Chapter 4
Evidence generation and synthesis to improve family planning, prevent unsafe abortion and prevent and control sexually transmitted and reproductive tract infections

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Contents

Abstract 107

Introduction 107

Methods 107

Results 107

Conclusions and recommendations 114

Summary 116

1 Introduction 117

2 Methods 117

2.1 Phase I: fact finding with WHO programme teams 118

2.2 Phase II: desk review and consultation with stakeholders 118

3 Rationale 118

4 Findings 119

4.1 General 119

4.2 Improving family planning: generating new evidence, marketing new products and protecting health and safety 120

5 Conclusions and recommendations 141

5.1 Summary 141

5.2 Impact 141

5.3 Recommendations 143

References 144

Annex 1: List of persons interviewed and methods of contact 148

Annex 2: Revised guidance: combined hormonal contraceptive use during the postpartum period 149

Recommendation 149

Annex 3: GRADE evidence profiles – systematic reviews of hormonal contraception use and HIV risk 150

A. GRADE evidence profile: hormonal contraception for women at high risk of HIV 150

B. GRADE evidence profile: risk of HIV transmission among women living with HIV and using hormonal contraceptives 151

C. GRADE evidence profile: HIV disease progression among women living with HIV and using hormonal contraception 152
Abbreviations

ANC  antenatal care
ART  antiretroviral therapy
BMA  British Medical Association
CAC  comprehensive abortion care
CERRUGUI  Cellule de Recherche en Santé de la Reproduction en Guinée (NGO in Guinea)
CCUP  comprehensive care for unwanted pregnancy
CHC  combined hormonal contraceptive
COC  combined oral contraceptive
COPUA  Coalition for Prevention of Unsafe Abortion
DAC  Development Assistance Committee (OECD)
DMPA  depot medroxyprogesterone acetate (an injectable hormonal contraceptive)
DSMC  data safety and monitoring committee
EC  emergency contraception
ECS  elimination of congenital syphilis
ERC  Ethical Review Committee (WHO)
EVA  electronic vacuum aspiration
FP  family planning
FSH  follicle-stimulating hormone
GRADE  grading of recommendations, assessment, development and evaluation (framework for reviewing evidence)
ICEC  International Consortium for Emergency Contraception
IEC  information, education and counseling
IUD  intrauterine device
LAC  Latin America and the Caribbean
LH  luteinizing hormone
LMP  last menstrual period
MDG  Millennium Development Goal
MEC  Medical eligibility for contraceptive use (WHO: 4th edition 2009)
MR  menstrual regulation
MTCT  mother-to-child transmission
MVA  manual vacuum aspiration
NET-EN  norethisterone enantate (an injectable progestin used as a contraceptive)
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
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</thead>
<tbody>
<tr>
<td>NGO</td>
<td>nongovernmental organization</td>
</tr>
<tr>
<td>OCP</td>
<td>oral contraceptives pill</td>
</tr>
<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td>OTC</td>
<td>over the counter</td>
</tr>
<tr>
<td>PAC</td>
<td>post-abortion care</td>
</tr>
<tr>
<td>PPTC</td>
<td>prevention of parent-to-child transmission (of HIV)</td>
</tr>
<tr>
<td>RHR</td>
<td>WHO Department of Reproductive Health and Research</td>
</tr>
<tr>
<td>RNA</td>
<td>ribonucleic acid</td>
</tr>
<tr>
<td>SRH</td>
<td>sexual and reproductive health</td>
</tr>
<tr>
<td>STI</td>
<td>sexually transmitted infection</td>
</tr>
<tr>
<td>TU</td>
<td>testosterone undecanoate (an injectable androgen)</td>
</tr>
<tr>
<td>UN</td>
<td>United Nations</td>
</tr>
<tr>
<td>UNAIDS</td>
<td>Joint United Nations Programme on HIV/AIDS</td>
</tr>
<tr>
<td>UNDP</td>
<td>United Nations Development Programme</td>
</tr>
<tr>
<td>UNFPA</td>
<td>United Nations Population Fund</td>
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<tr>
<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
</tr>
<tr>
<td>VTE</td>
<td>venous thromboembolism</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
Abstract

Introduction
The World Health Organization’s (WHO) Department of Reproductive Health and Research (RHR) is the implementing body for the multi-agency (United Nations Development Fund (UNDP)/United Nations Population Fund (UNFPA)/United Nations Children’s Fund (UNICEF)/WHO/World Bank) Special Programme of Research, Development and Research Training in Human Reproduction (HRP). The 2008–2012 case-study highlights HRP activities in the areas of (a) family planning (FP), (b) unsafe abortion and (c) sexually transmitted infections (STIs), by demonstrating HRP’s unique process of addressing sexual and reproductive health (SRH) issues, from problem identification to generating new knowledge, to global roll-out of solutions.

Methods
Meetings were held with team leaders in Geneva (18–20 April and 19–22 June 2012), to identify focal activities of the professional clusters. A desk audit of peer-reviewed publications and WHO reports was complemented by e-mail contact with collaborators. Highlighted work includes the development of a male contraceptive, marketing of emergency contraceptives and HRP’s response to evidence about hormonal contraceptive use and HIV risk. The application of the WHO strategic approach to reducing unsafe abortion and the initiative to eliminate congenital syphilis are also summarized.

Results

Family planning: developing a male contraceptive
A phase II, eight-country trial of two long-acting injectable hormones, testosterone undecanoate (TU), an androgen, and norethisterone enantate (NET-EN), a progestin, was undertaken to determine their safety, effectiveness and acceptability as a male contraceptive. While the regimen was effective in suppressing spermatogenesis, higher than expected rates of mood changes and increased libido led to a decision to stop the trial in April 2012. All sites should complete “close-out” visits by November 2012 and reporting is expected in 2013. While further testing of this drug combination is not expected to continue, the study will inform future development of a male contraceptive. The side-effects apply to the 1000 mg TU/200 mg NET-EN combination, and not to the drugs used alone for their approved indications.

Family planning: getting a new product to market – emergency contraception
The emergency contraceptive levonorgestrel can prevent pregnancy if taken within 120 hours of unprotected sexual intercourse. As it cannot terminate an established pregnancy, it is also acceptable where abortion is not. It is safe for over-the-counter (OTC) use and HRP has promoted its distribution through social marketing. As of 2010, 126 of 189 countries worldwide have an emergency contraception (EC) product registered, without the need for a prescription in 103 of these countries (see Table 1). Successful programmes (based on high-volume sales) were supported and/or promoted by governments. OTC sale at affordable prices, with discrete access through educated shop owners, pharmacists and health-care providers, facilitated sales. Barriers included lack of public-sector support; negative campaigns suggesting that EC acts as an abortifacient; prescription requirement; and limited public education.
Table 1
Countries with access to emergency contraception, by availability and region

<table>
<thead>
<tr>
<th>Region</th>
<th>Available without prescription (pharmacist/OTC)</th>
<th>Prescription required</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>Canada, Mexico United States of America (nine states no restriction)</td>
<td></td>
</tr>
<tr>
<td>Caribbean</td>
<td>Antigua and Barbuda, Aruba, the Bahamas, Barbados, Belize, Curacao, the Dominican Republic, French Guiana, Haiti, Jamaica, Puerto Rico, Saint Lucia, Trinidad and Tobago</td>
<td></td>
</tr>
<tr>
<td>Latin America</td>
<td>Argentina, the Bolivarian Republic of Venezuela, Ecuador, El Salvador, Guatemala, Nicaragua, the Plurinational State of Bolivia, Brazil, Chile, Colombia, Cuba, Paraguay, Peru</td>
<td></td>
</tr>
<tr>
<td>Western Europe</td>
<td>Austria, Belgium, Denmark, Iceland, Finland, France, Greece, Luxembourg, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, the United Kingdom of Great Britain and Northern Ireland, Germany, Italy, Lithuania</td>
<td></td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>Albania, Armenia, Azerbaijan, Belarus, Estonia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Poland, Romania, Serbia, Slovakia, Slovenia, Tajikistan, Ukraine, Bulgaria, Czech Republic, Georgia, Hungary, the Russian Federation</td>
<td></td>
</tr>
<tr>
<td>Africa</td>
<td>Algeria, Benin, Burkina Faso, Cameroon, the Congo, Côte d'Ivoire, the Democratic Republic of the Congo, Egypt, Ethiopia, Gabon, Ghana, Guinea, Kenya, Lesotho, Libya, Madagascar, Mali, Mauritius, Morocco, Namibia, the Niger, Nigeria, Senegal, South Africa, Togo, Tunisia, Uganda, the United Republic of Tanzania, Zambia</td>
<td>Botswana</td>
</tr>
<tr>
<td>Middle East</td>
<td>Cyprus, the Islamic Republic of Iran, Israel, Mauritius, Saudi Arabia, Turkey, Yemen</td>
<td>Lebanon</td>
</tr>
<tr>
<td>Asia</td>
<td>China, Hong Kong, India, Japan, the Lao People's Democratic Republic, South Korea, Sri Lanka, Thailand, Viet Nam</td>
<td>Bangladesh, Indonesia, Malaysia, Myanmar, Pakistan, Singapore, Taiwan</td>
</tr>
<tr>
<td>Oceania</td>
<td>Australia, French Polynesia, New Zealand</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>103</td>
<td>23</td>
</tr>
</tbody>
</table>

* Some states restrict use for adolescents aged <18 years or <16 years.
* Not for adolescents aged <15 years.

Family planning: monitoring product safety – hormonal contraception and risk of HIV acquisition

The WHO Medical eligibility criteria for contraceptive use (2009) indicate that hormonal contraceptives are safe for use by women at high risk of HIV or living with HIV; however, emerging evidence of associations between hormonal contraceptive use and risk of HIV infection, disease progression and transmission, suggested the need to review the current guidance. In early 2012, HRP convened a team of 75 experts to review the new evidence. They concluded that the available evidence did not establish a clear causal association between injectable contraceptives and HIV acquisition, but did not rule out a possible effect; therefore, use of hormonal contraceptives should remain unrestricted but further evidence should be closely monitored. Women at high risk of HIV infection can use all existing hormonal contraceptive methods without restriction, but should use condoms and other measures to prevent and reduce their risk of HIV/STIs. Women living with HIV infection can also use all hormonal contraceptive methods without restriction but should consistently use condoms to prevent HIV transmission to non-infected sexual partners.

Safe abortion services: application of the WHO strategic approach to unsafe abortion – experience in sub-Saharan Africa, eastern Europe and Asia

Worldwide, 55% of abortions are classified as unsafe, more so in Africa (97%). In eastern Europe, where abortion is legal, limited access to contraceptives results in overuse of abortion, with excess morbidity and mortality. In 2011, Bangladesh requested WHO assistance to im-
prove the quality of their menstrual regulation (MR)\textsuperscript{1} programme. The WHO strategic approach is a useful tool for tackling sensitive problems and has been applied to the prevention of unsafe abortion. The experiences of 11 countries that applied the approach to address unsafe abortion during 2008–2012 are summarized.

\textit{Stage 1: national strategic assessments}

Country assessment teams administered qualitative and quantitative interviews to a range of stakeholders and presented their findings at national dissemination workshops, where recommendations were reviewed and refined and interventions prioritized. Common barriers to safe abortion care across all settings included the lack of standards and guidelines for comprehensive abortion care and inadequate training of abortion providers. Some African countries that had ratified the 2003 Maputo Protocol on safe abortion reported that laws were in conflict with this protocol. Where laws had been revised, the public was generally unaware of the changes. Other challenges included gender inequality; limited access to education for girls; and girls being expelled from school when they become pregnant.

\textit{Stages 2 and 3: country-specific follow-up plans and activities}

Stage 2 activities in African countries included the development of national guidelines for abortion care; dissemination of information on legal indications for abortion; and strengthening of FP programmes, adolescent SRH services and sexuality education. In the Republic of Moldova, a comprehensive abortion care programme was piloted in three perinatal centres, which were later designated as training sites for the stage 3 roll-out. In 2011, the WHO \textit{Safe abortion: technical and policy guidance for health systems} was adapted for use in Bangladesh, with HRP assistance. The nature and pace of stage 3 scale-up depends on a health system’s readiness for change and available resources. Resistance to change has been reported where institutions or individuals benefited from the status quo.

\textit{Lessons learnt}

The participatory process of the strategic approach helps catalyse change through early engagement of stakeholders. Ministry of health participation is essential to enable the integration of recommendations into health policy and programmes. The process helps build local skills in planning, quantitative and qualitative data collection and analysis, intersectoral collaboration, evaluation and implementation. Engaging financial partners early is critical, so that implementation does not lose momentum.

Each country adapted the strategic assessment tool to the local context, with each intervention providing lessons for other country teams seeking ideas of where to begin. The methodology of the strategic approach is a powerful tool for addressing sensitive problems such as unsafe abortion and has robust applicability across a diverse range of settings.

\textit{Controlling sexually transmitted and reproductive tract infections: initiative to eliminate mother-to-child transmission of congenital syphilis}

Untreated syphilis in pregnancy can cause late abortion, stillbirth, prematurity/low birth weight, neonatal deaths and congenital infection. These adverse outcomes may be avoided by antenatal screening and treatment. In 2007, WHO launched the global initiative to eliminate congenital syphilis by at least 80\% in 10 high-burden countries (see Table 2) by 2015. Specific

\textsuperscript{1} Defined as “a procedure to make the menstrual cycle regular if menstruation is absent for a short duration” (\textit{National menstrual regulation services guidelines}. Dhaka, Ministry of Health and Family Welfare, People’s Republic of Bangladesh, 2011).
targets are that by 2015, at least 90% of pregnant women will be screened for syphilis and at least 90% of women who are syphilis seropositive will be appropriately treated.

Table 2
Countries applying the WHO strategic approach to safe abortion, by stage of the process, 2012

<table>
<thead>
<tr>
<th>WHO Region</th>
<th>Country</th>
<th>Initial year</th>
<th>Strategic stage in 2011/2012</th>
<th>Objective/output/outcome</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>African Region</td>
<td>Ghana</td>
<td>2005</td>
<td>Research/pilot programmes under way; scale-up initiated</td>
<td>Develop national standards and guidelines</td>
<td>Ipas; HRP</td>
</tr>
<tr>
<td></td>
<td>Guinea</td>
<td>2009</td>
<td>Dissemination workshop 2010; no further progress</td>
<td>Improve access to legal abortion; inform a national effort to reposition FP</td>
<td>HRP; CERRU-GUIa</td>
</tr>
<tr>
<td></td>
<td>Malawi</td>
<td>2009</td>
<td>Research/pilot programmes under way (provision of DMPA by community health workers)</td>
<td>Revise sexuality education curricula; strengthen FP and adolescent SRH; improve pregnancy advisory centre services (34)</td>
<td>Ipsas; HRP</td>
</tr>
<tr>
<td></td>
<td>Senegal</td>
<td>2010</td>
<td>Research/pilot programmes under way</td>
<td>Addressing gender equality and women’s SRH needs</td>
<td>Ipsas; HRP</td>
</tr>
<tr>
<td></td>
<td>Zambia</td>
<td>2008</td>
<td>Research/pilot programmes under way; scale-up initiated</td>
<td>na</td>
<td>Ipsas; HRP</td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td>Bangladesh</td>
<td>2011</td>
<td>Not applicable</td>
<td>Clinical norms/guidelines developed</td>
<td>HRP</td>
</tr>
<tr>
<td>European Region</td>
<td>The Republic of Moldova (personal communication, BR Johnson Jr, Scientist, WHO/HRP, 2012)</td>
<td>2005</td>
<td>Comprehensive abortion care (CAC) piloted in 3/12 perinatal centres (designated training sites); 1 district hospital; 1 youth-friendly clinic (medical abortion only); information, education and counselling (IEC) material disseminated nationally, including all 12 perinatal centres</td>
<td>Implement national standards and guidelines for CAC; revise training curricula based on new guidelines; develop indicators for national monitoring of the quality of abortion care; develop model outpatient services in selected sites</td>
<td>Reproductive health training centre; James Tudor Foundation; HRP</td>
</tr>
<tr>
<td></td>
<td>The Russian Federation</td>
<td>2009</td>
<td>Pilot testing</td>
<td>Proposal to test an educational intervention on use of manual vacuum aspiration was delayed by HRP 2011 budget shortfall</td>
<td>HRP</td>
</tr>
<tr>
<td></td>
<td>Ukraine (36)</td>
<td>2008</td>
<td>Pilot testing in three sites; preparation for scale-up</td>
<td>Develop new protocol for comprehensive care for unwanted pregnancy (CCUP); clinical protocols; in-service training of mid-level professionals; three model CCUP clinics established; pre-/post-abortion counselling introduced; develop and implement CCUP training curriculum</td>
<td>HRP; Women’s Health and Family Planning; Swiss Agency for Development and Cooperation; other NGOs</td>
</tr>
</tbody>
</table>

na, not available.

a Local research institution, Cellule de Recherche en Santé de la Reproduction en Guinée.

b Full assessment was not done; clinical guidelines were identified as needed and developed in collaboration with HRP.

Advocacy and technology to support the campaign

A strategy toolkit has been developed to provide technical support for screening, case identification and contact tracing and includes protocols for monitoring and surveillance. Core annual elimination of congenital syphilis (ECS) data are submitted to WHO or the Joint United Nations Programme on HIV/AIDS (UNAIDS), through WHO regional offices. Programme impact is measured by the progress toward the target incidence of congenital syphilis (≤0.5 per 1000 live births). An ECS website provides tools and information at http://www.who.int/reproductivehealth/topics/rtis/cs_global_updates/en/index.html.
### Progress

Table 3 highlights progress in Latin America and the Caribbean (LAC), Africa and Asia. LAC countries were best prepared to embrace the initiative and adopted a plan of action in 2010, which has been integrated into national plans in 22 of 41 countries. Eleven countries reported target incidence rates for congenital syphilis of ≤0.5 per 1000 live births. In Africa, progress has been slow, owing to weak systems to deliver services and challenges, because of the culture of late attendance for antenatal care (ANC). In 2011, the initiative was launched in the Asia-Pacific region, with some success reported in India, Malaysia and Myanmar.

### Table 3

**Stages 2 and 3: strategic approach, five African countries**

<table>
<thead>
<tr>
<th>Ghana</th>
<th>Guinea</th>
<th>Malawi</th>
<th>Senegal</th>
<th>Zambia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage 2: strategic development/pilot intervention</strong></td>
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<tr>
<td>Develop CAC services:</td>
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</tr>
<tr>
<td>• National standards, guidelines and protocols (2004, 2006)</td>
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<tr>
<td>• Update health information systems to monitor and evaluate abortion-related services</td>
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<tr>
<td>• Train mid-level staff to provide abortion using MVA up to 12 weeks’ gestation</td>
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<tr>
<td>Areas of focus include:</td>
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</tr>
<tr>
<td>• FP services</td>
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<tr>
<td>• Commodity security</td>
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<td></td>
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<tr>
<td>• Sexual health education</td>
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<tr>
<td>• Improve PAC</td>
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<tr>
<td>Develop national standards and guidelines for provision of abortion</td>
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<tr>
<td>MVA equipment added to Standard equipment list (2009); availability limited</td>
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<td></td>
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<tr>
<td>• Advocacy for legal reform initiated with creation of Coalition for Prevention of Unsafe Abortion (COPUA)</td>
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<tr>
<td>• Media sensitization</td>
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<tr>
<td>• Wide discussion of discordance between the Maputo Protocol (36) and the law</td>
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<tr>
<td>Medical Association of Malawi to develop clinical protocols for CAC</td>
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<tr>
<td><strong>Stage 3: scaling-up</strong></td>
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<tr>
<td>• Partner with public, private and nongovernmental organizations to expand services</td>
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</tr>
<tr>
<td>• CAC now available in 60 public and private facilities, including 12 hospitals</td>
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</tr>
<tr>
<td>• Incremental scaling-up to 18 more facilities; goal is national coverage</td>
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</tr>
<tr>
<td>• Given revisions to the law and lack of knowledge about changes, the team recommended:</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>• Develop clear legal guidance for application of the law</td>
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</tr>
<tr>
<td>• Wide dissemination of information on legal indications for abortion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Ministry of Health has started to strengthen PAC and CAC as legally permitted</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>• Infrastructure and equipment need to be assessed in 20 health centres in the capital, Lilongwe</td>
<td></td>
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</tr>
<tr>
<td>• MVA orientation workshops held</td>
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</tr>
<tr>
<td>• Plans are being developed to improve the quality of PAC, FP services and SRH education</td>
<td></td>
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<tr>
<td>• In two study provinces, additional facilities have been added in partnership with Marie Stopes International</td>
<td></td>
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</tbody>
</table>

**Goal**: Liberalization of current law to include grounds for rape/incest

- Draft bill prepared by the Association of Women Lawyers of Senegal based on the Maputo Protocol (36)
- Advocacy task force formed to conduct awareness raising among parliamentarians, religious leaders, journalists and civil society
- Development of CAC services

- National standards, guidelines and protocols (2009)
- CAC provided in 28 facilities in three of eight provinces
- Operations research undertaken to train nurse practitioners and clinical officers to deliver medical and surgical abortion services
<table>
<thead>
<tr>
<th></th>
<th>Ghana</th>
<th>Guinea</th>
<th>Malawi</th>
<th>Senegal</th>
<th>Zambia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enabling environment</strong></td>
<td>Medabon registered for use in public/private facilities</td>
<td>Misoprostol added to essential drug list for obstetric/gynaecological use</td>
<td>FP commodities in short supply</td>
<td>No legal reform expected</td>
<td>Legal requirement that three physicians approve every abortion is a barrier</td>
</tr>
<tr>
<td></td>
<td>Fixed price for abortion in public facilities</td>
<td>Medabon registered but use limited to obstetrics/gynaecology; availability limited</td>
<td></td>
<td></td>
<td>Medabon registered but use limited to obstetrics/gynaecology; availability limited</td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Services have increased</td>
<td>Women still opt to self-induce with misoprostol (PAC is free; safe abortion costs US$35–40)</td>
<td>Delivery of CAC seems long way off</td>
<td>Efforts needed to improve access to FP services/commodities</td>
<td>Civil society representatives, supported by The Ministry of Health and Prevention and the Ministry of Gender are advocating for legislative change regarding abortion</td>
</tr>
<tr>
<td></td>
<td>Lack of donor funds to support follow-up activities delayed implementing action plans</td>
<td></td>
<td></td>
<td></td>
<td>Project being scaled up nationally</td>
</tr>
</tbody>
</table>

**Effectiveness, efficiency and sustainability**

The willingness of development partners like the Global Fund to Fight AIDS, Tuberculosis and Malaria to support the integration of ECS into the HIV portfolio will help promote the initiative (see Table 4). Challenges include the persistence of vertical programmes (e.g. ANC, HIV), weak mid-level human resources skills, and inefficient logistical support. Technology transfer is needed to help scale up services, including strengthening of laboratory facilities, laboratory information systems, surveillance, and programme evaluation. Cultural and legal barriers, inconsistent funding and weak political will are threats to sustainability.
Table 4
Framework to enable access to comprehensive reproductive health and safe abortion care: the combined experiences of African and eastern European countries

<table>
<thead>
<tr>
<th>Areas for action</th>
<th>Legal and cultural behaviour change</th>
<th>Gendered attitudes and values</th>
<th>Skills and competencies of health providers</th>
<th>Appropriate environment to deliver safe abortion care</th>
<th>Planning and regulatory environment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objectives</strong></td>
<td>• Harmonize laws with international standards</td>
<td>• Improve SRH literacy</td>
<td>• Improve clinical and counselling skills and competencies</td>
<td>• Ensure access to care</td>
<td>• Enable safe abortion care</td>
</tr>
<tr>
<td></td>
<td>• Reduce stigma and discrimination</td>
<td></td>
<td></td>
<td>• Provide adequate resources</td>
<td>• Monitor access, safety, quality and outcome</td>
</tr>
<tr>
<td><strong>Targets</strong></td>
<td>• General public</td>
<td>• Enable SRH education in schools for boys and girls</td>
<td>• Develop and implement regulations so that middle-level providers may deliver FP/safe abortion care</td>
<td>• Add required drugs and equipment to essential drugs and equipment list</td>
<td>• Ensure comprehensive needs assessment, which includes diverse input (strategic assessment stage 1)</td>
</tr>
<tr>
<td></td>
<td>• Legislators</td>
<td>• Develop SRH educators</td>
<td>• Develop teaching skills and training teams (trainer of trainers: in service; tertiary)</td>
<td>• Upgrade facilities to provide care in a confidential, well-equipped environment</td>
<td>• Ensure adequate planning and identification of resources to enable a successful pilot stage (stage 2)</td>
</tr>
<tr>
<td></td>
<td>• Political leaders</td>
<td>• Provide public education aimed at dispelling local myths and negative attitudes</td>
<td>• Modify curricula at basic, undergraduate and postgraduate levels, consistent with current knowledge and evidence</td>
<td>• Ensure geographic access</td>
<td>• Have a clear strategy for how the scale-up will be financed and implemented (stage 3)</td>
</tr>
<tr>
<td></td>
<td>• Religious leaders</td>
<td>• Enable continuing education for health-care providers</td>
<td>• Enable continuing education for health-care providers</td>
<td>• Maintain and replace equipment as necessary</td>
<td>• Have a clear, integrated framework for monitoring safety, quality and outcome</td>
</tr>
</tbody>
</table>

* Or creatively avoid a public challenge to the existing law, as was done in Bangladesh.

**Summary**

The ECS campaign promotes the integration STI and SRH services based on a country’s level of readiness. High disease burden but good infrastructure allowed LAC to embrace the double goal to eliminate both congenital syphilis and mother-to-child transmission of HIV, while other settings focused only on the ECS target. By shifting the focus to syphilis, a treatable condition, teams could be encouraged by their success, and reap the bonus of reduced HIV transmission. This campaign is an excellent example of the public good created by HRP, which brings new technology to bear on a persistent problem, with the tangible possibility of improving health and survival. Partnerships with academic institutions, nongovernmental organizations and other international agencies enable high-quality research to inform decision-making about what works, marrying skills in high-income countries to the needs of low- and middle-income countries, while building inter-country collaboration between low- and middle-income countries to help each other. The achievement of target incidence rates for congenital syphilis of ≤0.5 per 1000 live births in 11 LAC countries is encouragement that the goal is not impossible.
Conclusions and recommendations

Impact

Tables 5 and 6 examine possible associations between these interventions and improvements in global health indicators. While achieving the first screen-and-treat ECS target is possible, as global access to ANC has increased, the third-trimester re-screen may not be feasible outside south east Asia and the LAC region. The higher observed contributions of women to reported HIV prevalence, despite stabilizing prevalence rates, may be a measurement artefact of improved antenatal surveillance, but we await the next round of indicators to decide whether new initiatives are needed to address the evolving situation. The stalled progress of abortion rates is cause for concern.

Table 5

Potential for syphilis elimination in the 10 high-impact countries

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>3 038 000</td>
<td>53 and 23</td>
<td>na</td>
<td>0.6 (2008)</td>
<td>128 500 (36)</td>
</tr>
<tr>
<td>India</td>
<td>27 165 000</td>
<td>75 and 51</td>
<td>65</td>
<td>0.3 (2010)</td>
<td>605 230 (22)</td>
</tr>
<tr>
<td>Indonesia</td>
<td>4 372 000</td>
<td>93 and 82</td>
<td>na</td>
<td>na</td>
<td>62 290 (15)</td>
</tr>
<tr>
<td>Kenya</td>
<td>1 529 000</td>
<td>92 and 47</td>
<td>59</td>
<td>1.8 (2010)</td>
<td>34 130 (22)</td>
</tr>
<tr>
<td>Madagascar</td>
<td>732 000</td>
<td>86 and 49</td>
<td>85</td>
<td>3.4 (2010)</td>
<td>14 590 (21)</td>
</tr>
<tr>
<td>Mozambique</td>
<td>883 000</td>
<td>92 and 53</td>
<td>68</td>
<td>6.0 (2010)</td>
<td>25 560 (28)</td>
</tr>
<tr>
<td>Rwanda</td>
<td>438 000</td>
<td>98 and 35</td>
<td>75</td>
<td>1.5 (2010)</td>
<td>9 620 (23)</td>
</tr>
<tr>
<td>South Africa</td>
<td>1 059 000</td>
<td>97 and 87</td>
<td>75</td>
<td>2.2 (2010)</td>
<td>22 560 (20)</td>
</tr>
<tr>
<td>United Republic of Tanzania</td>
<td>1 862 000</td>
<td>88 and 43</td>
<td>54</td>
<td>4.2 (2008)</td>
<td>47 550 (26)</td>
</tr>
<tr>
<td>Zambia</td>
<td>600 000</td>
<td>94 and 60</td>
<td>43</td>
<td>5.3 (2010)</td>
<td>14 380 (26)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>38 625 000</strong></td>
<td><strong>52–98 and 23–87</strong></td>
<td><strong>43–85</strong></td>
<td><strong>0.6–6.0 (2008–2010)</strong></td>
<td><strong>964 410 (15–36)</strong></td>
</tr>
</tbody>
</table>

na, not available.
Table 6
Summary of ECS implementation efforts, by region

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Latin America and the Caribbean</th>
<th>Africa</th>
<th>Asia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rationale/strategy</td>
<td>The region adopted a plan of action in 2010; most countries have developed strategies and plans for both ECS and MTCT of HIV</td>
<td>Progress has been limited to the development of country strategic frameworks (e.g. Kenya, South Africa)</td>
<td>The Asia Pacific United Nations Prevention of Parent-to-Child Transmission (PPTC) Task Force was launched in August 2011, to lead the initiative</td>
</tr>
<tr>
<td>Development of screening tools</td>
<td>Screening included in routine ANC; challenges reported in obtaining results in timely manner</td>
<td>Screening demonstrated to be cost effective (range of cost per DALY saved: US$3.97–10.5)</td>
<td>Variations in antenatal syphilis screening practices; routine screening of all ANC clients done in few countries – Malaysia, Papua New Guinea, Sri Lanka, Thailand (52)</td>
</tr>
<tr>
<td>Development of guidelines</td>
<td>Regional and national plans and clinical guidelines in place in 22 of 48 countries (e.g. Brazil, Cuba, Jamaica) (53)</td>
<td>Lack of guidelines for service providers</td>
<td>Monitoring and evaluation guide, fact sheets (12 countries) and costing tool developed (August 2011)</td>
</tr>
<tr>
<td>Roll-out in field: efficiency</td>
<td>Cuba has recorded the greatest success in the elimination initiative. Most countries reported 80% coverage on ANC and potential to provide the service; however, the quality of service varies across countries</td>
<td>Limited training and supervision of field staff</td>
<td>Limited data available on process issues</td>
</tr>
<tr>
<td>Monitoring effectiveness</td>
<td>ECS indicators reported annually; surveillance and health information systems challenged by data quality (e.g. 16/48 countries not reporting indicators); legal and technical frameworks strengthened through WHO regional/country-initiated efforts</td>
<td>Weak surveillance, monitoring and evaluation (e.g. Kenya, South Africa)</td>
<td>High rates of first ANC attendance – 79%</td>
</tr>
<tr>
<td>Impact</td>
<td>PMTCT coverage – 61% (2010)</td>
<td>Antenatal syphilis prevalence: 0.1–0.4% in China, India, Thailand</td>
<td>Antenatal syphilis prevalence: 0.1–0.4% in China, India, Malaysia; 6–7% in Papua New Guinea and Solomon Islands (52)</td>
</tr>
<tr>
<td>Sustainability</td>
<td>Declining political will and funding support</td>
<td>Need to scale up PMTCT programmes to reverse the trend in infections in neonates</td>
<td></td>
</tr>
</tbody>
</table>

DALY, disability-adjusted life-year. PMTCT, prevention of mother-to-child transmission.

*a Anguilla, Antigua and Barbuda, the Bahamas, Barbados, Canada, Cuba, Chile, Guadeloupe, Guyana, Panama and United States of America.

Recommendations

Input

A clear policy is needed to guide research regarding male reproductive health, including the development of male contraceptives. Within this framework, it may be necessary to revisit how costs and benefits of a male contraceptive are measured, as successful avoidance of unwanted pregnancy benefits not only the health of the female partner, but also the economic survival of the household and the community.
Process

Strategies are needed to measure access to emergency contraception, and its utilization and impact. Integration of indicators into demographic and health surveys or other reproductive health surveys may be a place to start.

Output/outcomes

To support the safe abortion and ECS goals, monitoring of indicators should be included in the Millennium Development Goal and other universally accepted country reporting frameworks.

Summary

Although it is relatively small, the HRP team in Geneva is impressive in its capacity to identify and coordinate a large network of investigators, collaborators and experts, drawn from academic and research institutions across all the WHO/United Nations regions of the world, capable of addressing acute problems and developing long-term solutions to global SRH challenges.

The cases demonstrate the global value of the Special Programme of Research, Development and Research Training in Human Reproduction, from problem identification (unsafe abortion) and problem clarification (the strategic approach), to generating new knowledge (male contraception) and marketing new products (emergency contraception), to piloting and roll-out of solutions to global problems (safe abortion; ECS), while monitoring the emergence of new knowledge (hormonal contraceptives and HIV) to maintain public trust in WHO/HRP as a reliable source of global SRH advice.
1 Introduction

The World Health Organization’s (WHO) Department of Reproductive Health and Research (RHR) is the implementing body for the multi-agency (United Nations Development Fund (UNDP)/United Nations Population Fund (UNFPA)/United Nations Children’s Fund (UNICEF)/WHO/World Bank) Special Programme of Research, Development and Research Training in Human Reproduction (HRP). The year 2012 marks the 40th year of a continuous and growing contribution of the team’s expertise to the development and synthesis of new knowledge aimed at improving the quality and outcome of global human reproductive activities. WHO is a respected source of reliable advice and guidance to countries and communities. RHR is best known for the development of normative guidance and technical support that integrates the best available evidence to guide reproductive health policy, programme development and clinical practice.

The WHO global strategy on reproductive health (1) provides the policy framework for RHR and thus the HRP agenda. The overarching aim is to accelerate progress towards attaining the highest achievable standard of sexual and reproductive health (SRH) for all, and this is embodied in Millennium Development Goals (MDGs) 4, 5 and 6 in particular. RHR organizes its work around five core aspects of SRH:

1. improving antenatal, perinatal, postpartum and newborn care;
2. providing high-quality services for family planning (FP), including infertility services;
3. eliminating unsafe abortion;
4. combating sexually transmitted infections (STIs), including HIV, reproductive tract infections, cervical cancer and other gynaecological morbidities;
5. promoting sexual health.

RHR recognizes the synergies of strengthening these five aspects of SRH and how activities in one area can impact the others. They also understand that, by strengthening existing health services, they help to ensure accessible entry points for new interventions (1). Technical assistance to countries employs action-oriented research and research-capacity strengthening, and the evidence generated is used to develop and improve norms and standards for care.

The 2008–2012 HRP external evaluation aims to inform the decision-making process for the Special Programme and its constituents in the following areas:

- the relevance and fulfilment of HRP’s objectives;
- its efficiency and effectiveness;
- its comparative advantage;
- the impact and sustainability of its work.

2 Methods

The case-study for the external evaluation was a desk review of peer-reviewed and WHO publications. This included consultations with relevant programme staff and collaborators. The process was guided by the key norms and standards set out by the Organisation for Economic Co-operation and Development (OECD) Development Assistance Committee (DAC) Network on Development Evaluation (2). Where appropriate, the review considered and addressed:
• **relevance**, by determining how HRP activities address the priorities and policies of countries and whether the activities and outputs are consistent with the intended impacts and effects;

• **effectiveness**, by exploring the extent to which stated objectives were achieved, mindful of barriers or facilitators to goal achievement;

• **impact**, by summarizing the ecological associations of activities with global reproductive health indicators.

In addition:

• as the work of HRP is intended to catalyse change and development in reproductive health care in target countries, the evaluation attempted to document what skill transfer has occurred to ensure the **sustainability** of intended benefits once initial interventions were concluded;

• while economic **efficiency** was beyond the scope of these case-studies, where feasible, the time frame for achieving the objectives was examined alongside possible barriers to timely implementation.

Programme staff were consulted at the following stages:

1. understanding programme activities (April to June 2012) and guidance concerning possible country visits;
2. feedback on the draft report and exploration of qualitative feedback from end-users (September to October 2012);
3. finalization of the report (November 2012).

### 2.1 Phase I: fact finding with WHO programme teams

Initial meetings were held with key staff members in Geneva from 18 to 20 April and 19 to 22 June 2012, to develop an understanding of the programme activities and the principal areas of focus of the professional teams, which were (see Annex 1):

1. promoting FP;
2. preventing unsafe abortion;
3. controlling sexually transmitted and reproductive tract infections.

### 2.2 Phase II: desk review and consultation with stakeholders

Based on phase I discussions, programme activities were selected by the consultant to demonstrate the leadership of the three teams in evidence generation, synthesis and programme implementation (Chapter 6 focuses on implementation research), to inform improvements in service delivery. During the evaluation, and in consultation with team leaders at WHO, stakeholders were consulted by e-mail for input or feedback on the draft report.

### 3 Rationale

The 2003–2007 case-study focused on one of the core areas – **improving antenatal, perinatal, postpartum and newborn care**. It examined the synthesis of evidence regarding which antenatal care (ANC) activities effectively improved pregnancy outcome. This was integrated into a revised ANC model, piloted and then field-tested in countries selected to represent culturally diverse regional and service-delivery capabilities.
A field visit to Thailand enabled observation of the national roll-out of this model and provided an opportunity to demonstrate how effective application of reproductive health research influences policy and, ultimately, practice.

The case-study for the 2008–2012 review examined three other areas of the Programme’s mandate – to improve FP; prevent unsafe abortion; and prevent and control sexually transmitted and reproductive tract infections. The review aimed to provide a synopsis of HRP’s work in action, across a range of settings and encompassing the processes of evidence generation, with synthesis of the evidence into programme guidance, through to national and international roll-out of proven strategies aimed at improving SRH. To this end, activities in multiple countries, not just one, were used to demonstrate the uptake of HRP guidance and leadership in SRH.

4 Findings

4.1 General

The WHO strategic approach to strengthening sexual and reproductive health policies and programmes is a strategic planning, policy and programme implementation tool that HRP teams use to evaluate and improve reproductive health services (3). It consists of three stages:

1. a strategic assessment to identify and prioritize needs;
2. introduction of interventions on a small scale, to address priority needs identified from the first stage, aimed at demonstrating their acceptability, feasibility and effectiveness;
3. scaling up proven interventions to expand their benefits to more people and strengthen institutional capacities.

An essential feature of the tool is its multidisciplinary, participatory framework, which enables a wide range of stakeholders, including beneficiaries, to participate in the evaluation and decision-making process. Other characteristics include:

- a staged implementation process, which links assessment, pilot-testing and scaling up;
- a systems framework that highlights relevant factors for decision-making about services;
- a reproductive health philosophy of reproductive rights, gender equity and empowerment;
- a focus on improving equitable access to and quality of care, so that services are client-centred and responsive to community needs;
- a participatory process, which consider the concerns of all relevant stakeholders;
- country ownership of the process and the results (4).

The process includes five overarching activities, derived from the WHO global Reproductive health strategy (1): (i) strengthening health-systems capacity; (ii) improving information for priority setting; (iii) mobilizing political will; (iv) creating supportive legislative and regulatory frameworks; and (v) strengthening monitoring, evaluation and accountability.

Elements of the strategic approach will be demonstrated by the case-studies. The FP case-study will summarize some of the challenges of generating new evidence (male contraception) and getting successes to market (emergency contraception), while maintaining a strong monitoring role that efficiently responds to new evidence (HIV acquisition and hormonal contraception). The safe abortion case-study demonstrates application of the strategic approach to a sensitive problem, enabling incremental, but certain progress toward improving health and
safety. The initiative to eliminate mother-to-child transmission (MTCT) of syphilis reveals how evidence generation, health systems research, surveillance, monitoring and evaluation combine to tackle a long-standing public health problem.

### 4.2 Improving family planning: generating new evidence, marketing new products and protecting health and safety

#### 4.2.1 Introduction

The FP agenda aims to improve the quality of FP methods and services. By utilizing epidemiological, social, behavioural and operations research, teams document unmet need; identify sociocultural barriers and health systems constraints that limit access to services, and test approaches to mitigate them; develop and assess the role of mid-level providers in improving access to services; and develop and test new tools to monitor how well gender issues and human rights are respected in FP services.

RHR is best known for the development of evidence-based FP guidelines and tools for service providers. The *Medical eligibility for contraceptive use* (MEC) now in its fourth edition (2009) (5) and translated into over 15 languages and covering 17 FP methods, was awarded a first prize at the British Medical Association (BMA) Book Awards2 in 2011, in the Obstetrics and Gynaecology category (6).

To ensure that guidelines are based on current knowledge, HRP monitors emerging evidence. This process has resulted in two consultations since the 2009 release of the MEC guidelines (5), concerning the use of hormonal contraceptives and related risk of venous thromboembolism (VTE) (7) and HIV, respectively. Revised guidelines were issued concerning VTE (see Annex 2), while the HIV risk did not generate new guidelines and will be detailed below. The marketing of levonorgestrel for emergency contraception (EC), and the efforts to develop a male contraceptive, will also be discussed.

#### 4.2.2 Creating new knowledge: developing a male contraceptive

**Background**

In recognition that inadequate attention has been paid to the SRH needs of men, in 2010 RHR established a working group on Men and Sexual and Reproductive Health, to formalize strategic programming in relation to men’s SRH needs (8, 9). Areas of work included understanding men’s roles in sexual decision-making and behaviour and their shared burden and responsibility for pregnancy prevention, including contraception. As part of improving the science of male reproductive function (andrology), RHR has been coordinating development of a hormonal regimen for male contraception (8).

**How male hormonal contraception works**

Hormonal methods of regulating male fertility utilize exogenous androgen (e.g. testosterone) to reduce the body’s ability to produce sperm (spermatogenesis). Suppression of sperm production is achieved by inhibiting hormones secreted by the pituitary gland (follicle-stimulating hormone (FSH) and luteinizing hormone (LH)), which in turn inhibit the production of testosterone by cells in the male testes. High levels of androgens in the testis are required for normal spermatogenesis; thus, very low levels of androgens in the testis result in significant suppres-

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2 The awards encourage and reward excellence in medical publishing; there are prizes in 21 categories, including an overall BMA Medical Book of the Year from among the category winners.
sion of, or no detectable, sperm. Suppression is achieved in most men when testosterone is administered with a progestin (10).

A combined long-acting injectable androgen, testosterone undecanoate (TU), with a long-acting progestin, norethisterone enantate (NET-EN), was tested for sperm suppression and demonstrated suppression of spermatogenesis in nearly all men (11). A dose of 1000 mg TU plus 200 mg NET-EN administered every 8 weeks was considered to be preferable to TU alone or to 750 mg TU plus NET-EN for contraception regimens, owing to more complete suppression of gonadotropins and spermatogenesis; this formed the basis for a multicentre trial (12). No major adverse events that would preclude development of the combination as a reversible male contraceptive were reported.

**Study objectives and methods**

The study was designed to evaluate whether the combination of NET-EN and TU would be a safe, effective, reversible and acceptable male contraceptive (13). The two drugs were administered by injection every 8 weeks. The study consisted of a suppression phase (up to 26 weeks), an efficacy phase (up to 56 weeks) and a recovery phase. In the initial drug-exposure phase, which has now been discontinued, men were monitored for suppression of spermatogenesis. Men who demonstrated adequate suppression proceeded into a 12-month contraceptive efficacy phase, which has also now been discontinued. This was followed by a recovery phase, which is still ongoing, in which the men are monitored for return to sperm levels that are indicative of fertility. Men whose sperm concentrations were not adequately suppressed initially, or whose sperm levels rose above the threshold during the efficacy phase, or who wished to withdraw from the study for any reason, also entered the recovery phase.

**Trial monitoring, expected side-effects, interim findings and the decision to stop the trial**

The trial was subject to annual reviews. At WHO, these were conducted by the research project review panel (RP2) and the WHO Ethical Review Committee (ERC). There was also periodic review by an independent data safety and monitoring committee (DSMC) and individual site ethical committees. These committees are intended to ensure that the rights, safety and well-being of study participants are protected. The WHO RP2 met in 2011 to review the status of the study and the available combined safety information from all sites.

Expected side-effects of androgen and progestin administration included acne, increased libido, injection-site pain, weight gain and mood changes. Participants were informed of the possibility of side-effects at enrolment but some occurred more often than expected. Reported side-effects of concern were depression and other mood changes, increase in sexual desire, and injection-site pain. Mood changes and increased libido were reported at a higher frequency than anticipated. Eight “serious adverse events” occurred, two of which were judged to be either possibly or probably related to the study regimen; the other six have been classified as unrelated to the study regimen.

The reviewers determined that the potential for side-effects was greater than the benefit of the study drug to the male participants (14). Given the reported side-effects, the WHO panel questioned whether this drug combination can be successfully developed and marketed as a male contraceptive, and opted to stop the trial. The RP2 recommended that injections of the two study drugs (TU and NET-EN) should not continue and all active participants should transition to the recovery phase. The ERC accepted this recommendation.
How many men are currently in the study and was the treatment effective?

A total of 321 men were enrolled at 10 research sites in eight countries.\(^3\) At 31 March 2011, 110 men had completed the full 12-month effectiveness phase. When the study was stopped, 103 men were receiving injections in the suppression or efficacy phase and were transferred to the recovery phase. All men in the initial suppression or efficacy phases attend two-monthly clinic visits until recovery of sperm to levels considered as fertile is demonstrated. By June 2012 (8 weeks post injection plus a scheduled 52-week recovery period), only five men had not recovered fully. Data collection should conclude by November 2012, when all sites have had their “close-out” visits. Sera from all sites will then be sent to a central laboratory for standardized analysis of hormones. Integration of the laboratory data with the clinical data and reporting is expected in 2013 (personal communication, D Colvard, Deputy Director for Programs, CONRAD, 17 September 2012: WHO-CONRAD Male contraceptive trial: update).

An earlier interim analysis indicated that the two hormones suppressed sperm production in nearly all men. Very few pregnancies occurred during the 12-month efficacy phase, when participants were asked to rely only on the study regimen for contraception. Anecdotally, many men were satisfied with the method, as were their partners. Male participants and female partners completed acceptability questionnaires several times during the study, and these data will be analysed when the study ends.

Conclusions: the future of male hormonal contraception development

Developing a new product is often a long and challenging process. CONRAD\(^4\) and WHO have supported research in male contraception, and while this drug combination in the current dosage will not move forward as a contraceptive method, this clinical trial provides valuable information on its effectiveness, safety and acceptability. Research is expected to continue on the development of a male contraceptive, whether hormonal or non-hormonal.

When unexpected findings arise in routinely monitored clinical trials, the first priority is to protect the health and well-being of participants. The WHO recommendation applies to this TU/NET-EN combination, not to the drugs used alone for their approved indications or in other combinations. The side-effects of concern observed during this study are not seen to the same extent when the drugs are used in their approved indications and dosing regimens.

The concerns about the risk–benefit ratio of this particular regimen should not apply to the development of other hormonal regimens for men. While all medications carry some risk, researchers and clinicians must ensure that the risks do not outweigh the benefits, especially in research. For female contraception, the risks of birth control are compared to the risks of pregnancy and its complications. The benefit of preventing pregnancy and its possible problems outweighs the risk of taking hormonal contraception for most women. With male contraceptive methods, the man is asked to bear the method’s risks without the direct benefit of preventing the risk of pregnancy. As a result, the risks of male hormone contraceptive methods may seem high compared to the benefits. However, a male contraceptive addresses the need of couples where women’s health concerns contraindicate the use of hormonal or other methods, and, secondly, a male option other than condoms addresses important issues about shared responsibilities in FP. There may be a need to revisit the risk–benefit assessment asso-

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\(^3\) The sites were: Melbourne and Sydney, Australia; Santiago, Chile; Halle and Munster, Germany; New Delhi, India; Jakarta, Indonesia; Bologna, Italy; Edinburgh and Manchester, United Kingdom of Great Britain and Northern Ireland.

\(^4\) CONRAD is a reproductive health research organization within the Department of Obstetrics and Gynecology of Eastern Virginia Medical School, United States of America.
associated with shared responsibility, as, while it is the woman who physically carries the child, it is the family unit not just the woman, that benefits from the successful avoidance of an unintended pregnancy.

4.2.3 Getting a new product to market: emergency contraception

Background

EC regimens have been available since the early 1990s (15), for use within 120 hours of unprotected sexual intercourse, to prevent pregnancy before it occurs, especially in circumstances such as rape, incest or non-use or failure of other methods (e.g. burst condom). EC acts primarily by preventing ovulation or by interfering with sperm so that they cannot fertilize the ovum. Because EC is not an abortifacient and cannot terminate an established pregnancy, it is acceptable in countries with highly restricted abortion laws, such as in Latin America (e.g. Argentina, the Bolivarian Republic of Venezuela, Brazil, Colombia, El Salvador) and former British colonies where the 1860s Offences Against the Person Act remain in force (e.g. Jamaica, Kenya, Pakistan) (16).

HRP has played a pioneering role in the development of EC and in making it easier and safer to use, and more widely available to women worldwide. HRP has conducted large multicentre randomized trials demonstrating the safety, efficacy and dosing of levonorgestrel for EC. Subsequent work from HRP has contributed to supporting the successful registration and increased utilization of single-dose levonorgestrel as an emergency contraceptive in several countries.

EC is commonly packaged as two levonorgestrel pills, although women are instructed to take both pills at once (17), owing to the dosing studies conducted by HRP.

WHO/HRP has collaborated with international partners such as the International Federation of Gynaecology and Obstetrics, International Planned Parenthood Federation and International Consortium for Emergency Contraception, to educate the public about the safety and use of EC and improve access to EC through advocacy to enable registration of EC products, preferably as a non-prescription over-the-counter (OTC) item, ensuring that EC is available to women at greatest risk of unwanted pregnancy (18). As part of their international commitments to reduce unwanted pregnancy and prevent pregnancy-related deaths and illnesses, governments worldwide are encouraged to take the essential first steps to ensure access to EC for every woman. Table 1 summarizes the status of EC availability in 2010. Of 189 countries worldwide, EC is available without prescription in 103 (54%) and by prescription in 23 (12%).
Table 1  

Countries with access to emergency contraception, by availability and region

<table>
<thead>
<tr>
<th>Region</th>
<th>Available without prescription (pharmacist/OTC)</th>
<th>Prescription required</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>Canada, Mexico United States of America (nine states no restriction)a</td>
<td></td>
</tr>
<tr>
<td>Caribbean</td>
<td>Antigua and Barbuda, Aruba, the Bahamas, Barbados, Belize, Curacao, the Dominican Republic, French Guiana, Haiti, Jamaica, Puerto Rico, Saint Lucia, Trinidad and Tobago</td>
<td>Brazil, Chile, Colombia, Cuba, Paraguay, Peru</td>
</tr>
<tr>
<td>Latin America</td>
<td>Argentina, the Bolivarian Republic of Venezuela, Ecuador, El Salvador, Guatemala, Nicaragua, the Plurinational State of Bolivia,</td>
<td></td>
</tr>
<tr>
<td>Western Europe</td>
<td>Austria, Belgium, Denmark, Iceland, Finland, France, Greece, Luxembourg, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, the United Kingdom of Great Britain and Northern Ireland</td>
<td>Bulgaria, Czech Republic, Georgia, Hungary, the Russian Federation</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>Albania, Armenia, Azerbaijan, Belarus, Estonia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Poland, Romania, Serbia, Slovakia, Slovenia, Tajikistan, Ukraine</td>
<td></td>
</tr>
<tr>
<td>Africa</td>
<td>Algeria, Benin, Burkina Faso, Cameroon, the Congo, Côte d’Ivoire, the Democratic Republic of the Congo, Egypt, Ethiopia, Gabon, Ghana, Guinea, Kenya, Lesotho, Libya, Madagascar, Mali, Mauritius, Morocco, Nambia, the Niger, Nigeria, Senegal, South Africa, Togo, Tunisia, Uganda, the United Republic of Tanzania, Zambia</td>
<td>Botswana</td>
</tr>
<tr>
<td>Middle East</td>
<td>Cyprus, the Islamic Republic of Iran, Israel, Mauritius, Saudi Arabia, Turkey, Yemen</td>
<td>Lebanon</td>
</tr>
<tr>
<td>Asia</td>
<td>China, Hong Kong, India, Japan, the Lao People’s Democratic Republic, South Korea, Sri Lanka, Thailand, Viet Nam</td>
<td>Bangladesh, Indonesia, Malaysia, Myanmar, Pakistan, Singapore, Taiwan</td>
</tr>
<tr>
<td>Oceania</td>
<td>Australia, French Polynesia, New Zealand</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>103</td>
<td>23</td>
</tr>
</tbody>
</table>

a Some states restrict use for adolescents aged <18 years or <16 years.

b Not for adolescents aged <15 years.

International collaborative efforts to promote and expand access to emergency contraception

Social marketing (5, 20) has been promoted for distributing EC, given its success with other reproductive health products such as condoms and oral contraceptives. The process operates through existing commercial channels, to place the products on the shelf along with other health- and household-related items. The International Consortium for Emergency Contraception (ICEC) has collaborated with HRP to monitor the social marketing of EC. In some settings, the products may be subsidized to ensure that the price is affordable for the intended users. Strategies include:

- use of a commercial partner to distribute the product through commercial outlets, while a nongovernmental organization (NGO) provides health services or support such as advocacy with policy-makers, training of providers and outreach to women;

- the NGO registers, imports and distributes the product, either through commercial outlets or through branded or “franchised” clinics, pharmacies or drug sellers (21).

An ICEC review of social marketing in a range of countries, including the Bolivarian Republic of Venezuela, Egypt, Ethiopia, India, Indonesia, Pakistan and Viet Nam, found that successful programmes, based on demonstrated high-volume sales, had some common characteristics, including:

- government support for advertising and public education (e.g. hotlines, dealer incentives, promotion with pharmacists and doctors, catchy radio advertisement campaigns);
• government approval of OTC sales;
• government support of social marketing as a population policy strategy;
• government distribution of EC within its FP programme;
• access to large urban populations;
• introduction of a single-pill product;
• affordable price and convenience (especially when available at local pharmacies);
• acceptability by women, and thus promotion by word of mouth;
• low use of other contraceptive methods, especially long-acting methods;
• high rates of unprotected sexual intercourse;
• convenience and discretion of private sector marketing;
• consumer education campaigns and promotional activities;
• promotion among providers in social franchise clinic networks;
• improved awareness by shop owners, staff, doctors, pharmacists and customers.

Barriers to inclusion or success of EC in social marketing and other commercial distribution programmes are:

• delays in the authorization process to have EC registered;
• lack of public sector funding for the introduction and promotion of EC;
• limited programme scope, because of political/legislative barriers;
• church protests, which include branding the product as an abortifacient;
• court decisions declaring EC acts as an abortifacient and prohibiting public sector distribution;
• requirement for a prescription;
• lack of donor funding to socially market EC in many countries;
• lack of client knowledge that EC is an option;
• stock-outs.

As EC has become more widely available and accepted, e.g. in Mexico and India, direct uptake by the commercial sector has reduced the need for social marketing agencies.

**Emergency contraception: access and impact**

EC is an acceptable post-coital method to prevent unwanted pregnancy, which can help reduce the number of unsafe abortions, especially in settings where abortion is not legal. Interventions designed to increase access to EC have not shown significant reductions in population-level rates of unintended pregnancy (22) or abortion, nor has its availability been associated with increasing promiscuous behaviour or unprotected sexual intercourse (23). High rates of unprotected sexual intercourse and rare use of EC probably limit population-level impact (24). If social marketing enables not only EC use but behaviour change toward more appropriate use of other contraceptive methods, attributing EC’s contribution to preventing unwanted pregnancy may be difficult. Routine measurement of knowledge, access and utilization of EC should be integrated into reproductive health or demographic and health surveys, to document its market penetration. While EC is a potentially valuable reproductive health product, like access
to safe abortion, there are political hurdles to overcome (25). Social marketing has the potential to expand access to and use of EC, especially when complemented with policy advocacy and educational activities directed at all stakeholders.

4.2.4 Monitoring product safety: hormonal contraception and risk of HIV acquisition

Background

Hormonal contraceptives include oral contraceptives pills (OCPs), injectables, patches, rings and implants. They are highly effective in preventing pregnancy, contribute to global public health targets such as reducing maternal morbidity and mortality, and translate into wider social and economic benefit for the family and community. The 2009 revision of the MEC (5) reports that hormonal contraceptives are safe for use by women who are at high risk of, or living with, HIV.

RHR monitors new research evidence to keep guidelines consistent with current knowledge. The emergence of a growing body of evidence suggesting an association between hormonal contraceptive use and risk of HIV infection acquisition among HIV-negative women, disease progression among women living with HIV, and transmission of HIV from women to non-infected male partners (26) suggested the need to review the 2009 guidance.

Methods

In collaboration with external experts and partners, HRP compiled three systematic reviews from peer-reviewed papers published up to 15 December 2011, focusing on findings published since the MEC revision meeting in 2008. Employing the grading of recommendations, assessment, development and evaluation (GRADE) approach, they examined the evidence regarding:

- hormonal contraception and acquisition in women who are HIV negative;
- hormonal contraception and disease progression in women who are HIV positive;
- hormonal contraception and transmission from women who are HIV positive to men who are HIV negative.

GRADE evidence profile summaries (see Annex 3) were peer reviewed by an advisory committee and circulated to a team of experts ahead of a technical consultation of 75 participants from 18 countries, representing 18 agencies, who met from 31 January to 1 February 2012, to consider the findings. The multidisciplinary panel included clinicians, epidemiologists, researchers, programme managers, policy-makers, guidelines methodologists, reproductive biologists and pharmacologists. Stakeholders included experts in international FP and HIV, as well as women’s health advocates.

After careful review of the evidence and extensive discussion, recommendations were reached through consensus. The process was reviewed by the WHO Guidelines Review Committee5 on 15 February 2012. The recommendations were approved and released the following day and are posted on the WHO website for easy availability to the global public (27, 28).

Summary of the evidence

Biological studies

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5 The Guidelines Review Committee is responsible for ensuring that all WHO recommendations are based on the best available evidence and have been developed in a transparent, unbiased and clearly reported manner.
Several biological mechanisms by which individual methods of hormonal contraception could influence HIV acquisition, progression and transmission were considered. Reviewers agreed that it remains unclear which, if any, are clinically relevant, as findings were inconsistent within and across contraceptive types. Different hormonal contraception could alter these factors in different ways and this depended on whether the preparations contained either or both estrogen or progestogen. Potential mechanisms included alteration of systemic and local immune responses and changes in the genital tract environment.

**Epidemiological studies**

The epidemiological studies mostly assessed combined oral contraceptives (COCs) or progestogen-only injectable contraceptives, including depot medroxyprogesterone acetate (DMPA) and NET-EN, and their relationship to acquisition of HIV infection among women who are HIV negative and at high risk of HIV, disease progression in women who are HIV positive or transmission from women who are HIV positive to men who are HIV negative, with the largest body of evidence related to disease progression.

**Acquisition in women who are HIV negative**

Twenty prospective studies assessed the risk of HIV acquisition among women who are HIV-negative. No significant association was found between OCP use and HIV infection, although point estimates varied and several had limited statistical power. Evidence on injectable contraception was mixed. While no statistically significant association was found with NET-EN, studies reported mixed results, varying from a significant increase in risk (48–100%) to no association for DMPA.

**Disease progression in women who are HIV positive**

Of 10 observational studies of various hormonal contraceptives and HIV disease progression (measured by mortality, time to CD4+ cell count <200 cells/mm³, initiation of antiretroviral therapy (ART), increased HIV-RNA (ribonucleic acid) viral load, or decreased CD4+ cell count), only one found a statistically significant association in a comparison of individuals using hormonal contraception with those using a copper intrauterine device (IUD). This study had methodological difficulties, including method switching and loss to follow-up, and the GRADE rating for this body of evidence was “low”.

**Transmission from women who are HIV positive to men who are HIV negative**

One study suggested a 2–3-fold increase in risk of female-to-male HIV transmission among users of injectable but not oral hormonal contraceptives. While the study had methodological strengths (statistical adjustment for multiple potential confounders, low loss to follow-up, frequent follow-up visits, large population studied), it had limited statistical power, owing to the small number of new HIV infections in men. The GRADE rating for the body of evidence on female-to-male HIV transmission was “low” for injectable contraception and “very low” for oral contraceptives.

**Recommendation**

As most concern focused around progestogen-only injectable contraception and risk of HIV acquisition in women, the experts decided that the available evidence did not establish a clear causal association between injectable contraception and HIV acquisition, but did not definitively rule out a possible effect. They agreed that use of hormonal contraceptives should remain unrestricted but that further research was needed and emerging evidence needed to be closely monitored.
Women at high risk of HIV infection were advised to:

- continue to use all existing hormonal contraceptive methods without restriction;
- access and use condoms, male or female, and, where appropriate, other measures to prevent and reduce their risk of HIV infection and STIs.

Women living with HIV infection were advised to:

- continue to use all hormonal contraceptive methods without restriction;
- consistently and correctly use condoms, male or female, to prevent HIV transmission to non-infected sexual partners.

Rodriguez et al modelled the risk of HIV acquisition against the risk of maternal death in four African countries (Chad, Kenya, South Africa and Uganda) if women were to stop using progestogen injectable hormonal contraception out of fear of acquiring HIV infection (29). The options included no method, an IUD or COCs. The authors concluded that if less than 70–100% of current users do not switch to an IUD or COC, an additional nine maternal deaths will occur for every case of HIV that is averted. This risk must therefore be considered in the counselling of women in settings where both HIV and maternal mortality risks are high. HRP will continue to monitor the evolving evidence and the team can be relied on to adjust their recommendations in light of the evidence, as necessary. There is, however, an indication of an emerging need to consider and develop alternatives for these populations.

4.2.5 Safe abortion services: application of the WHO strategic approach to unsafe abortion – experience in sub-Saharan Africa, eastern Europe and Asia

Background

While the global abortion rate declined from 35 per 1000 women aged 15–44 years in 1995 to 29 per 1000 in 2003, it seems to have stalled at 28 per 1000 in 2008 (30). In low- and middle-income countries in 2008, most abortions remained unsafe (55%), reaching 97% in Africa where access to safe abortion is generally restricted, with over 2000 abortion-related deaths every year (31). In eastern Europe, where abortion is legal, limited access to contraceptives results in overuse of abortion, and unacceptable morbidity and mortality.

In Bangladesh, menstrual regulation (MR), defined as “a procedure to make the menstrual cycle regular if menstruation is absent for a short duration” (33), was included in the national FP programme in 1979 to address contraceptive failure. MR procedures may be performed up to 10 weeks from the last menstrual period (LMP). When MR was introduced, no pregnancy test was done and uterine contents were not examined following MR. This legal grey area concerning pregnancy status was used by Bangladesh to make MR widely and legally available. In 2011, Bangladesh requested HRP technical assistance to revise their national menstrual regulation guidance in line with WHO safe abortion guidance (33).

The WHO strategic approach is a useful tool for tackling sensitive problems in a dispassionate way and has been applied to the prevention of unsafe abortion with good effect. Of 15 countries that have used the strategic approach to address unsafe abortion, Bangladesh, the former Yugoslav Republic of Macedonia, Ghana, Guinea, Kyrgyzstan, Malawi, Mongolia, the Republic of Moldova, Romania, the Russian Federation, Senegal, Sierra Leone, Ukraine, Viet Nam and Zambia.
lated and solutions developed to improve access to safe abortion services regardless of the environment. The status of country experiences is summarized in Table 2.

Table 2
Countries applying the WHO strategic approach to safe abortion, by stage of the process, 2012

<table>
<thead>
<tr>
<th>WHO Region</th>
<th>Country</th>
<th>Initial year</th>
<th>Strategic stage in 2011/2012</th>
<th>Objective/output/outcome</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>African Region</td>
<td>Ghana</td>
<td>2005</td>
<td>Research/pilot programmes underway; scale-up initiated</td>
<td>Develop national standards and guidelines</td>
<td>Ipas; HRP</td>
</tr>
<tr>
<td></td>
<td>Guinea</td>
<td>2009</td>
<td>Dissemination workshop 2010; no further progress</td>
<td>Improve access to legal abortion; inform a national effort to reposition FP</td>
<td>HRP; CERRUGUI^</td>
</tr>
<tr>
<td></td>
<td>Malawi</td>
<td>2009</td>
<td>Research/pilot programmes underway (provision of DMPA by community health workers)</td>
<td>Revise sexuality education curricula; strengthen FP and adolescent SRH; improve pregnancy advisory centre services (34)</td>
<td>Ipas, HRP</td>
</tr>
<tr>
<td></td>
<td>Senegal</td>
<td>2010</td>
<td>Research/pilot programmes underway</td>
<td>Addressing gender equality and women's SRH needs</td>
<td>Ipas, HRP</td>
</tr>
<tr>
<td></td>
<td>Zambia</td>
<td>2008</td>
<td>Research/pilot programmes underway; scale-up initiated</td>
<td>Development of national standards and guidelines</td>
<td>Ipas, HRP</td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td>Bangladesh^b</td>
<td>2011</td>
<td>Not applicable</td>
<td>Clinical norms/guidelines developed</td>
<td>HRP</td>
</tr>
<tr>
<td>European Region</td>
<td>The Republic of Moldova</td>
<td>2005</td>
<td>Comprehensive abortion care (CAC) piloted in 2/12 perinatal centres (designated training sites); 1 district hospital; 1 youth-friendly clinic (medical abortion only); information, education and counseling (IEC) material disseminated nationally, including all 12 perinatal centres</td>
<td>Implement national standards and guidelines for CAC; revise training curricula based on new guidelines; develop indicators for national monitoring of the quality of abortion care; develop model outpatient services in selected sites</td>
<td>Reproductive health training centre; James Tudor Foundation; HRP</td>
</tr>
<tr>
<td></td>
<td>The Russian Federation</td>
<td>2009</td>
<td>Pilot testing</td>
<td>Proposal to test an educational intervention on use of manual vacuum aspiration was delayed by HRP 2011 budget shortfall</td>
<td>HRP</td>
</tr>
<tr>
<td></td>
<td>Ukraine (36)</td>
<td>2008</td>
<td>Pilot testing in three sites; preparation for scale-up</td>
<td>Develop new protocol for comprehensive care for unwanted pregnancy (CCUP); clinical protocols; in-service training of mid-level professionals; three model CCUP clinics established; pre-/post-abortion counselling introduced; develop and implement CCUP training curriculum</td>
<td>HRP; Women's Health and Family Planning; Swiss Agency for Development and Cooperation; other NGOs</td>
</tr>
</tbody>
</table>

na, not available.
^a Local research institution, Cellule de Recherche en Santé de la Reproduction en Guinée.
^b Full assessment was not done; clinical guidelines were identified as needed and developed in collaboration with HRP.

The WHO strategic approach and safe abortion guidance were introduced to anglophone (2007) and francophone African (2008) stakeholders at two workshops. Following this, five countries (Ghana, Guinea, Malawi, Senegal and Zambia) requested support from WHO and/or Ipas for national strategic assessments on unintended pregnancy and abortion. Countries had to firstly submit a proposal to HRP outlining their needs. After approval by WHO’s Research Ethics Review Committee, the process began.

Country experiences

Since 2005, Ipas has partnered with HRP to support interventions to reduce unsafe abortion in Africa. HRP facilitated six strategic assessments from 2008 to 2011 and assisted Bangladesh to develop clinical guidelines (2011). In Ghana and the Republic of Moldova, follow-up activities
to the 2005 strategic assessment were supported by HRP. As data were being collected and/or analysed in Kyrgyzstan and Sierra Leone during the review, these experiences will not be included.

Stage 1: national strategic assessments

Country assessment teams (representatives of ministries of health; national and international NGOs; health-care providers; youth and women’s advocates; and religious leaders, among others) conducted qualitative, in-depth individual and group interviews (personal communication, E Jackson, Medical Officer, WHO/HRP, 2012). Male and female respondents were selected from among policy-makers, programme managers, women seeking reproductive health services and community members, and asked about unintended pregnancy and abortion; access to and availability of safe abortion services; quality of SRH services; policy; institutional capacity; laws; regulations; and human rights and health resources (human, physical, financing). Findings and recommendations were presented to stakeholders at national dissemination workshops, who reviewed, refined and prioritized the recommendations. Development of actions plans followed.

Major findings from assessments in the five African countries and the Republic of Moldova

Despite major cultural, political and economic differences, African countries identified similar barriers to safe abortion and pregnancy prevention, including lack of standards and guidelines for CAC, inadequate training of abortion providers and other reproductive health staff, poor monitoring of services and inadequate quality of care. Other common findings but important differences are detailed below.

Legal restrictions on abortion/access to contraceptives

While a favourable legal environment exists in Europe regarding access to abortion services, limited access and negative attitudes to contraception in Eastern Europe meant that abortion was routinely used to limit unintended pregnancies, with outdated practices leading to unsafe abortion, morbidity and mortality.

Abortions laws had been liberalized in Ghana and Zambia; however, stipulations that services could only be provided by physicians, or that three doctors had to approve every abortion request in writing, effectively limit access and prevent expansion of services by training mid-level providers. In countries that legally permitted abortion for specific indications, these grounds were rarely known, leading to an assumption that all abortion was illegal. While a 2000 revision to the law in Guinea allowed abortion in cases of rape, incest or fetal anomaly, or to preserve a woman’s life, none of the community members, health-care providers or policy-makers interviewed knew these legal indications for abortion. A similar lack of knowledge was seen in Ghana and Zambia, where laws had been liberalized much earlier.

Guinea, Malawi and Senegal had highly restricted access to abortion, limiting access to safe services, particularly for the poor, with demand for post-abortion care (PAC) exceeding supply. In Guinea, hospital committees must approve abortion requests but only two hospitals had such committees, both in the capital, Conakry. Assessors from Malawi and Senegal noted the lack of harmony between laws that only permit abortion to save the life of the woman, and the Maputo Protocol (2003) (36), ratified by Senegal (2004) and Malawi (2005), which calls for provision of abortion on broad-based legal grounds.

Systems of clandestine abortion provision had high associated costs for women

Even where safe legal services exist, women resort to clandestine care, often from doctors at privately negotiated prices, sometimes under the guise of PAC. The price depends on gestation
and provider qualifications. While generally safer than abortion provided by traditional practitioners, the higher cost and limitation to urban areas restrict access for poor, rural, young and otherwise vulnerable women. In Ghana and Zambia, some women buy drugs such as misoprostol from pharmacists or “chemical sellers”.

**Inadequate post-abortion care and weaknesses in family planning and sexuality education**

Although PAC was variably available, policy, practice and quality of care issues such as lack of, or poorly maintained, manual vacuum aspiration (MVA) equipment, or limited availability of services resulting in delays in uterine evacuation, often result in practitioners resorting to higher-risk sharp curettage procedures, which are only available in hospitals, further limiting access. PAC services often lacked contraceptive counselling.

Low contraceptive use was the main determinant of unsafe abortion. Barriers include limited infrastructure to provide contraception; stock-outs or lack of contraceptive commodities; myths and misperceptions about contraceptive use; gender inequity; and adolescent sexuality. Countries with severe legal restrictions on abortion are limited to strengthening FP and post-abortion contraception. Despite sexuality education in some schools, many teachers felt ill prepared to teach the subject, especially where open discussion of sexual intercourse and sexuality was largely taboo.

In Bangladesh, MR is performed by MVA by government-trained doctors and specially trained paramedics (family welfare visitors and female subassistant community medical officers). While several MR guidelines have been in use, the Ministry of Health saw the need for comprehensive *National menstrual regulation services guidelines* (32) to standardize norms, policy, regulations and performance descriptors using evidence-based clinical decision-making strategies.

**Religious, social and cultural contexts**

Abortion has been highly stigmatized and often shrouded in silence, with some health-care providers unwilling to deliver safe services. Religion often influences policy and legal reform. Religious values sometimes created shame and stigma, especially if pregnancy occurred outside of marriage, catapulting women toward seeking an abortion. Some interpreted maternal death, as “appropriate retribution” for both “sins”.

Religious teaching in Bangladesh did not challenge the practice of MR, as interventions were permitted “prior to ensoulment” of the fetus, while second-trimester abortion would not be allowed (37). No review of the 1860 British law occurred and no effort was made to legalize all abortion. By promoting MR for contraceptive failure, policy-makers, avoided second-trimester abortion, and the possible public backlash from conservative elements for the MR programme (33).

Other highlighted challenges included gender inequality, which limits access to education for girls; the requirement in some settings for spousal approval to use contraceptives, terminate a pregnancy or seek medical care; and girls being expelled from school when they become pregnant.

**Stages 2 and 3: country-specific follow-up plans and activities**

Stage 2 is the development and testing of appropriate interventions. Evaluation must be built into this stage, to ensure that interventions are feasible, acceptable, effective and sustainable and merit scaling up. Table 3 summarizes stage 2 and 3 activities for the five African countries. Common recommendations included development of national guidelines for abortion care, dissemination of information on legal indications for abortion, strengthening FP programmes, and improving adolescent SRH services and sexuality education. In the Republic of Moldova,
Three pilot centres were established to provide CAC and train providers in use of the newly developed guidelines and strategies. During stage 3, these centres were designated as training sites.

Table 3

<table>
<thead>
<tr>
<th>Ghana</th>
<th>Guinea</th>
<th>Malawi</th>
<th>Senegal</th>
<th>Zambia</th>
</tr>
</thead>
</table>

Stage 2: strategic development/pilot intervention

- Develop CAC services:
  - Update health information systems to monitor and evaluate abortion-related services
  - Train mid-level staff to provide abortion using MVA up to 12 weeks’ gestation
- Areas of focus include:
  - FP services
  - Commodity security
  - Sexual health education
  - Improve PAC
- Develop national standards and guidelines for provision of abortion
- MVA equipment added to Standard equipment list (2009); availability limited
- Advocacy for legal reform initiated with creation of Coalition for Prevention of Unsafe Abortion (COPUA)
- Media sensitization
- Wide discussion of discordance between the Maputo Protocol (36) and the law

Stage 3: scaling-up

- Partner with public, private and nongovernmental organizations to expand services
- CAC now available in 60 public and private facilities, including 12 hospitals
- Incremental scaling-up to 18 more facilities; goal is national coverage
- Given revisions to the law and lack of knowledge about changes, the team recommended:
  - Develop clear legal guidance for application of the law
  - Wide dissemination of information on legal indications for abortion
- Ministry of Health has started to strengthen PAC and CAC as legally permitted
- Infrastructure and equipment need to be assessed in 20 health centres in the capital, Lilongwe
- MVA orientation workshops held
- Plans are being developed to improve the quality of PAC, FP services and SRH education

Enabling environment

- Medabon registered for use in public/private facilities
- Misoprostol added to essential drug list for obstetric/gynaecological use
- Fixed price for abortion in public facilities
- FP commodities in short supply
- No legal reform expected
- Legal requirement that three physicians approve every abortion is a barrier
- Medabon registered but use limited to obstetrics/gynaecology; availability limited

Development of CAC services

- National standards, guidelines and protocols (2009)
- CAC provided in 28 facilities in three of eight provinces
- Operations research undertaken to train nurse practitioners and clinical officers to deliver medical and surgical abortion services
<table>
<thead>
<tr>
<th>Ghana</th>
<th>Guinea</th>
<th>Malawi</th>
<th>Senegal</th>
<th>Zambia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status</td>
<td>• Services have increased</td>
<td>• Lack of donor funds to support follow-up activities delayed implementing action plans</td>
<td>• Delivery of CAC seems long way off</td>
<td>• Civil society representatives, supported by The Ministry of Health and Prevention and the Ministry of Gender are advocating for legislative change regarding abortion</td>
</tr>
<tr>
<td></td>
<td>• Women still opt to self-induce with misoprostol (PAC is free; safe abortion costs US$35–40)</td>
<td>• Efforts needed to improve access to FP services/commodities</td>
<td>• Project being scaled up nationally</td>
<td></td>
</tr>
</tbody>
</table>

In 2011, in collaboration with HRP the WHO Safe abortion: technical and policy guidance for health systems was adapted for use in Bangladesh (32). These guidelines now require that the uterine size and/or time from the LMP be established as part of a medical examination before the procedure. After the procedure, aspirated uterine contents must be examined to ensure that the uterus has been completely evacuated. If inconclusive, guidelines for further assessment are included.

Stage 3 is intended to scale up proven interventions by building institutional and programmatic capacity to deliver them on a wide scale. The nature and pace of activities depends on the health system’s readiness for change, the broader political and sociocultural environment and available resources. The Republic of Moldova’s Ministry of Health started conservatively, only allowing outpatient CAC up to 8 weeks from a woman’s LMP. After a year of excellent safe practice, the limit was increased to 10 weeks, and will probably be increased to 12 weeks with further evidence of safety. As the high cost of medical abortion using mifepristone limited its use by poorer women in the Republic of Moldova, the government and an NGO, the Reproductive Health Training Centre, were exploring the registration of Medabon as a low-cost mifepristine–misoprostol medical abortion product.

**Lessons learnt**

**The situational analysis**

The participatory, field-oriented process of the strategic approach is suited to influencing policy and programmes. Ministry of health involvement is vital to ensuring the integration of findings into health policy and programmes. The process enables strengthening of local skills in planning, quantitative and qualitative data collection and analysis, intersectoral collaboration, translating research into policies and programmes, evaluation and scale-up of successful interventions. Teams often need technical support to facilitate discussions, given the sensitive and emotional nature of abortion. Engagement of financial partners early in the process is critical, otherwise implementation may become stalled midstream, leading to loss of momentum.

**Flexibility and adaptation**

Each country adapted the strategic assessment tool to national priorities and the local context. Where modifying the abortion law may not be feasible, creative Bangladeshi-type solutions may be possible. Other related determinants that could be addressed without legal reform included adolescent sexuality, violence against women, post-exposure EC for rape victims, “off licence” sale of abortifacients like misoprostol, and managing those entry points so that more acceptable SRH practices develop.
Impact

The Moldovan experience is being replicated in Ukraine. While the Republic of Moldova acknowledges the savings that derive from outpatient abortion care versus inpatient care, including PAC, they experienced professional tension as individual hospitals lost income. While contraceptive utilization has slowly improved in Romania, especially among rural women where the contraceptive prevalence rate increased from 21% in 1999 to 33% in 2004, better-quality care has been associated with falling abortion-related maternal mortality ratios, from 58 per 100 000 live births when restrictions on abortion were removed in 1999 to below 5 per 100 000 in 2006 (38).

Conclusions

The strategic approach methodology is a powerful tool to break through the silence of unsafe abortion by enabling diverse stakeholders to inform policies and services. Progress in helping women prevent and manage unwanted pregnancy and unsafe abortion ultimately depends on sustained commitment and leadership from governments, civil society and donors, through all three phases of the strategic-approach process. The experience across varying legal and cultural settings indicates that countries need not wait for legal reform to improve care. Even if the law is favourable, it does not guarantee that abortion care will be safe. Bangladesh demonstrated a creative solution for an inhospitable legal environment. As countries develop the enabling environment, there is a need to monitor implementation to ensure that the standard of care is consistent with current knowledge and practice.

These experiences demonstrate how political will, coupled with international and NGO technical and financial support, can deliver comprehensive reproductive health services aimed at improving women’s health and maternal morbidity and mortality. Romania, however, shows that without consistent attention to management of the supply chain for FP commodities, maintenance of MVA/EVA (electronic vacuum aspiration) equipment and continued training of new members of the health team, the likelihood of reverting to less safe practices is real (39). Table 4 summarizes a framework where countries can locate their barriers to safe abortion care from the country experiences in the case-study and identify possible areas for intervention, even if circumstances are far from ideal. HRP has developed a workable formula capable of reducing the risks of unsafe abortion across a range of settings.
Table 4
Framework to enable access to comprehensive reproductive health and safe abortion care: the combined experiences of African and eastern European countries

<table>
<thead>
<tr>
<th>Areas for action</th>
<th>Legal and cultural change</th>
<th>Gendered attitudes and values</th>
<th>Skills and competencies of health providers</th>
<th>Appropriate environment to deliver safe abortion care</th>
<th>Planning and regulatory environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objectives</td>
<td>• Harmonize laws with international standards</td>
<td>• Improve clinical and counselling skills and competencies</td>
<td>• Improve access to care</td>
<td>• Enable safe abortion care</td>
<td>• Monitor access, safety, quality and outcome</td>
</tr>
<tr>
<td>Targets</td>
<td>• General public</td>
<td>• Develop and implement regulations so that middle-level providers may deliver FP/safe abortion care</td>
<td>• Develop and implement regulations so that middle-level providers may deliver FP/safe abortion care</td>
<td>• Ensure comprehensive needs assessment, which includes diverse input (strategic assessment stage 1)</td>
<td>• Ensure adequate planning and identification of resources to enable a successful pilot stage (stage 2)</td>
</tr>
<tr>
<td></td>
<td>• Legislators</td>
<td>• Develop teaching skills and training teams (trainer of trainers: in service; tertiary)</td>
<td>• Add required drugs and equipment to essential drugs and equipment list</td>
<td>• Have a clear strategy for how the scale-up will be financed and implemented (stage 3)</td>
<td>• Have a clear, integrated framework for monitoring safety, quality and outcome</td>
</tr>
<tr>
<td></td>
<td>• Political leaders</td>
<td>• Modify curricula at basic, undergraduate and postgraduate levels, consistent with current knowledge and evidence</td>
<td>• Upgrade facilities to provide care in a confidential, well-equipped environment</td>
<td>• Enable continuing education for health-care providers</td>
<td>• Ensure geographic access</td>
</tr>
<tr>
<td></td>
<td>• Religious leaders</td>
<td>• Enable continuing education for health-care providers</td>
<td>• Ensure consistent supply of drugs, equipment and supplies</td>
<td>• Provide pre- and post-abortion counselling</td>
<td>• Provide public education aimed at dispelling local myths and negative attitudes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Maintain and replace equipment as necessary</td>
<td>• Ensure affordable access to FP</td>
<td>• Add required drugs and equipment to essential drugs and equipment list</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Provide post-abortion counselling</td>
<td>• Upgrade facilities to provide care in a confidential, well-equipped environment</td>
<td>• Develop SRH education in schools for boys and girls</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Ensure geographic access</td>
<td>• Have a clear strategy for how the scale-up will be financed and implemented (stage 3)</td>
<td>• Develop SRH educators</td>
</tr>
</tbody>
</table>

a Or creatively avoid a public challenge to the existing law, as was done in Bangladesh.

4.2.6 Controlling sexually transmitted and reproductive tract infections: initiative to eliminate mother-to-child transmission of congenital syphilis

Background

Untreated syphilis in pregnancy can cause late abortion, stillbirth (25% of cases), prematurity or low birth weight (13%), neonatal deaths (11%) and congenital infection (20%) (40). On-site antenatal screening and same day-treatment can, however, reduce all these adverse outcomes. While most countries have policies for antenatal syphilis screening, implementation has faltered from lack of training, inadequate supply of reagents, long turn-around time between testing and result availability, and limited access to drugs to treat infected individuals. In 2007, WHO launched the global initiative to eliminate congenital syphilis, aimed at achieving the following preventive outcomes:

- reduce the overall prevalence of syphilis in the adult population;
- deliver integrated SRH programmes;
- promote and ensure access to high-quality ANC for all pregnant women;
- provide syphilis screening and treatment within ANC services.
Elimination of congenital syphilis (ECS) is a feasible public health goal, which is more cost effective at preventing stillbirths than any other pregnancy intervention besides comprehensive emergency obstetric care (41). Global antenatal attendance rates are high (81% of women worldwide make at least one visit and 51% make four or more visits); screening tests are low cost (US$0.5–3.0) and technically feasible at the primary care level (rapid test reagents can be stored at room temperature for 9–18 months) (42); and treatment with penicillin is inexpensive (US$1.50 per treatment) and already on the essential medicines list of all countries (43). New rapid testing technology (42) can also enable joint syphilis and HIV screening in nearly any ANC setting. Despite these facilitating factors, screening pregnant women for syphilis is often not a priority public health intervention, and the burden of congenital syphilis is underappreciated.

The WHO strategy promotes early ANC (first visit before 16 weeks), testing of all women at the first antenatal visit, repeat testing in the third trimester and treatment of the partners of infected women (43). The main challenge is how to increase early attendance to improve the effectiveness of antenatal treatment. To achieve universal screening, the cost may need to be borne by the state, or those most in need of screening may be least likely to afford the cost of testing (44).

The WHO initiative for the global ECS aims to decrease the number of cases of congenital syphilis by at least 80% in 10 high-burden countries (Table 5) by 2015; these countries account for over 40% of the global syphilis burden (45). The specific targets of the global initiative are that, by 2015:

- at least 90% of pregnant women will be screened for syphilis;
- at least 90% of women who are syphilis seropositive will be appropriately treated.

### Table 5

**Potential for syphilis elimination in the 10 high-impact countries**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>3 038 000</td>
<td>53 and 23</td>
<td>na</td>
<td>0.6 (2008)</td>
<td>128 500 (36)</td>
</tr>
<tr>
<td>India</td>
<td>27 165 000</td>
<td>75 and 51</td>
<td>65</td>
<td>0.3 (2010)</td>
<td>605 230 (22)</td>
</tr>
<tr>
<td>Indonesia</td>
<td>4 372 000</td>
<td>93 and 82</td>
<td>na</td>
<td>na</td>
<td>62 290 (15)</td>
</tr>
<tr>
<td>Kenya</td>
<td>1 529 000</td>
<td>92 and 47</td>
<td>59</td>
<td>1.8 (2010)</td>
<td>34 130 (22)</td>
</tr>
<tr>
<td>Madagascar</td>
<td>732 000</td>
<td>86 and 49</td>
<td>85</td>
<td>3.4 (2010)</td>
<td>14 590 (21)</td>
</tr>
<tr>
<td>Mozambique</td>
<td>883 000</td>
<td>92 and 53</td>
<td>68</td>
<td>6.0 (2010)</td>
<td>25 560 (28)</td>
</tr>
<tr>
<td>Rwanda</td>
<td>438 000</td>
<td>98 and 35</td>
<td>75</td>
<td>1.5 (2010)</td>
<td>9 620 (23)</td>
</tr>
<tr>
<td>South Africa</td>
<td>1 059 000</td>
<td>97 and 87</td>
<td>75</td>
<td>2.2 (2010)</td>
<td>22 560 (20)</td>
</tr>
<tr>
<td>United Republic of Tanzania</td>
<td>1 862 000</td>
<td>88 and 43</td>
<td>54</td>
<td>4.2 (2008)</td>
<td>47 550 (26)</td>
</tr>
<tr>
<td>Zambia</td>
<td>600 000</td>
<td>94 and 60</td>
<td>43</td>
<td>5.3 (2010)</td>
<td>14 380 (26)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>38 625 000</strong></td>
<td><strong>52–98 and 23–87</strong></td>
<td><strong>43–85</strong></td>
<td><strong>0.6–6.0 (2008–2010)</strong></td>
<td><strong>964 410 (15–36)</strong></td>
</tr>
</tbody>
</table>

na, not available.

The ECS strategy consists of four critical pillars:

- I: ensure sustained political commitment and advocacy;
- II: increase access to, and quality of, maternal and newborn health services;
- III: screen all pregnant women and treat all those with positive test results;
- IV: implement surveillance, monitoring and evaluation systems.
Methods

RHR exploits the synergies of collaborative effort across HRP work clusters, across departments in WHO and across United Nations (UN) agencies. Strategies include joint ventures with HIV teams to introduce rapid tests; validate rapid test toolkits that use a single strip to test whole blood for both HIV and syphilis; develop bundled diagnostics for use during the perinatal/neonatal period by examining which combinations make sense; and find ways to support implementation. Expected barriers include concerns regarding penicillin anaphylaxis and addressing issues of timing so that reinfection has the least impact.

HRP provided leadership to synthesize global evidence on congenital syphilis, to develop screening and treatment protocols, implementation tools and guiding principles; and to develop surveillance and monitoring systems and guidelines for health-systems strengthening. The evidence has been generated from country research and case-studies of the efficacy and effectiveness of screening tests and programme interventions. An ECS website provides ready access to the most current tools and information (49).

Essential programme elements aim to:

- address enabling environments through a legislative agenda to ensure supportive laws and policies;
- promote appropriate health-seeking behaviours, treatment compliance and sexuality education;
- support health-care delivery, including STI case-finding in ANC, partner notification and care;
- provide a reliable supply of safe, effective medicines and commodities;
- support laboratory services, surveillance, research, training and information networks (50).

Advocacy and technology to support the campaign

The advocacy strategy aims to provide an enabling environment for implementation, including policy and legal reform, drawing on other successful campaigns. A strategy toolkit provides technical support for screening, case identification, contact tracing and protocols for monitoring/surveillance (51).

Case identification and treatment protocols

Cases should be identified with the use of rapid syphilis tests to screen women at routine antenatal clinics at the first visit, and all patients attending STI clinics. Partners are to be invited for care. Syphilis treatment protocols require treatment of pregnant women who test positive, their partners, and asymptomatic infants born to infected women. Infants should be followed up quarterly for the first year of life. A single dose of penicillin is recommended, unless contraindicated (51).

Monitoring outcome/surveillance

The monitoring framework encompasses regional, national and local contexts with defined output, outcomes and impact indicators and activities. Core annual ECS data are collected and verified at the country level and submitted to WHO or the Joint United Nations Programme on HIV/AIDS (UNAIDS) through WHO regional offices. Programme impact is measured by the progress toward the target incidence of congenital syphilis (≤0.5 per 1000 live births).
Progress

Table 6 highlights progress in Latin America and the Caribbean (LAC), Africa and Asia. Because of their pre-existing infrastructure, LAC countries were best prepared to embrace the initiative, and adopted a plan of action in 2010. Separate guidelines have been developed for LAC countries and have been integrated into national plans in 22 countries (53). Given its pre-existing health infrastructure and organization, Cuba has made the most progress; however, 11 countries report having achieved target incidence rates for congenital syphilis of less than 0.5 per 1000 live births. In Africa, progress has been slow, as more work needs to be done to develop systems to deliver the services and change the culture of late attendance for ANC. In 2011, the initiative was launched in the Asia-Pacific region, with some success reported in India, Malaysia and Myanmar (52).

Table 6
Summary of ECS implementation efforts, by region

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Latin America and the Caribbean</th>
<th>Africa</th>
<th>Asia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rationale/strategy</td>
<td>The region adopted a plan of action in 2010; most countries have developed strategies and plans for both ECS and MTCT of HIV</td>
<td>Progress has been limited to the development of country strategic frameworks (e.g. Kenya, South Africa)</td>
<td>The Asia Pacific United Nations Prevention of Parent-to-Child Transmission (PPTC) Task Force was launched in August 2011, to lead the initiative</td>
</tr>
<tr>
<td>Development of screening tools</td>
<td>Screening included in routine ANC; challenges reported in obtaining results in timely manner</td>
<td>Screening demonstrated to be cost effective (range of cost per DALY saved: US$3.97–10.5) Pregnant women present late for ANC: &gt;6 months' gestation (e.g. Kenya, South Africa)</td>
<td>Variations in antenatal syphilis screening practices; routine screening of all ANC clients done in few countries –Malaysia, Papua New Guinea, Sri Lanka, Thailand (52)</td>
</tr>
<tr>
<td>Development of guidelines</td>
<td>Regional and national plans and clinical guidelines in place in 22 of 48 countries (e.g. Brazil, Cuba, Jamaica) (53)</td>
<td>Lack of guidelines for service providers Lack of tracking systems for laboratory results – weak diagnosis/follow-up systems (e.g. Kenya, South Africa)</td>
<td>Monitoring and evaluation guide, fact sheets (12 countries) and costing tool developed (August 2011)</td>
</tr>
<tr>
<td>Roll-out in field: efficiency</td>
<td>Cuba has recorded the greatest success in the elimination initiative. Most countries reported 80% coverage on ANC and potential to provide the service; however, the quality of service varies across countries</td>
<td>Limited training and supervision of field staff Unavailability and poor management of drugs and supplies (e.g. Kenya, South Africa) Overall weak implementation (e.g. Ghana)</td>
<td>Limited data available on process issues High rates of first ANC attendance – 79%</td>
</tr>
<tr>
<td>Monitoring effectiveness</td>
<td>ECS indicators reported annually; surveillance and health information systems challenged by data quality (e.g. 16/48 countries not reporting indicators); legal and technical frameworks strengthened through WHO regional/country-initiated efforts</td>
<td>Weak surveillance, monitoring and evaluation (e.g. Kenya, South Africa)</td>
<td>WHO regional offices providing guidance on ECS indicators (e.g. Bangladesh, China, India, Thailand) Reported reduction in syphilis serology among pregnant women in ANC in India and Myanmar</td>
</tr>
<tr>
<td>Impact</td>
<td>PMTCT coverage – 61% (2010) Syphilis testing coverage – 61% (57) 11 countries* report a target for incidence of congenital syphilis of ≤0.5 per 1000 live births</td>
<td>Antenatal syphilis prevalence: 0.1–0.4% in China, India, Malaysia; 6–7% in Papua New Guinea and Solomon Islands (52)</td>
<td>Antenatal syphilis prevalence: 0.1–0.4% in China, India, Malaysia; 6–7% in Papua New Guinea and Solomon Islands (52)</td>
</tr>
<tr>
<td>Sustainability</td>
<td>Declining political will and funding support</td>
<td>Lack of sustained political commitment and advocacy (e.g. Kenya, South Africa)</td>
<td>Need to scale up PMTCT programmes to reverse the trend in infections in neonates</td>
</tr>
</tbody>
</table>

DALY, disability-adjusted life-year. PMTCT, prevention of mother-to-child transmission.

* Anguilla, Antigua and Barbuda, the Bahamas, Barbados, Canada, Cuba, Chile, Guadeloupe, Guyana, Panama and United States of America.
Effectiveness and efficiency

The availability of tools enabled regional teams to efficiently begin the process of adaptation to local needs. It was also valuable to have an evidence base that advocates could use to market the initiative to policy-makers, raise awareness among the public and enable the ECS initiative to receive priority political support. Some health teams had to be convinced that the problem should be addressed and that the goal could be achieved. The willingness of development partners like the Global Fund to support the integration of ECS into their HIV portfolio will help to promote the initiative, as addressing both problems simultaneously will improve outcomes (see Table 7).

Table 7
Effectiveness: can the ECS objectives be achieved?

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Weaknesses</th>
<th>Opportunities</th>
<th>Threats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa, Latin America, Asia: tools/guiding principles in use in Africa (Ghana), Asia (China), Latin America (Brazil) <strong>Africa</strong>: cost effectiveness of syphilis treatment demonstrated Asia: between 2007 and 2010 among pregnant women:  • syphilis prevalence has declined in some countries (e.g. Myanmar, from 3% to 0.7%; India, from 2.9% to 0.7%)  • in other countries, syphilis prevalence has stabilized at &lt;1% between 2007 and 2010 (e.g. Bangladesh, Sri Lanka, Thailand) (personal communication, L Newman, Medical Officer, WHO/HRP, 2012) <strong>Latin America</strong>: Paraguay – 2006–2009, screening for syphilis at first visit increased by 20% (personal communication, L Newman, Medical Officer, WHO/HRP, 2012) <strong>Global issues</strong>: a large proportion of the burden of congenital syphilis exists in only a few (10) countries (46)</td>
<td>Africa, Latin America, Asia:  • syphilis care is a low priority in many health ministries  • policy/decision-makers in Latin America (Plurinational State of Bolivia) and Africa (Kenya, South Africa) are unaware of syphilis problem and cost effectiveness of treatment  • health-care providers (Plurinational State of Bolivia, Kenya and South Africa) unaware of consequences  • community unaware of disease, results in incomplete treatment (Brazil, China)</td>
<td>Global issues:  • innovations in combination prevention strategies, integrated programming, political commitment  • community-based surveillance using skilled birth attendants and traditional healers to support referrals and report pregnancy complications, stillbirths and miscarriages  • Global Fund proposals to scale up interventions integrating STI and SRH services (e.g. Rwanda, United Republic of Tanzania, Zambia)</td>
<td>Global issues:  • Declining interest in STIs; declining resource allocation for PMTCT  • cultural barriers (i.e. gender norms that reduce women’s power to negotiate safer sexual intercourse; limited mobility and autonomy to make health decisions; culture of silence concerning SRH needs and issues)  • incomplete/inadequate reporting and information systems – reported figures need to be interpreted with caution</td>
</tr>
</tbody>
</table>

Factors that help programmes successfully get off the ground efficiently (see Table 8) include having evidence that demonstrates the value of integrating the initiative into existing SRH activities. Challenges include the persistence of vertical programmes (e.g. ANC, HIV) that are poorly integrated into SRH services, weak mid-level human resources skills, and inefficient logistical support. The strategy of bringing implementation teams together to share experiences helps new programmes understand what works, and demonstrates opportunities for integrating these successes into existing services.
The way forward: sustainability

Technology transfer is needed to help scale up services, especially where middle-level management capacity is weak, particularly in Africa and some Asian countries. Continued strengthening of laboratory facilities, laboratory information systems, surveillance and programme evaluation will improve programme efficiencies in all countries and improve country capacity to generate more reliable data for planning (S3). Cultural and legal barriers, inconsistent funding and weak political will to eliminate syphilis are threats to sustainability.

The development and implementation of the range of strategies is a dynamic process that will require sustained support from HRP (see Table 9). A 2011 meeting of six African countries (Central African Republic, Ghana, Madagascar, Mozambique, United Republic of Tanzania and Zambia), selected because of their high disease burden (antenatal syphilis rates of 4.4–7.1%), concluded with participants agreeing to draft national action plans to eliminate MTCT of syphilis and HIV in their respective countries. Steps outlined in their draft national action plans included the need to:

• improve access to and the quality of ANC services;
• introduce or scale up rapid syphilis and HIV testing (including CD4+ testing);
• develop indicators and targets for monitoring and evaluation;
• develop costed plans of action;
• promote advocacy with partners;
• create a supportive national policy environment (personal communication, L Newman, Medical Officer, WHO/HRP, 2012).

Table 9
Sustainability: capacity development to sustain ECS activity

<table>
<thead>
<tr>
<th>Skills transfer</th>
<th>Innovations</th>
<th>Opportunities</th>
<th>Threats</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Africa, Latin America and Asia:</strong></td>
<td>• more investment in transfer of skills at country level needs to occur, especially in the areas of management, surveillance, data collection, evaluation skills, laboratory testing, and sensitivity training to reduce discrimination and stigmatization of STI clients</td>
<td>• strengthening surveillance systems for HIV and syphilis (e.g. Argentina 2010)</td>
<td>• resource issues (funding)</td>
</tr>
<tr>
<td>LAC:</td>
<td>• need to prioritize expansion of access to diagnostic testing (S1); improving advocacy; involvement of community groups and NGOs</td>
<td>• many countries are now aware of the importance of syphilis screening and treatment</td>
<td>• cultural barriers (i.e. gender norms)</td>
</tr>
<tr>
<td>Global issues:</td>
<td>• syphilis treatment is cost effective</td>
<td>• missed opportunities for HIV and syphilis testing of partners of pregnant women in Argentina (S3)</td>
<td></td>
</tr>
</tbody>
</table>
The achievement of the target congenital syphilis incidence of ≤0.5 per 1000 live births in 11 LAC countries (54) provides encouragement that the goal is not impossible.

Conclusions

The ECS campaign has refocused attention on STIs and is a cost-effective goal. By scaling up interventions that integrate STI and SRH services, WHO has demonstrated to country teams strategies to roll out programmes starting from various levels of readiness of a health system and teams, and moving forward. With relatively high disease burden in LAC, this region was best able to tackle the double goal to eliminate both congenital syphilis and MTCT of HIV; other regions have focused on the ECS component. By focusing on a treatable condition such as syphilis, a reduction in HIV transmission rates is an added benefit. This campaign is an excellent example of the public good created by HRP, given its unique capacity to synthesize new technical development into effective clinical interventions that improve health and survival. Through partnerships with academic institutions, NGOs and other international agencies, high-quality research can be undertaken to inform decision-making about what works, and identify the most cost-effective approaches to solving public health problems, marrying skills in high-income countries to the needs of low- and middle-income countries, while building collaboration between low- and middle-income countries to help each other.

5 Conclusions and recommendations

5.1 Summary

Although it is relatively small, the HRP team in Geneva is impressive in its capacity to identify and coordinate a large network of investigators, collaborators and experts, drawn from academic and research institutions across all the WHO/UN regions of the world, often at short notice, to address acute, as well as long-term, development challenges. This vast network ensures that whatever problem arises, the best minds on the planet can be assembled to explore the problem, pore over existing evidence or gather new information (56), or innovate to come up with solutions. Sometimes there are setbacks, as the male hormonal contraceptive trial demonstrated, but the global community can be assured that HRP will always promote safe solutions to problems that may be old and intractable, as well as developing the best approach to addressing new challenges.

The cases demonstrate the global value of the Special Programme of Research, Development and Research Training in Human Reproduction, providing insight into the stages from problem identification (unsafe abortion), to problem clarification (the strategic approach), to generating new knowledge (male contraception) and strategies (emergency contraception), to global roll-out of solutions to old problems (ECS), while policing new knowledge (hormonal contraceptives and HIV) that ensures that advice given to individuals, communities and policy-makers is consistent with the best evidence and available expertise to evaluate this information and respond appropriately.

HRP has evolved procedures and practices that can provide a solution to most SRH problems. The strategic framework enables clarification of problems and crafting of solutions, even to sensitive problems such as unsafe abortion, and can adapt to a country’s level of readiness to address problems either incrementally or comprehensively.

5.2 Impact

Tables 10 and 11 look at possible associations between these interventions and changes in global health indicators. The capacity to achieve the first screen-and-treat ECS target is improving, as global access to ANC has grown across all regions. The challenge, however, will be to
provide the third-trimester screen outside of south-east Asia and the LAC region, as just half of the world’s mothers make four or more antenatal visits. Monitoring outcomes will also be challenging, as, in the most populous regions of the world, fewer than one in two mothers were attended by a skilled attendant at birth in 2010. The higher observed contribution of women to the stabilizing HIV prevalence rate may be a measurement artefact associated with improving antenatal surveillance. We await the next round of indicators to determine whether new initiatives are needed to address the evolving situation.

Table 10
Impact I: changes in Millennium Development Goal indicators, selected WHO regions, 2000–2010

<table>
<thead>
<tr>
<th>Impact</th>
<th>MDG and other related indicators</th>
<th>World 2010</th>
<th>Sub-Saharan Africa 2010</th>
<th>South Asia 2010</th>
<th>South-east Asia 2010</th>
<th>Latin America and the Caribbean 2010</th>
<th>Latin America and the Caribbean 2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal health</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANC – at least one visit (%)</td>
<td></td>
<td>80</td>
<td>71</td>
<td>77</td>
<td>71</td>
<td>54</td>
<td>93</td>
</tr>
<tr>
<td>ANC – at least 4 visits (%)</td>
<td></td>
<td>na</td>
<td>na</td>
<td>46</td>
<td>48</td>
<td>48</td>
<td>27</td>
</tr>
<tr>
<td>Skilled attendance at birth (%)</td>
<td></td>
<td>66</td>
<td>60</td>
<td>45</td>
<td>44</td>
<td>49</td>
<td>36</td>
</tr>
<tr>
<td>Maternal mortality ratio</td>
<td></td>
<td>210</td>
<td>320</td>
<td>500</td>
<td>740</td>
<td>220</td>
<td>400</td>
</tr>
<tr>
<td>Family planning</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraceptive prevalence rate (%)</td>
<td></td>
<td>63.4</td>
<td>61.5</td>
<td>24.6</td>
<td>18.4</td>
<td>55.6</td>
<td>48.2</td>
</tr>
<tr>
<td>Unmet need for family planning (%)</td>
<td></td>
<td>12.4</td>
<td>12.9</td>
<td>25.4</td>
<td>26.5</td>
<td>15.6</td>
<td>17.8</td>
</tr>
<tr>
<td>Adolescent fertility rate per 1000 population</td>
<td></td>
<td>48.6</td>
<td>50.9</td>
<td>119.5</td>
<td>121.9</td>
<td>46.0</td>
<td>58.5</td>
</tr>
<tr>
<td>HIV/STI control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV prevalence in adults aged 15–49 years (%)</td>
<td></td>
<td>0.8</td>
<td>0.8</td>
<td>4.8</td>
<td>5.6</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Cases in female adults aged 15+ years (%)</td>
<td></td>
<td>50</td>
<td>50</td>
<td>59</td>
<td>58</td>
<td>37</td>
<td>35</td>
</tr>
</tbody>
</table>

na, not available.

Table 11 indicates that previous improvements in the abortion rate seem to have stalled, with a rising proportion of global abortions considered unsafe. With efforts to improve the quality of abortion services and PAC, the data suggest that abortion-related deaths have decreased.

5.3 Recommendations

- A clear policy framework is needed to guide research efforts regarding male reproductive health, including the way forward in the development of male contraceptives. Within this framework, it may be necessary to revisit the costs and benefits of male contraception. Currently, while the health risks of a new male contraceptives are likely to be borne almost entirely by the user, and the health benefits appear to be largely to the partner, in terms of avoidance of the risks of unwanted pregnancy, there are social and economic benefits which accrue to the family unit. The economic costs of an unwanted pregnancy are often the responsibility of the male partner and needs to be factored into the equation.

- Efforts need to be explored to advance the social marketing and promotion of EC and other long-term contraceptives to adolescents in particular, as progress in reducing fertility in this age group has been slow.

- To support the goals for safe abortion and ECS, monitoring indicators should be included in the MDG or other universally accepted country reporting frameworks.

- Strategies are needed to effectively measure not only access to EC, but also utilization and impact. Integration of measurement tools into demographic and health surveys and other reproductive health surveys may be a place to start.

- The increasing HIV prevalence in the antenatal population needs to be monitored, especially in countries with high HIV prevalence. Revitalization of health-promotion initiatives targeting SRH behaviours among adolescents and youth may be a useful starting point.
References


## Annex 1: List of persons interviewed and methods of contact

<table>
<thead>
<tr>
<th>Area</th>
<th>Person contacted</th>
<th>Method of communication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promoting family planning</td>
<td>Mario Festin, Lead Specialist (WHO)</td>
<td>Face-to-face interview; e-mail</td>
</tr>
<tr>
<td></td>
<td>Moazzam Ali, Medical Officer (WHO)</td>
<td>Face-to-face interview</td>
</tr>
<tr>
<td></td>
<td>Mary Gaffield (WHO)</td>
<td>E-mail</td>
</tr>
<tr>
<td></td>
<td>Douglas Colvard (CONRAD)</td>
<td>E-mail</td>
</tr>
<tr>
<td>Preventing unsafe abortion</td>
<td>Bela Galantra, Lead Specialist (WHO)</td>
<td>Face-to-face interview; e-mail</td>
</tr>
<tr>
<td></td>
<td>Nathalie Kapp, Medical Officer (WHO)</td>
<td>Face-to-face interview; e-mail</td>
</tr>
<tr>
<td>Controlling sexually transmitted and reproductive tract infections</td>
<td>Lori Newman, Medical Officer</td>
<td>Face-to-face interview</td>
</tr>
<tr>
<td></td>
<td>Nathalie Broutet, Medical Officer</td>
<td>Face-to-face interview</td>
</tr>
</tbody>
</table>
Annex 2: Revised guidance: combined hormonal contraceptive use during the postpartum period

26 January 2010, Geneva, Switzerland

Recommendation

1. Consultation participants determined that current WHO guidance regarding the use of combined hormonal contraceptives (CHCs) in non-lactating postpartum women was discordant with the above evidence. The guidance inadequately reflected the gradually declining risk of VTE during the postpartum period, and the potential impact of multiple risk factors on VTE formation during this period.

2. In order to more closely fit the available data, WHO has revised their recommendations, stratifying guidance by the time since delivery (<21 days or ≥21 days after delivery), and the presence or absence of additional risk factors for VTE (including previous VTE, thrombophilia, immobility, transfusion at delivery, postpartum haemorrhage, body mass index >30 kg/m², pre-eclampsia and smoking, or immediately after a caesarean delivery). WHO discussed the impact of these additional risk factors for VTE on overall VTE risk, as well as return to fertility in non-lactating postpartum women. These revised recommendations are summarized below.

3. Four categories of risk associated with CHC use were outlined:
   - category 1 – no restriction on use of contraceptive method;
   - category 2 – advantages of the method generally outweigh the risks;
   - category 3 – the risks of contraceptive use usually outweigh the advantages;
   - category 4 – unacceptable health risk if the contraceptive method is used.

4. Prior to 21 days postpartum, the risks of CHC use generally outweigh the advantages and CHCs should generally not be used (category 3); for some women with additional risk factors for VTE other than being postpartum, CHCs should not be used (category 3/4). Women who are breastfeeding during the first 21 days postpartum should not use CHCs (category 4).

5. Between 21 and 42 days postpartum, the advantages of CHC use generally outweigh the risks and CHCs generally can be used (category 2), although for some women with additional risk factors for VTE, these methods should not be used unless other more appropriate methods are not available or acceptable (category 2/3).

6. For women up to 42 days postpartum with other risk factors for VTE, as outlined above, use of CHCs may pose an additional increased risk of VTE. Women’s risk should be assessed according to the number, severity and combination of VTE risk factors present. Because each woman is unique with respect to her personal risk profile, clinical judgment will be necessary to determine if she may safely use CHCs. Women who are breastfeeding between 21 and 42 days postpartum should not use CHCs (category 4).

7. Finally, in non-lactating women beyond 42 days postpartum, CHCs may be used without restriction. Although the risk of VTE is the same in breastfeeding as non-breastfeeding women, use of CHCs is generally not recommended prior to 6 months postpartum in women who are breastfeeding.

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9 These recommendations remain valid until 2012, when RHR will initiate a review of the Medical eligibility criteria for contraceptive use (5).
Annex 3: GRADE evidence profiles – systematic reviews of hormonal contraception use and HIV risk

A. GRADE evidence profile: hormonal contraception for women at high risk of HIV

**Use of hormonal contraception in women who are HIV negative**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Type/number of studies (number of participants)</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Imprecision</th>
<th>Indirectness</th>
<th>Quality</th>
<th>Estimate of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Injectable hormonal contraceptive use versus non-use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV acquisition</td>
<td>8 cohort studies meeting minimum quality criteria (26,512)</td>
<td>Serious limitations</td>
<td>Serious inconsistency</td>
<td>No serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR range 0.84–2.2: 3 studies increased risk (HR range 1.5–2.2) 3 studies trend towards decreased risk (HR range 0.84–0.94) 2 studies no clear effect (norethisteronea and DMPA reported separately; no clear association; opposite effects for each type of hormonal contraceptive)</td>
</tr>
<tr>
<td><strong>Oral hormonal contraceptive use versus non-use</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV acquisition</td>
<td>7 cohort studies meeting minimum quality criteria (25,518)</td>
<td>Serious limitations</td>
<td>Serious inconsistency</td>
<td>No serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR range 0.65–1.8: 1 study increased risk (HR 1.5, 95% CI 1.0 to 2.1) 3 studies trend towards increased risk (HR range 1.1–1.8) 3 studies trend towards decreased risk (HR range 0.65–0.91)</td>
</tr>
</tbody>
</table>

Note: Publication bias was not formally assessed. Estimates are based on adjusted risk estimates, results from marginal structural model analysis were used when available. CI, confidence interval; HR, hazard ratio.

* Three studies that reported risk estimates separately for norethisterone reported no statistically significant effect.

Source: [http://www.who.int/reproductivehealth/topics/family_planning/hc_hiv/en/](http://www.who.int/reproductivehealth/topics/family_planning/hc_hiv/en/)
### B. GRADE evidence profile: risk of HIV transmission among women living with HIV and using hormonal contraceptives

**Use of hormonal contraception in women who are HIV positive**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Type</th>
<th>Number of studies (number of participants)</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Imprecision</th>
<th>Indirectness</th>
<th>Quality</th>
<th>Estimate of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Injectable hormonal contraceptive use versus non-use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>HIV transmission</td>
<td>1 cohort study (2476)</td>
<td>Serious limitations</td>
<td>Not applicable (1 study)</td>
<td>Serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR = 3.0 (95% CI 1.5 to 6.2)</td>
<td></td>
</tr>
<tr>
<td><strong>Oral hormonal contraceptive use versus non-use</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>HIV transmission</td>
<td>1 cohort study (2476)</td>
<td>Serious limitations</td>
<td>Not applicable (1 study)</td>
<td>Very serious imprecision</td>
<td>No indirectness</td>
<td>Very low</td>
<td>HR = 2.4 (95% CI 0.79 to 7.0)</td>
<td></td>
</tr>
</tbody>
</table>

Note: Publication bias was not formally assessed.

Estimates are based on adjusted risk estimates, results from marginal structural model analysis were used when available.

CI, confidence interval; HR, hazard ratio.

* Combined estimate for injectable or oral hormonal contraceptive use versus non-use: HR 2.0 (95% CI 1.1 to 3.7); absolute increase about 1 transmission per 100 person-years.

Source: [http://www.who.int/reproductivehealth/topics/family_planning/hc_hiv/en/](http://www.who.int/reproductivehealth/topics/family_planning/hc_hiv/en/)
### C. GRADE evidence profile: HIV disease progression among women living with HIV and using hormonal contraception

#### Use of hormonal contraception in women who are HIV positive

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Type/number of studies (number of participants)</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Imprecision</th>
<th>Indirectness</th>
<th>Quality</th>
<th>Estimate of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hormonal contraception (oral or injectable) versus copper IUD</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>1 RCT (599)</td>
<td>Serious limitations (1 fair-quality)</td>
<td>Not applicable (one study)</td>
<td>Serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR 1.4 (95% CI 0.7 to 3.0); absolute risk increase 0.88 per 100 woman-years</td>
</tr>
<tr>
<td>Progression to CD4 count &lt;200 cells/mm³</td>
<td>1 RCT (599)</td>
<td>Serious limitations (1 fair-quality)</td>
<td>Not applicable (one study)</td>
<td>Serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR 1.6 (95% CI 1.0 to 2.3); absolute risk increase 3.7 per 100 woman-years</td>
</tr>
<tr>
<td>Mortality or progression to CD4 count &lt;200 cells/mm³</td>
<td>1 RCT (599)</td>
<td>Serious limitations (1 fair-quality)</td>
<td>Not applicable (one study)</td>
<td>Serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR 1.6 (95% CI 1.1 to 2.3)</td>
</tr>
<tr>
<td><strong>Injectable hormonal contraceptive use versus non-use</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>4 cohort studies (4399)</td>
<td>Serious limitations (1 good-, 2 fair-, and 1 poor-quality)</td>
<td>No serious inconsistency</td>
<td>No serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR range 0.41–1.0 (no estimate showed statistically significant effect)</td>
</tr>
<tr>
<td>Progression to AIDS or initiation of ART‡</td>
<td>3 cohort studies (3716)</td>
<td>Serious limitations (1 good-, 1 fair-, and 1 poor-quality)</td>
<td>No serious inconsistency</td>
<td>No serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR range 0.7–1.0 (no estimate showed statistically significant effect)</td>
</tr>
<tr>
<td>Mortality, progression to AIDS or initiation of ART‡</td>
<td>3 cohort studies (4044)</td>
<td>Serious limitations (2 good-, 1 fair-quality)</td>
<td>No serious inconsistency</td>
<td>No serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR range 0.72–1.0 (no estimate showed statistically significant effect)</td>
</tr>
<tr>
<td><strong>Oral hormonal contraceptive use versus non-use</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>4 cohort studies (1695)</td>
<td>Serious limitations (1 good, 1 fair-, and 2 poor-quality)</td>
<td>No serious inconsistency</td>
<td>Serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR range 0.28–1.1 (no estimate showed statistically significant difference)</td>
</tr>
<tr>
<td>Progression to AIDS or initiation of ART</td>
<td>4 cohort studies (4784)</td>
<td>Serious limitations (1 good-, 1 fair-, and 2 poor-quality)</td>
<td>No serious inconsistency</td>
<td>No serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR range 0.9–1.3 (no estimate showed statistically significant effect)</td>
</tr>
<tr>
<td>Mortality, progression to AIDS or initiation of ART</td>
<td>3 studies (4680)</td>
<td>Serious limitations (2 good-, 1 fair-quality)</td>
<td>No serious inconsistency</td>
<td>No serious imprecision</td>
<td>No indirectness</td>
<td>Low</td>
<td>HR range 0.65–1.0 (no estimate showed statistically significant effect)</td>
</tr>
</tbody>
</table>

Note: Publication bias was not formally assessed.

Estimates are based on adjusted risk estimates, results from marginal structural model analysis were used when available.

ART, antiretroviral therapy; CI, confidence interval; HR, hazard ratio; RCT, randomized controlled trial.

* Point estimates were higher for DMPA versus IUD compared with oral contraception versus IUD but confidence intervals were wide and overlapping

Source: [http://www.who.int/reproductivehealth/topics/family_planning/hc_hiv/en/](http://www.who.int/reproductivehealth/topics/family_planning/hc_hiv/en/)