovulation following a single injection of depo-medroxyprogesterone acetate: a pharmacokinetic and pharmacodynamic study. *Contraception* 1984;29:1–18.

331. Ortiz A, Hirol M, Stanczyk FZ, Goebelsmann U, Mishell DR. Serum medroxyprogesterone acetate (MPA) concentrations and ovarian function following intramuscular injection of depo-MPA. *J Clin Endocrinol Metab* 1977;44:32–8.

332. Saxena BN, Dusitsin N, Tankeyoon M, Chaudhury RR. Return of ovulation after the cessation of depot-medroxy progesterone acetate treatment in Thai women. *J Med Assoc Thai* 1980;63:66–9.

333. Pardthaisong T. Return of fertility after use of the injectable contraceptive Depo Provera: up-dated data analysis. *J Biosoc Sci* 1984;16:23–34.

334. Garza-Flores J, Cardenas S, Rodriguez V, Cravioto MC, Diaz-Sanchez V, Perez-Palacios G. Return to ovulation following the use of long-acting injectable contraceptives: a comparative study. *Contraception* 1985;31:361–6.

335. Pardthaisong T, Gray RH, McDaniel EB. Return of fertility after discontinuation of depot medroxyprogesterone acetate and intra-uterine devices in Northern Thailand. *Lancet* 1980;1:509–12.

336. Affandi B, Santoso SS, Djajadilaga, Hadisaputra W, Moeloek FA, Prihartono J, *et al*. Pregnancy after removal of Norplant implants contraceptive. *Contraception* 1987;36:203–9.

337. Morroni C, Grams M, Tiezzi L, Westhoff C. Immediate monthly combination contraception to facilitate initiation of the depot medroxyprogesterone acetate contraceptive injection. *Contraception* 2004;70:19–23.

338. Pharmacia Limited. Depo-Provera 150mg/ml injection. 2004 [emc.medicines.org.uk/emc/assets/c/html/displayDocPrinterFriendly.asp?documentid=11121] Accessed 17 September 2005.

339. Mohllajee AP, Curtis KM. *Progestogen-only Contraceptive Use Immediately After an Abortion*. World Health Organization, Division of Reproductive Health, Centers for Disease Control and Prevention, US Agency for International Development and National Institute of Child Health and Human Development; 2004.

340. Kaunitz AM. Injectable long-acting contraceptives. *Clin Obstet Gynaecol* 2001;44:73–91.

341. Baheiraei A, Ardsetani N, Ghazizadeh S. Effects of progestogen-only contraceptives on breast-feeding and infant growth. *Int J Gynaecol Obstet* 2001;74:203–5.

342. Halderman LD, Nelson AL. Impact of early postpartum administration of progestin-only hormonal contraceptives compared with nonhormonal contraceptives on short-term breast-feeding patterns. *Am J Obstet Gynecol* 2002;186:1250–6.

343. Hannon PR, Duggan AK, Serwint JR, Vogelhut JW, Witter F, DeAngelis C. The influence of medroxyprogesterone on the duration of breast-feeding in mothers in an urban community. *Arch Pediatr Adolesc Med* 1997;151:490–6.

344. Mattson RH, Cramer JA, Caldwell BV, Siconolfi BC. Treatment of seizures with medroxyprogesterone acetate: preliminary report. *Neurology* 1984;34:1255–8.

345. Baeten JM, Nyange PM, Richardson BA, Lavreys L, Chohan B, Martin HL Jr, *et al*. Hormonal contraception and risk of sexually transmitted disease acquisition: results from a prospective study. *Am J Obstet Gynecol* 2001;185:380–5.

346. McGregor JA, Hammill HA. Contraception and sexually transmitted diseases: interactions and opportunities. *Am J Obstet Gynecol* 1993;168(6 Pt 2):2033–41.

347. Louv WC, Austin H, Perlman J, Alexander WJ. Oral contraceptive use and the risk of chlamydial and gonococcal infections. *Am J Obstet Gynecol* 1989;160:396–402.

348. Lavreys L, Chohan V, Overbaugh J, Hassan W, McClelland RS, Kreiss J, *et al*. Hormonal contraception and risk of cervical infections among HIV-1-seropositive Kenyan women. *AIDS* 2004;18:2179–84.

349. Lavreys L, Baeten JM, Martin HL Jr, Overbaugh J, Mandaliya K, Ndinya-Achola J, *et al*. Hormonal contraception and risk of HIV-1 acquisition: results of a 10-year prospective study. *AIDS* 2004;18:695–7.

350. Keder LM, Rulin MC, Gruss J. Compliance with depot medroxyprogesterone acetate: a randomized, controlled trial of intensive reminders. *Am J Obstet Gynecol* 1998;179(3 Pt 1):583–5.

351. Croxatto HB. Mechanisms that explain the contraceptive action of progestin implants for women. *Contraception* 2002;65:21–7.

352. Makarainen L, van Beek A, Tuomivaara L, Asplund B, Coelingh Bennink HJ. Ovarian function during the use of a single contraceptive implant: Implanon compared with Norplant. *Fertil Steril* 1998;69:714–21.

353. Brache V, Alvarez-Sanchez F, Faundes A, Tejada AS, Cochon L. Ovarian endocrine function through five years of continuous treatment with NORPLANT subdermal contraceptive implants. *Contraception* 1990;41:169–77.

354. Croxatto HB, Diaz S, Pavez M, Miranda P, Brandeis A. Plasma progesterone levels during long-term treatment with levonorgestrel silastic implants. *Acta Endocrinol (Copenh)* 1982;101:307–11.

355. Newton J, Newton P. Implanon – The single-rod subdermal contraceptive implant. *J Drug Evaluation* 2003;1:181–218.

356. Edwards JE, Moore A. Implanon. A review of clinical studies. *Br J Fam Plann 1*999;24(4 Suppl):3–16.

357. Croxatto HB, Makarainen L. The pharmacodynamics and efficacy of Implanon. An overview of the data. *Contraception* 1998;58(Suppl 6):91S–97S.

358. Urbancsek J. An integrated analysis of nonmenstrual adverse events with Implanon. *Contraception* 1998;58(6 Suppl):109S–115S.

359. Affandi B. An integrated analysis of vaginal bleeding patterns in clinical trials of Implanon. *Contraception* 1998;58(6 Suppl):99S–107S.

360. Mascarenhas L. Insertion and removal of Implanon. *Contraception* 1998;58(6 Suppl):79S–83S.

361. Zheng SR, Zheng HM, Qian SZ, Sang GW, Kaper RF. A randomized multicenter study comparing the efficacy and bleeding pattern of a single-rod (Implanon) and a six-capsule (Norplant) hormonal contraceptive implant. *Contraception* 1999;60:1–8.

362. Croxatto HB. Clinical profile of Implanon: a single-rod etonogestrel contraceptive implant. *Eur J Contracept Reprod Health Care* 2000;5 Suppl 2:21–8.

363. Affandi B, Korver T, Geurts TB, Coelingh Bennink HJ. A pilot efficacy study with a single-rod contraceptive implant (Implanon) in 200 Indonesian women treated for < or = 4 years. *Contraception* 1999;59:167–74.

364. Zheng SR, Zheng HM, Qian SZ, Sang GW, Kaper RF. A long-term study of the efficacy and acceptability of a single-rod hormonal contraceptive implant (Implanon) in healthy women in China. *Eur J Contracept Reprod Health Care* 1999;4:85–93.

365. Kiriwat O, Patanayindee A, Koetsawang S, Korver T, Bennink HJ. A 4-year pilot study on the efficacy and safety of Implanon, a single-rod hormonal contraceptive implant, in healthy women in Thailand. *Eur J Contracept Reprod Health Care* 1998;3:85–91.

366. Medicines Evaluation Board. *Implanon still safe and effective: Europe adopts the Dutch position on Implanon.* [www.cbg-meb.nl/uk/nieuws/act0410a.htm] Accessed 11 September 2005.

367. Yao XY, Du MK. A randomized study comparing the efficacy and bleeding pattern of Implanon and Norplant hormonal contraceptive implant. [Chinese]. *Zhonghua Fu Chan Ke Za Zhi [Chinese Journal of Obstetrics and Gynecology]* 2003;38:419–22.

368. Mattos I, Martinez C, Ripolles M, Gomez de la CA, De Miguel S, Forcen L, *et al*. Satisfaction, efficacy and adverse effects of the subdermic implant (Implanon) in two women health assistance centers at Madrid community. [Spanish]. *Revista Iberoamericana de Fertilidad y Reproduccion Humana* 2004;21:93–9.

369. Rai K, Gupta S, Cotter S. Experience with Implanon in a northeast London family planning clinic. *Eur J Contracept Reprod Health Care* 2004;9:39–46.

370. Medicines and Healthcare products Regulatory Agency. *Adverse Drug Reactions Online Information Tracking: Implanon* (extracted for period 01/07/63 – 07/01/05. origin :UK). 2005.

371. Wenck BC, Johnston PJ. Implanon and medical indemnity: a case study of risk management using the Australian standard. *Med J Aust* 2004;181:117–9.

372. Harrison-Woolrych M, Hill R. Unintended pregnancies with the etonogestrel implant (Implanon): A case series from postmarketing experience in Australia. *Contraception* 2005;71:306–8.

373. Fleming D, Davie J, Glasier A. Continuation rates of long-acting methods of contraception. A comparative study of Norplant implants and intrauterine devices. *Contraception* 1998;57:19–21.

374. Lakha F, Glasier A. Continuation rates with Implanon: Abstract presented at the Annual Scientific Meeting of the FFPRHC, 26 and 27 May 2005 at the Royal Geographical Society, London, UK.

375. Bitzer J, Tschudin S, Alder J. Acceptability and side-effects of Implanon in Switzerland: A restrospective study by the Implanon Swiss Study Group. *Eur J Contracept Reprod Health Care* 2004;9:278–84.

376. Sergent F, Clamageran C, Bastard AM, Verspyck E, Marpeau L. Acceptability of the etonogestrel-containing contraceptive implant (Implanon). [French]. *J Gynecol Obstet Biol Reprod* 2004;33:407–15.

377. Gaffield ME. Implanon single rod implant. 2004. [Unpublished]

378. Andersch B, Milsom I. An epidemiologic study of young women with dysmenorrhea. *Am J Obstet Gynecol* 1982;144:655–60.

379. Belsey EM, Pinol AP. Menstrual bleeding patterns in untreated women. Task Force on Long-Acting Systemic Agents for Fertility Regulation. *Contraception* 1997;55:57–65.

380. Kaewrudee S, Taneepanichskul S, Jaisamraun U, Reinprayoon D. The effect of mefenamic acid on controlling irregular uterine bleeding secondary to Norplant(TM) use. *Contraception* 1999;60:25–30.

381. Alvarez-Sanchez F, Brache V, Thevenin F, Cochon L, Faundes A. Hormonal treatment for bleeding irregularities in Norplant implant users. *Am J Obstet Gynecol* 1996;174:919–22.

382. Witjaksono J, Lau TM, Affandi B, Rogers PA. Oestrogen treatment for increased bleeding in Norplant users: preliminary results. *Hum Reprod* 1996;11(Suppl 2):109–14.

383. Wu SL. [Changes in liver function and three metabolites before and after subdermal implantation with Norplant. [Chinese]. *Shengzhi Yu Biyun* 1992;12:74–5.

384. Subakir SB, Setiadi E, Affandi B, Pringgoutomo S, Freisleben HJ. Benefits of vitamin E supplementation to Norplant users – *In vitro* and *in vivo* studies. *Toxicology* 2002;148:173–8.

385. d'Arcangues C, Piaggio G, Brache V, Aissa RB, Hazelden C, Massai R, *et al*. Effectiveness and acceptability of vitamin-E and low-dose aspirin, alone or in combination, on Norplant-induced prolonged bleeding. *Contraception* 2004;70:451–62.

386. Cheng L, Zhu H, Wang A, Ren F, Chen J, Glasier A. Once a month administration of mifepristone improves bleeding patterns in women using subdermal contraceptive implants releasing levonorgestrel. *Hum Reprod* 2000;15:1969–72.

387. Massai MR, Pavez M, Fuentealba B, Croxatto HB, d'Arcangues C. Effect of intermittent treatment with mifepristone on bleeding patterns in Norplant implant users. *Contraception* 2004;70:47–54.

388. Egberg N, van Beek A, Gunnervik C, Hulkko S, Hirvonen E, Larsson-Cohn U, *et al*. Effects on the hemostatic system and liver function in relation to Implanon and Norplant. A prospective randomized clinical trial. *Contraception* 1998;58:93–8.

389. Mascarenhas L, van Beek A, Bennink HC, Newton J. Twenty-four month comparison of apolipoproteins A-1, A-II and B in contraceptive implant users (Norplant and Implanon) in Birmingham, United Kingdom. *Contraception* 1998;58:215–9.

390. Suherman SK, Affandi B, Korver T. The effects of Implanon on lipid metabolism in comparison with Norplant. *Contraception* 1999;60:281–7.

391. Biswas A, Viegas OAC, Roy AC. Effect of Implanon and Norplant subdermal contraceptive implants on serum lipids – A randomized comparative study. *Contraception* 2003;68:189–93.

392. Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK. Cardiovascular risk factors in confirmed prediabetic individuals. Does the clock for coronary heart disease start ticking before the onset of clinical diabetes? *JAMA* 1990;263:2893–8.

393. Biswas A, Viegas OA, Korver T, Ratnam SS. Implanon contraceptive implants: effects on carbohydrate metabolism. *Contraception* 2001;63:137–41.

394. Bachrach LK. Acquisition of optimal bone mass in childhood and adolescence. *Trends Endocrinol Metab* 2001;12:22–8.

395. Duursma SA, Raymakers JA, Boereboom FT, Scheven BA. Estrogen and bone metabolism. *Obstet Gynecol Surv* 1992;47:38–44.

396. Beerthuizen R, van Beek A, Massai R, Makarainen L, Hout J, Bennink HC. Bone mineral density during long-term use of the

progestagen contraceptive implant Implanon compared to a non-hormonal method of contraception. *Hum Reprod* 2000;15:118–22.

397. Sivin I, Campodonico I, Kiriwat O, Holma P, Diaz S, Wan L, *et al*. The performance of levonorgestrel rod and Norplant contraceptive implants: a 5 year randomized study. *Hum Reprod* 1998;13:3371–8.
398. Diaz S, Pavez M, Cardenas H, Croxatto HB. Recovery of fertility and outcome of planned pregnancies after the removal of Norplant subdermal implants or Copper-T IUDs. *Contraception* 1987;35:569–79.
399. Faculty of Family Planning and Reproductive Health Care. Royal College of Obstetricians and Gynaecologists. First prescription of combined oral contraception: recommendations for clinical practice. *Br J Fam Plann* 2000;26:27–38.
400. Huber J, Wenzl R. Pharmacokinetics of Implanon. An integrated analysis. *Contraception* 1998;58(Suppl):85S–90S.
401. Curtis KM, Chrisman C. *Systematic Review of the Evidence for Selected Practice Recommendations for Contraceptive Use: Background Paper*. Geneva: World Health Organization Department of Reproductive Health and Research; 2001.
402. Phemister DA, Laurent S, Harrison FN Jr. Use of Norplant contraceptive implants in the immediate postpartum period: safety and tolerance. *Am J Obstet Gynecol* 1995;172(1 Pt 1):175–9.
403. Mascarenhas L. Insertion and removal of Implanon: practical considerations. *Eur J Contracept Reprod Health Care* 2000;5(Suppl 2):29–34.
404. Faculty of Family Planning and Reproductive Health Care. *Training Requirements for Doctors Wishing to Obtain the Letter of Competence in Subdermal Contraceptive Implant Techniques (LOC SDI). 1-2*. London: Faculty of Family Planning and Reproductive Health Care; 2004.
405. Booranabunyat S, Taneepanichskul S. Implanon use in Thai women above the age of 35 years. *Contraception* 2004;69:489–91.
406. Cullins VE, Remsburg RE, Blumenthal PD, Huggins GR. Comparison of adolescent and adult experiences with Norplant levonorgestrel contraceptive implants. *Obstet Gynecol* 1994;83:1026–32.
407. Levine AS, Holmes MM, Haseldon C, Butler W, Tsai C. Subdermal contraceptive implant (Norplant) continuation rates among adolescents and adults in a family planning clinic. *J Pediatr Adolesc Gynecol* 1996;9:67–70.
408. Berenson AB, Wiemann CM, Rickerr VI, McCombs SL. Contraceptive outcomes among adolescents prescribed Norplant implants versus oral contraceptives after one year of use. *Am J Obstet Gynecol* 1997;176:586–92.
409. Dinerman LM, Wilson MD, Duggan AK, Joffe A. Outcomes of adolescents using levonorgestrel implants vs oral contraceptives or other contraceptive methods. *Arch Pediatr Adolesc Med* 1995;149:967–72.
410. Polaneczky M, Slap G, Forke C, Rappaport A, Sondheimer S. The use of levonorgestrel implants (Norplant) for contraception in adolescent mothers. *N Engl J Med* 1994;331:1201–6.
411. Dabrow SM, Merrick CL, Conlon M. Adolescent girls' attitudes toward contraceptive subdermal implants. *J Adolesc Health* 1995;16:360–6.
412. Reinprayoon D, Taneepanichskul S, Bunyavejchevin S, Thaithumyanon P, Punnahitananda S, Tosukhowong P, *et al*. Effects of the etonogestrel-releasing contraceptive implant (Implanon) on parameters of breastfeeding compared to those of an intrauterine device. *Contraception* 2000;62:239–46.
413. Diaz S, Reyes MV, Zepeda A, Gonzalez GB, Lopez JM, Campino C, *et al*. Norplant implants and progesterone vaginal rings do not affect maternal bone turnover and density during lactation and after weaning. *Hum Reprod* 1999;14:2499–505.
414. Haukkamaa M. Contraception by Norplant subdermal capsules is not reliable in epileptic patients on anticonvulsant treatment. *Contraception* 1986;33:559–65.
415. Gaffield ME. *Anti-convulsants and Hormonal Contraceptive Methods.* World Health Organization, Division of Reproductive Health, Centers for Disease Control and Prevention, US Agency for International Development and National Institute of Child Health and Human Development; 2004.
416. Sonnenberg FA, Burkman RT, Hagerty CG, Speroff L, Speroff T. Costs and net health effects of contraceptive methods. *Contraception* 2004;69:447–59.
417. Trussell J, Koenig J, Stewart F, Darroch JE. Medical care cost savings from adolescent contraceptive use. *Fam Plann Perspect* 1997;29:248–55.
418. Koenig JD, Strauss MJ, Henneberry J, Wilson TG. The social costs of inadequate contraception. *Int J Technol Assess Health Care* 1996;12:487–97.
419. Trussell J, Leveque JA, Koenig JD, London R, Borden S, Henneberry J, *et al*. The economic value of contraception: a comparison of 15 methods. *Am J Public Health* 1995;85:494–503.
420. Ortmeier BG, Sauer KA, Langley PC, Bealmear BK. A cost-benefit analysis of four hormonal contraceptive methods. *Clin Ther* 1994;16:707–13.
421. Chiou C-F, Trussell J, Reyes E, Knight K, Wallace J, Udani J, *et al*, Borenstein J. Economic analysis of contraceptives for women. *Contraception* 2003;68:3–10..
422. Ashraf T, Arnold SB, Maxfield M Jr. Cost-effectiveness of levonorgestrel subdermal implants. Comparison with other contraceptive methods available in the United States. *J Reprod Med* 1994;39:791–8.
423. Westfall JM, Main DS. The contraceptive implant and the injectable: a comparison of costs. *Fam Plann Perspect* 1995;27:34–6.
424. Janowitz B, Kanchanasinith K, Auamkul N, Amornwichet P, Soonthorndhada K, Hanebergh R. Introducing the contraceptive implant in Thailand: impact on method use and cost. *Int Fam Plann Perspect* 1994;20:131–6.
425. Phillips CJ. Economic analysis of long-term reversible contraceptives. Focus on Implanon. *Pharmacoeconomics* 2000;17:209–21.
426. McGuire A, Hughes D. The economics of family planning services. A report prepared for the Contraceptive Alliance. London: Family Planning Association, Contraceptive Alliance; 1995.
427. Hughes D, McGuire A. The cost-effectiveness of family planning service provision. *J Public Health Med* 1996;18:189–96.
428. Varney SJ, Guest JF. Relative cost effectiveness of Depo-Provera, Implanon, and Mirena in reversible long-term hormonal contraception in the UK. *Pharmacoeconomics* 2004;22:1141–51.

429. Hurskainen R, Teperi J, Rissanen P, Aalto A-M, Grenman S, Kivela A, *et al*. Clinical outcomes and costs with the levonorgestrel-releasing intrauterine system or hysterectomy for treatment of menorrhagia: randomized trial 5-year follow-up. *JAMA* 2004;291:1456–63.

430. Henshaw SK. Unintended pregnancy in the United States. *Fam Plann Perspect* 1998;30:24–9.

431. Forrest JD. Epidemiology of unintended pregnancy and contraceptive use. *Am J Obstet Gynecol* 1994;170:1485–9.

432. Denton AB, Scott KE. Unintended and unwanted pregnancy in Halifax: the rate and associated factors. *Can J Public Health* 1994;85:234–8.

433. Gadow EC, Paz JE, Lopez-Camelo JS, Dutra MG, Queenan JT, Simpson JL, *et al*. Unintended pregnancies in women delivering at 18 South American hospitals. NFP-ECLAMC Group. Latin American Collaborative Study of Congenital Malformations. *Hum Reprod* 1998;13:1991–5.

434. Rowlands S, Hannaford P. The incidence of sterilisation in the UK. *BJOG* 2003;110:819–24.

435. Trussell J. Contraceptive efficacy. In: Hatcher RA, Trussell J, Stewart F, Nelson A, Cates W, Guest F, *et al*., editors. *Contraceptive Technology*. 18th ed. New York: Ardent Media; 2004.

436. Department of Health. *Prescription Cost Analysis for England 2002*. London: Department of Health; 2003.

437. Department of Health. *NHS Reference Costs 2004*. London: Department of Health; 2005.

438. Department of Health. *Gp Fees and Allowances 2003–2004*. [www.dh.gov.uk/PolicyAndGuidance/OrganisationPolicy/PrimaryCare/GPFeesAndAllowances/fs/en] Accessed 12 September 2005.

439. Curtis L, Netten A. *Unit Costs of Health and Social Care 2004*. Canterbury: University of Kent at Canterbury, Personal Social Services Research Unit; 2004.

440. National Statistics. Conceptions in England and Wales, 2001. *Health Statistics Quarterly* 2003;17(Spring):72–4.

441. Scottish Office. Scottish Statistics 2002. Glasgow: Scottish Statistics; 2002.

442. Royal College of Obstetricians and Gynaecologists. *Male and Female Sterilisation: Evidence-based Clinical Guideline Number 4*. iii-114. London: RCOG Press; 2004.

443. Tay JI, Moore J, Walker JJ. Ectopic pregnancy. *BMJ* 2000;320:916–9. Erratum in: *BMJ* 2000;321:424.

444. Peterson HB, Xia Z, Hughes JM, Wilcox LS, Tylor LR, Trussell J. The risk of ectopic pregnancy after tubal sterilization. U. S. Collaborative Review of Sterilization Working Group. *N Engl J Med* 1997;336:762–7.

445. Furlong LA. Ectopic pregnancy risk when contraception fails. A review. *J Reprod Med* 2002;47:881–5.

446. National Institute for Clinical Excellence. *Guide to the Methods of Technology Appraisal*. London: NICE; 2004.

447. Macdowall W, Gerressu M, Nanchahal K, Wellings K. *Analysis of Natsal 2000 Data for Wales: a Report to the National Assembly for Wales*. 2002. [www.cmo.wales.gov.uk/content/work/sexualhealth/natsal-2000-e.pdf] Accessed 17 September 2005.

448. Scottish Programme for Clinical Effectiveness in Reproductive Health. *Scottish Audit of the Management of Early Pregnancy Loss*. SPCERH publication no. 19. Aberdeen: Scottish Programme for Clinical Effectiveness in Reproductive Health (SPCERH); 2003. [www.abdn.ac.uk/spcerh/publications/EPL%20report.pdf] Accessed 17 September 2005.

449. Glasier A, Gebbie A. *Handbook of Family Planning and Reproductive Healthcare*. 4th ed. London: Churchill Livingstone; 2000.

450. Emans SJ, Grace E, Woods ER. Adolescents' compliance with the use of oral contraceptives. *JAMA* 1987;257:3377–81.

451. Rosenberg MJ, Waugh MS, Meehan TE. Use and misuse of oral contraceptives: risk indicators for poor pill taking and discontinuation. *Contraception* 1995;51:283–8.