

**Department of Reproductive Health and Research**

including

**UNDP/UNFPA/WHO/World Bank Special Programme of Research,  
Development and Research Training in Human Reproduction**

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# Executive summary

## Executive summary

### THE DEPARTMENT

The Department of Reproductive Health and Research (RHR—referred to in this document as “the Department”) has set itself the mission of helping people to lead healthy sexual and reproductive lives. In pursuit of this mission the Department endeavours to strengthen the capacity of countries to enable people to promote and protect their own health and that of their partners as it relates to sexuality and reproduction, and to have access to and receive quality reproductive health services when needed.

The Department of Reproductive Health and Research was established in November 1998 by bringing together the UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP—referred to in this document as “the Programme”) and the former WHO Division of Reproductive Health (Technical Support) (RHT). The purpose of joining these two entities was to facilitate integration of research and programme development in reproductive health within WHO.

#### **UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP)**

The Programme was established in 1972 by WHO. In 1988, the United Nations Development Programme (UNDP), the United Nations Population Fund (UNFPA), and The World Bank joined WHO as the Programme’s cosponsors. The four cosponsoring agencies, together with the major financial contributors and other interested parties, make up the Programme’s governing body, the Policy and Coordination Committee (PCC), which sets policy, assesses progress, and reviews and approves the Programme’s budget and

programme of work. Broad strategic advice on the Programme’s work is provided by the Scientific and Technical Advisory Group (STAG) (Annex 1). In 1999, STAG assumed the responsibility for reviewing, and advising on, the work of the whole Department. The Scientific and Ethical Review Group (SERG) Panel (Annex 2) reviews all projects involving human subjects and research in animals and contributes to ethical debate on matters relating to reproductive health. The Toxicology Panel (Annex 3) is a complementary review body to the SERG Panel. It provides expertise in the evaluation of pharmacokinetic, metabolic, endocrinological, toxicological, teratogenicity, carcinogenicity and mutagenicity studies of drugs or devices developed or studied by the Programme or referred to it for advice. In addition, the Programme has several strategic review committees and specialist panels that advise on detailed research strategies.

### PROMOTING FAMILY PLANNING

#### **Research on users’ perspectives**

Research on users’ perspectives provides scientifically sound information on the needs and preferences of women and men for reproductive health technologies and services. This information is key to informed policy-making, and for designing programmes and services which best address the needs of users and potential users. Research findings also provide the basis for developing appropriate evidence-based norms and tools and improving existing, or developing new, reproductive health technologies.

A pioneering study that examines links between family planning and risk behaviour related to HIV/AIDS has been under way in African countries where the HIV epidemic is greatest:

Kenya, South Africa, Uganda, United Republic of Tanzania, Zambia, and Zimbabwe. Findings from this multicountry study entitled “Family planning and sexual behaviour in the era of HIV/STIs” were presented in Gaborone, Botswana, in July 2003 at a seminar organized by the International Union for the Scientific Study of Population (IUSSP) and the Department of Population Studies at the University of Botswana. The seminar provided an overview of what the South African research team dubbed “the quiet revolution”—condom use within marriage.

Because the condom’s association with prevention of sexually transmitted infections (STIs) and HIV has effectively over-ridden its family planning function, the researchers advised that programmes and policies should now include married couples among their target audiences. (Married women are among the most vulnerable to HIV infection, and are often unable to negotiate condom use with their husband.) Findings so far suggest that, while behaviour is slowly changing, there remains considerable potential for increasing condom use within stable relationships. Recommendations were also made for a refocusing of social marketing campaigns to ease the stigma of condom use within marriage and long-term partnerships.

Other work completed in 2003, using Demographic and Health Survey (DHS) data on contraceptive choice from 16 developing countries, further reinforces the above policy recommendations. It was found that a massive shift from more effective birth control pills to less effective condom use would not jeopardize the family-planning goal of reducing unintended pregnancies and abortions. Furthermore, such a shift will have the added benefit of preventing HIV/AIDS, especially in countries with generalized HIV epidemic.

Using DHS data for 495 000 women from 47 developing countries, work was also undertaken to estimate trends and levels of childlessness, and primary or secondary infertility.

#### *Selected highlights:*

- Research papers presented at the IUSSP seminar indicate that educated young African couples are using condoms with some consistency, suggesting that condom use within marriage may gain increasing social acceptance. Findings from South African studies also demonstrate that the second most powerful indicator of condom use within marriage, after education, is a woman’s perceived risk of infection from her spouse.
- A study in Senegal demonstrates that the implementation of a six-question checklist for family planning providers to rule out pregnancy significantly reduced the number of non-menstruating women turned away from family planning services from 10% to 4%.
- Research on users’ perspectives was published in 19 national or international journals.
- In 2003, three new research projects on quality of care were launched.

### **Research on the development of improved and new methods for fertility regulation**

The key objective of the Programme’s research in this area is to broaden the choice of contraceptive methods for users and potential users, by improving existing approaches and technologies, and by developing entirely new ones. The Programme has successfully collaborated with other funding partners and with the private sector to identify research and development needs and to design and execute relevant research in the field of fertility regulation.

The Programme pursues high-priority leads for novel, innovative methods that are easier to use, simplify service delivery, are associated with fewer and less severe side-effects, and respond to the needs of users, including men. The Programme’s goals link this work to subsequent large-scale trials determining safety and efficacy. Behavioural and acceptability research is also conducted, as appropriate

#### *Selected highlights:*

- Results of the Phase II trial of the male contraceptive, based on monthly injections of testosterone undecanoate, were published in 2003. Data demonstrate a failure rate of 5.2 per 100 couple-years of use. No significant adverse events or safety concerns were reported, illustrating the potential for this regimen as a safe, effective, acceptable and reversible male contraceptive method.
- Interim analysis of the ongoing Phase III trial of testosterone undecanoate, the first-ever Phase III trial of a male hormonal contraceptive method, suggests that failure to respond adequately to the regimen may be more common than indicated in the Phase II trial, although the response rate is in an acceptable range.
- A large multicentre study in China, involving nearly 5000 women and 32 centres, further confirmed the efficacy and safety of a low dose of mifepristone (10 mg) when used for emergency contraception.
- Phase I clinical trials and supplementary animal safety studies of a totally new method of contraception based on the production of an immune response against human chorionic gonadotrophin (hCG) are scheduled to begin in 2004 subject to availability of funds. The GMP batch of the matrix formulation of the hCG immunocontraceptive has been prepared and approved for release by drug regulatory authorities in Sweden for Phase I trials.
- A product development plan was drawn up as part of a collaborative strategy involving WHO, NIH, CONRAD, the Concept Foundation and industry for the further development and preclinical and clinical evaluation of

levonorgestrel butanoate as a three-monthly injectable contraceptive for women.

- Studies to determine the mechanism of action of levonorgestrel in emergency contraception indicate that the pregnancy-prevention effect is mainly due to inhibition of ovulation.
- The collaborative initiative between the Programme and the Rockefeller Foundation for basic research in implantation has completed its fifth and final year. Discussions with industry have led to the formulation of a number of collaborative research and development plans. Final reports of the research undertaken in the six centres participating in the initiative over the past five years will be published in scientific journals.

### Research on safety and effectiveness of contraceptives

Research on the safety and effectiveness of existing methods of contraceptives forms an important part of the work of the Programme. Most information on the safety and effectiveness of contraceptive methods comes from studies conducted in developed countries or from research conducted on carefully screened and monitored groups of users. The safety profile under actual conditions of use may be very different, however, making it difficult to extrapolate results to developing countries. Therefore, the overall research objectives in this area are: (i) to collect evidence on the safety and efficacy of contraceptives with particular emphasis on developing countries; and (ii) to address priority unanswered questions on existing methods of fertility regulation when used in developing countries.

#### Selected highlights:

- Research continued on the safety and effectiveness of the levonorgestrel-releasing intrauterine device and on the long-term safety and effectiveness of the TCU 380A intrauterine device.
- A multicountry study was launched on the comparative clinical performance of two second-generation implantable progestogen-only contraceptive methods, Implanon and Jadelle.
- A review of evidence suggesting an association between cervical cancer and long-term use of combined oral contraceptives continues.

### Promoting family planning norms and tools

The overall objective of this area of work is to create evidence-based and consensus-driven guidance to support the provision of high-quality family planning services globally.

#### Selected highlights:

- The third edition of *Medical eligibility criteria for contraceptive use*—a guide for policy-makers, family planning programme managers and the scientific community—was prepared. Whereas its counterpart, *Selected practice recommendations for contraceptive use*, addresses *how* to use contraceptive methods and offers guidance on common clinical issues, the *Medical eligibility criteria for contraceptive use* addresses *who* can safely and effectively use contraceptive methods.
- Field-testing was under way of the *Decision-making tool for family planning clients and providers*, an interactive tool which provides assistance in the choice of the most appropriate method of contraception. This tool includes guidance on dual protection for those at risk of both pregnancy and STIs, including HIV.
- Development of a handbook for health care providers, which will serve as a companion guide to the *Decision-making tool for family planning clients and providers* continues. This tool is intended to give in-depth information on how to provide high-quality family planning services.
- A system was developed for ensuring that family planning guidance is created, and maintained, based on the best available evidence. This system includes a continuous and comprehensive process of identifying, critically appraising, and synthesizing new evidence as it becomes available.

### MAKING PREGNANCY SAFER

One of the most striking examples of health inequality in the world is the state of maternal-newborn health. Today, a woman in the poorest countries has a risk of dying of pregnancy-related causes that is higher than that risk was 100 years ago in wealthy countries. Furthermore, the disparity in maternal deaths between rich and poor countries is startling. Nearly 90% of maternal deaths occur in Asia and sub-Saharan Africa, while less than 1% occur in the developed countries.

The Making Pregnancy Safer (MPR) initiative represents WHO's contribution to the global safe motherhood movement. The United Nations Millennium Declaration has set targets which include reducing the maternal mortality ratio by three-quarters, between 1990 and 2015, and achieving a two-thirds reduction in under-five mortality by 2015 by reducing, inter alia, the number of newborn deaths.

The work of the Department in this area consists of: (i) conducting research to map effective interventions and to improve the quality of services (see below *Generating new evidence for maternal and perinatal health*); and (ii) providing normative guidance and technical support to countries for the development, implementation and evaluation of cost-effective

tive interventions to reduce maternal and newborn morbidity and mortality (see below *Implementation of evidence-based programmes*).

Regions and countries are heavily involved in discussions on the future work of the global Making Pregnancy Safer initiative in order to assure that WHO's plans, structures, and commitments are responsive to their identified needs and constraints. Despite severe funding shortages faced by the Department in 2003, much progress was made in achieving country objectives by fostering closer collaboration and coordination with other United Nations agencies and partners. In 2003, WHO became host to the Secretariat of the Partnership for Safe Motherhood and Newborn Health.

### Generating new evidence for maternal and perinatal health

The objective of research in this area is to provide up-to-date epidemiological data on maternal and perinatal health conditions and offer solid evidence on the effectiveness of interventions and treatments that will significantly improve maternal and newborn health worldwide. The Programme expects to continue playing a leading role in this endeavour, as demonstrated by its landmark global achievement in 2003—the completion, as planned in 1997, of the first WHO Programme of Work for Maternal and Health Research 1998–2003, with an impressive 90% implementation rate for 108 research activities conducted throughout the world during this time period.

The Department's recent initiative, "From Research to Action," with its emphasis on nutritional interventions during pregnancy and strategies to prevent postpartum haemorrhage, continues to impact positively on the quality of maternal-newborn health in more than 14 countries.

Two comprehensive, new initiatives on a global scale began in 2003: a global collaboration with funding agencies and academic institutions worldwide to develop fundamental and clinical research for the prevention of pre-eclampsia; and the WHO Global Survey for Monitoring Maternal and Perinatal Health which began in Africa and Latin America in 2003, and will encompass 56 countries on all continents by the year 2005. By that time, data from over 400 000 deliveries, occurring in over 1000 randomly-selected facilities worldwide, will have been collected.

#### *Selected highlights:*

- In 2003, several research projects were completed. These included the calcium supplementation trial for the prevention of pre-eclampsia, which included two ancillary studies involving 8338 women, and the systematic review of maternal morbidity in developing countries, which included data from over 4000 publications. In addition, two conceptual documents requested by major international agencies to guide their institutional strategies in maternal and perinatal nutrition were published. A similar document on the future of maternal and perinatal health research was prepared for the 25<sup>th</sup> anniversary of the United Kingdom National Perinatal Epidemiology Unit; all of these position papers are contributing to the global research agenda for the next decade.
- Considerable efforts were made to disseminate the results of previous research and secondary analyses of data collected in the context of several trials. In 2003, 21 publications were produced. The primary results of the trial evaluating a strategy to reduce unnecessary caesarean sections will be published in 2004, together with reports on women's and providers' perceptions of care and the economic evaluation of interventions tested in the context of the WHO Caesarean Section Trial and the WHO Antenatal Care Trial.
- Implementation of recommendations underscored in the initiative "From Research to Action" is under way in Argentina, Australia, Bolivia, Brazil, Chile, Cuba, Ethiopia, Haiti, Oman, Pakistan, Spain, Syria, Thailand, and Zambia. In the Latin American and Caribbean region, the new model of antenatal care is now being promoted by the WHO Regional Office for the Americas in 11 focal countries.
- Eight new specific projects were initiated, including four randomized clinical trials to evaluate therapeutic and preventive interventions during pregnancy together with two ancillary studies, a study to develop a diagnostic tool for birth asphyxia at community level, and an initiative on maternal and newborn health and poverty.

### Implementation of evidence-based programmes

During 2003, the Making Pregnancy Safer team extensively consulted with regional and country focal points to finalize the Making Pregnancy Safer strategy. Intensive work to refine the strategy has sharpened WHO's focus and contribution to assist Member States to galvanize broad-based political support in order to strengthen existing efforts and programmes for maternal and newborn health. The strategy was finalized following consultations with regional office staff at the Second Global Team Meeting of Making Pregnancy Safer held in May 2003.

The strategy outlines evidence-based guidance on what countries, international agencies, and other partners can do to address the huge global disparities in maternal and newborn health and help reduce morbidity and mortality in this area. In particular, the strategy promotes access for all pregnant women and their newborn, particularly poor and underserved populations, to a "continuum of care" for pregnancy, birth and the postnatal period. The Department's Scientific and Technical Advisory Group in 2003 recommended activities to promote, intensify and coordinate work in this area. Projects, involving technical support provided by Making

Pregnancy Safer teams from WHO headquarters, regional and country offices at the policy and strategy level, as well as at the maternal and newborn health programme development and implementation level, are under way in 82 countries.

Despite severe funding constraints, much was accomplished in 2003. A significant number of key guidance tools were finalized, translated and published, and are being used by countries throughout the world. Other major tools which address policy, strategy, clinical services, training and advocacy are near completion. Future efforts will continue to shift from development of guidance towards greater support to countries. Still, work will need to continue to strengthen the evidence base to assure that WHO continues to provide the most up-to-date information and guidance in the field.

#### *Selected highlights—development of tools and guidelines:*

- The Integrated Management of Pregnancy and Childbirth is a comprehensive set of tools designed to provide guidance to countries for improving maternal and newborn health. An overview of the tools is regularly updated on the Department's web site. *Managing complications in pregnancy and childbirth: a guide for midwives and doctors* is being used in several countries to improve national standards of emergency obstetric care. Translations into Chinese, Lao, Mongolian, Spanish, and Vietnamese were completed in 2003. By 2004, the guide will be available in over 10 languages, including French, Arabic and Portuguese. The companion guide, *Managing newborn problems: a guide for doctors, nurses and midwives* was endorsed by UNFPA, UNICEF, the World Bank, FIGO, the International Pediatric Association and the International Confederation of Midwives. *Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice* was endorsed in 2003 by UNFPA, UNICEF, and the World Bank. Its adaptation is under way in Africa and the Western Pacific. Validation studies were conducted in Brazil in 2003 and similar studies are planned for Sudan and Uganda.
- During 2003, the Making Pregnancy Safer team worked closely with the WHO Roll Back Malaria (Malaria in Pregnancy) team and the WHO Regional Office for Africa to finalize a tool provisionally entitled *A policy framework for malaria prevention and control during pregnancy in the African Region*. This tool provides policy-makers and national programme managers with guidance on prevention and case management of malaria in pregnant women (the main adult target group in Africa).
- *Kangaroo mother care: a practical guide* is being translated into several languages—Albanian, Bengali, Bahasa Indonesia, Japanese, Portuguese, and Vietnamese.
- Tools finalized and ready for printing and/or field-testing include: *Handbook for communication and counselling*

*with pregnancy, childbirth, postpartum and newborn care: a guide for essential practice* (field reviews in Malawi and the Philippines); *Beyond the numbers: reviewing maternal deaths and complications for making pregnancy safer* (regional facilitators are being trained in South-East Asia and Africa); the revised WHO midwifery education modules; the *Strengthening midwifery toolkit*; the *Reference guide on HIV-related care and support to women and children*.

- Major tools in the final stages of development included (provisional titles): *Standards for maternal and neonatal care*; *Antenatal care reference guide*; *Making pregnancy safer education and training strategy*; *Making pregnancy safer planning guide*; *Human rights assessment tool for maternal and neonatal health: a multisectoral approach for improving laws, policies and standards of care*; and on CD-ROM, *Making pregnancy safer essential health technology package*.

#### *Selected highlights—technical support to countries:*

- In Africa, a major achievement of 2003 was the establishment or strengthening of Making Pregnancy Safer/ Safe Motherhood national task forces or partner coordination committees. Task forces are meeting routinely in Ethiopia, Mauritania, Mozambique, Nigeria, and Uganda and efforts are being intensified to revitalize similar task forces in the other countries of the region.
- During 2003, the WHO Regional Office for the Americas provided intensive technical assistance to priority countries (Bolivia, Brazil, Dominican Republic, Ecuador, El Salvador, Guatemala, Guyana, Haiti, Honduras, Nicaragua, Paraguay, and Peru) to operationalize the regional strategy for maternal morbidity and mortality reduction at national and local levels.
- In the WHO Eastern Mediterranean Region, technical and financial support has been maintained to strengthen and expand Making Pregnancy Safer strategies in priority countries such as Afghanistan, Djibouti, Iraq, Pakistan, Somalia, Sudan, and the Republic of Yemen.
- Other notable accomplishments in 2003 include: increased numbers of midwifery students in Sudan; upgrading of skills in emergency and obstetric case management, particularly in rural and remote areas in Afghanistan, Djibouti, Somalia and the Sudan; improving health care providers' skills in neonatal resuscitation and control of newborn infections, as well as emergency obstetric and gynaecology services in Syria; review of the Safe Motherhood strategy and programme in Morocco and in two provinces in Yemen; and undertaking a national survey on perinatal health care in Syria.
- Introduction of the Making Pregnancy Safer strategy was continued in 10 priority countries in the European

Region (Albania, Armenia, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Romania, Russian Federation, Tajikistan, Turkmenistan and Uzbekistan). Azerbaijan, Macedonia, Poland and Turkey have requested introduction of the strategy in 2004–2005.

- Initial orientation and planning meetings involving staff from the Ministry of Health, key stakeholders, and partners were held in 2003 in all 10 priority countries. National plans of action were developed, including training of trainers, supervisors, top-level clinicians and decision-makers, and the building-up of model sites.
- Full support for Making Pregnancy Safer was achieved at policy level in most of the 10 countries of the European region. In Uzbekistan, outdated laws that constitute a barrier to implementing evidence-based care will be substituted with a new legal framework.
- In the South-East Asia region, special emphasis has been placed on promoting skilled birth attendance, especially in Bangladesh, India, Nepal, and Timor Leste.
- In October 2003, SEARO together with WPRO, UNICEF and UNFPA organized a bi-regional workshop, 'Progress on maternal mortality reduction', at which high-level government officials and major partners reviewed progress and shared lessons learnt.
- The Government of India launched, together with SEARO, a "National Safe Motherhood day" on 11 April 2003. This has provided crucial political commitment to the agenda of safe motherhood—not only in India but also in other countries in the region.
- The Making Pregnancy Safer web site <[www.who.int/reproductive-health/MNB/index.htm](http://www.who.int/reproductive-health/MNB/index.htm)> was further developed in 2003. Another web site has also been set-up, with detailed information about WHO activities in making pregnancy safer in the European region: <[www.who.dk/pregnancy](http://www.who.dk/pregnancy)>.

## CONTROLLING SEXUALLY TRANSMITTED AND REPRODUCTIVE TRACT INFECTIONS

The key objectives of the Controlling Sexually Transmitted and Reproductive Tract Infections team are: (i) to increase the availability of high-quality, culture- and gender-sensitive and non-stigmatizing services for the prevention, care and management of sexually transmitted infections (STIs) and reproductive tract infections (RTIs) and their complications; (ii) to broaden the range of safe, effective and affordable methods to prevent and manage STIs and RTIs and mother-to-child transmission (MTCT) of HIV and STIs; and (iii) to contribute to the strengthening of national health system capacity to deliver these services.

### Selected highlights:

- An updated global strategy for STI prevention and control that reflects recent evidence and experience in STI control and its impact on the HIV epidemic is ready to be presented and discussed at a series of regional and international consultations. A strategy for the elimination of congenital syphilis and control of syphilis in the general population is under development.
- A package of guidelines and tools that will assist programme managers to plan and implement effective and appropriate interventions to prevent, control and manage STIs and RTIs was compiled. The package includes: Programme guidance tool for sexually transmitted and reproductive tract infections (under development); the *Sexually transmitted and other reproductive tract infections: a guide to essential practice* (in press); the *Guidelines for the management of sexually transmitted infections*; *Training modules for the management of sexually transmitted infections*; and a new guide, *Comprehensive cervical cancer control: a guide to essential practice*.
- Updated *Male latex condom specification and guidelines for condom procurement* was published to improve the quality of condoms manufactured and used in countries for STI and HIV prevention.
- Azithromycin was included on the WHO *Model list of essential medicines* for the treatment of genital Chlamydia infection and trachoma, as part of the strategy to improve access to and sustainability of drugs required for STI control at country level.
- The contraceptive effectiveness of the female condom compared with the male condom is being assessed in over 1000 volunteers from family planning clinics in China, Nigeria, Panama and South Africa.
- A project to assess the comparative efficacy of male and female condoms against exposure to sexually transmitted pathogens is scheduled to start in 2004.
- In partnership with CONRAD, the Programme successfully concluded a three-centre, randomized double-blind Phase I study of the safety and acceptability of 6% cellulose sulfate gel compared with placebo (K-Y Jelly) among healthy women volunteers in India, Nigeria, and Uganda. Further evaluation of cellulose sulfate for the prevention of HIV infection is now warranted.
- The WHO-CONRAD *Manual for the standardization of colposcopy for the evaluation of vaginal products* was updated. This is a central technique in the safety assessment of topical microbicides developed to fight STIs/HIV.

- A protocol was finalized and cleared to study the impact of a triple-combination antiretroviral prophylactic therapy on the rate of mother-to-child transmission (MTCT) of HIV. The study is a response to the critical issue of safe breastfeeding for women who are HIV positive.

### PREVENTING UNSAFE ABORTION

Approximately 19 million unsafe abortions occur worldwide each year, resulting in many tragic consequences. The two main objectives of the Programme's work in this area are preventing unsafe abortion and its consequences, and improving the safety of current abortion procedures and postabortion care. To this end, the workplan focuses on generating scientifically sound evidence for providers and policy-makers to enable them to make informed decisions about implementing best practices and resource allocation.

Projects include documentation of global and regional levels of unsafe abortion and associated morbidity and mortality, social science research to better understand the pathways to safe and unsafe abortion, clinical trials to evaluate medical abortion techniques, the development and implementation of guidelines for safe abortion, and technical support to countries to improve abortion care.

#### *Selected highlights:*

- New global and regional estimates of unsafe abortion-related mortality became available in 2003 and show that 68 000 women die each year due to unsafe abortion, while another five million women suffer temporary or permanent disability.
- Recent studies indicate that abortion and contraceptive use may increase concurrently in countries where fertility rates are rapidly declining and family planning services are unable to meet the growing demand for contraceptives.
- Age patterns of unsafe abortion vary by region. In Africa, for example, nearly 60% of unsafe abortions occur in women less than 25 years of age, while in Asia, 50% of all unsafe abortions occur in women 25–35 years of age.
- The systematic review of medical methods for first trimester abortion shows that combined regimens are more effective than single agents. In the combined regimen, the dose of mifepristone can be lowered to 200 mg without significantly affecting the method effectiveness.
- The Programme is planning a conference in Bellagio, Italy, in 2004 to reach a consensus on the optimal regimen for medical abortion and the service requirements for the provision of this method.

- The Programme continues to assist countries with improving the quality of abortion services, including counselling, in Romania and Viet Nam, and it assisted the Ministry of Health of Mongolia in conducting a strategic assessment of issues related to abortion. In all three countries, Ministries of Health are implementing recommendations resulting from the strategic assessments.

- *Safe abortion: technical and policy guidance for health systems* was released in 2003 and distributed to Ministries of Health through WHO regional offices. This document is in high demand and is being translated into French, Polish, Portuguese, Russian and Spanish.

### PROMOTING SEXUAL AND REPRODUCTIVE HEALTH OF ADOLESCENTS

The objective of the Department's work in this area is to generate evidence to promote healthy sexual development and maturation and to strengthen the capacity of adolescents to have equitable and responsible relationships. Activities primarily focus on supporting research and developing the evidence base on the sexual and reproductive health situation, needs, and perspectives of adolescents in developing countries. Related to this work are activities intended to strengthen national capacity for research in this area and dissemination of findings.

#### *Selected highlights:*

- Sixty papers detailing WHO's social science research initiative on adolescent sexual and reproductive health were published in national or international journals and results from selected studies were presented at international seminars or conferences.
- Analysis of Demographic and Health Survey (DHS) data for never-married young women in Colombia and Peru showed that during the 1990s, condom use rose dramatically, becoming the first most commonly-used method in Colombia and the second in Peru. While use of contraceptives, especially condoms, increased, there was an even greater rise in sexual activity among young, never-married women in the two countries, resulting in unintended pregnancy and abortion.
- Small-scale focused studies (13) from Latin America, supported under current research initiatives, show the persistence of double standards for men and women, lack of sexual communication and negotiation, and negative social norms which constrain a young person's access to sexual and reproductive health services.
- Results from an operations research project in Benin, Côte d'Ivoire, Cameroon, Guinea and Senegal show that reproductive health services, especially those in

the public sector, are beyond the reach of most young people for a number of reasons: cost, negative attitudes of providers, and prevailing societal values against sexual activity outside marriage.

- The network of investigators engaged in adolescent research was provided continued assistance in developing papers for presentation at conferences and for submission to journals.
- Core instruments developed for the study of adolescent sexual risk behaviours (focus group discussion guidelines, in-depth interview guides and a survey questionnaire) and an annotated bibliography of relevant materials were provided to a large number of researchers. These tools are available on the Department's web site.
- Ongoing research projects include: investigating the extent to which hormonal contraception suppresses peak bone mass in adolescents; factors underlying reports of unusually high levels of lower genital tract infection among pre-adolescents in Mongolia; and the reproductive health needs of young migrants in the Greater Mekong region.
- The unique needs of adolescents are highlighted in tools and guidelines developed by the Department to promote reproductive health.
- A meeting was organized jointly with the Population Council (New Delhi) and the Family Health International/YouthNet project to review the evidence on non-consensual sexual experiences among young people in developing countries and to identify research and intervention priorities and appropriate methodologies.
- Collaboration continued with the WHO Department of Child and Adolescent Health and Development (CAH) in a number of activities, including joint planning of meetings and review of documents.

## GENDER AND REPRODUCTIVE RIGHTS IN REPRODUCTIVE HEALTH

The Department's objectives are: (i) to develop and evaluate strategies and mechanisms for promoting gender equality and human rights in reproductive health research, programming and technical support; (ii) to support countries to ensure that reproductive health programmes and policies respect, protect and fulfil human rights and promote gender equity and equality; and (iii) to ensure that the promotion of gender equity and equality and human rights principles are integrated into the Department's work.

### Selected highlights:

- A validation study of the *Health and human rights policy action tool* was finalized and prepared for field-testing in Brazil and Mozambique.
- The Department participated in the development of a framework for indicators that can be used to measure governments' progress in fulfilling their human rights obligations relating to health.
- *Transforming health systems: gender and rights in reproductive health*, a 3-week training curriculum for health managers, was produced on CD-ROM. The Spanish translation was published in August 2003.
- The Ministry of Health and the WHO Office in Myanmar conducted a two-week training course on Gender and rights in reproductive health, adapted from the WHO curriculum noted above. Similar courses are planned for Kazakhstan and the Sudan in 2004.
- The Department provided, to four United Nations Treaty Monitoring Bodies, information on the sexual and reproductive health situation in 10 countries that were required to report to the Treaty Bodies about their adherence to various rights-related international treaties. The Department also contributed to reports made by the Department on Child and Adolescent Health and Development on three countries reporting to the Convention on the Rights of the Child.

## PROMOTING SEXUAL HEALTH

The goal of the new cross-cutting area of sexual health is to promote optimal sexual health and an affirmative view of sexuality for women, men and young people. The Department will focus on: (i) building the evidence base for high-quality, non-discriminatory, acceptable and sustainable sexual health education and service programmes; and (ii) increasing knowledge and understanding of the social and cultural factors related to harmful sexual practices in order to develop strategies to abolish such practices.

### Selected highlights:

- In 2003, the Department elaborated a Medium-term Programme of Work on sexual health and began to develop a conceptual framework on sexual health based on extensive consultation within and outside WHO, which will be published in the planned sexual health document series in 2004.
- *Integrating sexual health into reproductive health programmes* was finalized for publication, with assistance from scientists from the Royal Tropical Institute (KIT) Amsterdam, Netherlands, and the London School of Hygiene and Tropical Medicine, London, United Kingdom.

- A research methods design workshop was held in Bangkok, Thailand, as a first step in the planning of a multicountry study on gender, sexuality and vaginal practices.

## TECHNICAL COOPERATION WITH COUNTRIES

### Overview of activities—inter-regional activities and collaboration with WHO Regional Offices

The main objectives in the area of technical cooperation with countries are: (i) to assist developing countries in identifying priority areas where research is required to address reproductive health needs; (ii) to support national planning and programming, including the introduction of reproductive health technologies and the adaptation and application of practice guidelines essential for improving reproductive health; (iii) to provide assistance to developing countries to strengthen their capacity to undertake research, and to disseminate and apply results of reproductive health research; and (iv) to collaborate with countries in the monitoring of effects of policies and initiatives related to health sector reforms on reproductive health programmes and outcomes.

#### *Selected highlights:*

- With support from the Programme and from national and international sources, 761 research projects are currently under way in collaborating research institutions. A total of 736 research articles were published, and/or disseminated through congress abstracts presented at national, regional and international scientific events.
- A total 27 institutions (or national research coordinating committees) were receiving support through either Long-term Institutional Development grants or through Resource Maintenance Grants. Research Training Grants were awarded to 24 scientists from these institutions, most of whom received their training within their respective regions.

### The WHO Regions of Africa and the Eastern Mediterranean

The main objective in the African and Eastern Mediterranean regions is to build and develop the research capacity of institutions in order to enhance their potential to implement reproductive health research relevant to national and regional needs and to facilitate their participation in the global research effort.

In 2002–2003, the Programme collaborated with 47 institutions or research groups in 28 countries in these two regions. Seven institutions received Long-term Institutional Development grants, and three received Resource Maintenance Grants.

#### *Selected highlights:*

- A total of 129 studies were carried out by the 10 centres receiving Long-term Institutional Development grants or Resource Maintenance Grants. From these 10 centres, 45 studies were published in national and international journals, and staff of these centres served in 52 different advisory roles at national, regional and international levels.
- Data collection for the study on obstetric sequelae of female genital mutilation (FGM) was completed in six countries and preliminary analyses were carried out. Three proposals on sociocultural aspects of FGM were approved and a grant from the European Commission was received for research on decision-making related to FGM and for developing and implementing models for fighting against this practice.
- A protocol for the operations research project “Community and facility-based interventions towards improving maternal and newborn health” was approved.
- Support was given to the Department of Obstetrics and Gynaecology, University of Harare, Zimbabwe, to conduct a workshop on cervical cancer screening by visual inspection with acetic acid (VIA) and to pilot-test in district hospitals in five countries this promising method for identifying high-grade precancerous lesions.
- Support was given to the African Task Force of Reproductive Health, and to 74 participants in workshops and courses on research methodology, semenology and operations research.
- Operations research on improving reproductive health services for adolescents continued in Benin, Cameroon, Côte d'Ivoire and Guinea and was completed in Senegal.
- An operations research training initiative for French-speaking African countries was launched in collaboration with FRONTIERS, and the first orientation workshop was held in Bamako, Mali for decision-makers, programme managers and researchers from six countries.

### The WHO Region of the Americas

Collaboration was under way with seven institutions in the Region of the Americas which are conducting an impressive number of research projects—187 studies conducted during 2002–2003—on topics relevant to regional and national reproductive health problems.

#### *Selected highlights:*

- Of the 187 projects, only 15% received direct funding support from WHO, indicating an increased reliance on

national funding sources and support from other international agencies.

- Nineteen staff from regional centres underwent training outside their home countries, and the seven centres receiving research capacity-strengthening support (in the form of Resource Maintenance Grants) trained 847 professional and technical staff from other local institutions. Sixty-two fellows participated in formal courses and 4006 attended short, group-learning activities such as seminars and workshops organized by the centres.
- During 2002–2003, a total of 299 research articles, including 268 original papers and 31 review articles, were published and 77 books and book chapters were authored by staff from the centres receiving research capacity-strengthening support.
- A national workshop attended by researchers, policy-makers and other stakeholders (most from regions where maternal mortality ratios are high) was organized in Buenos Aires, Argentina in December 2003. Researchers addressed the two main contributors to maternal mortality: hypertensive disorders of pregnancy and postpartum haemorrhage. Workshop participants agreed to utilize recommended practices learned at the workshop and meet within the year to discuss the degree to which services offered to pregnant women have been optimized in their hospitals.

### The WHO Regions of South-East Asia and the Western Pacific

An integral part of the Programme's work to improve reproductive health in the WHO Regions of South-East Asia and the Western Pacific is the continued development of relevant skills for enhancing national leadership, priority-setting, advocacy, communication, networking and negotiation, and the use of research results and partnerships. To achieve these objectives, the Programme continues to help developing countries build and maintain networks, and enhance their capacity to identify their needs for improving national reproductive health research through institutional development and training grants. These activities should result in greater participation in national, regional and global research, in accordance with the highest scientific and ethical standards, as well as increased dissemination and application of the results of reproductive health research to national policies and programmes.

#### *Selected highlights:*

- Efforts to build and maintain networks in research and training continued. Research links were strengthened between Prince Henry's Institute of Medical Research, Melbourne, Australia and the Shanghai Institute of Planned Parenthood Research, Shanghai, China.

Research training initiatives involved collaboration between universities in Galle, Sri Lanka and Münster, Germany.

- Six centres in five countries were receiving support through Long-term Institutional Development grants and 13 centres in four countries were receiving Resource Maintenance Grants.
- A regional research initiative, "Adolescent migrants and reproductive health in the Greater Mekong Region", brought together researchers from social research centres in China, the Lao People's Democratic Republic, Thailand and Viet Nam. Another multicentre regional project, "Patterns and predictors of caesarean section in Asia", involved 13 centres from 10 countries.
- Partnerships were forged on a regional or international level with the Forum for Ethical Review Committees in Asia and the Western Pacific (FERCAP) for training researchers on ethical issues in research; with the Population Council, Regional Office, Asia, on operations research training; and with the Fudan University School of Public Health, Shanghai, China, and the Geneva Foundation for Medical Education and Research, Geneva, Switzerland, to conduct training courses on reproductive health in China.

### Central and Eastern Europe, including the Newly Independent States and Central Asian Republics

The WHO European Health Report of 2002 stated that an East-West health divide has opened up in the European Region with a significantly worsening situation in the East. Recent surveys indicate some disturbing trends common to countries of Central and Eastern Europe and Newly Independent States: (i) levels of maternal death up to five times higher than in the West despite universal health coverage; (ii) emerging HIV/AIDS epidemic due to an explosion of STIs, intravenous drug use, growing sex trade, and increased sexual contact among young people; (iii) reliance on repeat abortions as a means of birth control; (iv) persistently high unmet needs for modern contraception.

Furthermore, with population size shrinking or stalling due to very low birth rates, some policy-makers in the European Region now consider family planning unnecessary or counterproductive.

The Programme's main objectives in the European Region are: (i) to strengthen national capacity in reproductive health research, with particular focus on providing training opportunities for Central and Eastern Europe, Newly Independent States and Central Asian Republics; and (ii) to assist the WHO Regional Office for Europe (EURO) in providing technical support to countries to implement reproductive health programmes.

*Selected highlights:*

- The third meeting of the European Regional Advisory Panel, held in Estonia in August 2003, deliberated three main issues: (i) research and capacity building; (ii) continued information dissemination through the magazine *Entre Nous*; (iii) support to EURO to implement its strategy for sexual and reproductive health, including adaptation of the WHO gender and rights in reproductive health course (*Transforming health systems: gender and rights in reproductive health*).
- The second WHO/Frontiers course on operations research, held at the Kazakhstan School of Public Health in April 2003, focused on Russian-speaking countries. Several research proposals emanating from this course are being reviewed for possible funding.
- Technical and financial support was provided to the 11<sup>th</sup> session of the postgraduate course on reproductive medicine and reproductive biology, organized annually by the WHO Collaborating Centre, University of Geneva, Geneva, Switzerland.

**Policy and programmatic issues**

The Department's objectives in this area are to review, develop and test methodologies to assist countries in the planning and implementation of reproductive health services and to provide technical support to countries. Central to this work are the testing, refinement and promotion of the Strategic Approach to improve the quality of care of reproductive health services.

The Strategic Approach is a three-stage process to assist national-level decision-making to improve the quality of care of reproductive health services. Stage I strategic assessments examine users' needs and perspectives, available technologies and services and the capacity of the service delivery system, so as to determine appropriate strategies for improving the quality of care. Stage II involves policy development and action research to design and test optimal models for introducing or reintroducing health services or technologies. Stage III uses research results and lessons learned in Stage II for policy and programme development and the scaling-up of activities.

*Selected highlights:*

- Work began on a new, easily adaptable field guide for implementing all three stages of the Strategic Approach. This new document will supplement the existing guide that focuses on contraceptive introduction.
- In 20 countries throughout the world, continued adaptation of the Strategic Approach is helping to address

a wide range of reproductive health issues. A strategic assessment of comprehensive, integrated reproductive health services that emphasizes access to and utilization of services by the poor was completed in Yunnan, China, and will soon take place in Rajasthan, India. A strategic assessment of abortion-related issues was conducted in Mongolia. An assessment focusing on maternal and newborn health will take place in Paraguay in early 2004. In Nigeria, an assessment of adolescent reproductive health issues is being planned.

- Stage II activities continued in China, Ethiopia, Myanmar and Viet Nam.
- Scaling-up of tested interventions is under way in Stage III activities in Bolivia, Brazil, Myanmar, Viet Nam and Zambia.
- The results of systematic reviews of available data on the safety and efficacy of IUDs and hormonal contraceptive methods, provided through China's national family planning programme, will be presented to national policy-makers in early 2004 to support their selection of the safest and most effective products for provision.
- A three-year initiative to examine the impact of health sector reforms on reproductive health services and outcomes began in 2003 in collaboration with the Women's Health Project of the University of Witwatersrand, Johannesburg, South Africa. The "Sexual Rights and Reforms Project" brings together members of nongovernmental women's health organizations from Africa, Asia, and Latin America to develop an agenda for research and advocacy on sexual and reproductive health and rights.

**Implementing best practices**

The Implementing Best Practices (IBP) initiative is a global collaborative effort, involving 20 partner agencies committed to working with regional and country health professionals to introduce, adapt (according to country needs) and apply evidence-based practices to improve access to and the quality of reproductive health services. This is implemented, inter alia, through on-site visits and an electronic communication system to facilitate in-country and country-to-country sharing of experience, best practices and lessons learnt. IBP partners undertake activities on a cost-sharing basis and are committed to providing countries with the ongoing support necessary to take guidelines into practice. The IBP Consortium is also developing a mentorship and follow-up programme.

Activities in the "WHO Programme to Map Best Reproductive Health Practices" include primary research, research synthesis, dissemination and capacity-strengthening in evidence-based decision-making worldwide.

*Selected highlights:*

- Twenty partner agencies signed a Memorandum of Understanding to form the Implementing Best Practices Consortium and developed a number of knowledge-sharing tools to support the dissemination of reproductive health best practices.
- In India, an in-country team of 11 agencies organized the IBP initiative launch in four States at a meeting involving 280 health professionals.
- The randomized controlled trial of an active dissemination strategy for evidence-based reproductive health information using *The WHO reproductive health library* (RHL) was completed. Results will be available in 2004.
- Cochrane and non-Cochrane systematic reviews covering high-priority reproductive health topics continue to form the backbone of the work on implementing best practices. Three new Cochrane reviews and five Cochrane review protocols were published. Thirteen systematic reviews were updated.
- Subscription to RHL exceeded 13 000 in 2003, and a total of 22 000 copies in English and 10 000 in Spanish were distributed.
- RHL editors and scientists from partner institutions conducted 77 RHL presentations or workshops worldwide.
- Draft manuals for the training initiative developed jointly with the WHO Regional Office for Africa and the South African Cochrane Centre were produced and a technical meeting was held to develop a similar programme in the WHO South-East Asia Region.

### MONITORING AND EVALUATING REPRODUCTIVE HEALTH

The Department's aim is to monitor progress in attaining reproductive health-related goals and targets, including the Millennium Development Goals of reduction of maternal and under-five mortality.

*Selected highlights:*

- A systematic review of global maternal morbidity and mortality for 1997–2003 was completed. More than 60 000 reports were screened, with 2500 selected for inclusion in the review. A report on the methodology of the review was submitted for publication. The global maternal mortality estimates for 2000 were released. The morbidity reports will be published in 2004.
- Global, regional and subregional estimates of the proportions of births attended by skilled health personnel were updated.
- A systematic review of the prevalence, associated factors and consequences of genital organ prolapse was completed and the report is being revised.
- A database of 17 reproductive health indicators short-listed for global monitoring was developed and published on the Department's web site in early 2003, and provides up-to-date information at the national, regional, and global levels.
- At a technical meeting, organized in collaboration with UNFPA, to measure access to reproductive health services, a set of four access indicators and future priority areas of work were identified.

### COMMUNICATION, ADVOCACY AND DISSEMINATION OF INFORMATION

The Department seeks to facilitate access within and outside the Department to reproductive health knowledge including that resulting from the Programme's work, through communication, advocacy, and dissemination of information.

*Selected highlights:*

- A total of 30 information products were developed.
- The Department's *Annual technical report 2002* was issued on a professionally-designed, interactive CD-ROM, which also includes the complete contents of the Department's web site.
- Issue No. 6 of *The WHO reproductive health library* (RHL) was produced in English and Spanish and widely distributed.
- A 10-minute training video on caesarean section was produced for inclusion in RHL No. 7.
- The Department's web site received over half a million visitors who downloaded more than one million files.
- A new training component on research proposal writing was developed and tested in a scientific writing workshop conducted in Chiang Mai, Thailand, at which 37 scientists were trained.
- Training material for a new scientific writing workshop dedicated to social science research was developed and tested in collaboration with FRONTIERS (Population Council).

## CLINICAL TRIALS AND INFORMATICS SUPPORT

This group provides statistical and data processing support for all multicentre and some single-centre research projects undertaken by the Programme. The group also provides support to research capability strengthening in collaborating institutions by offering technical expertise, as needed, to strengthen data processing procedures and policies and to refine the application of biostatistics in research studies and clinical trials.

### *Selected highlights:*

- Methodological research on statistical issues related to the meta-analysis of observational studies, and work on guidelines for the reporting of clinical trials continued.
- Support was provided to 64 single- and multicentre research projects.
- Staff from the group supervised data collection and monitored data quality at several collaborating centres in Egypt, South Africa, and the Sudan that are participating in international multicentre studies.
- Editing of Standard Operating Procedures, drafted for implementation of WHO's Good Clinical Practice guidelines in all of the Programme's research activities, was completed.

## Annex 1

## SCIENTIFIC AND TECHNICAL ADVISORY GROUP IN 2003

## Members

Lawrence Adeokun, Association for Reproductive and Family Health, Ibadan, Nigeria  
 Yagob Y. Al-Mazrou, Assistant Deputy Minister, Ministry of Health, Riyadh, Saudi Arabia  
 John Cleland, London School of Hygiene and Tropical Medicine, University of London, London, United Kingdom  
 Jock Findlay, Prince Henry's Institute of Medical Research, Clayton, Australia (*Chairman*)  
 Anna Glasier, Lothian Primary Care NHS Trust, Edinburgh, United Kingdom  
 Barbara Hulka, University of North Carolina, Chapel Hill, NC, USA (*Vice-chairperson*)  
 Nasreen Huq, ActionAid Bangladesh, Dhaka, Bangladesh  
 Angela Kamara, Regional Prevention of Maternal Mortality Programme, Accra, Ghana  
 Salim Abdool Karim, University of Natal, Durban, South Africa  
 Hoda Rashad, The American University in Cairo, Cairo, Egypt  
 Gaston Sorgho, Harvard School of Public Health, Boston, MA, USA  
 Reijo Vihko, The Academy of Finland, Helsinki, Finland  
 Xiao Shaobo, State Family Planning Commission, Beijing, China

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	7	54			6	46	13
Women	3	23			2	15	5
<b>from:</b>							
AFRO	3	23					3
AMRO					2	15	2
EMRO	2	15					2
EURO					3	23	3
SEARO	1	8					1
WPRO	1	8			1	8	2

## Annex 2

## SCIENTIFIC AND ETHICAL REVIEW GROUP PANEL IN 2003

Gordon Ada, John Curtin School of Medical Research, Canberra, Australia  
 Abdul-Aziz Al Meshari, King Saud University, Riyadh, Saudi Arabia  
 Karen Beattie, EngenderHealth, New York, NY, USA  
 Iain Cameron, Princess Anne Hospital, Southampton, United Kingdom  
 Jean Cohen, Paris, France  
 Andrea Genazzani, Institute of Obstetrics and Gynaecology, Modena, Italy  
 Ronald Gray, Johns Hopkins University, Baltimore, MD, USA  
 Kerstin Hagenfeldt, Karolinska Hospital, Stockholm, Sweden (*Chairwoman*)  
 Timothy Hargreave, Western General Hospital, Edinburgh, United Kingdom  
 Dwip Kitayaporn, Mahidol University, Bangkok, Thailand  
 Korrie de Koning, Royal Tropical Institute, Amsterdam, Netherlands  
 Fernando Larrea, National Institute of Nutrition, Mexico City, Mexico  
 Ruth Macklin, Albert Einstein College of Medicine, Bronx, NY, USA  
 Oscar Mateo de Acosta, National Institute of Endocrinology, Havana, Cuba  
 Marvellous Mhloyi, Population Studies Center, Harare, Zimbabwe  
 Yuji Murata, Osaka University Medical School, Osaka, Japan  
 Ngeow Yun Fong, University of Malaya, Kuala Lumpur, Malaysia  
 Charles Ngwenya, Centre for Health Systems Research and Development, University of the Free State,  
 Bloemfontein, South Africa  
 Edith Pantelides, Population Studies Centre, Buenos Aires, Argentina  
 Manee Piya-Anant, Siriraj Hospital, Bangkok, Thailand  
 Chai Podhisita, Institute for Population and Social Research, Nakhon Pathom, Thailand  
 Kazuo Satoh, Nihon University School of Medicine, Tokyo, Japan  
 John Sciarra, Northwestern University Medical School, Chicago, IL, USA  
 Carmel Shalev, The Gertner Institute for Health Policy, Tel Hashomer, Israel  
 Carlos Simon, Institute of Infertility, Valencia University, Valencia, Spain  
 Sonia Tabacova, National Centre of Hygiene, Ecology and Nutrition, Sofia, Bulgaria  
 Godfrey B. Tangwa, University of Yaoundé I, Yaoundé, Cameroon  
 Zhao Baige, National Population and Family Planning Commission, Beijing, China

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	13	46	1	3	14	50	28
Women	7	25	1	3	4	14	12
<b>from:</b>							
AFRO	3	11					3
AMRO	3	11			4	17	7
EMRO	1	3					1
EURO	1	3	1	3	7	25	9
SEARO	3	11					3
WPRO	2	6			3	11	5

## Annex 3

## TOXICOLOGY PANEL IN 2003

Colin L. Berry, The London Hospital Medical College, London, United Kingdom

Ranjit R. Chaudhury, National Institute of Immunology, New Delhi, India

Ralph Heywood, The Larches, The Lanes, Huntingdon, United Kingdom

Alex Jordan, Division of Reproductive and Urologic Drug Products, Food and Drug Administration, Rockville, MD, USA

Shirley Price, University of Surrey, Guildford, United Kingdom

Sonia Tabacova, National Centre of Hygiene, Ecology and Nutrition, Sofia, Bulgaria

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	1	17	1	17	4	67	6
Women			1	17	1	17	2
<b>from:</b>							
AFRO							
AMRO					1	17	1
EMRO							
EURO			1	17	3	50	4
SEARO	1	17					1
WPRO							



# **Section 1**

## **Promoting family planning**

# Users' perspectives in the context of reproductive health

I. Warriner and I.H. Shah

## INTRODUCTION

As part of the global effort to achieve improved levels of reproductive health through informed policies, programmes and services, understanding men's and women's reproductive health needs and preferences as well as the constraints to the use of services has become increasingly important. Perspectives and needs of users are shaped by their interactions with providers, the available reproductive health services and supplies, and their assessment of the dual risks of unintended pregnancy and sexually transmitted infections (STIs), including HIV/AIDS. Their reproductive health behaviour, including contraceptive practice and acceptability of various methods, is also influenced by the quality of the care they receive, their perceptions and attitudes, and the socio-cultural context in which people live and services are provided.

The primary focus of the Programme's work in this area is to understand better men's and women's behaviours and perspectives as users or potential users of reproductive health services or technologies, and of emerging or currently available fertility-regulating methods. The second objective is to understand the constraints and sociocultural contexts that influence users' practices, behaviours, and perspectives. The third objective is to address neglected aspects of quality of care that have an important bearing on the access to and use of reproductive health services. Findings on users' perspectives provide policy-makers and programme managers with evidence-based recommendations for improved care. These findings also indicate the acceptability of reproductive health services and technologies for both users and potential users while identifying unmet needs of clients. The work also covers selected issues related to infertility, which is an integral, but frequently neglected, part of reproductive health.

## RESEARCH ACTIVITIES

### Specific objectives of research

Research on users' perspectives aims to understand better how reproductive health decisions are made by both women and men, and it analyses perceptions about, and needs for, reproductive health technologies and services. Several projects focus on various aspects of users' perspectives, some of which are supported under a social science research initiative on quality of care.

### Progress

#### *Condom use within marriage: the untapped potential*

In a pioneering attempt to assess the interactions between family planning and risk behaviour related to HIV/AIDS, a multicountry research project has been ongoing in six eastern and southern African countries where HIV infection rates are greatest: Kenya, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe. The study is designed to address three main objectives: firstly, to determine the perspectives of sexually active individuals about the dual risks of STIs (including HIV/AIDS) and unintended pregnancy. A second objective is to gain knowledge of strategies that sexually active individuals would consider appropriate, practical and effective in coping with these risks. Thirdly, the study explores opportunities for and constraints to behavioural change.

A seminar on "Taking stock of the condom in the era of HIV/AIDS" was organized by the International Union for the Scientific Study of Population and the Department of Population Studies at the University of Botswana, in Gaborone, in July

2003 and included papers which were selected on a competitive basis. Investigators from the multicountry study presented a cluster of papers providing an overview of condom use within marriage and stable partnerships with the following range of topics: The quiet revolution: condom use within marriage in South Africa; Factors affecting condom use in primary sexual relationships in Kenya; Making inroads: the use of condoms within marriage in Uganda; and Condom use within marriages and consensual unions in Zimbabwe.

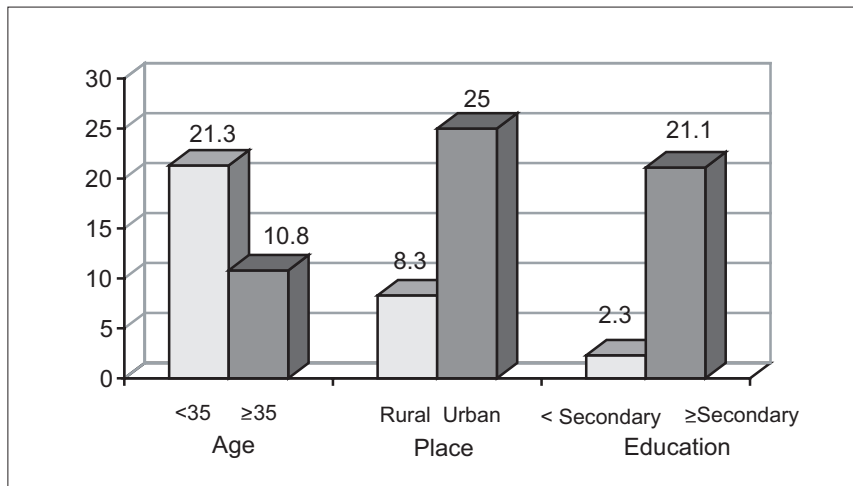
Substantial progress has been made in understanding the dynamics of condom use outside of marriage, both with commercial sex workers and with short-term partners. What

is less well-documented are the dynamics within marriage that both prevent condom use and provide opportunities for introducing condoms as either a form of family planning or as a means of STI prevention, or both. By focusing on respondents who are either married or who are in stable relationships, the study provides an opportunity to understand and document the potential for condom use within these relationships. Married women are among the most vulnerable to HIV infection but are the least able to negotiate condom use with their husbands. Increasing condom use among infected married men and women is imperative to prevent further spread of the disease. Findings from the study suggest that there is untapped potential for increasing condom use within

these relationships and that behaviour is indeed changing, albeit slowly, and that condom use can be reasonably expected to rise within marital relationships in the countries studied.

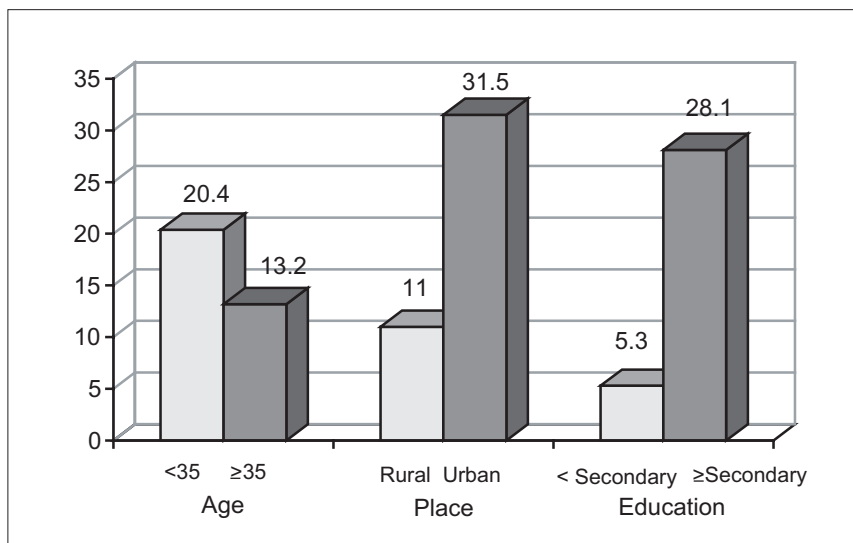
Findings from all four countries show that educated couples are more likely to use condoms than couples with little or no education. In two of the four countries (South Africa and Uganda), younger people are more likely to use condoms with stable partners than are their older counterparts. Figures 1.1 and 1.2 illustrate the differentials in the use of condom within marriage among men and women in South Africa. These findings suggest considerable potential for increase in condom use through the social diffusion of new forms of behaviour from educated, urban elites to rural, less educated segments of society—much as the decline in fertility became the norm in wealthy, educated groups in society and slowly spread to the general population. Furthermore, as young couples increasingly use condoms within marriage, their behaviour may gain increasing social acceptance to become a potent factor in challenging the stigma of condom use with a long-term partner. Findings from South Africa also indicate that the second most powerful predictor of condom use within marriage after education is the perceived risk of infection from a spouse. Some 25% of women who perceived the risk of infection to come from their husband were likely to use the condom, compared to 7% who did not. This suggests that individuals are developing awareness and strategies for self-protection in face of a spouse's risky behaviour.

Figure 1.1. Percentage of men reporting using condom within marriage, by background characteristics, South Africa



Source: Maharaj and Cleland, forthcoming

Figure 1.2. Percentage of women reporting using condom within marriage, by background characteristics, South Africa



Source: Maharaj and Cleland, forthcoming

Knowledge of the condom as a barrier to HIV transmission is nearly universal among respondents in the four countries. Barriers to condom use within marriage include well-documented gender power imbalances that negatively impact women's ability to negotiate condom use and the links between condom use and unfaithfulness. For example, an urban woman from Zimbabwe stated, "If men accept condoms, we women are ready. [But] men do not want to have sweet wrapped in paper."

Refocused social marketing campaigns could do much to ease the stigma associated with condom use in stable relationships. Because the condom's association with STI/HIV prevention has effectively overridden its family planning function, programmes and policies now need to include married couples among their target audiences.

Other work completed in 2003, using the Demographic Health Survey (DHS) data for 16 developing countries, further reinforces the above policy recommendations. It was found that a massive shift from more effective oral contraceptive pills to the less effective condom would not jeopardize the family planning policy goal of reducing unintended pregnancies and abortions. However, such a shift will have the benefit of preventing HIV infections, especially in countries with generalized HIV epidemic.

### *Quality of care in family planning and maternal health services*

In 2000, a research initiative on quality of care was launched, focusing on research that seeks to assess the quality of reproductive health services from the perspectives of clients, potential clients, providers, and/or objective standards of care. Additionally, the initiative sought proposals designed to assess the effects of improved service quality on intermediate outcomes (e.g. provider behaviour, client knowledge, client satisfaction, client behaviour especially with regard to the continuation of contraceptive use). Research that explores quality of care in such relatively under-studied areas of reproductive health as, for example, maternal health, providers' perspectives, abortion or STI treatment has been especially encouraged.

New findings from the social science research initiative on quality of care in reproductive health services became available in 2003. Studies have assessed the barriers to family planning access in several African countries, analysed provider perspectives on the provision of family planning services in several countries, and conducted research to understand and further document poor-quality maternal care in Turkey.

Findings from a study in Mali and Senegal address an often-overlooked barrier to contraceptive access. In many developing countries, family planning providers deny contraceptives to non-menstruating clients, believing that contraceptives may harm an unrecognized pregnancy. Using

WHO-approved criteria for ruling out pregnancy, the projects in Mali and Senegal, where the menstruation requirement is considered a substantial barrier to contraceptive access, involved implementing a six-question checklist for health care providers. Researchers there collected basic personal and service delivery information from an average of 100 new clients in each of six clinics per country, before and after the intervention. The intervention consisted of training providers from each of the six clinics and supplying them with laminated copies of the checklist. Results indicate that the intervention had significant impact in Senegal, where the percentage of new clients denied services due to lack of menses declined from 10% to 4% (a decline from 25% to 8% of new, non-menstruating clients). In Mali, researchers were surprised to find that, at least in the urban and peri-urban centres studied, menstruation requirements were not rigidly enforced. Thus, there was little room for improvement, and denial rates remained flat at the low level of 4%. However, because pregnancy cannot reasonably be ruled out for some women, this finding is consistent with correct use of the check-list.

Findings from a study on provider perspectives on quality of family planning care in Uganda became available in 2003. The project examined the following under-researched areas: provider definitions of quality, perceptions of services rendered, perceptions of clients' view of services rendered, perceptions of clients in general, provider motivation, and provider perceptions of their work environment. The results of this project indicate that providers identified availability of a variety of contraceptives, competence of providers, and good client-provider interaction as key elements of quality of care. Overall, providers and their supervisors alike were concerned about the quality of family planning services and did not think that government and private clinics provide good-quality family planning services. Providers felt constrained in their ability to provide quality family planning care by factors that they have little control over, for example, ensuring privacy. Other key findings include the lack of a national policy for training family planning providers. However, almost all providers and supervisors felt that the introduction of the health sub-district concept into Uganda's health care delivery system has been contributing to the recent improvement in the quality of family planning services in Uganda.

Hospital-based maternity care in cities in the developing world is often characterized by overuse of technology, unnecessary and/or inappropriate procedures, and lack of social support. There is a need for conceptual frameworks and methods to evaluate the quality of maternity care in these settings in order to identify problems, gain an in-depth understanding of why they occur, and develop appropriate interventions. Findings are available from a study that closely examined the maternity care in hospitals providing services to low-income women in Istanbul, Turkey. The study used qualitative and quantitative research methods to examine services from the perspectives of women, health care providers, administrators, and evidence-based medicine. A conceptual framework for the quality of reproductive health

services formulated by Judith Bruce was adapted for use in the evaluation of maternity care. Three typical hospitals (two public and one inexpensive private hospital), each with around 300 births per month, participated in the study. Methods used over a two-month period at each hospital included interviews with administrators, examination of hospital statistics, in-depth interviews with health workers and postpartum women, semi-structured interviews with 50 pregnant and 50 postpartum women, and semi-structured observations of antenatal, labour and delivery, and postpartum service delivery.

Important problems identified with antenatal care included neglect of simple but important procedures such as blood pressure monitoring and insufficient provision of information and counselling. Problems with labour and delivery services included excessive use of technological interventions, lack of emotional support, insufficient beds and other supplies, infrequent monitoring of postpartum women, and lack of support for breastfeeding. General problems included inadequate attention to infection control, difficult working conditions, and poor interpersonal relations. At the private hospital, the all-female maternity staff had much better interpersonal relations with clients than staff at the two public hospitals. Patient satisfaction was also found to be significantly higher at the private hospital. On the other hand, the research team identified some important problems with the technical aspects of maternity care at the private hospital. Given that many of the problems with maternity care identified in this study are related to general characteristics of the health system and health worker training, it is likely that similar problems exist in many other Turkish hospitals. In addition, the conceptual framework and methods used in this study were found to be useful in identifying and understanding problems with hospital-based maternity services and could be adapted for use in other countries.

Findings from a number of additional studies became available and were published in 2003. For the sake of brevity, these are not reported here (see Annex 3).

## **New projects initiated during the year**

### *Quality of care research initiative*

Three new studies on quality of care were approved from among 14 proposals and 15 concept papers which were reviewed in 2003. Two of these studies address quality of care in maternal health, while the third examines the quality of services providing contraceptives.

Under the Soviet regime, excellence in clinical birthing practice followed a predominantly physician-focused approach, rather than a family-centered system of care. Since the breakdown of the Soviet Union, some hospitals in Lithuania have been striving to balance excellence in medical care with concern for psychosocial aspects of the birth experience. A newly-approved study will examine women's and their part-

ners' attitudes and perceptions of perinatal care received in two hospitals in Lithuania. One of the two hospitals has been actively introducing family-centered and evidence-based care practices since the early 1990s. This provides researchers with an opportunity to evaluate the effect of these practices on perceptions of perinatal care by comparing women and partner responses from the two hospitals, which are otherwise similar. The results of this study will be used in evidence-based training programmes for hospital personnel and administrators in Lithuania and throughout the former Soviet Union. The assessment will be done through self-administered questionnaires given to 350 women and their partners in each hospital.

In Cameroon, the few studies that have been conducted on quality of prenatal care have focused on various indicators of maternal care rather than on providers' and clients' perceptions. The objective of a new three-province study on maternal care is to conduct a baseline assessment of prenatal quality of care in Cameroon to inform programmes and policies designed to reduce the risks of maternal morbidity and mortality. The proposed methodology is based on the Population Council's quality of care assessment guidelines. In all three provinces, study instruments will include a survey of providers, exit interviews of pregnant women, a household survey, and an observation phase.

In Guatemala, a major reproductive health concern continues to be the low rate of contraceptive use. To address this problem, the current Government, through the Ministry of Public Health (MSPAS), has developed strategies aimed at improving reproductive health among Guatemalans through implementation of the National Reproductive Health Programme. One method of particular interest to MSPAS is the injectable depot-medroxyprogesterone acetate (DMPA), which has become increasingly popular among Guatemalan women in recent years. The study consists of a longitudinal follow-up of randomly selected providers and their clients to evaluate the introduction of injectable contraception. The study will be carried out in four municipalities of the Department of Sololá. The intervention to be evaluated will include the use of a checklist for screening and method choice and the training of community-based workers to provide counselling and DMPA. The investigators propose to follow 115 service providers and 690 clients throughout the course of a year. The study will collect data on providers' knowledge, attitudes and practices, as well as on their satisfaction through follow-up interviews with providers and with clients. In addition, the study will use random observations to evaluate injection techniques.

### *Infertility and childlessness in developing countries*

In collaboration with Opinion Research Co-operation (ORC) Macro, work continued on a major study measuring infertility, infertility and childlessness in developing countries. DHS data from nationally-representative surveys conducted during 1995–2000 in 47 developing countries were analysed.

Data were collected from 495 000 women between the ages of 15 and 49. Topics covered in the analyses included the magnitude of childlessness, primary involuntary infertility, self-reported infecundity, secondary involuntary infertility, secondary infecundity, and differentials and trends in childlessness and in infertility. Overall, 2.5% of couples in the developing world, excluding China, were estimated to experience primary involuntary infertility. Important regional, socioeconomic, and demographic differentials were noted. The associations between STIs, including HIV/AIDS, and infertility were explored at the population level. Work is in progress to document the extent of adoption or fostering among childless couples surveyed in DHS.

### *Future workplans*

In the coming years, the work on users' perspectives will focus on four major activities. First, the results from the multicountry study on 'Family planning and sexual behaviour in the era of HIV/STIs' will continue to be disseminated nationally and internationally through presentations of findings and publications of papers.

Second, jointly with the staff of the University of London School of Hygiene and Tropical Medicine, a compendium will be developed to provide comparative information on contraceptive use, method continuation and method switching in developing countries. This compendium will also provide information on such key aspects as unmet need, unintended fertility, postpartum contraceptive protection, and antecedents of sterilization. Work on the uptake of contraception following childbirth or pregnancy termination will be completed and implications of quality of care in developing countries will also be identified.

Third, research proposals on quality of care and on users' perspectives on reproductive health services and technologies will continue to be considered for support.

Fourth, a comparative report on involuntary childlessness and infertility in developing countries will be completed.

### **TECHNICAL COOPERATION WITH COUNTRIES**

Technical cooperation with countries in 2003 included a research workshop held in Gaborone, Botswana, and a site visit to develop a quality of care research initiative in Tunisia. An analysis workshop with country investigators was held in Gaborone, Botswana, in conjunction with the seminar on "Taking stock of the condom in the era of HIV/AIDS", mentioned above. The main objectives of the workshop were to: (i) review results from the study "Family planning and sexual behaviour in the era of HIV/STIs"; (ii) plan and initiate further analysis and write-up; and (iii) develop plans for dissemination and further work.

Technical assistance was provided to the Office National de la Famille et de la Population (ONFP) in Tunis, Tunisia, to develop a social science research strategy for quality of care in reproductive health in Tunisia and to review the activities of the centre. A network was established bringing together researchers working on quality of care in Tunisia to share resources and research agendas for projects on quality of care. Plans are being made to hold a national consultation to identify research priorities and develop a national research agenda.

## Annex 1

## SPECIALIST PANEL FOR SOCIAL SCIENCE AND OPERATIONS RESEARCH ON REPRODUCTIVE HEALTH

## Members

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	8	89			1	11	9
Women	4	44					4
<b>from:</b>							
AFRO	2	22					2
AMRO	2	22			1	11	3
EMRO							
EURO	1	11					1
SEARO	2	22					2
WPRO	1	11					1

## Collaborating agency scientists

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Annex 2

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	31	100					31
Women	16	52					16
<b>from:</b>							
AFRO	12	39					12
AMRO	7	23					7
EMRO	4	13					4
EURO	2	6					2
SEARO	2	6					2
WPRO	4	13					4

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	3	43			4	57	7
Women					1	14	1
<b>from:</b>							
AFRO							
AMRO					3	43	3
EMRO	2	29					2
EURO					1	14	1
SEARO	1	14					1
WPRO							

Annex 3

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# Development of improved and new methods of fertility regulation

P.D. Griffin, K.M. Vogelsong, H. von Hertzen, E. Vayena, C. d'Arcangues

## INTRODUCTION

In 2003, the United Nations Population Division reported that approximately 635 million couples worldwide regularly used some method of family planning. Because use does not necessarily mean acceptance, this statistic offers only a glimpse at the behaviours that determine a couple's decision to use a method of fertility regulation. Nearly one-half of users of a reversible method discontinue its use within a year, owing to a variety of reasons including health concerns and the occurrence of an unplanned pregnancy. On the other hand, at least 123 million couples do not use any method of family planning, despite expressing a desire to space or limit the number of their children. Obstacles to the use of contraceptive methods include ambivalence towards modern contraception (especially attributed to a fear of side-effects) and lack of access to high-quality services. Experts have determined that the availability of improved or totally new methods of family planning could lead to a significant public health benefit and could meet the need and demand of millions of men, women, and families.

The Programme's research on improved and new methods for fertility regulation provides one of the several inter-connecting building blocks required for the delivery of quality family planning services. The Programme has pursued high-priority leads for new methods and approaches that are easier to use and simplify service delivery, that are associated with fewer and less severe side-effects, and that respond to the needs of various users, including men. The Programme's goals link this work to the introduction of methods and subsequent large-scale trials of their safety and efficacy. Users' perspectives are gathered during the product development, introduction and routine service provision phases. Together with clinical trial data, this information provides input into the

development of norms, guidelines and other tools for providers and family planning acceptors.

## RESEARCH ACTIVITIES

### Emergency contraception

#### *Specific objectives of research*

For the past ten years, the Programme has been in the forefront of research on new technologies for emergency contraception. The aim is to improve further the safety, efficacy, acceptability and ease of service delivery of methods for this indication. After demonstrating the superiority of levonorgestrel over the regimen of combined oral contraceptives, the Programme has further simplified the levonorgestrel regimen and compared it to low-dose mifepristone. Possible mechanisms of action of levonorgestrel and mifepristone in emergency contraception have also been studied.

#### *Progress*

##### *Levonorgestrel*

During 2003, the data from completed trials have been combined to perform various meta-analyses. The results of a large multinational trial published last year (*Lancet* 2002;360:1803–1810) demonstrated a similar efficacy of two levonorgestrel regimens (0.75 mg given twice at 12-hour interval and a single dose of 1.5 mg levonorgestrel) and the 10 mg dose of mifepristone for emergency contraception, when given up to 120 hours after unprotected intercourse. The data on levonorgestrel from this trial and the data from an earlier trial comparing the two-dose regimen of levonorgestrel with the

Yuzpe regimen (*Lancet* 1998;352:428–433) were used to investigate the effect of delay in the administration of levonorgestrel on the efficacy of the treatment. The analysis included data on 3757 women participating in the two above-mentioned randomized trials. Logistic regression techniques were used to assess the extent and type of decrease in effectiveness when levonorgestrel was administered in the successive five days after an unprotected act of intercourse. The results showed a significant effect of delay on the proportion of pregnant women ( $p=0.0062$ ). The pregnancy rate increased from 1.3% (22/1644) when levonorgestrel was administered within 24 hours of unprotected intercourse to 4.8% (6/126) when administered on the fifth day (OR=3.37,  $p=0.0108$ ). Thus, delaying levonorgestrel administration until the fifth day after intercourse increased the probability of pregnancy by more than three-fold compared with administration within 24 hours. Because most women request emergency contraception within the first 2–3 days after intercourse, the number of women who came later than this, who were included in the analysis, was rather small. Therefore, more research is needed to confirm effectiveness after day three.

To this end, the data from a double-blind, multicentre trial carried out in collaboration with investigators in Hong Kong will be added to perform a further meta-analysis in 2004. This Chinese study compared the effectiveness of two tablets of 0.75 mg of levonorgestrel when given with a 12-hour interval or with a 24-hour interval between the two doses. The study included 2071 women requesting emergency contraception within 120 hours of unprotected intercourse. The outcome was unknown for 53 women (29 in the 12-h group and 24 in 24-hour group). Among the remaining 2018 women the crude pregnancy rate was 2.0% in the 12-hour group and 1.9% in the 24-hour group. The percentage of pregnancies prevented was estimated to be 72–75%. Side-effects were rare and mild in both groups. About 40% of women had menses earlier than expected. The results of this study will be published in 2004.

Levonorgestrel is also being studied in a seven-centre study in Nigeria. The efficacy and side-effects of a one-dose regimen of 1.5 mg will be compared with a two-dose regimen (0.75 mg taken twice, with a 24-hour interval between doses). The target is to include a total of 3150 women. Due to unforeseen problems (strikes at universities and other local problems) recruitment has been slower than expected. By November 2003 a total of 1068 women had been recruited at the seven participating centres. An additional aim of this study is to develop the capability of the centres to carry out research according to Good Clinical Practice (GCP) standards.

The data on side-effects among women in the trial of levonorgestrel versus the Yuzpe regimen (*Lancet* 1998; 352:428–433) were compared to side-effects among 52 adolescents, aged 13–16 years, participating in a study in California, USA. When compared to the WHO study in adults, adolescents reported

higher frequencies of nausea ( $p=0.012$ ), fatigue ( $p=0.001$ ), headaches ( $p<0.001$ ), diarrhoea ( $p=0.001$ ) and dizziness ( $p=0.001$ ). However, in both studies, the participants experienced similar levels of vomiting, breast-tenderness and lower abdominal pain.

The data on the Yuzpe regimen from the above-mentioned Programme trial and from a study by the Population Council were used to calculate new estimates of conception probabilities by cycle day of intercourse to propose a new approach for estimating the effectiveness of emergency contraceptive pills (ECPs). In this approach the cycle day was measured with day 1 being the first day of bleeding in a cycle. The expected pregnancy rate among typical users was 6.2% in the Population Council trial and 7.4% in the WHO trial based on conception probabilities by cycle day relative to the day of ovulation. Based on conception probabilities by cycle day relative to the first day of bleeding, the expected pregnancy rates dropped to 5.4% and 5.2%, respectively. The two trials yielded conflicting evidence regarding whether effectiveness declines with treatment delay. The results suggest that in previous studies the absolute levels of effectiveness for the Yuzpe regimen of emergency contraception were probably overestimated based on conception probabilities by cycle day, relative to day of ovulation.

### *Mifepristone*

To test further the low-dose mifepristone regimen for emergency contraception, the Programme collaborated with Chinese investigators in a three-year initiative funded by the Rockefeller Foundation. The December 2003 issue of the journal *Contraception* contains a total of 14 papers resulting from this collaboration.

Two large multicentre trials of emergency contraception were carried out during this initiative. In addition, the efficacy and side-effects of 100 mg of mifepristone followed two days later by 0.4 mg oral misoprostol were investigated among 699 women who either came too late, i.e. beyond five days, or had more than one unprotected act of intercourse at any time during the cycle in which they requested emergency contraception.

The results of the first multicentre study, a randomized, double-blind study comparing the effectiveness and side-effects of 10 mg and 25 mg doses of mifepristone, were reported last year (*Human Reproduction*, 2002; 17:3084–3089). The two doses were equally effective, with a raw pregnancy rate of 1.1%. The treatments led to very few, if any, reported side-effects. The 10 mg dose was tested further in a larger prospective study at 32 clinics in 19 provinces of China among 4945 women requesting emergency contraception within 120 hours of one unprotected act of intercourse. A total of 28 women were lost to follow-up, and 4917 women were included in the analysis, of whom 69 became pregnant. The overall pregnancy rate was 1.4% (95% CI: 1.0–1.9). The pregnancy risk was double among nulliparous women com-

pared to parous women (2.3% vs 1.0%), and it increased by a factor of 1.5 when the treatment was administered at 25–48 hours and 49–72 hours compared to administration within 24 hours, although this association was not statistically significant. The risk of pregnancy was higher if intercourse took place during the follicular or pre-ovulatory phase of the cycle. Women having repeated intercourse after treatment without using any contraceptive methods had a dramatic increase in the risk of pregnancy, while those who used contraceptives had a similar risk to those without further acts.

A meta-analysis was carried out combining the estimates of efficacy and side-effects of 10 mg mifepristone for emergency contraception obtained from 13 randomized trials. A total of 6283 women receiving 10 mg mifepristone for emergency contraception up to 120 hours of intercourse were analysed for efficacy. Of these, 3601 women were analysed for delay of menses of more than seven days. The percentage of pregnancies prevented, the effect of delay of treatment and the effect of further acts of intercourse after treatment administration were analysed in 3440 women for whom individual data were available.

The combined pregnancy rate from all 13 trials was 1.7%, and it was 1.3% from three trials providing individual data. The estimate of pregnancies prevented was 83.4%. There was a sharp decline in efficacy when treatment was administered during the fifth day after intercourse, compared to administration during the first day. The odds of pregnancy increased by a factor of 6.0 (95% CI 2.1–17.2). The relative risk of pregnancy was about 16 times higher among women reporting unprotected acts of coitus between treatment administration and the start of next menses compared to women reporting no such acts. The increase in risk for women reporting protected acts of intercourse during this interval was not statistically significant.

The pharmacokinetics of 10 mg of mifepristone was studied in eight healthy female volunteers, who received a single oral dose of mifepristone on the 10<sup>th</sup> or 11<sup>th</sup> day of their menstrual cycle. Blood samples were collected at 0, 1, 2, 4 and 8 hours, and daily for the next 6 days and on day 10 after mifepristone. Mifepristone concentrations were determined by radioimmuno assay (RIA) preceded by column chromatography. A peak level of  $1413 \pm 307$  nmol/l (mean  $\pm$  SD) was measured at 1 hour. Individual elimination phase half-lives varied from 15.3 hours to 26.8 hours, the mean ( $\pm$  SD) value being  $19.6 \pm 4.5$  hours. Serum mifepristone concentrations exceeded 2.5 nmo/l in all volunteers for five days. These data on 10 mg of mifepristone were in line with previous pharmacokinetic and clinical data, and encouraged further development of the 10 mg dose in emergency contraception.

No methods of emergency contraception have been shown to be effective when treatment is administered more than five days after a single unprotected act or after several unprotected acts. Therefore, the potential of 100 mg of mifepristone followed two days later by 0.4 mg of misoprostol orally

was tested among 699 Chinese women when administered during the luteal phase of the cycle. A urinary pregnancy test had to be negative at the time of treatment. Despite treatment, 25 women (2.7%) became pregnant. Among women with treatment delayed more than five days, the pregnancy rate was related to the number of acts of intercourse before treatment, being 1.4% with one episode and increasing to 6.5% when the number of episodes was two or more (relative risk=4.62, 95% CI: 1.06–20.18). The increase was significant when treatment was delayed by more than five days after the last of two or more episodes, compared to treatment within five days (relative risk=2.29, 95% CI 1.02–5.13). The pregnancy risk was also related to unprotected intercourse after treatment and it increased by more than four-fold when women had further acts of unprotected intercourse. Side-effects were mild and most women (57.2%) had menstruation within three days as expected. While it was concluded that an occasional treatment with mifepristone and misoprostol could provide an option for preventing unwanted pregnancies in women who are late for emergency contraception, this treatment did not seem to be very effective.

#### *Mechanism of action studies*

Several studies are being undertaken by the Programme's collaborating centres to investigate possible mechanisms of action of emergency contraceptives. A study in Santiago, Chile, investigated the effects of levonorgestrel in the *Cebus apella* monkey. Levonorgestrel or placebo was administered either in oral tablets or subcutaneously within the first 24 hours after mating that occurred very close to the time of ovulation. Females that became pregnant had induced abortion and re-entered the study after a resting cycle until each of 12 females had contributed, in a randomized fashion, to the data set with two levonorgestrel and two placebo cycles. The pregnancy rate was identical after placebo and levonorgestrel treatment. In addition, the effect of levonorgestrel on ovulation was studied in 30 cycles, 15 cycles with a follicular size smaller than 5 mm and 15 cycles with a follicular size larger than 5 mm. Levonorgestrel inhibited or delayed ovulation only when the follicular size was <5 mm. Researchers concluded that in the cebus monkey, levonorgestrel can inhibit or delay ovulation, but once fertilization has taken place, it cannot prevent the establishment of pregnancy.

Another study in Chile examined the effects of a single dose (1.5 mg) of levonorgestrel on follicular growth and ovulation in the human. The pharmacokinetics as well as the levels of the steroid in endometrial tissue were determined after oral and vaginal administration. Preliminary results suggest lower plasma levels are achieved following vaginal administration. The results of hormone analyses and steroid levels in endometrial tissue will be available in early 2004.

#### *Other activities*

Several invited presentations on the work of the Programme in the area of emergency contraception were given in inter-

national and national conferences during 2003 including the International Congress of Obstetrics and Gynaecology (FIGO) in Santiago. Within the International Consortium on Emergency Contraception Programme staff were actively involved in the revision of international guidelines for service providers.

#### *New projects initiated during the year*

No new trials were launched during 2003.

### **Six-monthly, non-steroidal, injectable immunocontraceptive for women**

#### *Specific objectives of research*

The development of a totally new method of contraception, based on the production of an immune response to reproduction-specific molecules, has been the subject of extensive investigation supported by a number of international and national agencies for several decades. A large number of animal studies and a limited amount of clinical experience have shown that, depending on the approach used and the type of preparation developed, such a method could provide a relatively long-acting, but not a permanent, safe and effective, immunocontraceptive method.

The research being supported by the Programme in this area is the development of an immunocontraceptive based on, and directed against, human chorionic gonadotrophin (hCG). This work has been in the forefront of what has now become recognized as the new field of immunopharmaceuticals—that is, preparations that have a profile of action akin to that of a pharmaceutical but which mediate their effect through the immune system by the production of a specific and time-limited immune response.

The objective of the Programme's work is to develop a long-acting, non-hormonal method of contraception that can provide approximately six months' protection following a single injection and that does not produce the endocrine and other metabolic disturbances often experienced with long-acting steroid hormone preparations currently on the market and under development. A preparation that is capable of meeting these requirements has been developed and consists of hCG peptide:diphtheria toxoid (DT) immunogen conjugates and a muramyl dipeptide (MDP) immunostimulant incorporated in biocompatible, biodegradable inorganic matrix particles and suspended in a water-in-oil emulsion vehicle formed from squalene and phosphate-buffered saline, using mannide mono-oleate as the emulsifying agent.

#### *Progress*

A clinical trial application was submitted to the regulatory authorities in Sweden in May 2002 to carry out a Phase I

clinical trial with the matrix formulation of the hCG immunocontraceptive described above. However, changes in regulatory requirements occurred shortly after the application was filed. This necessitated finding a new manufacturing facility capable of producing and packaging the matrix-incorporated immunogen materials to be used in the proposed clinical trial and in conducting additional safety studies in animals. A manufacturing company that meets the new regulatory requirements was identified and a contract for preparing the clinical trial supplies was negotiated and finalized. Approval to proceed with this preparation was temporarily delayed pending STAG's endorsement of the proposed work at its February 2003 meeting, and again was delayed for a few months pending funding availability. The project is proceeding once again. Materials have been prepared and in October 2003, the associated Good Manufacturing Practice (GMP) documentation was compiled into a supplementary submission to regulatory authorities in Sweden.

During the past year, development work has continued to provide evidence to support the use of the matrix formulation of the hCG immunocontraceptive in the planned Phase I clinical trial in Sweden. The testing of immunogenicity and safety of a GMP batch of this material prepared in 2001 was completed and similar evaluations of the new batch, made in 2003, have been initiated. These include dose-finding studies for booster immunizations and assessment of local injection site reactions in rabbits. Further studies have also been conducted on the preparation and testing of alternative versions of the hCG immunocontraceptive consisting of totally synthetic chimeric peptides representing B-cell and T-cell epitopes of hCG and DT, respectively, and the hCG peptide:DT conjugate incorporated into an alternative delivery system consisting of biodegradable polylactide/glycolide microspheres.

#### *Dose-response studies*

Previous studies in rabbits, with the batch of the matrix formulation of the hCG immunocontraceptive manufactured in 2001, identified doses that were effective for eliciting putatively protective levels of antibodies for a six-month period following a single injection, and for an additional six months following a booster injection. It was found that the booster injection at six months need be only 50% of the primary immunization dose to stimulate the production of antibody levels above those attained from the first injection. Dose-finding studies are proceeding with the new lot of matrix immunogen particles prepared in 2003 to identify the most appropriate dose for the booster injection. Booster injections of less than 50% of the primary immunization dose are being tested to determine the minimum dose needed to maintain putatively protective levels of anti-hCG antibodies. It is anticipated that using these reduced doses for booster injections will result in correspondingly reduced local reactions at the injection sites, which is crucial to the clinical acceptability of the method.

### Stability testing

To be suitable for use in clinical trials and for eventual manufacture, the matrix formulation of the hCG immunocontraceptive must be stable for at least 12 months and preferably for as long as 24 months. The compilation of product stability data is, therefore, an essential part of ascertaining the shelf-life of the GMP materials when conducting the planned Phase I clinical trial and its associated supplementary animal safety studies. Stability studies carried out on the matrix particles stored at 4°C for 12 months showed no reduction in immunogenicity and no increase in tissue reactivity compared to recently made materials. Similar tests carried out on matrix particles stored under the same conditions for 27 months showed some loss of immunogenicity (Figure 1.3).

The new GMP batch of the matrix formulation made in 2003 is currently under storage at 4°C and will be evaluated for stability after 1, 3, 9, 12, 18, and 24 months.

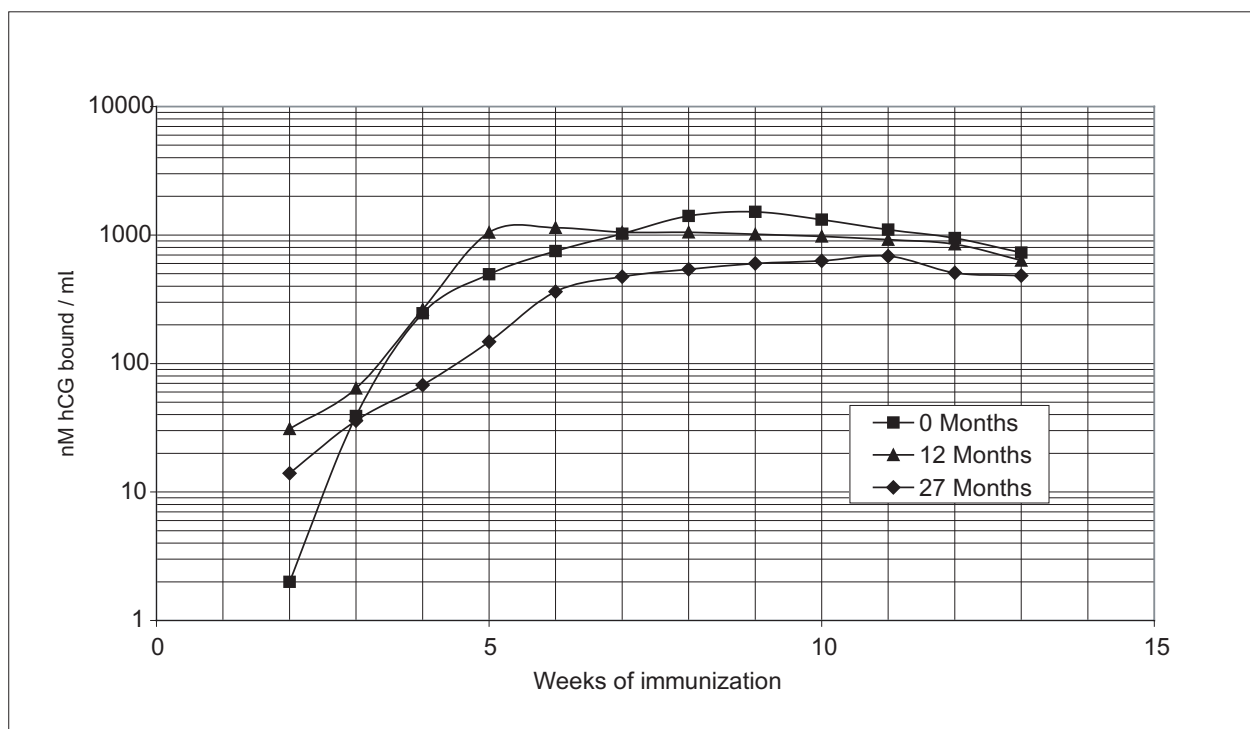
### Studies for improving manufacturing procedures

The method currently used for preparing the dosage form involves weighing and placing very small amounts of the immunogen matrix particles into sterile syringes and mixing them with the viscous emulsion vehicle immediately prior to injection. While this is an acceptable and feasible approach for use in preclinical safety studies and clinical trials, it may not be practical for routine clinical use. Several studies aimed

at devising a more suitable manufacturing method have been conducted during the past year. These involved the addition of empty matrix particles as a “filler” to make weighing easier and/or the use of less viscous vehicles to permit mixing by simple vial shaking. The addition of the empty matrix particles did make weighing easier but the increased amount of the matrix material in the resulting preparation was found to produce unacceptable local reactions at the injection sites. The work with the less viscous emulsions was similarly unsuccessful because these emulsions were found to be stable for only a few weeks.

Studies were also carried out on the stability of the eventual dosage form, in which the matrix formulation of the hCG immunocontraceptive immunogen was suspended in the emulsion vehicle, dispensed into syringes, and stored at 4°C. The immunogenicity of this material was tested after 0, 3, 6, 9 and 12 months of storage and was found to be essentially the same at each of these time points. These preliminary data suggest that it may be possible for the hCG immunocontraceptive to be prepared and packed in its final dosage form. This would enable future clinical trials to be conducted using a vaccine manufactured and prepared in a standard manner, that is practical for widespread use, and that meet the requirements for commercial production. Further evaluations of the stability of the fully formulated material will be conducted using the most recently manufactured lot of GMP immunogen matrix particles.

Figure 1.3. Comparison of the mean anti-hCG antibody levels in serum from rabbits immunized\* with the matrix formulation of the hCG immunogen at the time of its preparation and after storage for 12 and 27 months



\*All injections given at time zero.

### *Testing of biodegradable microspheres as a vaccine delivery system*

In addition to tests and evaluations of the matrix formulation of the hCG immunocontraceptive currently being proposed for the Phase I clinical trial, research has continued on the assessment of biodegradable polylactide/glycolide (PLG) microspheres as an alternative formulation approach. This copolymer material has been used extensively in humans in surgical and other settings and has a long history of proven safety. Previously conducted studies have demonstrated that chimeric peptides—containing hCG B-cell epitopes and T-cell epitopes of tetanus toxoid or measles proteins—incorporated in PLG microspheres and administered in the standard emulsion vehicle, can elicit antibody profiles similar to those produced with the immunogen conjugate incorporated in the inorganic matrix particles. In addition, these PLG microspheres were able to elicit these types of immune responses when administered in a simple phosphate-buffered saline vehicle which produces very little reaction at the injection sites, offering the possibility of an equally potent but simpler and less reactive formulation.

These studies have been continued during the past year and expanded to include evaluation of the immunogenicity of hCG peptide/DT immunogen conjugates incorporated in PLG microspheres. Since structural integrity of the immunogen is critical for maintaining the level and specificity of the induced immune response, the immunogens were entrapped in polymer solutions containing various concentrations of an inorganic salt, magnesium carbonate. This basic salt neutralizes the lactic acid that is released as the PLG microspheres degrade and prevents structural changes to the immunogen in the low pH conditions that would otherwise have occurred in and around the degrading microspheres. In addition, the salt has adjuvant properties which eliminate the need for inclusion of the MDP adjuvant. Studies have been conducted using PLG polymers of varying molecular weights and various immunogen loadings. The findings to date suggest that lower molecular weight polymers and low immunogen loads are the best combinations for use with the chimeric peptides, whereas medium molecular weight polymers and somewhat higher immunogen loads work best for the hCG peptide/DT conjugates. Antibody levels elicited by both of these types of immunogen delivered in microspheres, at comparable doses, are lower than those produced by the inorganic matrix but were above the levels considered to be needed for contraceptive efficacy. The PLG polymers may warrant further investigation as an alternative formulation approach for future hCG immunocontraceptives.

### **Injectable hormonal contraceptives**

#### *Specific objectives of research*

A number of long-acting injectable esters of levonorgestrel were prepared in a chemical synthesis programme conducted by the National Institute of Child Health and Human

Development (NICHD) of the United States National Institutes of Health (NIH) and the Programme in the late 1970s and early 1980s. One of these, levonorgestrel butanoate (LNG-B), has been investigated as a possible improved alternative to depot-medroxyprogesterone acetate (DMPA). Formulation problems encountered in the 1990s, however, led to an interruption of this work. While a new formulation has since been prepared, preparation of a GMP batch of this material has been hampered by the absence of an industrial partner and funding shortages.

#### *Progress*

##### *Levonorgestrel butanoate*

In November 2003, a meeting involving WHO, NIH, CONRAD, the Concept Foundation and industry, was held in Geneva, Switzerland, to review the history and current status of the work on LNG-B and to propose a strategy for future studies with this compound. The participants in the meeting were unanimous that LNG-B was an attractive alternative to DMPA as a three-monthly injectable contraceptive and agreed to collaborate on its further development. A product development plan was drawn up listing the steps required, assigning responsibilities for, and determining the costs involved in, taking LNG-B through to the stage of a Phase II clinical trial.

### **Combined vaginal ring**

#### *Specific objectives of research*

Acceptability studies show that women need long-acting methods of contraception which do not require daily interventions and which are under their control. The vaginal ring is one approach that meets these needs. Most steroid hormones are absorbed efficiently through the vaginal wall and can be released from a Silastic ring. The ring can be easily inserted and replaced by the woman herself. It can be worn continuously for a number of weeks. Its use is not coitally related. The contraceptive ring provides a constant rate of drug release resulting in a steady plasma level of the minimum dose required for contraception; metabolic side-effects of the steroidal hormones are reduced by avoiding the first-pass effect through the liver. Upon removal of the vaginal ring, fertility returns rapidly.

#### *Progress*

The Population Council will launch a Phase III clinical trial of a combined contraceptive vaginal ring releasing 150 µg of norgestrel and 15 µg of ethinyl estradiol daily over the course of a year. In mid-2003, the Council signed a contract for the production of vaginal rings which are expected to be delivered in mid-2004. A small pharmacokinetic study will be carried out first, to verify the performance profile of the rings, followed by a Phase III clinical trial. The Programme is planning to provide support to two clinical research centres to take part in the Phase III trial.

## Basic research on implantation

### *Specific objectives of research*

A method of fertility regulation that needs to be taken on only one occasion in any menstrual cycle would be an attractive option for many individuals and couples. The use of such a method would be more popular if it does not need to be taken regularly in every cycle, but strictly on an "as needed" basis—for example, in the case of occasional otherwise unprotected intercourse, or, as a backup in the case of known method failures such as condom breakage. Ideally, a method with these attributes would also be largely free of the logistical difficulties and side-effects associated with many other existing methods of contraception. Because of its infrequent use, this contraceptive should also be relatively inexpensive, making it affordable to women in many parts of the world.

At the end of 1998, a collaborative five-year initiative in the area of basic research in implantation was established between the Rockefeller Foundation and the Programme. The primary objective of this research is to identify promising leads for development—in eventual collaboration with industry—of novel once-a-month birth control methods, which are safe, effective, acceptable in their mode of administration and mechanism of action, and which can be self-administered.

The continuing focus of the research during the past and final year of the above joint initiative has been on: (i) the implantation window in the primate, at the endometrial level; (ii) the development and demise of the primate corpus luteum; and (iii) preimplantation embryo–uterus–corpus luteum interactions. The work is being carried out in a network of six centres in Australia, China, Germany, India, the United Kingdom and the USA, with financial support being provided by the Rockefeller Foundation and technical oversight being provided by the Programme.

### *Progress*

During the past year, further information has been obtained on the complicated and interactive structural and functional changes that occur in the mouse, monkey and human uterus and the monkey corpus luteum at the site and time of implantation, respectively. Systemic or local—intrafollicular—injection of angiogenesis inhibitors demonstrated the ability of these compounds to inhibit folliculogenesis temporarily, or to prevent ovulation, or to inhibit the development of the corpus luteum, depending on the time in the cycle that they were administered. Also investigated was the 'cocktail' approach in which a number of different molecules, each with its own discrete mechanism of action at the endometrial level, are used together to achieve a multi-point anti-implantation effect. Other studies have investigated the controlled cell fusion that leads to the formation of the syncytial trophoblast and assessed the role of various genes, hormones, enzymes,

cytokines and other molecules that appear to be associated with the survival, transport, attachment and implantation of the embryo.

### *New projects initiated during the year*

Because the past year was the fifth and final year of funding, no new projects were started as part of the initiative during 2003. However, several collaborative projects are being planned as a result of a joint meeting held at the Rockefeller Foundation Study and Conference Center in Bellagio, Italy, in May 2003. The meeting brought together the principal investigators and Project Review Committee of the joint initiative and their counterparts from the complementary programme supported by CONRAD/CICCR. Representatives of large and small pharmaceutical companies that had expressed an interest in this area of work were also invited to participate in this meeting. As a result of the presentations made at the meeting, and subsequent public and private discussions that took place, a number of collaborative projects were identified and discussed with the industry representatives. These discussions, and the plans for collaborative activities that evolved from them, were facilitated by the patents that many of these investigators had been encouraged to take out in order to protect their discoveries and to provide an attractive environment for industry involvement.

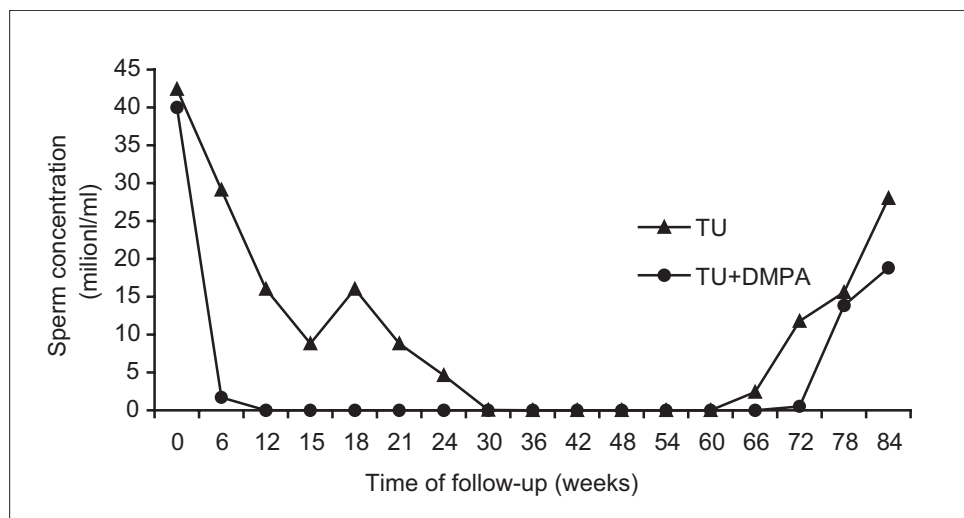
Publication of the work done over the past five years is planned, either as a special edition or a supplement of a journal. The six centres have been asked to prepare a report of their activities once the ongoing work has been completed (around the first quarter of 2004). A meeting of the Project Review Committee will then be held to review the reports, which will be prepared according to a common format and edited for publication.

## Basic research on endometrial bleeding

### *Specific objectives of research*

A large proportion of the more than 15 million women using progestogen-only methods of contraception endure irregularities in vaginal bleeding that these methods induce. This has significant implications not only for their sexual lives, but also for the sociocultural, economic and, for some, religious dimensions of their lives. Few options are available to women to prevent or alleviate bleeding irregularities. As a result, counselling is the main, and often the only form of assistance that women who experience this problem can expect from providers. Clearly, in order to formulate appropriate treatments and to develop new methods free of these side-effects, there is an indisputable need to understand better the mechanisms of menstruation and irregular bleeding, and how they are affected by contraceptive steroids, particularly progestogens.

Figure 1.4. Average sperm concentrations in men receiving TU every 6 weeks, either alone or with DMPA every 12 weeks, for 48 weeks



### Progress

A double-blind, randomized, placebo-controlled, multicentre clinical trial was conducted to test the effect of vitamin E as an anti-oxidant, and of low-dose aspirin as an anti-inflammatory agent, alone and in combination, on Norplant-induced prolonged bleeding, as described in the *Annual technical report 2002*. None of the treatments had a significant beneficial effect on bleeding patterns in the study population, as previously reported. The study and analysis were completed in 2003 and a manuscript has been submitted for publication.

A systematic review of the evidence for the efficacy of various therapies in the treatment or prevention of progestogen-induced endometrial bleeding irregularities is being supported by the Programme, through the Fertility Regulation Group of the Cochrane Collaboration. An updated protocol for the review was published in 2003. The review is ongoing and should be completed by mid-2004.

A basic science project designed to provide insight into the cellular and molecular mechanisms that underlie progestogen-induced breakthrough bleeding, "Studies on the role of progestins in endometrial breakthrough bleeding," was initiated in 2002. In the second year of this three-year project, the investigators thoroughly characterized the expression and production of chemokines in the normal cycle and progestogen-exposed human endometrium. Three of these proteins have been selected for further studies, as preliminary evidence suggests that they are differentially regulated by progestogens and may, therefore, contribute to the endometrial fragility seen in women using progestogen-only contraceptives. Additional current research results suggest that chemokines, in turn, differentially regulate the amounts of cellular matrix metalloproteinases, supporting the inves-

tigators' hypothesis that progestogens may bring about the breakdown of the endometrium by altering matrix metalloproteinase expression and activation through the regulation of various chemokines. Additional progress in this area includes establishment of a suitable cell line for the *in vitro* cellular investigation of the role of progestogens in breakthrough endometrial bleeding.

### Male hormonal contraception—clinical and social science research

#### Specific objectives of research

The Programme has taken a leadership role in the development of male contraceptives. A research agenda in male contraceptive development must identify and pursue leads that are feasible and show the most promise, such as a hormonal method that suppresses spermatogenesis and produces temporary infertility. The Programme's clinical trials are complemented by acceptability and behavioural research.

#### Progress

##### Androgen alone

Results of the Phase II clinical trial of the contraceptive efficacy of the injectable androgen testosterone undecanoate (TU), described in previous *Annual technical reports*, were published in early 2003.

The follow-on Phase III study of the safety and contraceptive efficacy of TU was initiated in late 2001. This four-year trial is evaluating the effects of a monthly injection of 500 mg TU on the fertility of 1000 men, from 10 centres in China. The study is progressing according to schedule (see Table 1.1), with recruitment completed in December 2002. In August 2003,

Table 1.1. Current status of 1045 volunteers enrolled in Phase III\* trial of TU alone as a male contraceptive

Study phase	Number of volunteers
Suppression (first 6 months)	0
Efficacy (24 months)	786
Early discontinuation:	
lost to follow-up	72
change in contraceptive method	40
inadequate response	43
missed injection	35
other	69
Total	1045

\* Volunteers receive monthly injections of TU (1000 mg in the first injection and 500 mg thereafter) and are followed for sperm suppression during the first 6 months (Suppression phase). If sperm concentrations are suppressed to  $\leq 1$  million/ml, the volunteers continue to receive monthly injections and are followed for contraceptive efficacy for 24 months (Efficacy phase). If sperm concentrations are not adequately suppressed, the volunteer is discontinued from the study. All men who discontinue early for any reason are followed until their sperm concentrations return to levels generally considered to be fertile ( $\geq 20$  million/ml).

research teams from all the centres attended a mid-term meeting to report progress to date and discuss the conduct of the remainder of the study. Preliminary data analyses indicated that a higher than anticipated number of participants failed to respond adequately to the regimen, leading to a primary failure rate of 4.34 per 100 couple-years, a rate within an acceptable range. Age, height, weight, body mass index, testes volume and semen values at baseline were not predictive of the response to the regimen. The preliminary cumulative continuation rate for the study is determined to be 83.83 per 100 couple-years.

#### *Androgen/progestogen combinations*

In 2002, a Phase II trial to evaluate the suppression of spermatogenesis resulting from the administration of an androgen/progestogen combination, TU + DMPA, to Indonesian men was completed, as described in the previous *Annual technical report* (Figure 1.4). In 2003, the analysis was completed and a manuscript describing the results was prepared. The final manuscript will be submitted for publication in early 2004.

In order to simplify the regimen of TU and DMPA, lengthen the interval between injections, and determine the lowest effective doses of both components, the study will be revised and expanded, as appropriate, when a new formulation of TU (see below) is available.

The initiation of a multicentre Phase IIb trial of TU combined with the progestogen norethisterone enantate (NET-EN) was again delayed due to non-availability of the study compounds. The protocol has been approved by the Programme's Toxicology Panel and negotiations with the manufacturer are ongoing; a 2004 start date is anticipated. The study will be funded and conducted in collaboration with CONRAD.

#### *Behavioural and social science research*

In conjunction with the clinical trial of the TU + DMPA regimen (above), a study to assess users' perspectives and acceptability of the study compounds was completed in 2002. Results of this study will be submitted for publication in 2004.

The Programme is supporting a study to pilot-test instruments to assess the acceptability of, and mood or behavioural changes following, the administration of the TU + NET-EN regimen as a potential contraceptive in Italian men. Instruments have been developed and validated; data collection was completed in 2003 and analysis is ongoing. Preliminary evidence indicates that sexual behaviour and mood are not altered as a result of the hormone administration. It is anticipated that these instruments will be used in future clinical trials of male hormonal contraceptive methods.

#### *New projects initiated during the year*

A protocol to evaluate the pharmacokinetics and pharmacodynamics of a novel formulation of TU in hypogonadal men

is under development and review. The Xianju Pharmaceutical Corporation, Zhejiang, China, has developed a higher concentration preparation of the steroid. This will: allow the injection volume to be halved; reduce pain at the injection site; and improve acceptability, as compared to the formulation currently manufactured and available in China. A study of the pharmacokinetics of this formulation in monkeys was initiated in 2003; preliminary data suggest that the new formulation does not have a pharmacokinetic profile significantly different from other formulations of TU that are currently used commercially and in research. If the manufacturer is interested in pursuing this lead and public sector access to the equivalent commercial product is limited or restricted, a decision on going forward with the clinical trial will be made once the monkey data have been analysed (expected in early 2004).

### **Basic science leads toward the development of novel approaches to male fertility regulation**

#### *Specific objectives of research*

As a complement to clinical research related to male fertility regulation, the Programme supports innovative, goal-oriented basic research on sperm and testicular physiology. Potential research targets include the identification, characterization and manipulation of developmental events such as: acrosome and flagellar formation; the expression and function of sperm-specific proteins; and specific intracellular pathways or events required for sperm function. Investigators are required to focus on the unique aspects of their research that have implications for male contraceptive development.

#### *Progress*

In 1998–1999 and 2000–2001, the Programme issued calls for proposals for basic science activities targeted toward the identification of a novel target for a male contraceptive approach. The following activities were approved through a competitive peer-review process, and were ongoing in 2003.

#### *Delivery of antibodies to the male reproductive ducts to achieve immunocontraception*

This study seeks to determine whether a sufficient titre of antibody can be delivered to the lumen of the male reproductive ducts to saturate a target antigen, in order to achieve immunocontraception. Results indicate that IgG and IgA do enter the rete testes and prostatic fluids of the mouse and rat. In 2003, the investigators immunized mice against *Chlamydia* as a model to determine if preparations of prostatic fluid from these mice contain adequate antibody titres to kill cultures of *Chlamydia*. Preliminary results are encouraging. Immunization of male mice with preparations of sperm surface proteins had no effect on fertility. Antibody titres in the male reproductive fluids of these mice are under investigation, in order to assess the effectiveness of the immunizations in delivering antibodies against sperm to the male reproductive ducts.

#### *Investigation of the possible presence of the C progesterone receptor isoform at the level of the human sperm plasma membrane*

This project was designed to characterize and clone a putative sperm membrane progesterone receptor, as described in previous *Annual technical reports*. The study was completed in 2003; however, due to a variety of technical difficulties, the group was unable to accomplish the work as planned.

#### *Anti-spermatogenic effects of luteinizing and thyroid hormones*

Data from this pilot-study indicate that, in three-month-old Sprague Dawley rats, thyroxin, administered continuously by means of a subcutaneous pump, exerts an anti-spermatogenic effect. In 2003, work continued to establish the dose–response characteristics and possible mechanisms of this effect; the study was completed at the end of 2003. Serum and intratesticular hormone assays, measurements of testicular androgen concentrations and sperm counts are ongoing. Final results will be available in 2004.

#### *The prostasome as a potential new target for fertility regulation in men*

Work in 2002 had demonstrated that of 116 infertile men with anti-sperm antibodies, 97% had antibodies against prostasomes, suggesting that prostasomes could be a major target for anti-sperm antibodies. Eighty-five percent of these men had antibodies to proteins of 70–75 kDa; 80% reacted with a protein of 50–55 kDa. Researchers hypothesized that these two potential immunogens may be interesting candidates as anti-fertility targets. However, further research demonstrated a lack of tissue specificity of the identified prostasome proteins, so the study ended in 2003.

#### *Human sperm mitogen-activated protein kinase cascades and their role in sperm functions*

In this study, natural and potential sperm ligands are used to investigate the presence and role of a series of kinases in ligand-stimulated human sperm function. Initial results were described in the *Annual technical report 2002*. In 2003, the investigators determined that extracellular signal-related kinase (ERK) is downstream from protein kinase C. They also described a potentially novel mitogen-activated protein kinase in sperm and propose that human sperm progressive motility is maintained by the ratio of ERK to this protein, as regulated, in part, by progesterone. Both of the proteins are also involved in the human sperm acrosome reaction. The study is expected to continue, pending availability of funds.

#### *New projects initiated during the year*

A proposal to study the molecular and functional characteristics of the human sperm GnRH receptor was reviewed and approved. The work could begin in 2004, if funding allows.

## Annex 1a

## RESEARCH GROUP ON POST-OVULATORY METHODS FOR FERTILITY REGULATION IN 2003

## Members

György Bartfai, Albert Szent-György Medical University, Szeged, Hungary

Cheng Linan, Shanghai Institute of Family Planning Technical Instruction, Shanghai, China

Luigi Devoto, University of Chile, Santiago, Chile

Kristina Gemzell-Danielsson, Karolinska Hospital, Stockholm, Sweden

Pak Chung Ho, University of Hong Kong, Hong Kong, Special Administrative Region of China (*Chairman*)

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	3	60	1	20	1	20	5
Women	1	20			1	20	2
<b>from:</b>							
AFRO							
AMRO	1	20					1
EMRO							
EURO			1	20	1	20	2
SEARO							
WPRO	2	40					2

Annex 1b

**RESEARCH GROUP ON IMMUNOCONTRACEPTIVES IN 2003**

**Members**

John Beale, Cranbrook, Kent, United Kingdom  
 Marc Bygdeman, Karolinska Hospital, Stockholm, Sweden  
 Richard Elton, Tuscon, AZ, USA  
 Warren Jones, Flinders Medical Centre, Adelaide, Australia (*Chairman*)  
 Rob Loblay, Clinical Immunology Research Centre, Sydney, Australia  
 Viveca Odling, University Hospital, Uppsala, Sweden  
 Susan Pierce, Northwestern University, Evanston, IL, USA  
 Faye Schrater, Smith College, Project on Women and Social Change, Northampton, MA, USA  
 Shobha Sehgal, Postgraduate Institute of Medical Education and Research, Chandigarh, India  
 Gennadi Sukhikh, International Institute of Biological Medicine, Moscow, Russian Federation

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	1	10	1	10	8	80	10
Women	1	10			3	30	4
<b>from:</b>							
AFRO							
AMRO					3	30	3
EMRO							
EURO			1	10	3	30	4
SEARO	1	10					1
WPRO					2	20	2

**Collaborating agency scientist**

Doug Colvard, CONRAD, Arlington, VA, USA

## Annex 1c

## RESEARCH GROUP ON METHODS FOR THE REGULATION OF MALE FERTILITY IN 2003

## Members

Richard Anderson, MRC Human Reproductive Sciences Unit, Edinburgh, United Kingdom  
 Kiagus Arsyad, Sriwijaya University, Palembang, Indonesia  
 Hermann Behre, Martin Luther University, Halle, Germany (*Chairman*)  
 William Bremner, University of Washington, Seattle, WA, USA  
 Kai Dada, Ogun State University Teaching Hospital, Sagamu, Nigeria  
 Gu Yi-Qun, National Research Institute for Family Planning, Beijing, China  
 Ilpo Huhtaniemi, University of Turku, Turku, Finland  
 Robert McLachlan, Prince Henry's Institute of Medical Research, Victoria, Australia  
 Cristina Meriggiola, University of Bologna, Bologna, Italy  
 Nukman Moeloek, University of Indonesia, Jakarta, Indonesia  
 Eberhard Nieschlag, Institute of Reproductive Medicine, Münster, Germany  
 Zephne van der Spuy, University of Cape Town, Observatory, South Africa  
 Christina Wang, Harbor-University of California at Los Angeles Medical Center, Torrance, CA, USA  
 Frederick Wu, University of Manchester, Manchester, United Kingdom

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	5	36			9	64	14
Women	1	7			2	14	3
<b>from:</b>							
AFRO	2	14					2
AMRO					2	14	2
EMRO							
EURO					6	43	6
SEARO	2	14					2
WPRO	1	7			1	7	2

## Sub-Committee for the review of male basic science research

Stella Campo, Endocrinology Research Centre (CEDIE), Buenos Aires, Argentina  
 Patricia Cuasnicu, Institute of Biology and Experimental Medicine, Buenos Aires, Argentina  
 Anton Grootegoed, Erasmus University Rotterdam, Rotterdam, Netherlands  
 David Hamilton, University of Minneapolis Medical School, MN, USA  
 Norman Hecht, University of Pennsylvania, Philadelphia, PA, USA  
 Ilpo Huhtaniemi, University of Turku, Turku, Finland (*Chairman*)

## Collaborating agency scientists

Mark Barone, EngenderHealth, New York, NY, USA  
 Diana Blithe, National Institute of Child Health and Human Development, Bethesda, MD, USA  
 Douglas Colvard, CONRAD, Arlington, VA, USA  
 Henry Gabelnick, CONRAD, Arlington, VA, USA  
 Judy Manning, United States Agency for International Development, Washington, DC, USA  
 Régine Sitruk-Ware, Population Council, New York, NY, USA

Annex 1d

**WHO/ROCKEFELLER FOUNDATION INITIATIVE ON IMPLANTATION RESEARCH IN 2003**

**Members**

Ruben Gonzalez, Boston Biomedical Research Institute, Watertown, MA, USA

Michael Harper, Consortium for Industrial Collaboration in Contraceptive Research (CICCR), Arlington, VA, USA

Hideharu Kanzaki, Kansai Medical University, Osaka, Japan

Stephen Killick, Princess Royal Hospital, Hull, United Kingdom

John White, Hammersmith Hospital, London, United Kingdom

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members					5	100	5
Women							
<b>from:</b>							
AFRO							
AMRO					2	40	2
EMRO							
EURO					2	40	2
SEARO							
WPRO					1	20	1

**Collaborating agency scientists**

Mahmoud Fathalla, Assiut, Egypt

Evelyn Majidi, Rockefeller Foundation, New York, NY, USA

## Annex 2a

## RESEARCH GROUP ON POST-OVULATORY METHODS FOR FERTILITY REGULATION

## Scientists in 2003

*Principal investigators*

Cheng Linan, Shanghai Institute of Family Planning Technical Instruction, Shanghai, China  
 Horacio Croxatto, Chilean Institute of Reproductive Medicine, Santiago, Chile  
 Luigi Devoto, University of Chile, Santiago, Chile  
 Robert Garfield, University of Texas Medical Branch, Galveston, TX, USA  
 Jiejie Dai, Medical Primate Research Centre of China, Kunming, China  
 Lena Marions, Karolinska Institute, Stockholm, Sweden  
 Cora Ngai, University of Hong Kong, Hong Kong, Special Administrative Region of China  
 Maria Elena Ortiz, Catholic University of Chile, Santiago, Chile  
 Shi Shao-Qing, University of Texas Medical Branch, Galveston, TX, USA  
 Wang Jie-dong, National Research Institute for Family Planning, Beijing, China  
 Wu Shang-chun, National Research Institute for Family Planning, Beijing, China

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	8	73			3	27	11
Women	4	36			1	9	5
<b>from:</b>							
AFRO							
AMRO	3	27			2	18	5
EMRO							
EURO	1	9					1
SEARO							
WPRO	5	45					5

*Other scientists*

Mark Bygdeman, Karolinska Institute, Stockholm, Sweden  
 Kristina Gemzell-Danielsson, Karolinska Hospital, Stockholm, Sweden  
 Oskari Heikinheimo, Helsinki University Central Hospital, Helsinki, Finland  
 Pak Chung Ho, University of Hong Kong, Hong Kong, Special Administrative Region of China  
 Joachim Oehler, Concept Foundation, Pathumthani, Thailand  
 László Kovács, Albert Szent-György Medical University, Szeged, Hungary  
 Suneeta Mittal, All India Institute of Medical Sciences, New Delhi, India  
 Jayasree Sengupta, All India Institute of Medical Sciences, New Delhi, India  
 Régine Sitruk-Ware, Center for Biomedical Research, Population Council, New York, NY, USA  
 Xiao Bilian, National Research Institute for Family Planning, Beijing, China  
 Zhao Heng, National Research Institute for Family Planning, Beijing, China

Annex 2a (continued)

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	6	55	1	9	4	36	11
Women	3	27			2	18	5
<b>from:</b>							
AFRO							
AMRO					1	9	1
EMRO							
EURO	3	27	1	9			4
SEARO	3	27					3
WPRO	3	27					3

## Annex 2b

## RESEARCH GROUP ON LONG-ACTING SYSTEMIC AGENTS FOR FERTILITY REGULATION

## Scientists 2003

*Principal investigators*

Hany Abdel-Aleem, Assiut University, Assiut, Egypt  
 Rim Ben Aissa, Research Centre for Human Reproduction, Tunis, Tunisia  
 Vivian Brache, PROFAMILIA, Santo Domingo, Dominican Republic  
 Gu Sujuan, Beijing Municipal Research Institute for Family Planning, Beijing, China  
 Rebecca Massai, Chilean Institute of Reproductive Medicine (ICMER), Santiago, Chile  
 Peter Rogers, Monash Medical Centre, Clayton, Australia  
 Lois Salamonsen, Prince Henry's Institute of Medical Research, Clayton, Australia  
 Sri Bakti Subakir, University of Indonesia, Jakarta, Indonesia

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	6	75			2	25	8
Women	5	63			1	13	6
<b>from:</b>							
AFRO							
AMRO	2	25					2
EMRO	2	25					2
EURO							
SEARO	1	13					1
WPRO	1	13			2	25	3

*Other scientists*

Frank Alvarez, PROFAMILIA, Santo Domingo, Dominican Republic  
 Melissa Brasted, Prince Henry's Institute of Medical Research, Clayton, Australia  
 Horacio Croxatto, Chilean Institute of Reproductive Medicine (ICMER), Santiago, Chile  
 Rebecca Jones, Prince Henry's Institute of Medical Research, Clayton, Australia  
 Hayet Mansour, Research Centre for Human Reproduction, Tunis, Tunisia  
 Marion Marsh, Prince Henry's Institute of Medical Research, Clayton, Australia

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	3	50			3	50	6
Women	1	17			3	50	4
<b>from:</b>							
AFRO							
AMRO	2	33					2
EMRO	1	17					1
EURO							
SEARO							
WPRO					3	50	3

## Annex 2c

## RESEARCH GROUP ON IMMUNOCONTRACEPTIVES

## Scientists in 2003

*Principal investigators*

Richard Ascione, Aphton Corporation, Woodland, CA, USA  
 James Hampton, Peninsula Laboratories, San Carlos, CA, USA  
 Vernon Stevens, Ohio State University, Columbus, OH, USA

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members					3	100	3
Women							
<b>from:</b>							
AFRO							
AMRO					3	100	3
EMRO							
EURO							
SEARO							
WPRO							

*Other scientists*

Faz Chowdury, Aphton Corporation, Loughborough, United Kingdom  
 Peter Fagan, Quintiles Pharmaceutical Services, Edinburgh, United Kingdom  
 Frederick Frye, Comparative Medical, Surgical and Pathology Consultation, Davis, CA, USA  
 Stephen Grimes, Aphton Corporation, Woodland, CA, USA  
 Susan Hagan, Aphton Corporation, Loughborough, United Kingdom  
 Pravin Kaumaya, Ohio State University, Columbus, OH, USA  
 Dov Michaeli, Aphton Corporation, Woodland, CA, USA  
 John Powell, Ohio State University, Columbus, OH, USA  
 Peter Rees, Huntingdon Life Sciences, Huntingdon, United Kingdom  
 Theo de Roij, Aphton Corporation, Tervuren, Belgium  
 Peter White, Nova Laboratories Limited, Leicester, United Kingdom

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members					11	100	11
Women					1	9	1
<b>from:</b>							
AFRO							
AMRO					5	45	5
EMRO							
EURO					6	55	6
SEARO							
WPRO							

## Annex 2d

## RESEARCH GROUP ON METHODS FOR THE REGULATION OF MALE FERTILITY

## Scientists in 2003

*Principal investigators*

Kiagus Arsyad, Sriwijaya University, Palembang, Indonesia  
 Gianni Forti, University of Florence, Florence, Italy  
 Gu Yi-Qun, National Research Institute for Family Planning, Beijing, China  
 Chandindrami Handagama, University of Tennessee, Knoxville, TN, USA  
 Russell Jones, University of Newcastle, New South Wales, Australia  
 Maria Cristina Meriggiola, University of Bologna, Bologna, Italy  
 Nukman Moeloek, University of Indonesia, Jakarta, Indonesia  
 Zvi Naor, Tel-Aviv University, Ramat Aviv, Israel  
 Eberhard Nieschlag, Institute of Reproductive Medicine, Münster, Germany  
 Ove Nilsson, Uppsala University, Uppsala, Sweden

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	4	40			6	60	10
Women					2	20	2
<b>from:</b>							
AFRO							
AMRO					1	10	1
EMRO							
EURO	1	10			4	40	5
SEARO	2	20					2
WPRO	1	10			1	10	2

*Other scientists*

Elisabetta Baldi, University of Florence, Florence, Italy  
 Richard Blye, National Institute of Child Health and Human Development, Bethesda, MD, USA  
 Bo Li-Wei, Henan Family Planning Research Institute, Henan, China  
 Cheng Li-Fa, Henan Family Planning Research Institute, Henan, China  
 Antonietta Costantino, S. Orsola Hospital, Bologna, Italy  
 David Handelsman, University of Sydney, Sydney, Australia  
 Li Han-Min, Birth-Control Institution, Guizhou, China  
 Liang Xiaowei, National Research Institute for Family Planning, Beijing, China  
 Lin Peng, Yunnan Family Planning Research Institute, Yunnan, China  
 Liu Xiao-Zhang, Sichuan Family Planning Research Institute, Sichuan, China  
 Michaela Luconi, University of Florence, Florence, Italy  
 Song Shu-Xiu, Hebei Family Planning Research Institute, Hebei, China  
 Ronald Swerdloff, Harbor-University of California at Los Angeles Medical Center, Torrance, CA, USA  
 Tong Jian-Sun, Jiangsu Family Planning Institute, Jiangsu, China  
 Wu Wei-Xiong, Family Planning Research Institute, Guangzhou, China  
 Xiong Cheng-Liang, Institute of Family Planning, Tongji Medical University, Hubei, China  
 Yao Kang-Shou, Zhejiang Institute of Planned Parenthood Research, Zhejiang, China  
 Kathryn Yount, Emory University, Atlanta, GA, USA  
 Zhao Heng, National Research Institute for Family Planning, Beijing, China

Annex 2d (continued)

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	12	63			7	37	19
Women	3	16			4	21	7
<b>from:</b>							
AFRO							
AMRO					3	16	3
EMRO							
EURO					3	16	3
SEARO							
WPRO	12	63			1	5	13

## Annex 2e

## RESEARCH GROUP ON NATURAL REGULATION OF FERTILITY

## Scientists 2003

*Principal investigators*

Stan Becker, Johns Hopkins University, Baltimore, MD, USA

Shakuntala Bhatnaar, National Institute of Health and Family Welfare, New Delhi, India

Len Blackwell, Massey University, Palmerston North, New Zealand

James Brown, Royal Women's Hospital, Melbourne, Australia

Hernan Delgado, Institute of Nutrition of Central America and Panama, Guatemala City, Guatemala

Kathy Kennedy, Denver, CO, USA

Pablo Lavin, University of Chile, Santiago, Chile

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	3	43			4	57	7
Women	1	14			1	14	2
<b>from:</b>							
AFRO							
AMRO	2	29			2	29	4
EMRO							
EURO							
SEARO	1	14					1
WPRO					2	29	2

Annex 2f

**WHO/ROCKEFELLER FOUNDATION INITIATIVE ON IMPLANTATION RESEARCH**

**Scientists in 2003**

*Principal investigators*

Peter Kaufmann, University of Aachen, Aachen, Germany

Liu Yi-Xun, State Key Laboratory of Reproductive Biology, Institute of Zoology, Beijing, China

Lois Salamonsen, Prince Henry's Institute of Medical Research, Clayton, Australia

Jayasree Sengupta, All India Institute of Medical Sciences, New Delhi, India

Stephen Smith, Rosie Maternity Hospital, Cambridge, United Kingdom

Richard Stouffer, Oregon Regional Primate Research Center, Beaverton, OR, USA

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	2	33			4	67	6
Women	1	17			1	17	2
<b>from:</b>							
AFRO							
AMRO					1	17	1
EMRO							
EURO					2	33	2
SEARO	1	17					1
WPRO	1	17			1	17	2

## Annex 3a

**RESEARCH GROUP ON POST-OVULATORY METHODS FOR FERTILITY REGULATION****Publications in 2003**

- Croxatto HB. Mifepristone for luteal phase contraception. *Contraception*, 2003, 68:483–488.
- Harper CC et al. Safety of levonorgestrel emergency contraception among adolescents. *Obstetrics and Gynecology* (submitted).
- Gemzell-Danielsson K, Mandl I, Marions L. Mechanisms of action of mifepristone when used for emergency contraception. *Contraception*, 2003, 68:471–476.
- Heikinheimo O, Kekkonen R, Lähteenmäki. Pharmacokinetics of mifepristone in the human reveal insights into differential mechanisms of antiprogesterin action. *Contraception*, 2003, 68:421–426.
- von Hertzen H, Bygdeman M. Summary of evidence and research needs on the use of mifepristone in fertility regulation: consensus from the conference. *Contraception*, 2003, 68:401–407.
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- Leminen R et al. Pharmacokinetics of 10 mg of mifepristone. *Contraception*, 2003, 68:427–429.
- Ortiz ME et al. Post-coital administration of levonorgestrel does not interfere with post-fertilization events in the new-world monkey *Cebus apella*. *Human Reproduction* (submitted).
- Piaggio G et al. Meta-analyses of randomized trials comparing different doses of mifepristone in emergency contraception. *Contraception*, 2003, 68:447–452.
- Piaggio G et al. Combined estimates of effectiveness of mifepristone 10 mg in emergency contraception. *Contraception*, 2003 68:439–446.
- Sengupta J et al. A multiparametric study of the action of mifepristone used in emergency contraception using the rhesus monkey as a primate model. *Contraception*, 2003, 68:453–469.
- Shi L et al. Synergistic effects of antiprogesterins and iNOS or aromatase inhibitors on establishment and maintenance of pregnancy. *Steroids*, 2003, 68:1077–1084.
- Sitruk-Ware R, Spitz IM. Pharmacological properties of mifepristone toxicology and safety in animal and human studies. *Contraception*, 2003, 68 (in press).
- Trussell J et al. Estimating the effectiveness of emergency contraceptive pills. *Contraception*, 2003,67:259–265.
- Wu J et al. Effects of a single and low dose of mifepristone on integrin expression in human endometrium during the peri-implantation period. *Reproduction and Contraception*, 2002, 13:214–221.
- Xiao B et al. Expanded clinical trial of emergency contraception with 10 mg mifepristone. *Contraception*, 2003, 68:431–437.
- Xiao B et al. Luteal phase treatment with mifepristone and misoprostol for fertility regulation. *Contraception*, 2003, 68:477–482.

**Annex 3b**

**RESEARCH GROUP ON LONG-ACTING SYSTEMIC AGENTS FOR FERTILITY REGULATION**

**Publications in 2003**

*Basic research on endometrial bleeding*

Hannan HJ et al. Co-expression of fractalkine and its receptor in normal human endometrium and in endometrium from users of progestin-only contraception supports a role for fractalkine in leukocyte recruitment and endometrial re-modelling. *Journal of Clinical Endocrinology and Metabolism*, 2003 (submitted).

Stepito NK, Rogers PAW. Cytosensor monitoring of microvascular endothelial cells. Proceedings of the 34<sup>th</sup> annual scientific meeting of the Society for Reproductive Biology, Melbourne, Australia. *Reproduction, Fertility and Development*, 2003; 15 (suppl):99.

## Annex 3c

**RESEARCH GROUP ON METHODS FOR THE REGULATION OF MALE FERTILITY****Publications in 2003**

Carlsson L et al. A new test for immunological infertility: an ELISA based on prostasomes. *International Journal of Andrology* (accepted).

Carlsson L, Ronquist G, Nilsson BO, Larsson A. Prolactin-induced protein and clusterin are the predominant prostasomal antigens for ASA of patients with immunological infertility. *Journal of Andrology* (submitted).

Gu Y-Q, Wang X-H, Xu D, Peng L, Cheng L-F, Huang M-K, Huang Z-J, Zhang G-Y. A multicenter contraceptive efficacy study of injectable testosterone undecanoate in healthy Chinese men. *Journal of Clinical Endocrinology and Metabolism*, 2003, 88: 562–568.

Jones RC, Dacheux JL. Pathophysiology of the epididymis. In: Kandeel F, ed. *Pathophysiology and treatment of the male sexual and reproductive dysfunction*. New York, Marcel Dekker, Inc. (accepted).

Luconi M et al. Human spermatozoa as a model for studying membrane receptors mediating rapid nongenomic effects of progesterone and estrogens. *Steroids*, 2004 (in press).

Merigiola MC, Farley TMM, Mbizvo MT. A review of androgen-progestin regimens for male contraception. *Journal of Andrology*, 2003, 24(4):466–483.

O'Connor DB, Archer J, Wu FCW. Effects of testosterone on mood, aggression and sexual behavior in young men: a double-blind, placebo-controlled, cross-over study. *Journal of Clinical Endocrinology and Metabolism* (submitted).

Pomering M et al. Restricted entry of IgG into male and female rabbit reproductive ducts following immunization with recombinant rabbit PH-20. *American Journal of Reproductive Immunology*, 2002, 47:174–182.

**Annex 3d**

**RESEARCH GROUP ON NATURAL REGULATION OF FERTILITY**

**Publications in 2003**

Becker S, Ahmed S. Dynamics of contraceptive use and breastfeeding during the post-partum period in Peru and Indonesia. *Population Studies*, 2003, 55:165–179.

Becker S, Rutstein S, Labbok MH. Estimation of births averted due to breast-feeding and increases in levels of contraception needed to substitute for breast-feeding. *Journal of Biosocial Science*, 2003, 35:559–574.

Bhatnagar S, for the WHO Task Force on Methods for the Natural Regulation of Fertility. Infant feeding patterns and lactational amenorrhoea in New Delhi. *International Journal of Public Health* (submitted).

Blackwell LF et al. Hormonal monitoring of ovarian activity using the Ovarian Monitor, Part I. Validation of home and laboratory results obtained during ovulatory cycles by comparison with radioimmunoassay. *Steroids*: 2003, 68:465–476.

Blackwell LF, Brown JB. Hormonal monitoring of ovarian activity using the Ovarian Monitor, Part II. Characteristics of the normal menstrual cycle (submitted).

Blackwell LF et al. Hormonal monitoring of ovarian activity using the Ovarian Monitor, Part III. Multicentre study of the hormonal definition of the fertile days of the cycle by home hormonal monitoring for natural family planning. A comparison with the basal body temperature and cervical mucus symptoms (submitted).

## Annex 3e

## WHO/ROCKEFELLER FOUNDATION INITIATIVE ON IMPLANTATION RESEARCH

## Publications in 2003

- Black S et al. Syncytial fusion of human trophoblast depends on caspase 8. *Cell Death and Differentiation*, 2004, 11:90–98.
- Borges M et al. A two-colour fluorescence assay for the measurement of syncytial fusion between trophoblast-derived cell lines. *Placenta*, 2003, 24:959–964.
- Borthwick JM et al. Determination of the transcript profile of human endometrium. *Molecular Human Reproduction*, 2003, 9: 19–33.
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- Chen XL et al. Regulatory effect of IFN- $\gamma$  on expression of TGF $\beta$ 1, T $\beta$ R-II, and StAR in corpus luteum of pregnant rhesus monkey. *Acta Pharmacologica Sinica*, 2003, 24:435–441.
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- Evans AL et al. Generation and use of a tailored gene array to investigate vascular biology. *Angiogenesis*, 2003, 6:93–104.
- Ghosh D, Bell SC, Sengupta J. Immunohistochemical localization of insulin-like growth factor binding protein-1 in primary implantation site and trauma-induced decidual tissues of the rhesus monkey. *Placenta* 2004, 25:197–207.
- Hastings JM et al. Soluble vascular endothelial growth factor receptor 1 inhibits edema and epithelial proliferation induced by 17 $\beta$ -estradiol in the mouse uterus. *Endocrinology*, 2003, 144:326–334.
- Hull ML et al. Antiangiogenic agents are effective inhibitors of endometriosis. *Journal of Clinical Endocrinology and Metabolism*, 2003, 88:2889–2899.
- Huppertz B, Kaufmann P, Kingdom J. Renouvellement normal et pathologique du trophoblaste villositaire. *Reproduction Humaine et Hormones*, 2003, 16:53–58.
- Liu K et al. Expression and regulation of plasminogen activators, plasminogen activator inhibitor type-1, and steroidogenic acute regulatory protein in the rhesus monkey corpus luteum. *Endocrinology*, 2003, 144: 3611–3617.
- Lu KC et al. Endometrial expression of calbindin-d9k & calbindin-d28k: species differences and regulation during early pregnancy. *Biology of Reproduction* (submitted).
- Nie GY et al. Identification and cloning of two isoforms of human HtrA3, characterisation of its genomic structure and comparison of its tissue distribution with HtrA1 and HtrA2. *Biochemical Journal*, 2003, 371:39–48.
- Nie GY et al. Specific and transient up-regulation of proprotein convertase 6 (PC6) at the site of embryo implantation and identification of a unique transcript in mouse uterus during early pregnancy. *Biology of Reproduction*, 2003, 68:439–447.
- Nie GY et al. A novel serine protease of the mammalian HtrA family is dramatically up-regulated during placentation in the mouse. *Molecular Human Reproduction*, 2003, 9:279–290.
- Poetgens AJG et al. A positive immunoselection method to isolate villous cytotrophoblast cells from first trimester and term placenta to high purity. *Placenta*, 2003, 24:412–423.
- Salamonsen LA et al. Complex regulation of decidualization: a role for cytokines and proteases. *Placenta*, 2003, 17 (suppl. A): S76–S85.
- Sengupta J, Dhawan L, Ghosh D. Immunohistochemical localization of leukemia inhibitory factor, interleukins 1 and 6 at the primary implantation site in the rhesus monkey. *Cytokine*, 2003, 24:277–285.
- Sengupta J et al. A multiparametric study of the action of mifepristone used in emergency contraception using the rhesus monkey as a primate model. *Contraception*, 2003, 68:453–469.
- Sengupta J, Ghosh D. Experimental models for human implantation. *Indian Journal of Physiology and Pharmacology*, 2003, 47:10–26.
- Sharkey AM, Smith SK. The endometrium as a cause of implantation failure (review). *Best Practice & Research Clinical Obstetrics & Gynaecology*, 2003, 17:289–307.
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# Safety and effectiveness of existing methods of fertility regulation

T.M.M. Farley and J. Schmidt

## INTRODUCTION

Most of the information on the safety and clinical performance of fertility-regulating methods is generated in developed countries and it is not necessarily appropriate to extrapolate to developing countries. The health and social situations are very different and there may be interactions with endemic conditions not seen in the developed countries. The Department's work on the safety and effectiveness of existing methods of fertility regulation is concerned with reviewing the evidence and building the evidence base on the safety and performance of fertility-regulating methods in developing countries. Clinical trials leading to product registration are conducted under ideal conditions with carefully screened and monitored volunteers. These may not reflect what happens when the products are made available to a wider population of users, and observational epidemiological methods must be used to study the safety and effectiveness under actual conditions of use. This evidence forms the basis for the development and promotion of norms, guidelines and training materials for the use of different methods of fertility regulation and for the development of high-quality family planning services. Progress in those areas is summarized in other chapters of this document.

### Objectives

The overall objectives of the work on the safety and effectiveness of existing methods of fertility regulation are (i) to assess evidence on the safety and effectiveness of different methods of contraception among women and men in developing countries, and (ii) to address priority unanswered questions on existing methods of fertility regulation when used in developing countries.

## RESEARCH ACTIVITIES

### Progress

#### *Hormonal factors in breast cancer*

The Programme supported The Collaborative Group on Hormonal Factors in Breast Cancer to compile individual patient data from epidemiological studies of breast cancer. The database includes over 50 000 cases of breast cancer and almost 100 000 women without the disease. Previous analyses addressed the relationship between breast cancer and hormonal contraception, hormone replacement therapy and family history of breast cancer, as well as the impact of breastfeeding and its duration on breast cancer risk. A recent investigation focused on the effect of alcohol and tobacco consumption on breast cancer risk using data on 58 515 women with breast cancer and 95 067 women without the disease from 53 epidemiological studies. The results suggest that while alcohol appears to exert an independent effect, smoking has little or no effect on the risk of developing breast cancer. Specifically, compared with women who reported drinking no alcohol, the relative risk of breast cancer was 1.32 (95% confidence interval [CI] 1.19–1.45) for an intake of 35–44 g/day alcohol, and 1.46 (95% CI 1.33–1.61) for  $\geq 45$  g/day alcohol. The relative risk of breast cancer increased by 7.1% (95% CI 5.5–8.7) for each additional 10 g/day intake of alcohol. The increase was the same in ever-smokers and never-smokers. By contrast, the relationship between smoking and breast cancer was substantially confounded by the effect of alcohol. When the analysis was restricted to women with breast cancer (N = 22 255) and women without the disease (N = 40,832) who reported drinking no alcohol, smoking was not associated with breast cancer. Assuming the observed relationship for alcohol is causal, the study

suggests that about 4% of breast cancer cases in developed countries are attributable to alcohol.

### *Bone mineral density and progestogen-only contraception*

Worldwide, over 20 million women are estimated to be currently using progestogen-only contraceptives, including injectables, implants, vaginal rings, the levonorgestrel-releasing intrauterine device and oral preparations. Concerns have been raised that progestogen-only preparations can decrease bone mineral density and thus increase subsequent risk of osteoporotic fracture. It is unclear whether any decrease in bone density noted with current use of progestogen-only contraception is transient or persistent.

Investigators at the Reproductive Health Research Unit, Durban, South Africa, are conducting a prospective study of the impact of progestogen-only contraception among women in the age ranges 15–19 years and 42–49 years. The younger age group covers the period of maximal bone mass acquisition, and any decrease due to progestogen-only contraception may affect the peak bone mass achieved. In the older age group, a transient decrease in bone mass with progestogen-only contraception may result in a woman starting her menopause-related decline in bone mass from a lower level.

Recruitment was completed with at least 100 women in each of eight subgroups: depot-medroxyprogesterone acetate (DMPA), norethisterone enantate (NET-EN), combined oral contraceptive (OC), and non-hormonal method users in each of two age groups (15–19 years and 42–49 years). Since most young women in South Africa are given the two-monthly injectable NET-EN, it was difficult to identify young DMPA users. All women are being followed at six-monthly intervals for up to five years. Full results for women in the 42–49 age group are expected in 2004.

One of the methodological problems faced by the study is the reliable identification of menopause and its timing, particularly among women using injectable contraceptives since these disrupt the normal menstrual pattern. Upon enrolment in the study, follicle-stimulating hormone (FSH) levels were measured and showed that 32% of the non-users had FSH levels in the menopausal range >25.8 IU/L compared to 28% of the DMPA users and 9% of the NET-EN group. After adjusting for age, there was no significant difference between the three groups ( $P = 0.13$ ). An increase of one year in age corresponded to an increase in the FSH level of 3 IU/L ( $p < 0.001$ ). All the hormonal contraceptive users were between 1 day and 12 weeks of their injection interval. Many had been using the injectable contraceptive method for over 10 years and almost all were amenorrhoeic at the time. The data show that a raised FSH level can be detected during use of DMPA and NET-EN and could be used as a menopausal indicator, particularly if taken late in the injection cycle, without interrupting method use in this group of contraceptive users.

These results were published in *Contraception* 2003, 68: 339–343.

### *Long-term safety and effectiveness of copper intrauterine devices*

Up to 147 million women world wide use intrauterine devices (IUDs) for family planning. IUDs have the advantage of being long-acting and relatively easy to remove, with a rapid return of fertility upon removal. The demonstration of their long-term safety and efficacy is an important aspect of the work of the Programme.

The long-term follow-up of cohorts of women using the copper-releasing TCu 380A device continues. In the period from 1989 to 1998, a total of 5953 women had this device inserted as part of Programme-sponsored randomized trials comparing the safety and effectiveness of different devices. The majority of the insertions took place from 1990 to 1991. The first large cohort of users completed 10 years of use at the end of 2001, and over 500 are expected to have completed 13 years of use by the end of 2003. The Programme will continue to follow users up to 15 years from insertion, thus providing unique information on long-term contraceptive safety and efficacy of this device. Previous data from the Programme's research have been used to extend progressively the approved lifespan of the device from the initial three to ten years. It is anticipated that the 12- and 15-year data will be used to extend the approved lifespan of these devices even further.

The randomized comparative study of the TCu 380A and the Multiload (ML) 375 copper-releasing devices started in the early 1990s, and the interim 10-year results are shown in Table 1.2. Both devices are highly effective in preventing pregnancy and have similar overall continuation rates. However, the intrauterine pregnancy rate with the TCu 380A is about half the rate of the ML 375 device at all times since insertion (Figure 1.5). There were few ectopic pregnancies, none of which occurred beyond the fifth year of use.

Just over half (54%) the women participating in this study lived in China. These women had an overall continuation rate of 55 per 100 after 10 years of use compared with only 15 per 100 among women from the other countries (Table 1.3). The pregnancy rates with both devices were higher among women in China than in the other countries, consistent with observations from previous multinational research on IUDs conducted by the Programme.

### *Clinical performance of the levonorgestrel-releasing intrauterine device*

The clinical performance of the 20 µg/day levonorgestrel (LNG)-releasing IUD (Mirena®) compared with the TCu 380A device is being assessed in a multicentre study involving a total of 3815 insertions. The interim results six years after insertion are presented in Table 1.4. The pregnancy rate for

Table 1.2. Cumulative net probabilities of discontinuation, and overall continuation rate, of use of IUD (standard error) per 100 women after ten years (interim data, to 30 September 2003)

Reason for discontinuation of use	TCu-380A	Multiload 375	P value
Pregnancy	3.4 (0.5)	5.3 (0.7)	0.029
Ectopic pregnancy	0.8 (0.3)	0.1 (0.1)	0.011
Intrauterine pregnancy	2.7 (0.5)	5.2 (0.7)	0.002
Expulsion	11.2 (1.0)	14.7 (1.2)	0.023
Medical reason	29.4 (1.4)	28.8 (1.5)	0.80
Pelvic inflammatory disease	0.4 (0.2)	0.5 (0.2)	0.82
Lost to follow-up	12.7 (1.0)	12.2 (1.1)	0.72
Overall continuation rate	40.2 (1.3)	37.5 (1.3)	0.14
Total woman-years	10 469	10 019	
Number of women completing 10 years	375	352	

the levonorgestrel device is significantly lower than for the TCu 380A, but there is a high rate of device removal for menstrual-related reasons, in particular amenorrhoea, with the levonorgestrel-releasing device. The overall continuation rate at six years was 43.4 per 100 women for the levonorgestrel device and 65.6 per 100 women for the TCu 380A.

*HIV and steroid contraception*

To assess the impact of different contraceptive methods on the clinical course of human immunodeficiency virus (HIV) infection, the Programme is sponsoring a multicentre study in Brazil, Kenya, Thailand and Zimbabwe. Women with HIV

Figure 1.5. Cumulative intrauterine and ectopic pregnancy rates by device (interim data, cut off 30 Sept 2003)

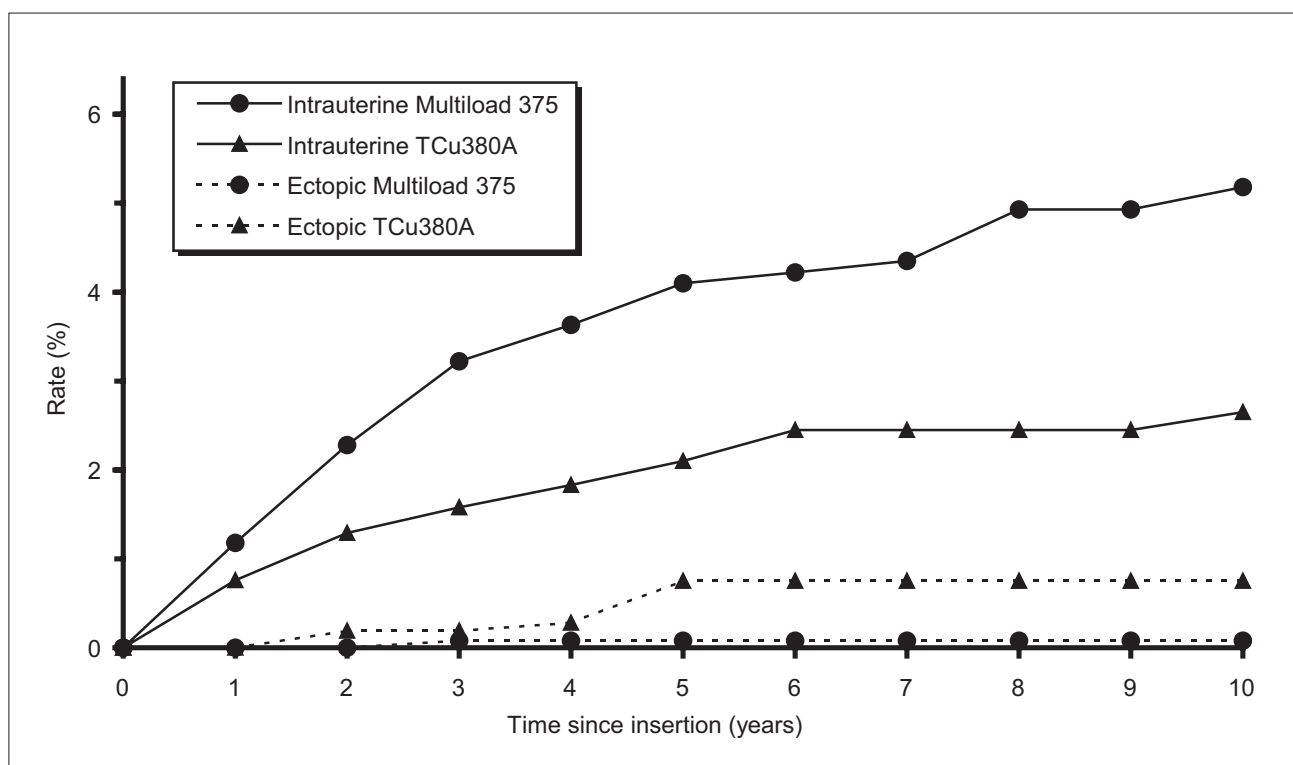


Table 1.3. Cumulative net probabilities of discontinuation, and overall continuation rate, of use of IUD (standard error) per 100 women after ten years in Chinese and Non-Chinese centres (interim data, cut off 30 Sept 2003)

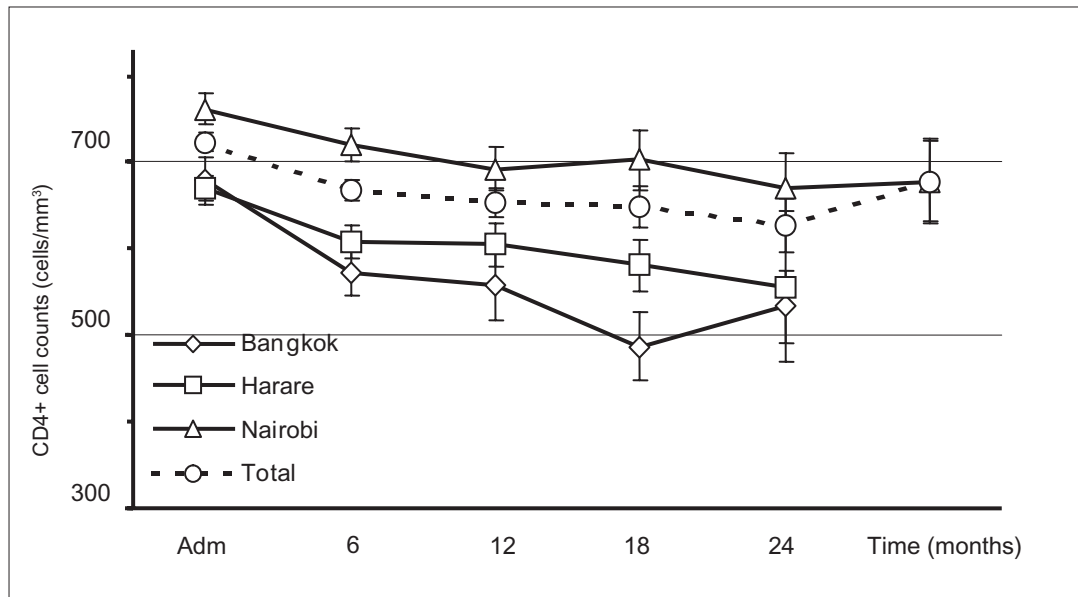
	Chinese centres		Non-Chinese centres	
	TCu 380A	Multiload 375	TCu 380A	Multiload 375
Total pregnancy	4.0 (0.7)	6.7 (0.9)	2.1 (0.6)	2.1 (0.6)
Ectopic pregnancy	0.9 (0.4)	0.1 (0.1)	0.3 (0.2)	-
Intrauterine pregnancy	3.1 (0.6)	6.6 (0.9)	1.8 (0.6)	2.1 (0.6)
Expulsions	11.4 (1.2)	16.2 (1.4)	9.9 (1.8)	9.8 (1.6)
Total medical removals	20.0 (1.5)	17.3 (1.5)	52.0 (3.3)	53.8 (3.3)
Pelvic inflammatory disease	-	-	1.6 (1.2)	1.6 (0.8)
Loss to follow-up	5.9 (0.9)	6.8 (1.1)	25.9 (2.7)	21.8 (2.6)
Overall continuation rate	57.5 (1.7)	52.9 (1.8)	14.9 (1.6)	15.2 (1.6)
Total woman-years	6780	6672	3365	3343
Number of women completing 10 years	322	295	53	57

Table 1.4. Cumulative net probabilities of discontinuation of use of IUD (standard error) per 100 women after six years of use (interim data, to 30 September 2003)

Reason for discontinuation of use	TCu-380A	Mirena	P value
Pregnancy	2.0 (0.5)	0.5 (0.2)	<0.001
Ectopic pregnancy	0.1 (0.1)	-	0.162
Intrauterine pregnancy	1.9 (0.4)	0.5 (0.2)	<0.001
Expulsion	8.2 (0.8)	7.5 (0.8)	0.51
Pelvic inflammatory disease	0.1 (0.1)	0.3 (0.1)	0.29
Menstrual disturbance	10.9 (0.9)	35.9 (1.4)	< 0.001
Amenorrhoea	0.5 (0.3)	23.6 (1.3)	< 0.001
Reduced bleeding	3.1 (0.5)	10.9 (1.0)	< 0.001
Increased bleeding	7.1 (0.7)	5.9 (0.7)	0.074
Total device-related removals	25.5 (1.1)	47.8 (1.3)	< 0.001
Lost to follow-up	7.9 (0.7)	5.8 (0.7)	0.036
Total woman-years	7421	6382	
Number of women completing 6 years	629	506	

infection are invited to participate in an observational cohort study with six-monthly follow-up visits for four years. Study endpoints include HIV disease progression, the incidence of opportunistic infections, and changes in CD4+ cell counts. These will be analysed according to the contraceptive methods used.

By December 2003, a total of 626 women had been enrolled in Kenya (308), Thailand (116) and Zimbabwe (202). Recruitment in the study was not possible in Brazil since antiretroviral (ARV) therapy is available nationally for all patients and few patients had CD4+ counts of at least 500 cells/mm<sup>3</sup>. The majority of women enrolled used hormonal contraception (primarily DMPA in Nairobi and combined OCs in Harare) and non-hormonal methods

Figure 1.6. Decline in CD4+ cell counts (cells/mm<sup>3</sup>) by centre

were used by 25% of the study cohort. Recruitment to the cohort was stopped at the end of December 2003. The rates of CD4+ cell count decline are much steeper in Bangkok and Harare compared with Nairobi (Figure 1.6), possibly reflecting the impact of different HIV subtypes.

As a result of increasing access to sustainable ARV therapy in the study sites, the protocol has been adapted to introduce ARV drugs in a structured way to women in the cohort as they become eligible for therapy according to WHO and national guidelines. This will permit a preliminary assessment of differences in clinical response to first-line ARV therapy by type of hormonal contraception. However, the study is moderate in size and will provide useful comparative information for DMPA and combined OC users only. Results on initial clinical response to therapy in hormonal users are expected in 2005.

Additional questions on the interactions between hormonal contraception and ARV therapy are becoming more urgent as therapy becomes more widely available in resource-limited settings. These include:

- response to first-line ARV therapy in users of different contraceptive methods (intrauterine devices, combined OCs, DMPA, NET-EN, implants);
- acceptability and tolerance of different contraceptive methods among women starting first-line ARV therapy; and
- pharmacokinetic and pharmacodynamic studies of the interactions between hormonal contraceptives and ARV therapy in women from developing countries.

Results from such studies will form the basis for evidence-based recommendations regarding contraceptive choices for HIV-positive women who are under ARV therapy. The Programme is seeking ways to assemble larger cohorts of women to answer these questions.

#### *HIV and vaginal epithelium*

Progestogen-only contraception has been associated with increased susceptibility to HIV infection. In a study in Umeå, Sweden, vaginal biopsies were taken from 15 women using combined OCs, DMPA and Norplant and from 15 women not using hormonal contraception to assess the impact of different contraceptive methods on the thickness and on immune cell parameters of the normal human vaginal epithelium. The epithelium was significantly thicker in all three groups of women using hormonal contraceptives compared with controls (mean thickness 333  $\mu$ m and 261  $\mu$ m, respectively) and exhibited a hyperplastic superficial layer. Compared with controls, significant changes occurred in the intraepithelial leukocyte population in DMPA users ( $P < 0.001$ ) and Norplant users ( $P < 0.04$ ), whereas no such changes were observed in combined OC users. In DMPA users, changes were explained by a relative increase in CD8+ cells, a subset of T lymphocytes. The altered immune protection capacity of the vaginal epithelium in DMPA and Norplant users may have implications for the risk of acquiring sexually transmitted infections.

#### *Mifepristone-induced abortion and outcome of subsequent pregnancy*

Investigators in China assessed whether a mifepristone-induced early abortion in nulliparous women affects the outcome of a subsequent wanted pregnancy. In a prospective

study, 4925 women with no history of induced abortion, 4931 with one previous mifepristone-induced abortion, and 4800 with one previous surgical abortion were enrolled from antenatal clinics in Beijing, Chengdu and Shanghai and followed through pregnancy and delivery. The adjusted odds ratio for preterm delivery in women with past mifepristone-induced abortion compared with women with no abortion was 0.77 (95% confidential interval: 0.61–0.98). The mean birthweight of infants born to women with mifepristone-induced abortion was marginally higher than that of those born to women with no abortion, with an adjusted difference of 33 g (95% CI: 17–49), but the rates of low birthweight and mean pregnancy duration were similar. There were no significant differences in risk of preterm delivery, low birthweight, or mean infant birthweight in the comparisons between women with previous mifepristone-induced or surgically-induced abortion, though the mean pregnancy duration was marginally longer among the latter. This study suggests that one early abortion induced by mifepristone has no adverse effects on the outcome of a subsequent wanted pregnancy in nulliparous women.

#### *HPV, cervical cancer and steroid hormone contraception*

Whether use of oral contraceptives is causally associated with an increased risk of cervical cancer has been controversial. A WHO Scientific Group concluded in 1990 that use of oral contraceptive for more than five years was associated with a modest (1.3–1.8-fold) increased risk of cervical cancer. However, it was unclear whether that risk reflected a biological relationship or was attributable to other factors, such as differences in lifestyle between contraceptive method users, or patterns of sexually transmitted infections, particularly with human papilloma virus (HPV). Results published in early 2002 (Moreno et al, *Lancet*, 2002, 359: 1085–1092) showed that among women who tested positive for HPV infection, those who had used hormonal contraceptives for between five and nine years had a 2.8-fold increased risk of cervical cancer, while women who had used hormonal contraception for 10 or more years had a 4-fold increased risk. The Programme convened a consultation in March 2002 to review these results and other information on the relationship between cervical cancer and hormonal contraception. A systematic review on combined oral contraceptive use and the risk of cervical cancer was commissioned (Smith et al, *Lancet*, 2003, 361:1159–1167). The review confirmed that long duration of use of oral contraceptives was associated with an increased risk of cervical cancer. Previous reports have shown that the relative risk of cervical cancer associated with oral contraceptive use might decline after discontinuation of use. However, the review was hampered by the lack of data needed to address this question. The Consultation therefore recommended to establish an individual record meta-analysis from all relevant studies to address better the key question of effect of duration of use within categories of time since last use.

Data from relevant studies have been consolidated into a common database in Oxford, United Kingdom. With primary support from the Programme, the investigators from all studies met at the International Agency for Research on Cancer (IARC) in Lyon, France, on 7–8 November 2003 to review preliminary results from the consolidated data and to plan future activities and publications. Thirty-six collaborators and 18 IARC staff gathered at the meeting, assembling data from 31 studies on 10 907 cases of invasive cancer, 4959 cases of cervical intraepithelial neoplasia (CIN) grade three or *in situ* cancer, and 33 726 controls (total: 49 592 women). Preliminary results on hormonal contraceptives, sexual and reproductive factors, and smoking were discussed. Specific suggestions for stratification and adjustment for confounding were made and an agreement was reached regarding future key analyses and their possible interpretation. Among the next steps were the identification of new data on hormonal factors and cervical cancer and the search for additional studies on smoking and cervical cancer. The first papers on OCs, as well as sexual and reproductive factors, will be drafted on the basis of existing data and updated as the database is being finalized.

#### *Natural history of HPV infections and cervical intraepithelial neoplasia*

With partial support from the Programme and in collaboration with the Colombian National Institute of Cancer, IARC scientists conducted two studies on the natural history of HPV infection in women who were cytologically normal. Both studies were conducted with subsamples from a large population-based cohort of 1995 women aged 13–85 years drawn from a low-income population in Bogota, Colombia.

The first study aimed to report type-specific prevalence and determinants of HPV infection in 1859 women with normal cytology (Molano et al, *British Journal of Cancer*, 2002, 87: 324–333). The overall HPV prevalence was 14.8%, of which 9% were infected with the high-risk types, 3.1% with low-risk types, 2.3% with both high-risk/low-risk types, and 0.4% by uncharacterized types. A total of 32 different types were detected. The HPV prevalence was higher among women younger than 20 years (26%), and low (2.3%) in women above 45 years of age. Besides age, multiplicity of sexual partners and OC use predicted infection risk.

In the second study, a subset of 227 women with prevalent HPV infection and a normal cytology were followed over five years to investigate determinants of clearance of HPV infections (Molano et al, *American Journal of Epidemiology*, 2003, 158:486–494), where clearance of a given HPV type is defined as disappearance of the HPV type that had been detected at enrolment. The overall clearance rate was not constant, and was highest during the first six months of follow-up. Thirty-eight percent of HPV infections were still present at one year and 7% at five years. HPV16 had a significantly lower clearance rate than infections with low-risk types. Infections with single and multiple HPV types had

similar clearance rates. Parity was significantly associated with slower clearance, ever-use of OCs with faster clearance. Less than half of prevalent HPV infections persisted after one year, and over 7% after five years. The strongest risk factor for persistence of infection was the presence of HPV type 16.

### *Risk factors of women with low-grade squamous intraepithelial lesions*

Using data from the same Colombian study population, a cross-sectional case-control study was conducted to compare the risk profile of women with low-grade squamous intraepithelial lesions (LSIL) with that of HPV-negative and positive women with normal cytology (Molano et al, *British Journal of Cancer*, 2002, 87:1417–1421). While the estimated prevalence of HPV among women with normal cytology was 14.9%, it was 55.7% among women with LSIL. More severe lesions were associated with higher prevalence of HPV, higher prevalence of high-risk HPV types and higher odds ratios. When LSIL cases were compared to HPV-negative controls, no association with tobacco smoking or the number of sexual partners was observed, and a reduced risk of LSIL was associated with ever-use of oral contraceptives. This result was not consistent with results from previous research, and may be due to the small number of LSIL cases.

### *Possible cofactors in the etiology of invasive cervical cancer*

Three papers addressed the issue of possible HPV cofactors in the etiology of invasive cervical cancer (ICC). The first paper reported a cross-sectional study using data from the Colombian study population (Molano et al, submitted for publication). The aim of the study was to determine the prevalence and determinants of *Chlamydia trachomatis* infection and its association with HPV infection. While the overall *C. trachomatis* prevalence (5%) did not differ from that in other geographical areas, no difference in prevalence was observed between women with normal and abnormal cervical cytology, and between women with and without HPV infection. Among HPV-infected women *C. trachomatis* infection was significantly more prevalent among women with multiple HPV infection (9.5%) compared with women with single HPV infection (5.9%). Besides young age, multiple HPV infection was the only risk factor independently associated with *C. trachomatis* infection.

The second paper reported a study conducted in São Paulo, Brazil, and Manila, the Philippines, which examined genital *C. trachomatis* infection as a possible cofactor for ICC among HPV-infected women (Smith et al, *Journal of Infectious Diseases*, 2002, 185:324–331). The study indicated a moderate, yet significant, association between *C. trachomatis* infection and ICC in the presence of HPV infection.

The third paper reported a pooled analysis of seven case-control studies conducted in Brazil, Colombia, Morocco, Peru, Philippines, Spain and Thailand, to examine the influence of genital Herpes simplex virus-2 (HSV-2) infection in the etiology of ICC (Smith et al, *Journal of the National Cancer Institute*, 2002, 94:1604–1613). The results suggest that although HSV-2 infection may act in conjunction with HPV infection to increase the risk of ICC, the effect of HSV-2 infection on ICC risk is modest, compared with the strong effect of HPV infection on ICC risk.

### *Vasectomy and prostate cancer risk*

Using hospital discharge data, researchers from the University of Copenhagen, Copenhagen, Denmark studied the risk of prostate cancer after vasectomy in men who had been hospitalized for vasectomy between 1977 and 1989 (N=57 931). The observed number of patients with cancer in the cohort (N=46) did not differ from the number expected based on the cancer incidence rate for all Danish men. Time since vasectomy or age at vasectomy did not reveal any trend. This study adds to the evidence that there is no excess prostate cancer risk associated with vasectomy (Lynge E, *Journal of Urology*, 2002, 168:488–490).

## **New projects initiated during the year**

### *Randomized trial of two implantable contraceptives for women*

The Programme initiated a multinational randomized comparative trial of Jadelle® and Implanon® to determine differences in clinical performance and contraceptive efficacy of the two implantable devices. Primary endpoints include pregnancy rates, incidence of adverse effects, method acceptability and continuation rates. A total of 2000 women will be enrolled and randomly assigned to use one of the two implants. While non-reproductive system complaints such as headache, dizziness, skin alterations, and mood changes are commonly associated with progestogen-only implants, interpretation of their clinical significance is difficult. Therefore, in addition to the implant users, an age-matched cohort of 1000 women who choose the TCU 380A IUD will be enrolled in parallel with the randomized study. These women will provide data on the incidence of non-reproductive system complaints in users of a non-hormonal method in order to place the observations from the implant users in context.

Ten sites in nine countries are participating: Ankara (Turkey), Bangkok (Thailand), Campinas (Brazil), Beijing and Shanghai (China), Harare (Zimbabwe), Ljubljana (Slovenia), Santiago (Chile), Santo Domingo (Dominican Republic) and Szeged (Hungary). Recruitment has begun and interim results on the one-year experience are expected in 2005. Final results on study endpoints, three years after insertion, will be available in 2007.

## Annex 1a

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	4	36			7	64	11
Women	1	9			3	27	4
<b>from:</b>							
AFRO	1	9					1
AMRO	2	18					2
EMRO							
EURO					5	45	5
SEARO							
WPRO	1	9			2	18	3

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	10	29			24	71	34
Women	3	9			14	41	17
<b>from:</b>							
AFRO	2	6					2
AMRO	4	12			7	21	11
EMRO	1	3					1
EURO					16	47	16
SEARO	2	6					2
WPRO	1	3			1	3	2

## Annex 2

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## Annex 2 (continued)

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	41	84	4	8	4	8	49
Women	19	39	1	2	3	6	23
<b>from:</b>							
AFRO	6	12					6
AMRO	8	16			1	2	9
EMRO	2	4					2
EURO	1	2	4	8	3	6	8
SEARO	4	8					4
WPRO	20	41					20

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**Annex 2 (continued)**

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	42	81	5	10	5	10	52
Women	18	35	2	4	2	4	22
<b>from:</b>							
AFRO	1	2					1
AMRO	2	4			2	4	4
EMRO	1	2					1
EURO	1	2	5	10	2	4	8
SEARO	2	4					2
WPRO	35	67			1	2	36

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# Norms and guidelines for use of methods of fertility regulation

H.B. Peterson, K. Church, S. Johnson, E. Vayena

## INTRODUCTION

Family planning programmes are facing the challenge of finding better ways to deliver high-quality family planning services to the millions of people who would use family planning if they had access to it. However, many family planning programmes have substantial progress to make in improving quality of care. The Department is contributing to these efforts by creating four cornerstones of evidence-based and consensus-driven guidance for family planning. This new series includes two guidelines—the *Medical eligibility criteria for contraceptive use* and the *Selected practice recommendations for contraceptive use*—and two tools—the *Decision-making tool for family planning clients and providers* and a handbook for family planning providers. A system has also been created to assure that this global family planning guidance is based on the best available evidence through a continuous, systematic process of identifying, critically appraising, and synthesizing new evidence as it becomes available.

The creation of evidence-based guidelines and tools alone, while important, is insufficient to assure that family planning services are improved. The ultimate impact of the Department's norms and tools will be contingent on the development of successful strategies for implementation.

## OVERALL OBJECTIVE

The overall objective of the Department in the area of promoting family planning norms and tools is to create evidence-based and consensus-driven guidance to support the provision of high-quality family planning services globally.

To achieve this objective, the Department is:

- establishing the context for norms and tools within a programme of research for promoting family planning;
- developing four cornerstones of evidence-based guidance for promoting family planning;
- creating a system for developing guidelines based on the best available evidence and assuring that they are kept up-to-date; and
- developing an implementation strategy for, and providing support to countries with, adopting and adapting WHO's family planning guidance.

## Establishing the context

The context for developing norms and tools in family planning is based on a framework that links the four major goals of the Department in promoting family planning:

- to develop new and improved methods of contraception (including methods for dual protection);
- to evaluate the safety and effectiveness of existing methods of family planning;
- to assess the sociocultural and behavioural determinants of successful family planning use;
- to translate available evidence into guidelines that can be used successfully at country level.

The first three goals are supported by research activities of the Programme and the fourth is based on the research findings derived from those activities and other relevant research. Thus, the findings from social science research (see Users' perspectives in the context of reproductive health, page 22) and research on the safety and efficacy of contraceptive methods (see page 31) feed directly into the evidence base for norms and tools. As new methods are developed and evaluated, research on safety and efficacy, as well as acceptability of the method, becomes part of the evidence base. Further, a feedback loop exists between the guidelines and the research priorities. Key gaps in evidence are identified as available evidence is appraised, synthesized and considered for guidelines. Some of these gaps, in turn, become research priorities for social science or safety and efficacy research.

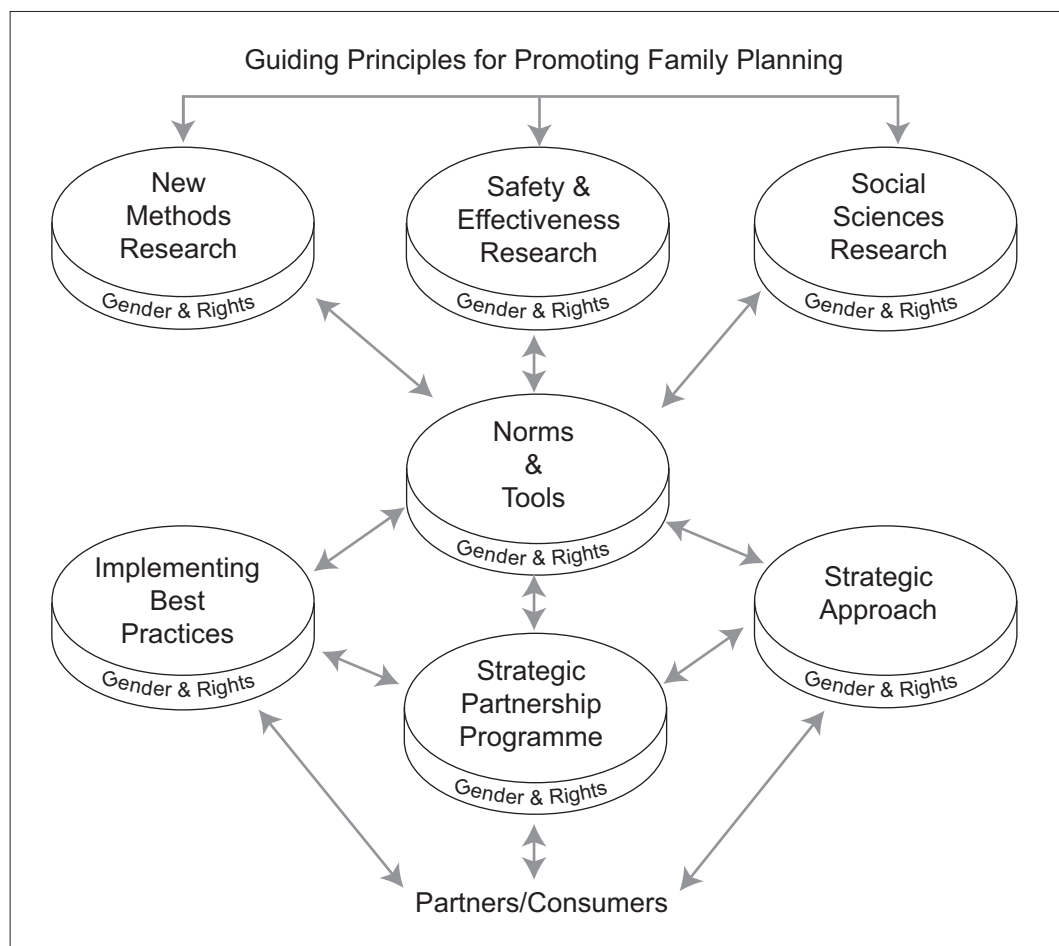
The creation of evidence-based guidelines, while important, is insufficient to assure the delivery of quality services in family planning. The dissemination, adaptation and utilization of guidelines is also critical. The ultimate impact of guidelines will be contingent on the development of strategies for the successful implementation of best practices in family planning. The Implementing Best Practices initiative (see page 223)

and the Strategic Approach (see page 213) are examples of such strategies currently being implemented by the Department. A new initiative between WHO and the United Nations Population Fund (UNFPA), the Strategic Partnership Programme, will likewise support the implementation of best practices in family planning at country level. The needs of the users at the country level will, in turn, help determine priorities for creating and implementing guidelines (Figure 1.7).

### Developing the four cornerstones of evidence-based guidance for promoting family planning

The *Medical eligibility criteria for contraceptive use* and the *Selected practice recommendations for contraceptive use* are the first two cornerstones of the evidence and consensus-based foundation of WHO's family planning guidance. They are intended for policy-makers, family planning programme managers, and the scientific community and aim to assist in the preparation of guidelines for service delivery. In effect, they provide 'guidance for guides'. The *Medical eligibility criteria for contraceptive use* provides guidance regarding *who* can safely use contraceptive methods. The *Selected practice recommendations for contraceptive use* provides guidance regarding *how* to use contraceptive methods safely and

Figure 1.7. Schematic presentation of the role of different areas in the development of norms and tools to promote family planning



effectively. Recommendations include instructions on when and how to start contraceptive use and what to do in problem situations. The *Medical eligibility criteria for contraceptive use* was updated with recommendations from an expert working group in October 2003 and the *Selected practice recommendations for contraceptive use* will be updated in 2004.

The *Decision-making tool for family planning clients and providers* and a handbook for family planning providers are the third and fourth cornerstones of WHO's family planning guidance respectively, and will be derived primarily from the *Medical eligibility criteria for contraceptive use* and the *Selected practice recommendations for contraceptive use*, but will also include best evidence from social science research on how to meet the needs of the family planning client. They are intended to be used by family planning providers during their discussions with clients searching family planning advice, and are designed to improve the quality of care—they provide 'guidance for providers and clients'. These two tools will also be accompanied by an adaptation guide, training package, and materials for clients.

### Creating a system

The *Medical eligibility criteria for contraceptive use* and the *Selected practice recommendations for contraceptive use* are evidence-based and consensus-driven guidelines. They provide recommendations made by expert working groups based on an appraisal of relevant evidence. They are reviewed and updated in a timely manner.

A system has been developed to assure that this global family planning guidance is created and maintained based on the best available evidence. This system, called CIRE (Continuous Identification of Research Evidence), includes a continuous and comprehensive process of identifying, critically appraising, and synthesizing new evidence as it becomes available. The system is a collaborative effort between the Department, the Johns Hopkins University Bloomberg School of Public Health's Center for Communication Programs (JHU/CCP) and the Centers for Disease Control and Prevention (CDC)/WHO Collaborating Centre for Reproductive Health (CDC/WHOCC).

The initial activity of the system is conducted by JHU/CCP, and consists of an ongoing, comprehensive bibliographic search using the POPLINE database to identify studies that may be of relevance to the guidance. This is achieved by: (i) screening input to the POPLINE database (averaging 850 records per month) to identify research reports that may be relevant; (ii) posting bibliographic information to a database; and (iii) categorizing the bibliographic data according to the research issue it addresses.

The second activity of the system is conducted by CDC, and consists of: (i) determining which new research reports are relevant; (ii) critically appraising new, relevant reports; (iii) preparing systematic reviews; (iv) obtaining peer review of

systematic reviews and revising as appropriate; and (v) providing final systematic reviews to the Department.

The third activity of the system is conducted by WHO, and consists of working with CDC and the WHO Promoting Family Planning Guidelines Steering Group. This group was created in response to WHO's new "Guidelines for Guidelines", to provide ongoing oversight and advice on the preparation of the *Medical eligibility criteria for contraceptive use* and the *Selected practice recommendations for contraceptive use*. The Guidelines Steering Group assists the Department in planning the guideline update process, including advice on the conduct of the expert working group meetings. An important additional responsibility of the group is to provide interim guidance on behalf of the expert working group when it determines that such guidance is warranted. Updates are provided electronically pending the next printing of the guidelines. The first electronic update providing such interim guidance was published on the Department's web site in 2003.

The CIRE System became operational in November 2002, and is ongoing (Figure 1.8). It was used to prepare the evidence for the third edition of the *Medical eligibility criteria for contraceptive use*, and will be used for further editions. Likewise, the second edition of *Selected practice recommendations for contraceptive use* will also benefit from the CIRE System.

### Developing an implementation strategy

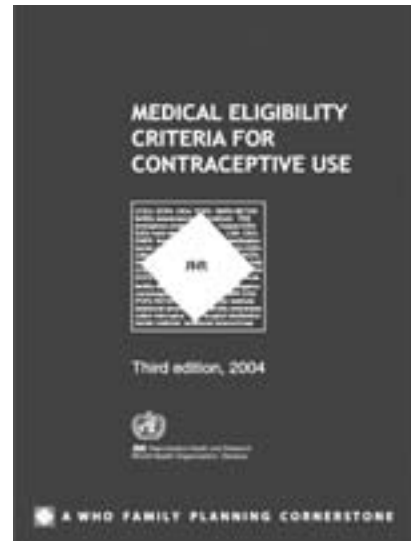
The creation of evidence-based guidelines alone is insufficient to assure the delivery of quality services in family planning. To assure that the guidance has impact, the Department provides technical assistance and support for effective implementation, including training in the use and adaptation of the guidance to the local context. The Department is committed to strengthening the technical link between the creation and the implementation of its guidance; in this regard the Department works with WHO regional and country offices and its global partners to achieve maximum impact.

In a bid to improve further the impact of its guidelines, a new partnership was initiated in October 2003 with UNFPA. Through this new Strategic Partnership Programme, WHO and UNFPA will work together to assure a link between the creation of evidence-based guidelines and tools at WHO headquarters and their adaptation and adoption in countries through UNFPA Country Support Teams (CSTs), WHO regional and country offices, and other partner organizations. The partnership is in its initial planning stage, but will involve the development of training programmes to strengthen the technical capacity of the CSTs and WHO regional offices to implement WHO's family planning guidelines and tools. The partnership will also develop specific adaptation and training guides for the guidelines and tools to help the CSTs, WHO regional and country offices, national programme managers, and policy-makers implement them at country level.

**NEW NORMS/TOOLS DEVELOPED**

The third edition of the *Medical eligibility criteria for contraceptive use* updates the 2000 edition and provides detailed guidance regarding the medical appropriateness of initiating and continuing contraceptive use for women and men with medical problems or selected conditions. The *Medical eligibility criteria for contraceptive use* has been an important step in a process for improving access to quality of care in family planning and has provided guidance to national family planning/reproductive health programmes in the preparation and revision of national medical and service provision guidelines. Prior editions of the document have been translated into at least eight languages, including Arabic, Chinese, French, Bahasa Indonesia, Romanian, Russian, Spanish and Vietnamese. With the help of the US Agency for International Development (USAID) and other collaborating partners, this document has been used in over 50 countries in the preparation and revision of national service delivery guidelines for family planning.

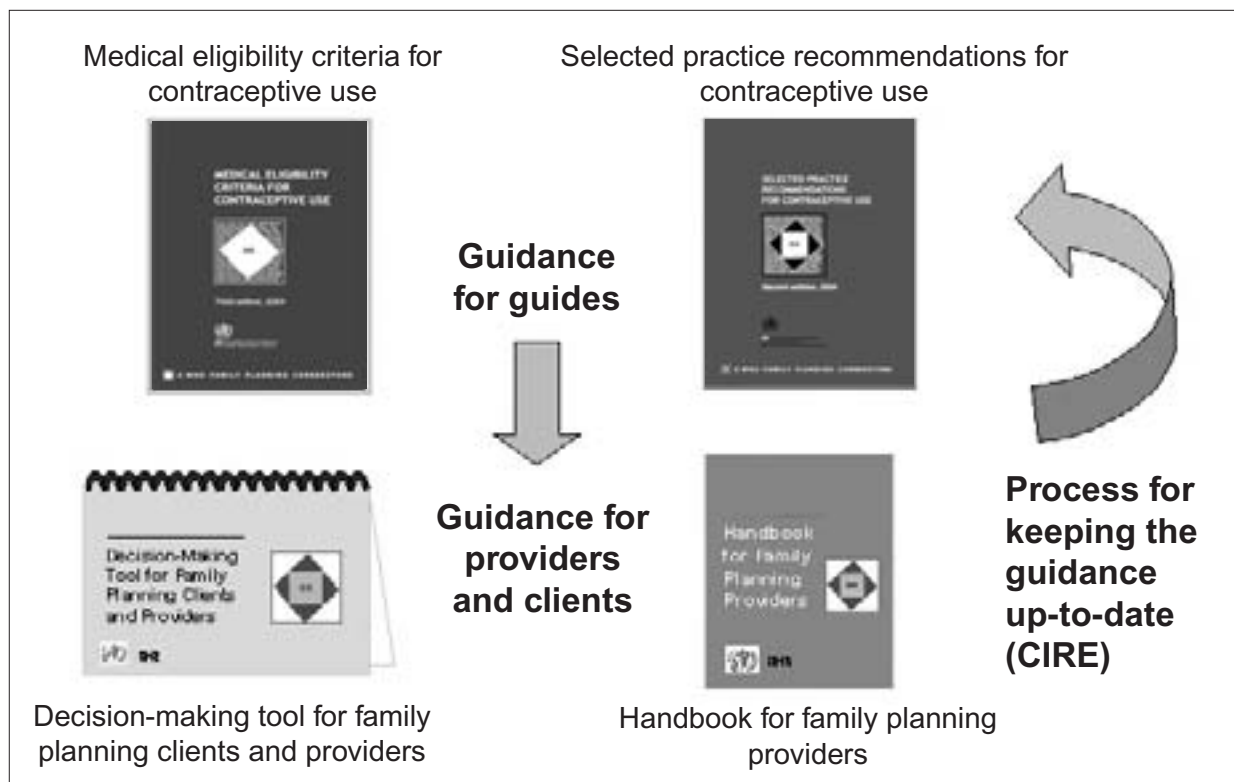
The third edition of the document summarizes the main recommendations of a scientific working group meeting held in Geneva, Switzerland, on 21–24 October 2003. The working group brought together 36 participants from 18 countries, including representatives of many different agencies and organizations. The group reviewed new evidence obtained through a systematic, comprehensive search of the bibliographic databases, including MEDLINE. The search yielded



all primary studies through August 2003 that provided direct evidence regarding the use of contraceptive methods among women with the medical conditions selected for the review. Programmatic implications of the recommendations were also considered by the working group.

The third edition provides guidance regarding the use of contraceptives in relation to over 70 medical problems or conditions in women, offering over 1 700 possible combinations of recommendations. The document adds guidance for three new contraceptive methods, and now includes: low-dose

Figure 1.8. The four cornerstones of evidence-based guidance and the system to assure that the guidance remains current and based on the best available evidence



combined oral contraceptives, combined injectable contraceptives, combined hormonal patches, combined hormonal rings, progestogen-only pills, depot-medroxyprogesterone acetate, norethisterone enantate, levonorgestrel and etonogestrel implants, emergency contraceptive pills, copper-bearing intrauterine devices (IUDs), levonorgestrel-releasing IUDs, IUDs for emergency contraception, barrier methods, fertility awareness-based methods, coitus interruptus, lactational amenorrhoea method, and female and male sterilization. Guidance on new conditions was also added, including recommendations on contraceptive use by women taking antiretroviral medications for treatment of HIV infection.

The counterpart document, the *Selected practice recommendations for contraceptive use* (published in 2002), addresses *how* to use contraceptive methods safely and effectively. It provides practical guidance on common clinical issues, for example, what a woman should do if she misses oral contraceptive pills. This guidance will be updated through an expert working group meeting in 2004, based on evidence from systematic reviews currently being prepared. The new edition will address approximately 15 new contraceptive management controversies and concerns, and will update the 23 existing recommendations. New recommendations will include guidance regarding how women using antibiotics, anticonvulsants or antiretroviral drugs can use hormonal contraceptives safely and effectively; how long after unprotected intercourse women can use emergency contraceptive pills; and how long after vasectomy men should abstain or use additional contraception.



The Department is taking strides toward ensuring the implementation of its guidance at the national level. As part of this effort, the Department will build on lessons learned in the implementation of these guidelines in 2003 by the Department of Health in South Africa, the Faculty of Family Planning in the United Kingdom, and the Ministry of Health in Romania.

## NORMS/TOOLS UNDER DEVELOPMENT

The *Decision-making tool for family planning clients and providers*, along with the handbook for family planning providers, are two tools that are part of WHO's evidence-based guidance for family planning. These tools are designed to be used by family planning providers when discussing options with their clients.

The *Decision-making tool for family planning clients and providers* was derived from, and will be supported by, the *Medical eligibility criteria for contraceptive use* and the *Selected practice recommendations for contraceptive use*. In addition, training and educational materials for clients and providers, and an adaptation guide are being developed to support the tool.

The primary objectives of the *Decision-making tool* are:

- to promote clients' informed choice and role in family planning service delivery;
- to enable providers to apply evidence-based best practices in the client-provider interaction during delivery of family planning services;
- to provide the technical information necessary for optimal delivery of non-surgical contraceptive methods; and
- to encourage providers and health systems to promote best practices in client-provider interaction as an integral part of service delivery.

The guiding principles to support these objectives are the following:

- The process for family planning decision-making is client-driven and interactive.
- The client's needs as *expressed by the client* are met to the extent possible.
- Evidence-based best practices in client-provider communication are used.
- Technical information needed for appropriate choice and for safe and effective use of family planning methods is provided.
- The discussion and the process are tailored to the needs of the individual client with provider's statements or actions depending, as much as possible, on the client's previous answer or statement.
- The client should be enabled to express her/his purposes quickly in the encounter and the provider should be able to respond appropriately.

The *Decision-making tool for family planning clients and providers* has been developed in partnership with JHU/CCP, with technical input from many other experts in reproductive health and health communication. It has undergone expert reviews on the counselling/communication component, as well as the technical information. Over the past year, the tool has been extensively field-tested in four developing countries.

Phase One field-testing began in late 2002, and involved meetings with providers to get initial feedback on the usability of the tool. Feedback meetings were undertaken with partner organizations in South Africa (Reproductive Health Research Unit of the University of Witwatersrand), Indonesia (Sustaining Technical Achievements in Reproductive Health—STARH—Program of JHU/CCP), and Trinidad and Tobago (International Planned Parenthood Federation—IPPF).

Phase Two field-testing was undertaken in the first half of 2003, and involved two observational studies with providers and clients. Working with the Population Council in Mexico City, Mexico, and the STARH Program in Indonesia, researchers at JHU/CCP compared the family planning counselling skills of providers at baseline (without the tool), with their skills after a short training course and a month's practice using the tool in clinics. The results showed improvements in client-provider interactions, including improvements in provider information-giving, client participation and satisfaction, client decision-making, and discussion of dual protection. Design problems with the tool were addressed in subsequent revisions and the latest draft will be tested in Uganda in early 2004.

Phase Three field-testing in 2004, is planned by researchers at JHU/CCP, and will include an impact evaluation of the use of the tool in Nicaragua.

In addition to participating in the field-testing, several of the partners and countries involved have initiated national or regional dissemination of the draft tool. Local adaptations are currently under way in both Indonesia and South Africa. IPPF has also initiated a regional training programme on quality of care in the Latin American region using the *Decision-making tool for family planning clients and providers*.

### NEW NORMS/TOOLS INITIATED

The new handbook for family planning providers will be a companion to the *Decision-making tool for family planning clients and providers*, intended to give in-depth and detailed information for providers on the provision of high-quality family planning services. To build on an already widely known and successful resource, the handbook will be based on the *Essentials of contraceptive technology* produced by JHU/CCP. The new book will be developed in collaboration with JHU/CCP, members of the Implementing Best Practices Consortium (including at least 20 organizations), as well as other key international partners. The development process will include an expansion in scope of the current book, to include selected reproductive health issues, as well as new family planning methods. In May 2004, WHO will convene an expert working group to gain global consensus on selected technical issues that are not currently addressed in its other evidence-based guidelines. This consensus-building process will enhance the likelihood that providers are given sound and consistent messages.

The handbook will be completed by the end of 2004 and will incorporate the latest WHO recommendations from the updates of the *Medical eligibility criteria for contraceptive use* and the *Selected practice recommendations for contraceptive use*.

## **Section 2**

# **Making pregnancy safer**

# Generating new evidence for maternal and perinatal health

J. Villar, M. Gülmezoglu, M. Merialdi, J. Zupan, Z. Matthews

## INTRODUCTION

Maternal-newborn health continues to be one of the most striking examples of health inequality in the world. Sadly, women in the poorest countries today face a risk of dying of pregnancy-related causes that is higher than what it was in wealthy countries 100 years ago. The disproportion in maternal deaths between rich and poor countries is startling. Nearly 90% of maternal deaths occur in Asia and sub-Saharan Africa; approximately 10% in other developing regions of the world, whereas less than 1% occur in the developed countries. Similarly, most of the perinatal and neonatal deaths occur in sub-Saharan Africa and in South Asia, in the poorest countries of the world. The disparity between rich and poor countries in neonatal mortality is unacceptably large and continues to increase.

Unfortunately, most initiatives launched in the past have failed to reduce maternal and newborn mortality in developing countries. In addition, perinatal conditions such as preterm births have not been reduced, even in developed countries. What is most surprising is the limited solid scientific evidence upon which some of the proposed interventions for pregnancy-specific conditions have been built. Two decades have passed since the launch of the Safe Motherhood initiative and we still do not have solid epidemiological data on the extent of maternal and newborn morbidity. In addition, we still do not know the etiologies of some of the major conditions responsible for the deaths of mothers and their infants in developing countries. Therefore, primary prevention is limited. Preeclampsia, obstructed labour, postpartum haemorrhage, preterm delivery, restricted fetal growth and birth asphyxia are complex syndromes without a determined or single cause. They remain difficult to predict, prevent, or treat, especially in developing countries where access to adequate obstetric and neonatal care is limited.

The Programme's maternal and perinatal health research is committed to contributing effectively to the reduction of maternal and newborn mortality and morbidity globally by implementing a programme which is innovative, feasible, and collaborative. Most importantly, the research focus on developing countries aims to address the specific and critical needs of these countries.

On the basis of the extensive research experience accumulated thus far, and with the advice of internationally recognized experts, a comprehensive research programme was developed that applies the latest research and technological developments to the reality and needs of developing countries. From this perspective, it is recognized that research produced in developed countries has often failed to address the needs of the poorest nations. Programmatic interventions initiated so far have focused on providing surrogates of western standards that have not always benefited the populations of the developing world, and, in some instances, have generated additional costs and introduced non-useful practices.

A research programme based on the latest scientific developments is the only way to assure that programmatic interventions aimed at improving maternal and newborn health worldwide will be targeted effectively. This is the basic principle that guided the development of the 1998–2003 research programme, in which more than 300 000 mothers and infants have been studied (Table 2.1), and which formed the basis for the 2004–2009 programme.

## RESEARCH ACTIVITIES

### Specific objectives of research

The overall goal of the 1998–2003 programme of work was to reduce maternal morbidity and mortality through the

development of acceptable and affordable evidence-based health programmes. The implementation of this programme has been achieved by (i) evaluating the effectiveness of practices; (ii) improving the understanding of sociocultural and economic factors influencing maternal health care; (iii) reviewing methodological issues related to maternal health research; (iv) conducting follow-up studies of the populations included in pregnancy-related research; (v) evaluating implementation strategies of research results; (vi) stimulating fundamental research on outstanding obstetric problems of global importance; and (vii) mapping the magnitude of maternal ill-health.

## Progress

### *Evaluating the effectiveness of practices*

#### *The WHO randomized controlled trial for the evaluation of a new antenatal care programme*

The new WHO antenatal care programme limits the tests, clinical procedures, and follow-up actions to those scientifically demonstrated to be effective in improving maternal and newborn outcomes. The new antenatal care model was found to be as effective as the standard model and to be acceptable by women and providers, and may reduce cost. Secondary analyses of the data set, including analysis of women's

opinions, costs of antenatal care, and the epidemiology of anaemia were prepared for publication in 2003.

#### *The WHO multicentre randomized trial of misoprostol in the management of the third stage of labour*

The results of this trial demonstrate that 10 IU oxytocin is preferable to 600 µg oral misoprostol in the active management of the third stage of labour. After publication of the main results of the study, the results of a pharmacokinetic study of misoprostol and the methodological issues related to the implementation of such a complex trial were published in 2003, thus completing the evaluation of strategies for the prevention of postpartum haemorrhage.

#### *The Latin American randomized controlled trial of mandatory second opinion for the reduction of the rate of caesarean section*

This study evaluated the effect of establishing a mandatory second opinion policy, based on the best available evidence about effective and safe management of childbirth, before every non-emergency caesarean section. The trial did not demonstrate a clinically relevant reduction in caesarean section rate associated with the intervention in the hospitals where the trial was conducted. The main report has been accepted for publication in *The Lancet* for 2004.

Table 2.1. Summary of Programme's randomized clinical trials on maternal health interventions up to 2003

	Countries	Women	Status
Antenatal care	4	24 678	Published
Postpartum haemorrhage	9	18 530	Published
Treatment of pre-eclampsia*	31	10 141	Published
Caesarean section	5	149 276	In press
Prevention of pre-eclampsia (calcium)	6	8338	Completed
Multifaceted educational intervention to change practices***	2	76 053	Final evaluation phase
Screening and treatment of urinary tract infection	4	18 000	Ongoing
Prevention of pre-eclampsia (antioxidants)	3	4044	Ongoing
Prevention of pre-eclampsia (treatment of hypertension)	5	1600	In preparation
Treatment of postpartum haemorrhage	4	1000	In preparation
<b>TOTAL</b>	<b>25**</b>	<b>311 660</b>	

\* The Programme was not responsible for the management of this trial.

\*\* Some countries have been involved in more than one study. The total excludes the 31 countries involved in the trial on Treatment of pre-eclampsia.

\*\*\* Based on *The WHO Reproductive Health Library*.

### *The WHO randomized double-blind controlled trial of calcium supplementation provided during pregnancy to women with low calcium intake for the prevention of pre-eclampsia*

The protective effect of calcium supplementation provided during pregnancy to women with low calcium intake was evaluated by the Programme in populations from Argentina, Egypt, India, Peru, South Africa and Viet Nam. Follow-up of the 8338 pregnant women recruited in the trial was completed. Results will be ready for publication in early 2004.

### *Cochrane systematic reviews*

Systematic reviews are conducted in collaboration with the Department's Programme to Map Best Reproductive Health Practices. In the area of maternal health care interventions, five systematic reviews and a protocol for a systematic review were published by staff of the Programme or by scientists from developing countries with support from the Programme in the 2003 issues of *The Cochrane Library*. They will be included in *The WHO Reproductive Health Library* in 2004.

### *Overview of evidence of effectiveness*

In 2003, the Programme was invited to participate in the Wellcome Trust/United States Agency for International Development (USAID) initiative, "Nutrition as prevention strategy against adverse maternal pregnancy outcomes" and to prepare as background documents two overviews of systematic reviews of the effectiveness of nutritional interventions during pregnancy to prevent and treat maternal morbidity, mortality, preterm delivery and intrauterine growth impairment. The two overviews, which are now used by these agencies for decision-making, were published in the *Journal of Nutrition* in 2003 and are the basis for the new issue on *Nutrition in Pregnancy* of the series, "From Research to Action" (see also From research to action, page 83).

### *Improve the understanding of sociocultural and economic factors influencing maternal health care*

#### *Women's and providers' perceptions of the quality of antenatal care*

Women's and providers' perceptions of the quality of antenatal care were assessed alongside the WHO Antenatal Care Trial. Results of this analysis were published and incorporated into the *Antenatal Care: From Research to Action* dissemination material (see also From research to action, page 83). A similar evaluation was conducted in the context of the trial of mandatory second opinion for caesarean section and two reports were prepared.

### *The economic evaluation of a rational package for antenatal care conducted alongside a multicentre randomized controlled trial*

This economic evaluation was completed in collaboration with the University of East Anglia, Norwich, United Kingdom and the London School of Hygiene and Tropical Medicine, London, United Kingdom. Its overall aim was to assess whether the new programme of antenatal care tested in the WHO Antenatal Care Trial was more cost-effective than the existing level of services, both for women using the services and for health care providers. Results of this analysis demonstrate that the main determinant of average cost of antenatal care is staffing pattern and productivity. The study also showed that the main determinants of health-service use include: the illness and risk status of patients; the practices and habits of health personnel; and the model of antenatal care being practised. This economic analysis will be published in 2004.

### *Review of research methodology related to maternal health*

#### *Methodological considerations for the design, analysis and meta-analysis of cluster randomization trials*

This activity is conducted in collaboration with the Department of Epidemiology and Biostatistics, University of Western Ontario, Canada. Utilizing the experience gained from the WHO Antenatal Care Trial and the caesarean section trial, work is carried out on statistical issues related to trial design, sample size and power calculations. A methodological paper on power calculations for cluster randomized trials was published in 2003. This experience has been applied to define the cluster survey methodology for the WHO Global Survey for Maternal and Perinatal Health (see page 82).

### *Clinical trials methodology*

The Programme's multicentre randomized controlled trial to evaluate the use of misoprostol in the management of the third stage of labour, mentioned above, presented special methodological challenges, both because of its size and the type of intervention. The methods of sequence generation, allocation concealment, and blinding used in this trial were described in a unique methodology paper published in 2003 that also describes how the possible existence of ascertainment bias, discussed in the literature, can be assessed.

### *Methodology for meta-analysis of observational studies*

A novel and unprecedented research effort was completed to define the methodology of meta-analysis of observational studies. This methodology was applied to the Department's systematic review aimed at mapping the magnitude of maternal ill-health completed during 2003. A report on this methodology was submitted for publication and, on this basis, a

series of publications describing the up-to-date epidemiology of maternal health conditions has now been completed.

#### *Follow-up studies of populations included in pregnancy-related research*

Follow-up of the infants born to mothers who participated in epidemiological studies is a necessary complement of any research effort aimed at evaluating the long-term outcomes of therapeutic and preventive interventions in pregnancy. Two major studies based on this approach are presently being conducted.

#### *The effect of high calcium exposure in utero on blood pressure during late childhood: 10-year follow-up of subjects enrolled in a randomized controlled trial*

This is a prospective follow-up study of 600 pre-adolescent children born to women enrolled in a previously conducted randomized trial of calcium supplementation during pregnancy. It explores the long-term effect of a nutritional intervention (calcium supplementation during pregnancy) on the offspring's blood pressure during pre-adolescence. This postnatal effect, possibly related to the Barker hypothesis, had been observed inconsistently in previous studies and seldom in randomized trials. Contrary to the results of previous follow-up studies, including an examination of the same children at seven years of age, no effect on blood pressure from calcium supplements was observed in the 10-year follow-up.

#### *Follow-up of the MAGPIE trial study population*

This is a follow-up (up to two years of age) of children born to mothers enrolled in the MAGPIE trial, in which magnesium sulfate was tested for the treatment of pre-eclampsia. Growth, development and morbidity are evaluated. Data collection is ongoing in Colombia, Cuba, and Nigeria.

#### *Evaluation of implementation strategies of research results*

*A randomized controlled trial to evaluate a programme promoting evidence-based medicine based on The WHO Reproductive Health Library*

In order to evaluate the uptake of information from the *WHO Reproductive Health Library* (RHL) with subsequent changes in health care practices, a randomized controlled trial of an educational outreach strategy was undertaken, using maternal care practices as indicators. The trial is now completed and the data have been analysed (see chapter on Implementing best practices, page 223).

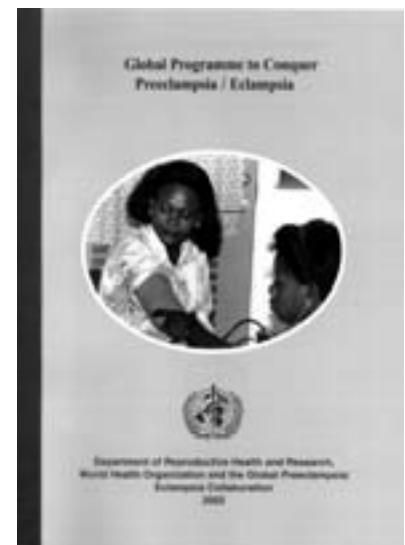
#### *Stimulate fundamental research on outstanding obstetric problems of global importance*

There are two highly prevalent maternal morbidities in developing countries for which there is very little knowledge of pathophysiology on which to base preventive and therapeutic interventions: hypertensive disorders of pregnancy and impaired fetal growth. Currently available interventions consist largely of symptomatic treatment for the mother and intensive care of a preterm or growth-impaired infant. It is unlikely that morbidity and costs can be reduced without identifying effective preventive measures, and this will require considerable efforts in implementing basic research aimed at understanding their pathophysiological process. Therefore, in 2003, the Programme started two major research collaborations that will continue in 2004: The Global Programme to Conquer Pre-eclampsia/Eclampsia and the initiative for the development of fetal growth monitoring standards for international applications.

#### *The Global Programme to Conquer Pre-eclampsia/Eclampsia*

In collaboration with a network of institutions in both developing and developed countries, a new comprehensive research and service programme entitled "Global Programme to Conquer Pre-eclampsia-Eclampsia", based on the concept of systematic reviews and priority research areas, was launched in 2002 and its full implementation started in 2003. The initial phase included

the preparation of a systematic review on screening methods for pre-eclampsia and two reviews on promising etiological and pathophysiological hypotheses to be tested in future research. In addition, a conference is being organized to prepare the basis for a large multicountry study of the genetic origins of pre-eclampsia, intrauterine growth restriction and preterm delivery. Researchers from several leading institutions have already joined this initiative and have collaborated on the submission of a letter-of-intent to the US National Institutes of Health Grand Challenges in Global Health initiative for obtaining funds to support the multicountry study. Identifying the genes involved in the origin and development of these conditions could allow the prompt identification of women at risk and their appropriate and timely care. In addition, by studying the functions related to the genes involved, more insights may be gained into the pathological processes,



thus providing the scientific evidence needed to develop effective preventive and treatment interventions.

*Development of fetal growth monitoring standards for international applications*

In 1995, the WHO Expert Committee on Physical Status indicated the need for the development of growth reference data suitable for international applications. Consequently, WHO implemented a multicentre study for the development of infant and child growth charts. An international research effort was initiated in collaboration with the National Institute of Child Health and Human Development, National Institutes of Health, USA, to extend the results of the WHO child growth study to the period of fetal life, assessing fetal growth *in utero* by means of fetal ultrasonography and at birth by neonatal anthropometry in the context of a multinational study. This will contribute to the development of comprehensive growth reference data, extending from intrauterine life to childhood, suitable for international use. A preliminary meeting of experts to define the protocol of the study will be held in March 2004 at the US National Institute of Child Health and Human Development. As a preparatory activity, a meeting was held in Houston, TX, USA, in November 2003 to produce a computerized system for fetal growth assessment. Participants at this meeting included staff of the Programme, the Baylor College of Medicine, Houston, TX, USA, and the Centro Rosarino de Estudios Perinatales (CREP), Rosario, Argentina.

*Mapping the magnitude of maternal ill-health*

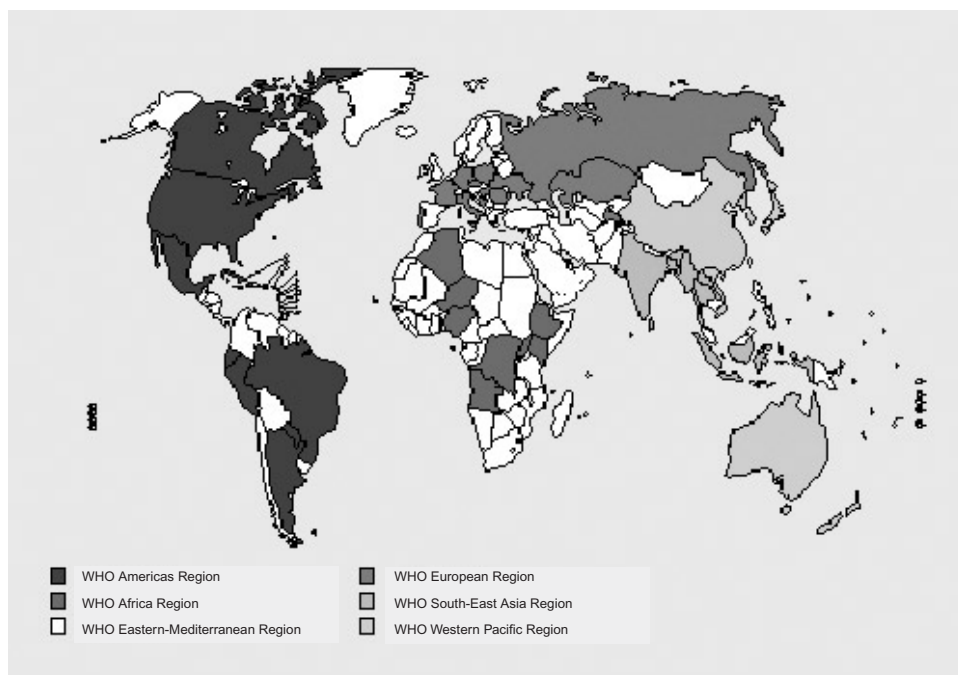
*The systematic review of the epidemiology of maternal morbidity*

In 2002, a systematic review of epidemiological data available between 1997 and 2002 on the incidence and prevalence of maternal morbidity was initiated. This unique systematic review was completed in 2003 and will constitute the background work for the development of the WHO Global Survey for Maternal and Perinatal Health.

*WHO Global Survey for Maternal and Perinatal Health*

A global effort was initiated to assess the relationship between the already quantified burden of disease and the services currently provided in the area of maternal and perinatal health: the WHO Global Survey for Maternal and Perinatal Health. The gap between interventions shown to be effective and those implemented by present services will be identified. To reach this goal, a network of randomly-selected institutions and their corresponding geographical areas that collects focused information for monitoring maternal and perinatal health services worldwide will be created. This network will operate by conducting, systematically and periodically, a global assessment using a simple, very specific, short data-collection instrument. The first preparatory phase of the global survey began in 2003 and will be conducted in early 2004 in the African (8 countries) and American (11 countries) regions (Figure 2.1).

Figure 2.1. Countries participating in the WHO Global Survey for Maternal and Perinatal Morbidity and Mortality



*Radiation and reproductive health: assessment of reproductive health in relation to radiation exposure around the nuclear test site in Semipalatinsk, Kazakhstan*

Radiation has the potential to influence reproductive outcome negatively in three ways: (i) direct irradiation of the embryo or the fetus could influence the outcome of the pregnancy and/or the health of the baby and have carcinogenic effects, which would manifest in later life; (ii) irradiation of the gonads can lead to genetic effects, which in turn could affect the health of the offspring; and (iii) irradiation of the gonads can also affect fertility, through radiation-induced death of germinal cells. However, very few data are available in this area which has important implications for the reproductive health of people with occupational or accidental exposure to radiation.

A collaborative research project between the Programme, the Institute for Cancer Research in London, United Kingdom and the Scientific Research Institute for Radiation Medicine and Ecology in Semipalatinsk, Kazakhstan was launched in 2001 to investigate the consequences for reproductive health of exposure to radiation in the area of Semipalatinsk in Kazakhstan. This area had been a nuclear weapons testing site from 1947 to 1989, resulting in considerable radioactive contamination of large territories and in radiation exposure to inhabitants. The study is now in its second year of activities. Data on approximately two-thirds of the *a priori* calculated sample size (50 000 subjects) have been collected.

### From research to action

Dissemination of research results is a high priority and needs to go beyond the publication of study results in major medical journals. Specifically-designed dissemination material is produced and actively distributed worldwide to facilitate the translation of research results into clinical and public health practice. The dissemination packages for the WHO antenatal care model and for the prevention of postpartum haemorrhage are two examples of highly appreciated and successful dissemination strategies that are being used at country level as working tools for effective implementation of best health care practices. Recently, a third package, *Nutrition in pregnancy*, has been added to the series.



The following sections describe the dissemination and implementation activities so far conducted by using the dissemination package for the WHO antenatal care model. Similar activities are planned for the other two dissemination packages and will be conducted in 2004.

### *Dissemination of the new antenatal care model*

In 2003, an extensive dissemination effort of the research results of the WHO Antenatal Care Trial was conducted, by means of presentations and training workshops at national and international conferences. A total of 17 presentations, nine of which were part of training workshops, took place in 13 countries. In total, 2290 manuals of the antenatal care model have been distributed to date.

### *Implementation of the new antenatal care model*

The new WHO antenatal care model is now being implemented in several countries. In Thailand, it was introduced in Khon Kaen where it is currently being monitored and evaluated. A similar evaluation is ongoing in the Province of Corrientes in Argentina. Significantly, the Pan American Health Organization (PAHO) presented the WHO antenatal care model at a conference in Quito, Ecuador in November 2003. The conference was organized by PAHO, the US Agency for International Development and the Programme and attended by representatives of ministries of health of the Latin America and Caribbean region. In addition, during 2003, specific efforts to introduce the new WHO antenatal care model began in Argentina, Australia, Brazil, Bolivia, Chile, Cuba, El Salvador, Ethiopia, Haiti, Italy, Oman, Pakistan, Spain, Syria, Thailand and Zambia.

### New projects initiated in 2003

In 2003, the Programme's Scientific and Technical Advisory Group (STAG) recommended that priority should be given to research programmes with results expected in the near future in order to generate positive interest by donors. Following this recommendation, seven research activities were initiated that will produce results with both public health and clinical implications. Some of these activities have been completed while others will be continued in 2004. The multinational dimension of those research activities and the collaborative agreements with major research institutions on which they are based assure that large number of subjects will be studied in relatively short time and that research activities will be given international visibility.

### *A randomized controlled trial evaluating strategies for the routine screening and treatment of urinary tract infection during pregnancy*

Activities are being implemented by collaborating centres in Argentina, Philippines, Thailand, and Viet Nam to evaluate the most effective strategies for the screening, laboratory procedures, and treatment of urinary tract infection during

pregnancy. The research programme includes all the methodological steps from the systematic review of publications evaluating treatment regimens, which has now been completed, to the implementation of a clinical trial and health service research (including cost analysis) of different screening and treatment modalities. Preparatory activities were initiated during 2003 and recruitment of study subjects will start in February 2004.

*A multicentre randomized clinical trial of vitamins C and E supplementation in pregnancy for the prevention of pre-eclampsia*

Recently, the cause of pre-eclampsia has been related to oxidative stress which may potentially be reversed by giving antioxidants (Vitamins C and E). The specific aim of the proposed study will be to determine whether daily administration of 1000 mg of vitamin C and 400 IU of vitamin E, from the second trimester, to high-risk women, would be associated with a reduction in the incidence of pre-eclampsia. This objective will be accomplished by conducting a collaborative research effort between the Programme and the Maternal and Fetal Research Unit, St. Thomas Hospital, London, United Kingdom. Should this clinical trial demonstrate a beneficial effect of antioxidant supplementation in pregnancy on the risk of pre-eclampsia, relatively inexpensive and feasible nutritional interventions during pregnancy could be recommended to prevent the occurrence of this condition. The study will start in January 2004.

*Ancillary and explanatory studies to the WHO trial of calcium supplementation provided to women with low calcium intake for the prevention of pre-eclampsia*

*Ancillary study to determine the effect of calcium supplementation on fetal growth and maternal and fetal blood flow assessed by ultrasound and Doppler velocimetry*

This study is being performed to determine the effect of calcium supplementation on fetal growth and maternal and fetal blood flow assessed by ultrasonography and Doppler velocimetry. The study is being conducted at CREP, Rosario, Argentina, with consultants from the Baylor College of Medicine, Houston, TX, USA, the University of Cincinnati, Cincinnati, OH, USA and the Universidad Catolica de Chile, Santiago, Chile. The required sample size of 500 pregnant women has been recruited and followed up. Results will be available early in 2004.

*Ancillary study to determine the effect of calcium supplementation on biochemical "markers" for hypertensive disorders of pregnancy*

This study, conducted in South Africa, is being undertaken to determine the effect of calcium supplementation on biochemical markers (platelets and blood uric acid levels) for

hypertensive disorders of pregnancy. These markers reflect damage to organ systems thought to underlie the pathophysiology of pre-eclampsia, such as the endothelium, platelets and kidneys. All study subjects (1000) have been recruited and analysis of the data is in process.

*Treatment of mild to moderate hypertension during pregnancy: a randomized controlled trial*

Hypertension complicates approximately 10% of pregnancies. Women with mild hypertension alone have a similar outcome to those who are normotensive. If they progress to pre-eclampsia, however, complications arise. Treatment of mild-moderate hypertension has been proposed as a strategy to delay progression to more severe disease. Therefore, a multicentre randomized placebo-controlled trial evaluating the effectiveness of labetalol for the treatment of moderate hypertension in pregnancy has been prepared. If funds are available, the study will be implemented in 2004 in collaboration with the Global Network for Women's and Children's Health, National Institute of Child Health and Human Development, Bethesda, MD, USA.

*The contribution of birth asphyxia to neonatal mortality and morbidity at community level: development and validation of a disease surveillance system for birth asphyxia-related perinatal mortality and morbidity at community level*

Neonatal mortality rates have remained high during the last decades, while under-five and infant mortality rates have decreased. This suggests that further reduction in child mortality could be obtained by targeting the perinatal period. Most neonatal deaths occur in developing countries and at home. However, data on perinatal and neonatal mortality and morbidity in developing countries are scarce and usually based on hospital surveys.

Birth asphyxia has been estimated to account for approximately 30% of all neonatal deaths occurring in developing countries. Because of the limited availability of data, and despite its enormous magnitude, this figure is likely to underestimate the real magnitude of the problem. Epidemiological research is needed to estimate accurately the contribution of birth asphyxia to perinatal morbidity and mortality at community level. Thus, the Programme has started a collaboration with the Saving Newborn Lives initiative (SNL), Save the Children, USA, to develop and validate a diagnostic instrument for birth asphyxia that could be implemented at community level to estimate rates of mortality and morbidity due to birth asphyxia in developing countries. A study protocol has been prepared and was finalized during a meeting of experts in January 2004 in Geneva. A paper focusing on the burden of disease associated with birth asphyxia has been submitted for publication.

*A randomized controlled trial evaluating strategies for the treatment of postpartum haemorrhage*

As many as 40 maternal deaths per 100 000 births in rural areas in developing countries are due to postpartum haemorrhage. Results from preliminary studies have suggested that, among the drugs used to treat postpartum haemorrhage, oral misoprostol may be effective. Systematic reviews of randomized and non-randomized trials were prepared and a multicentre randomized trial to evaluate the effectiveness of misoprostol for the treatment of postpartum haemorrhage is being prepared for implementation in Gambia, Nigeria, South Africa and Zambia.

*Maternal and newborn health and poverty*

While the importance of maternal and newborn morbidity and mortality is recognized, little is known about the actual impact and cost of maternal and newborn illness and death at individual, family and societal levels, and their effects on poverty. Furthermore, while there is growing evidence on the efficacy and cost-effectiveness of maternal and newborn health interventions, there is little information on the effectiveness of these interventions in reaching the poor. To address this knowledge gap, the Department, together with collaborating institutions, has commissioned papers and reviews on this issue. A conference of experts is being planned where these papers will be reviewed and compiled in a technical report.

**The future**

The Programme and its network of collaborating centres have completed 90% of the maternal and perinatal health research programme approved by STAG for the period 1998–2003. A total of 122 reports were produced and published in the scientific literature. For the future, the first challenge remains how best to transfer this knowledge from research into practice in many developing countries. The second challenge is to implement and maintain long-term capacity building efforts

in maternal and perinatal health research, allowing countries both to conduct their own priority research and to be part of global initiatives. Other challenges are even more formidable. There is still a considerable gap in the understanding of most of the specific pregnancy-related conditions to implement effective prevention programmes. One example is the case of pre-eclampsia/eclampsia, which is addressed by the Global Programme to Conquer Pre-eclampsia/Eclampsia. In addition, there are no effective preventive measures for preterm labour and intrauterine growth restriction, two pregnancy-specific conditions that are leading causes of newborn morbidity and mortality.

Finally, recent evidence from developed and developing countries suggests intra- and inter-generational effects of pregnancy-related events. For example, there is evidence of an association between short stature and obstructed labour, as well as between fetal malnutrition and chronic diseases in adult life. The latter effects, if confirmed in populations from developing countries, could have great importance for those countries in their epidemiological transition, e.g. where ischaemic heart disease is already the second most common cause of death.

While health services can now incorporate effective treatments and emergency medical and surgical strategies to reduce maternal mortality and severe morbidity, there remains an alarming lack of scientific understanding of pregnancy-specific conditions which endanger mother and child. Increasing the body of knowledge in this area would help prevent future morbidity and mortality, and add to a sound understanding of the epidemiology of these conditions in developing countries. The Programme's maternal and perinatal health research, by implementing its 2004–2009 programme of work, expects to continue playing a leading role in generating new scientific evidence that will help to design effective intervention programmes, thus improving maternal and newborn health worldwide.

Annex 1

**RESEARCH GROUP ON MATERNAL AND PERINATAL HEALTH IN 2003**

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Marisa Rebagliato, University Miguel Hernández, Valencia, Spain

Fiona Stanley, Telethon Institute for Child Health, Perth, Australia

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	4	57			3	43	7
Women	2	29			3	43	5
<b>from:</b>							
AFRO	2	29					2
AMRO	2	29			1	14	3
EMRO							
EURO					1	14	1
SEARO							
WPRO					1	14	1

## Annex 2

## SCIENTISTS IN 2003

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	17	57			13	43	30
Women	7	23			6	20	13
<b>from:</b>							
AFRO	2	7					2
AMRO	8	27			5	17	13
EMRO	2	7					2
EURO					8	27	8
SEARO	3	10					3
WPRO	2	7					2

## Annex 3

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# Implementation of evidence-based programmes

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## INTRODUCTION

As part of the global efforts for Safe Motherhood, the Making Pregnancy Safer initiative aims to contribute to the improvement of maternal and newborn health and to the achievement of the related international goals, in particular the Millennium Development Goals (MDGs).

Specifically, the Making Pregnancy Safer area of work addresses MDG No. 5: "Improve maternal health" and its associated target No. 6 "Reduce by three quarters, between 1990 and 2015, the maternal mortality ratio". These are closely linked to other MDGs and targets, including those of reducing under-five mortality (of which 20–25% is due to perinatal causes), of halting the spread of HIV/AIDS, of controlling malaria, of promoting gender equality and empowerment of women, and of eradicating extreme poverty.

A few countries have made remarkable progress and demonstrated that reductions of maternal deaths and of pregnancy-related morbidity are possible, even while socioeconomic development is taking place. However, it is clear that if present trends continue, many countries will not be able to achieve target No. 6, without accelerated efforts at national and district levels. The Making Pregnancy Safer strategy has been developed with this aim in mind.

## STRATEGIC DIRECTIONS

### The Making Pregnancy Safer strategy

The intensive work to refine the global Making Pregnancy Safer strategy has given a sharper focus to WHO's contribution in assisting Member States galvanize broad-based

political commitment and action to strengthen existing efforts and programmes for maternal and newborn health. The strategy was finalized following consultations with WHO regional offices and decisions made at the Second Global Team Meeting of Making Pregnancy Safer held in May 2003.

In particular, the strategy promotes access for all pregnant women and their newborn, especially poor and under-served populations, to a 'continuum of care' for pregnancy, birth and the postnatal period. The continuum starts with the woman and her family in the woman's home—i.e. self-care and prevention. It is followed by the first level of health care (either a health post, clinic or in the home), and involves the provision of high-quality midwifery care and access to an essential package of care, especially to essential and emergency services at referral levels when complications occur in women and/or their newborn. The strategy defines the essential package for maternal and neonatal health services, pregnancy, labour, birth, postnatal and early newborn care, family planning, postabortion care and, where legally permissible, safe abortion. While each country will define the exact contents of its own package, these should be formulated on evidence-based standards.

To ensure the continuum of care, four key interlinked elements of the health system have been highlighted. These are:

1. Human resources: strengthening capacities, management and deployment and increasing numbers where needed.
2. Provision, access, and quality of maternal and newborn health and other essential reproductive health services, including emergency obstetric care (EmOC).

3. Capacities of women, their families and communities to take measures to improve maternal and newborn health including self-care in the home, decisions on seeking care, including obtaining access to skilled birth attendants, and community responsiveness to maternal and newborn health needs.
4. Collaboration with other key primary health care programmes, such as nutrition, family planning, prevention and treatment of sexually transmitted infections (STIs) and HIV. This will improve the delivery of maternal and newborn health services, as well as maximize scarce resources and provide childbearing women and their families with an integrated primary health care service package.

In addition to assisting countries in strengthening their national programmes, especially in relation to the above, WHO will continue to provide the evidence and guidance necessary to improve the effectiveness of programmes, and to generate and disseminate new evidence on outstanding issues concerning maternal and newborn health, as required. Furthermore, WHO will monitor and regularly report on global progress, as well as document and share lessons learnt from countries. In particular, work will continue on gathering the evidence base for the links between poverty and maternal and newborn health, as the strategy calls for greater emphasis to be given to the needs of poor and marginalized groups.

In refining and finalizing the strategy, it was ensured that the strategic directions outlined above are highlighted in the reproductive health strategy developed by WHO at the request of the World Health Assembly, and that there is complementarity between the two strategies. The workplan and budget for the 2004–2005 biennium are also being adjusted accordingly.

Finally, areas for closer collaboration and coordination with other UN agencies and partners at global, regional and country levels have been identified. It is envisaged that this will be enhanced significantly by the decision taken in 2003 that WHO will host the Secretariat of the Partnership for Safe Motherhood and Newborn Health.

### Human resources

The percentage of births attended by skilled health personnel has been identified as one of the two indicators of MDG No. 5. Indeed, the issue of human resources is key for the provision of quality maternal and newborn health services, and, therefore, it has been identified as a priority in the Making Pregnancy Safer strategy, and one where WHO should take the lead, particularly because no other organizations have included this issue in their programmes. In 2002, an advocacy document was prepared and presented to the Meeting of Interested Parties (MIP) proposing a global movement for galvanizing action to increase access to skilled

attendants during pregnancy, childbirth and the postpartum period. The document which identifies five strategies and five stakeholders, is called *the 5+5 strategy*. Accordingly, in 2003 a detailed workplan was elaborated. The document entitled “90% by 2015—Skilled attendants; human resources needs for achieving the MDGs for maternal and child health” delineates what WHO and partners must do to address the human resources issues to meet the ambitious MDG target of 90% of all births attended by a skilled health person by 2015. This document is being used as a basis for discussion with countries, partners and donors on human resources issues for Making Pregnancy Safer. Work in this area will be conducted in collaboration with the WHO Department of Human Resources for Health.

In addition, a joint document on skilled attendants has been developed with the International Federation of Gynaecology and Obstetrics (FIGO) and the International Confederation of Midwives (ICM) and will be published in early 2004. The purpose of this statement is to provide guidance to countries on the definition of a skilled attendant, to assist with and improve reporting on the skilled birth attendant indicator, as well as to help identify areas for attention in national plans of action.

### Increasing provision, access, utilization and quality of services

Improving the quality and coverage of maternal and newborn health services, postabortion care, family planning and related services is vital for addressing maternal and newborn health. In this regard, the Making Pregnancy Safer strategy calls on countries to review their essential package of maternal and newborn health services, and to define national standards for both clinical care and the health systems requirements for delivering this care. A number of tools have been identified and developed to assist countries with this work. Thus, efforts can have greater focus on providing technical support and guidance, through working with countries to strengthen, monitor and evaluate their essential maternal and newborn health services package.

### Strengthening the capacities of individuals, families and communities for maternal and newborn health

The concept and strategy paper *Working with individuals, families and communities to improve maternal and newborn health* was finalized in 2003 and translated into French and Spanish. Discussions on its implementation have begun with countries as reported under the section on “Technical cooperation with countries”.

The Department has taken part in the preparation of a protocol being developed for a multicountry study in the WHO African Region to look at community and facility interventions to reduce three key delays in receiving needed care. A regional meeting is being planned with the WHO Regional Office for Africa (AFRO) to introduce the community framework they

have developed for addressing the three delays and supporting interventions and tools.

The Department organized an informal working group on community interventions for improved health in collaboration with other departments of the WHO Family and Community Health Cluster and with the WHO Department of Health Service Provision. A common area of work, i.e. the linkages between the health services and the community, has been identified for further collaboration.

A key role for WHO will be sharing lessons learned and working with the research community to develop the evidence base. Collaboration with the Cochrane Collaboration's Health Promotion and Public Health Field has assured the inclusion of community maternal and newborn health interventions on the global priority list of research topics.

### Strengthening collaboration and integration with other primary health care programmes

Work has continued with other departments across the Organization to ensure that key information from other programmes is identified adequately within the Making Pregnancy Safer normative work and vice versa. Given the importance of this as a key component of the Making Pregnancy Safer strategy, the Department convened a cross-cluster meeting in 2003 to address issues of integration and strengthening collaboration. From this initial meeting a number of initiatives and meetings with individual programmes have ensued.

### Maternal and newborn health and poverty

As stated before, the new Making Pregnancy Safer strategy focuses on addressing the needs of the poor and underserved. It is the poor who are likely to bear the greatest burden of ill-health, as they are unlikely to have the economic capacity to pay for treatments of obstetric<sup>1</sup> emergencies. The poor are also the ones who have least access to and least utilize skilled care, especially at the time of birth. To advance understanding of the relationship between maternal and newborn health and poverty, evidence is now being consolidated into a comprehensive review, to include 26 commissioned background papers under five main subtopics or "working areas"<sup>2</sup>. During 2003 these topics were finalized and work commenced on identifying suitable authors.

This work is being conducted in close collaboration with other teams in the Department and WHO, such as Capacity strengthening for planning and management (SPM), Gender and reproductive rights (GRR), Choosing interventions: effectiveness, quality, costs, gender and ethics (EQC), Epidemiology and burden of disease (EBD), Poverty and health financing (PHF), Technical cooperation with countries (TCC), and Policy and programmatic issues (PPI). The process of commissioning the background papers has led to strengthened continuing engagement with the equity and poverty research community<sup>3</sup>. A web site showing short summaries of the background papers was established towards the end of 2003. It is expected that the full set of papers, reports and policy briefs, will be finalized during 2004. Gaps in the evidence base identified during this process will be brought to the attention of the research community for action.

## NORMATIVE TOOLS AND GUIDELINES

The Integrated Management of Pregnancy and Childbirth (IMPAC) is a comprehensive set of tools designed to provide guidance to countries on improving maternal and newborn health. These normative tools and guidelines address policy, strategy, health systems (including clinical and other services), training and advocacy issues. They are developed in collaboration with WHO regional offices and countries; WHO regional offices have also been involved in commissioning many of the translations into other languages of these tools. An overview of the tools is regularly updated and is available on the Department's web site. Given the large number of tools, the section below lists only: (i) the tools that have been finalized and published during 2003; (ii) those finalized and ready for printing or field-testing in 2004; (iii) the major ones still under development; and (iv) those produced by other WHO departments, but to which this Department made a significant input.

### Tools finalized and published during 2003

- ***Managing complications in pregnancy and childbirth: a guide for midwives and doctors.*** Translations into Chinese, Lao, Mongolian, Spanish and Vietnamese were completed in 2003. Arabic and Portuguese translations will be completed in 2004, so that altogether, the guide will be available in over 10 languages. In several

<sup>1</sup> Including neonatal emergencies at birth or soon after.

<sup>2</sup> These working areas are: global burden of disease from maternal and newborn ill-health; impact of maternal and newborn illness and death on individuals, households and communities; macroeconomic consequences of maternal and newborn ill-health; making health systems respond to the health needs of mothers and their children, especially the poor and marginalized, during pregnancy, childbirth and the postpartum period; and benefits of investing in maternal and newborn health for wider socioeconomic development and equity and society-wide consequences of maternal and newborn ill-health.

<sup>3</sup> Key collaborators include: United Nations Population Fund, International Labour Office, Initiative for Maternal Mortality Programme Assessment, World Bank, MDG Task Force no. 4, Swiss Centre for International Health, London School of Hygiene and Tropical Medicine, and Harvard School of Public Health.

countries, introduction of this manual is being used as an opportunity to revise national standards of care, in particular those related to emergency obstetric care.

- **Managing newborn problems: a guide for doctors, nurses and midwives.** This is a companion to the above guide and follows a similar format, but focuses on the management of newborn complications. It was endorsed by the United Nations Population Fund (UNFPA), United Nations Children's Fund (UNICEF), The World Bank, the International Federation for Gynaecology and Obstetrics (FIGO), the International Pediatric Association (IPA) and the International Confederation of Midwives (ICM). This guide is being translated into Bahasa Indonesian.
- **Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice.** This guide was previously referred to as the Essential Care Practice Guide or ECPG, and was endorsed by UNFPA, UNICEF and The World Bank in 2003. Adaptation and translations are already under way in the WHO Regional Offices for Africa (AFRO) and the Western Pacific (WPRO). Validation studies of the "rapid assessment" and the "newborn examination" charts in this guide were conducted in Brazil during 2003. Similar validation studies will be conducted in Sudan and Uganda as soon as funds become available in 2004. The results of the entire validation exercise will be available by the end of 2004.
- **Kangaroo mother care: a practical guide.** This guide is already available in Vietnamese. Translations into Albanian, Bengali, Bahasa Indonesia, Japanese and Portuguese are under way and will be available in 2004.
- **Strategic framework for malaria control during pregnancy in the WHO African Region.** During 2003, Department staff worked in close collaboration with the WHO Roll Back Malaria (Malaria in Pregnancy) team and AFRO to finalize this tool. The framework aims to contribute to the achievement of the Abuja goal of 60% coverage of pregnancies with intermittent preventive treatment (IPT) and insecticide-treated nets (ITNs) by 2005. The tool provides policy-makers and national programme managers with guidance on prevention and case management of malaria in pregnant women (the main adult target group in Africa). An accompanying framework on *Monitoring and evaluation of malaria during pregnancy* at the health-facility level has also been developed and is under pilot-testing.

#### Tools finalized and ready for printing and/or field-testing in 2004

- **Handbook on communication and counselling with pregnancy, childbirth, postpartum and newborn care: a guide for essential practice.** This draft handbook, designed to develop the skills of skilled attendants in communicating and counselling for maternal and

newborn health, was completed in 2003. Field reviews were conducted in Malawi and the Philippines. Further review in two other countries, Indonesia and Sudan, planned for 2003, has been postponed until 2004 due to lack of funds. In 2004, regional representatives and other experts in the area of counselling and communication will assess the handbook. The final version will be available in September 2004.

- **Beyond the numbers: reviewing maternal deaths and complications for making pregnancy safer.** Three regional workshops were conducted during 2003, one in the WHO South-East Asia Region and two in the African Region, to finalize the document. Many of the countries that attended the workshops have already begun to introduce the methodologies described, or are in the final stages of planning for implementation. The final printed version of the guide and a CD-ROM of sample questionnaires will be released in 2004. The launch will be accompanied by a workshop to train experts from each region in the methodologies, in order that they may act as regional facilitators. Also, in 2004 the WHO Regional Office for the Americas (AMRO) will be revising its manual for maternal mortality surveillance, incorporating the content and methodologies of this document. A global partnership of interested agencies and organizations is to be established to build on strengths and experiences, and to develop a coherent and cohesive global approach to maximize resources and skills and avoid duplication of efforts. A global database of ongoing audits and experiences will be developed and made available on the web.
- **The revised WHO midwifery education modules.** The revised modules, including an additional module on *Managing incomplete abortion and postabortion care* are ready and will be printed and distributed as soon as funding is available. The French translation of the modules is almost complete. During 2003, funding was identified for the translation and printing of a Portuguese version.
- **Strengthening midwifery toolkit.** This toolkit, consisting of six separate guidance documents, each dealing with a specific aspect critical for strengthening midwifery, was further elaborated during 2003 and now contains a simple needs' assessment tool for helping users to prioritize actions within each component. The final tool is ready for discussions with regional office staff and experts in 2004.
- **Reference guide on HIV-related care and support to women and children.** This guide is being developed in collaboration with the Department of HIV/AIDS. It provides an inventory of key interventions and recommendations for HIV-related care, treatment and support of HIV-infected women and their children in the context of reproductive health and maternal and child health ser-

vices in resource-constrained settings. The guide will be published in early 2004. This guidance formed the basis for the development of *Guidelines on HIV-related care, treatment and support of HIV-infected women and their children*.

### Major tools published in 2003 by others, to which the Department made significant inputs

- **Manual on surgical care at the district hospital.** Developed by the WHO Department of Blood Safety and Clinical Technology, this manual provides practical guidance on surgical procedures that are commonly performed by non-specialist clinicians working in first-level referral hospitals with limited resources. Its aim is to improve the quality of surgical care, particularly for essential procedures in surgery, obstetrics, gynaecology, orthopaedics, anaesthesia and trauma care. It is promoted in collaboration with the Department of Essential Health Technologies.
- Other tools include *Guideline on prevention and control of maternal and congenital syphilis*; *Clinical guidelines for management of pregnant women with HIV*; *Patient safety strategy*; list of essential reproductive health commodities.
- **Making Pregnancy Safer planning guide.** Intended to assist district managers and planners in the planning and implementation of the Making Pregnancy Safer strategy, this guide will include information on the health systems issues and evidence-based interventions related to maternal and newborn health services, as well as guidance in planning these services. It will focus on how to select the most relevant programming processes, methods and tools, and on how to adapt these to the local context. Guidance on the planning processes of budgeting, monitoring and evaluation will also be included. Field-testing and finalisation of the guide will take place in 2004, along with the *Making Pregnancy Safer planning workshop manual* developed during 2002.
- **Making Pregnancy Safer—essential health technology package (MPR-EHTP).** This is a software tool, delivered on CD-ROM, that facilitates the analysis of resources and technologies required for the key maternal and newborn health interventions in the IMPAC tools. It builds on the *Mother-baby package costing spreadsheet*, and is being developed in close collaboration with the Department of Health Service Provision and the WHO Collaborating Centre for Essential Technologies for Health in Cape Town, South Africa. The package was reviewed in 2003 for technical content and functionality with a demo field-testing version that includes training and simulation of the tool. It is anticipated that the package will be finalized in 2004.

### Major tools under development

- **Standards for maternal and neonatal care.** This document is designed for policy-makers, programme managers and health care providers, and sets evidence-based standards of care during pregnancy, childbirth and the postnatal period. It complements the IMPAC clinical guidelines for first and second levels of care and will be used for national standards-setting and auditing of maternal and newborn health services. Each standard is complemented by a table of supporting evidence. Publication of the first set of 30 standards is expected in 2004.
- **Antenatal care reference guide.** This guide is for health care providers at the first level of referral. It compiles the evidence for essential antenatal care for pregnant women with non-emergency problems. Work commenced in 2003, but has been delayed due to lack of funds. The first draft is expected in April 2004.
- **Making Pregnancy Safer education and training strategy.** This strategy aims to strengthen the capacity of teachers of health care providers to train health practitioners for maternal and child health care. It is based on a comprehensive set of tools produced in 2003 by the Department of Child and Adolescent Health and Development (CAH) with input from this Department. It addresses strengthening recruitment, education and training, and the skills needed for the management of human resources.
- **Human rights assessment tool for maternal and neonatal health: a multi-sectoral approach for improving laws, policies and standards of care.** This tool is being developed in collaboration with the Department's Gender and Reproductive Rights (GRR) group. It is a health systems tool using a human rights approach to assist countries in assessing and improving the legal, policy, regulatory and practice environment that influences maternal and newborn health services. A user's guide and an adaptation guide accompany the tool. Based on the results of the validation study conducted in Switzerland in 2003, the tool will be further elaborated for a three-country field-test that will begin in 2004 (see page 161).

### TECHNICAL COOPERATION WITH COUNTRIES

This section summarizes the progress and major achievements obtained through the provision of technical support by staff of the Making Pregnancy Safer initiative (in WHO headquarters, regional and country offices) at the policy and strategy level, as well as at the maternal and newborn health programme development and implementation level. By 2003, activities increased to reach approximately 82 countries.

## African Region

- A major achievement of 2003 was the establishment or strengthening of Making Pregnancy Safer/Safe Motherhood (SM) national task forces or partner co-ordination committees. They are now meeting routinely in Ethiopia, Mauritania, Mozambique, Nigeria, and Uganda. Efforts are being intensified to revitalize similar task forces in the other countries in the region.
- It is noteworthy that there has been improved coordination among donors and partners (especially between UNFPA, UNICEF and The World Bank), resulting in improved use of resources and reduction in duplication and piecemeal efforts to improve maternal and newborn health. Key issues pertaining to making pregnancy safer have been discussed at all levels—regional, national, and sub-national—particularly during the annual Reproductive Health Task Force meeting which took place in October 2003.
- AFRO organized regional meetings to increase political commitment, and prioritize resources needed, to accelerate the reduction of maternal mortality. A roundtable meeting was organized during the 53<sup>rd</sup> session of the WHO Regional Committee for Africa in September 2003 and working sessions were held during a regional meeting in Senegal in October 2003.
- AFRO also finalized the development of an advocacy tool for making pregnancy safer, using the REDUCE model, that includes policy briefs, leaflets, videos and presentation slides. The tool was developed for use at the regional level. To date, Ethiopia, Mauritania, Mozambique, Nigeria and Uganda have adapted and implemented the tool.
- In Mauritania, financial incentives have been put in place to attract health care providers to work in rural areas.
- In Ethiopia, a pledge was made by the Government in parliament to establish the monitoring of maternal deaths as a priority.
- Training of trainers on emergency obstetric care, based on *Managing complications in pregnancy and childbirth: a guide for midwives and doctors*, was conducted in Ethiopia, Ghana, Kenya, Mozambique, Nigeria and Uganda.
- AFRO contributed to the provision of equipment for essential obstetric care and to the strengthening of reporting of maternal mortality and severe morbidity. This has helped to assess provider performance and improve quality of care in Ethiopia, Mauritania, Mozambique, Nigeria and Uganda.
- Collaboration was strengthened with other programmes for those conditions that have an impact on maternal and newborn health and survival, namely HIV, malaria,

and human rights. Collaboration with Roll Back Malaria is outlined above. In addition, the teams have collaborated in undertaking a survey of malaria in pregnancy and national malaria policies. Steps were also taken to develop a common framework for integration of malaria, HIV/AIDS, and antenatal care programmes in three countries (Kenya, Nigeria and Uganda).

## Americas Region

- During 2003, AMRO provided intensive technical assistance to priority countries (Bolivia, Brazil, Dominican Republic, Ecuador, El Salvador, Guatemala, Guyana, Haiti, Honduras, Nicaragua, Paraguay and Peru) to operationalize the regional strategy for maternal morbidity and mortality reduction at national and local levels.
- The Regional Inter-agency Task Force for maternal mortality reduction continued its efforts to advance the regional agenda. A “Strategic Consensus Document” for maternal mortality reduction was completed and approved by all participating agencies in 2003. The document has been translated (and printed) into French, Portuguese, and Spanish, and it is expected to be disseminated in the first quarter of 2004.
- A technical consultation on ‘Skilled attendance at birth’ was held in June 2003 in Bolivia, with participation of more than 100 regional experts including decision-makers, academics, non-physician providers, community groups, and women’s health representatives. The consultation’s target was to analyse the importance of skilled care, define the abilities and competencies of skilled attendants, develop strategies to promote skilled care, and build alliances and links between different sectors and professions.
- Maternal mortality reduction plans were successfully developed in Bolivia, Guatemala, and Haiti. Improving essential obstetric care and skilled attendance at birth have been highlighted as the key intervention in the national health development plan in all three countries. In Haiti, maternal mortality was defined as a national priority and as the entry point to strengthen the health system. In Honduras, a Presidential Declaration was issued on reducing maternal and infant mortality.
- In Paraguay, a decision was made to focus on essential obstetric care, family planning, and strengthening effective links between health service delivery and the community. Fieldwork will begin during the first quarter of 2004 and the final report is expected by August 2004.
- A policy document on *Monitoring maternal mortality and morbidity reduction* was completed and presented at several meetings during 2003. This document provides guidance on how to develop a monitoring system that addresses maternal health. The document is currently

being disseminated in several countries of the region for implementation.

- A regional meeting on the WHO antenatal care model was held in November 2003, in Quito, Ecuador, to discuss the model and possible approaches to deliver care, including interventions to empower women, families, and communities.
- The *Maternal mortality surveillance system*, published in 1996 by AMRO and the United States Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA, is being revised and updated, based on lessons learnt from countries in the region. Updates will be finalized in 2004. In addition, the Latin American Centre of Perinatology (CLAP), Montevideo, Uruguay, has provided technical assistance in implementing the 'Perinatal information system (SIP)' in the priority countries.
- Collaboration with regional professional associations, such as the Latin American Federation of Societies of Obstetrics and Gynecology (FLASOG) and the Pan-American Federation of Nursing and Midwifery, has been established to advance the agenda of maternal mortality reduction and to implement effective interventions such as promoting skilled attendance at birth, providing essential obstetric care services, and ensuring audits of all maternal deaths.

### Eastern Mediterranean Region

- The WHO Regional Office for the Eastern Mediterranean (EMRO) has adopted the Making Pregnancy Safer strategy as a priority strategy to reduce maternal and perinatal mortality in the region. Technical and financial support has been maintained to strengthen and expand activities in priority countries such as Afghanistan, Djibouti, Iraq, Pakistan, Somalia, Sudan, and the Republic of Yemen.
- As a result of intensified efforts by WHO Member States in the region, the proportion of births attended by a skilled health professional has increased from 27% in 1990 to 51% in 2000. The adoption of the Making Pregnancy Safer strategy is expected to accelerate the reduction of maternal and neonatal mortality and morbidity through improvement of the quality, availability, accessibility, and utilization of essential maternal and newborn health services.
- WHO staff at headquarters, regional and country levels have actively supported the national programmes for safe motherhood through a series of intercountry planning/training consultations, meetings, and workshops. Activities have focused on improving the knowledge and skills of national maternal and newborn health programme managers and planners for the planning, management and monitoring of maternal and newborn health-related

plans and actions at national and district levels. Examples of activities conducted in 2003 include:

- Materials for training on the use of data to improve decision-making in maternal and newborn health were developed by EMRO in collaboration with CDC, and have been extensively disseminated to all Member States in the region.
- A database on reproductive health research was developed in close collaboration with the Department to enable easy access and exchange of relevant evidence between and within the countries in the region. EMRO has encouraged countries in the region to use this databank in their maternal and newborn health programme development and implementation work.
- Regional training guidelines on "Total quality management in maternal and perinatal health care" were finalized in 2003 in close collaboration with CDC. These guidelines are aimed at developing the managerial skills of programme managers and planners at district level to improve and better integrate maternal and perinatal health care into existing services.
- The League of Arab States executed the 'Pan-Arab project for family health' (PAP-FAM) in close collaboration with EMRO. The project consists of updating surveys related to family health issues, including maternal health. PAP-FAM surveys were completed in Syria and Tunisia in 2003, while survey fieldwork was conducted in Djibouti and the Republic of Yemen. Implementation of this survey is under consideration in Lebanon, Morocco, Somalia, and Sudan for 2004.
- A joint UNICEF/WHO plan of action was formulated for the region to contribute to the achievement of the Making Pregnancy Safer objectives. Efforts were made to establish effective partnerships at country level between the two organizations to ensure better coordination of technical support to and resources for maternal and newborn health activities, as well as monitoring and evaluation of safe motherhood programmes. Activities were put in place to advocate jointly to all policy-makers and other interested partners that the concept of safe motherhood continue to be kept high on their health and development agendas. Joint support was also provided to Djibouti, Sudan, and Yemen to strengthen their emergency obstetric care.
- Technical support by EMRO has mainly been focused on assisting Member States expand availability of maternal and newborn health services at the community level and emergency obstetric care at the referral levels. Specific examples of support and accomplishments in

2003 include: increasing intake of midwifery students in Sudan; upgrading skills in emergency and obstetric case management, particularly in rural and remote areas in selected provinces in Afghanistan, Djibouti, Somalia and the Sudan; improving health care providers' skills in neonatal resuscitation and control of newborn infections, as well as emergency obstetric care services in Syria; review of the safe motherhood strategy and programme in Morocco and in two provinces in Yemen; and undertaking a national survey on perinatal health care in Syria.

### European Region

- Work in the WHO European Region is coordinated by the WHO Regional Office for Europe (EURO). Introduction of the Making Pregnancy Safer strategy was conducted in 10 priority countries in the WHO European Region (Albania, Armenia, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Romania, Russian Federation, Tajikistan, Turkmenistan and Uzbekistan). Azerbaijan, Macedonia, Poland and Turkey have requested introduction of the strategy in 2004–2005.
- Initial orientation and planning meetings involving staff from the Ministry of Health, key stakeholders, and partners were held in 2003 in all 10 countries. National plans of action were developed, which included activities such as: training of trainers at provider level; training for continuous supervision; building-up of model sites; training in evidence-based maternal and newborn care for top-level clinicians; training in appropriate planning for perinatal care for decision-makers.
- Full support for making pregnancy safer was achieved at policy level in most of the 10 countries, particularly in Moldova and Uzbekistan. In Uzbekistan, policy changes included the establishment of a new general legal framework for maternal and newborn health which will substitute outdated laws that constituted a barrier to implementing evidence-based care.
- Coordination among major partners and donor agencies of activities at national and regional levels has also been accomplished during 2003. Regional capacity building has been expanded and an increased number of professionals (including midwives) from Eastern European countries are now included in the Making Pregnancy Safer team of regional experts.
- Tools, training courses, and materials were developed for regional use, e.g. "Making Pregnancy Safer evidence-based mother and newborn care" course, "Making Pregnancy Safer planning for appropriate perinatal care" as well as the updating of the material for the obstetric and neonatal training course. In Moldova, national clinical guidelines for maternal and newborn health were updated, officially endorsed by the Ministry of Health and

published in 2003; clinical guidelines for the prevention of HIV among mothers and children are to be developed in 2004.

- Another set of activities accomplished in Moldova focused on strengthening midwifery. Local midwives are now part of the regional expert team and provide technical support to other countries. In the field of pre-service training, a local technical working group has been set up, international consultancy provided, and a new curriculum for midwives prepared, which will be tested in 2004.
- To strengthen further the midwifery component at the national midwifery school in Moldova, training material developed by WHO was provided; training of trainers (including all midwives' trainers) with practical sessions in maternal care was also undertaken. Review of the clinical practice component of the maternal programme was also conducted in 2003.
- Also in Moldova, a making pregnancy safer documentation centre has been set up to provide technical support to activities and links with similar programmes in the field.
- The Council of Europe developed a document on maternal health, which recommends that the Making Pregnancy Safer strategy be implemented as a key activity to reduce maternal and newborn morbidity and mortality in the region. Countries in the region are encouraged to develop national plans of activities to implement the strategy within their context, with Moldova's achievements serving as a model.
- A web site has been set-up, with detailed information about Making Pregnancy Safer activities in the European region: <<http://www.who.dk/pregnancy>>.

### South-East Asia Region

- A major focus for the WHO Regional Office for South-East Asia (SEARO) during 2003 has been to provide adequate support to countries for preparing and implementing coordinated plans to make pregnancy safer, including monitoring and evaluation. Special emphasis has been placed on promoting the use of skilled attendants at birth, especially in Bangladesh, India, Nepal, and Timor Leste. While SEARO has continued to be very active in supporting the making pregnancy safer work in Indonesia, activities have begun to provide assistance to other countries to implement the Making Pregnancy Safer strategy and develop national plans and activities to reduce maternal and perinatal mortality.
- SEARO assisted India in developing a competency-based 12-month course with the view to developing a cadre of community-level skilled birth attendants. The curriculum has been developed and training material,

including a facilitator's guide and job aids, is being prepared. Field-testing was carried out in one state and will be expanded to seven states.

- Timor Leste made efforts to increase skilled birth attendants through the recruitment, training, and deployment of midwives in community health centres. SEARO provided assistance in improving the skills of health care providers through training in: safe and clean delivery, breastfeeding counselling, and management of sexually transmitted infections using the syndromic approach. Adaptation and implementation of the WHO standards of midwifery practice were also undertaken, as well as the development of a national reproductive health strategy.
- Also in Timor Leste, a course for MB BS doctors in "Life-saving anaesthetic skills for emergency obstetrics care" has been developed and tested. A core group consisting of experts from the fields of anaesthesiology and obstetrics and gynaecology developed the course curriculum and carried out the first skills- and competency-based training.
- The use and implementation of maternal death reviews, using *Beyond the numbers: reviewing maternal deaths and complications for making pregnancy safer*, was initiated in 10 countries in the region. This document is now acknowledged as a key tool for assisting countries to identify the causes and possible solutions for reducing maternal mortality and case fatalities at the facility level.
- In October 2003, SEARO, together with WPRO, UNICEF and UNFPA, organized a biregional workshop on 'Progress on maternal mortality reduction'. This workshop brought together high-level government officials from countries in both regions, as well as the major partners, to review progress and share lessons learnt.
- Together with SEARO, the Government of India launched a "National Safe Motherhood Day" on 11 April 2003. This has provided crucial political commitment to the agenda of safe motherhood, not only in India but also in other countries in the region.
- Efforts have been made in Indonesia to improve the quality of maternal and newborn health services. SEARO supported the evaluation of the midwifery in-service training programme and the scaling-up of the implementation of the *WHO SEARO standards of practice for midwives*, adapted for use in Indonesia.
- Strengthening planning and management capacity at district level to improve maternal and newborn health services is increasingly becoming a priority area. SEARO provided technical assistance in approximately 20 districts in Indonesia to improve maternal and newborn health programme planning.

- SEARO has taken an active lead in developing consensus and in strengthening coordination among partners at regional and country levels. WHO participated in the evaluation of The World Bank project "Safe motherhood partnership and family approach" in Indonesia and in the evaluation of a maternal and newborn health project conducted by the Johns Hopkins Program of International Education in Gynecology and Obstetrics (JHPIEGO).
- Technical assistance has been provided to India in expanding safe abortion services and up-grading skills among health care providers. In order to facilitate the expansion of safe abortion services in India, the Medical Termination of Pregnancy Act has been amended. The Act now includes medical methods of abortion, and ensures greater involvement of the private sector in the provision of services. SEARO provided support to the training of 250 medical experts in India in the medical methods of abortion and plans to assist Indonesia in the training of 240 medical officers in manual vacuum aspiration (MVA) in 2004. MVA guidelines and standardized training tools were developed in 2003. Training courses were conducted in eight states in India during 2003. Currently, training for district medical officers is under way. In addition, monitoring forms as well as checklists for supportive supervision were developed. MVA has already been included in the next phase of India's Reproductive Health & Child Health Programme.

### Western Pacific Region

- The main focus for the WHO Regional Office for the Western Pacific (WPRO) has been to increase the number of skilled attendants and develop appropriate routine monitoring and evaluation mechanisms to monitor progress and improve decision-making at national and district levels. WPRO initiated the development of action plans for Making Pregnancy Safer in all priority countries in the region (Cambodia, Lao People's Democratic Republic, Mongolia, Papua New Guinea, the Pacific Islands, Philippines, and Viet Nam). These action plans were reviewed at a biregional workshop with SEARO in October.
- Service protocols for reproductive health were developed in Cambodia, Lao People's Democratic Republic, and Viet Nam. An assessment tool for mother-friendly hospitals was developed and pre-tested in Mongolia. Training courses have also been conducted in these countries.
- With WPRO's technical support, monitoring or recording/reporting systems for reproductive, maternal, and child health were strengthened in Cambodia, Lao People's Democratic Republic, Mongolia, Papua New Guinea, the Pacific Islands, Philippines, and Viet Nam.
- Maternal death audits have been conducted in Cambodia, China, Mongolia, and Papua New Guinea with a

view to improving quality of care and to use this information to mobilize increased government investment and community involvement.

- Increased awareness of and attention to women's health and gender issues have also been emphasized during 2003, including women's suicide and violence against pregnant women in China, and domestic violence in the Republic of Korea.
- Increased collaboration and coordination among major partners, governments, international agencies, and nongovernmental organizations at national and regional levels for providing preventative and curative care for maternal and newborn health have been accomplished during 2003.
- A research proposal on the prevalence and risk factors for anaemia among pregnant women was developed. The project will be conducted in Mongolia in 2004. Activities for the "Operation trial of maternity waiting homes and essential obstetric care" have begun in two pilot districts in Lao People's Democratic Republic in 2003.

## OTHER ACTIVITIES

### The Making Pregnancy Safer web site

The web site <<http://www.who.int/reproductive-health/MNB/index.htm>> was further developed in 2003 and will be

updated in 2004 with the maternal and newborn health and poverty page.

### Glossary of terms relevant to maternal and newborn health

A glossary of terms relevant to maternal and newborn health has been compiled along with a fully-referenced set of definitions of commonly used indicators relevant to maternal health. This information will also be available on the web site in 2004.

### New perinatal estimates

Estimates of the incidence of low birthweight were developed with UNICEF and are available in the UNICEF publication *The state of the world's children 2003*. A publication with details of the methodology used in compiling the estimates is in preparation.

Estimates of perinatal mortality were also developed and will be released in 2004, along with estimates of the proportion of stillbirths that occur intrapartum.

In collaboration with the WHO Department of Nutrition for Health and Development (NHD) and the unit of Leadership, Management and Fellowships within the WHO Department of Human Resources for Health (HRH), the Department organized a consultation "Towards the development of a strategy for promoting optimal fetal growth". Based on background documents that reviewed the causes, determinants

Table 2.2. Cost-effective interventions for selected maternal conditions

Maternal condition	Intervention
Obstructed labour	Assisted vaginal delivery
	Caesarean section
	Symphiotomy
	External cephalic version
	Surgical repair of fistula
Postpartum haemorrhage	Active management during the third stage of labour
	Medical management (hysterectomy, blood transfusion)
Sepsis	Prophylactic antibiotics
	Antibiotic treatment
Hypertensive disorders	Magnesium sulfate for pre-eclampsia
	Magnesium sulfate for eclampsia
Unsafe abortion	Access to safe abortion: vacuum aspiration
	Access to safe abortion: dilatation and curettage
Overall maternal conditions	Family planning

and interventions, groups of experts at the consultation made recommendations for strategy development. Highlights include the importance of pre-conception health and nutrition throughout the life cycle, the significance of maternity health care services in optimizing fetal development and early and distant outcomes, and the limited role of nutrient supplementation in pregnancy except for iron and iodine when required.

### **Cost-effectiveness studies of maternal and neonatal health interventions**

In order to assist countries in their planning and priority-setting, the Department has continued to work with the Choosing Interventions: Effectiveness, Quality, Costs, Gender and Ethics (EQC) team to review and conduct cost-effectiveness studies of beneficial maternal and newborn health interventions listed in *The WHO Reproductive Health Library* (RHL). To date, cost-effectiveness studies have been conducted on the interventions listed in Table 2.2.

Additional studies are planned for newborn health interventions. Work is also under way to produce databases reporting the costs and effectiveness of the above interventions for 17 WHO subregions, on the basis of their epidemiology, infrastructure, and economic situation. Once these databases have been established, basic assumptions can be modified for country-specific analyses and the data will be summarized and made available on the Internet. Difficulties have been encountered in including additional interventions, as adequate information does not exist on their efficacy. Thus, it has been decided to undertake a Delphi review, based on estimates produced by a global panel of 30–40 experts, including obstetricians, midwives, neonatologists as well as public health specialists from a wide-range of practice environments. The 'Making Pregnancy Safer intervention efficacy Delphi process' is planned to take place in 2004 in three rounds of two months each, carried out electronically. This work is being conducted in collaboration with the WHO Department of Health Financing and Stewardship (HFS).

### **Developing health systems profiles**

The Department is making efforts to increase the knowledge base and understanding of key elements of health systems including laws, policies, socioeconomic, sociocultural and demographic parameters as an *a priori* to developing and implementing maternal and newborn health programmes. As such, health system profiles are being developed in order to lay the basis for monitoring progress and evaluating achievements as needed, and to facilitate comparisons within and among countries. Work has begun on the development of the health system profile template and desk reviews have been conducted on Ethiopia, Indonesia, Mozambique, and Nigeria. The template will be finalized and made ready for adaptation and use for planning purposes by other countries during 2004.

### **Mapping midwifery services in the world**

Work has commenced to compile data on midwifery services in the world. This work will allow a more detailed analysis of the situation in terms of service coverage, equipment and staffing patterns of health facilities, and of adequacy of policies and regulations regarding midwifery. It will assist in identifying gaps and inform decision-makers on norms and models of care needed to provide equitable, quality midwifery services under different scenarios. This work is being conducted in close collaboration with other departments in WHO headquarters, regional and country offices, as well as partners such as ICM, the International Council of Nurses (ICN), FIGO and other relevant nongovernmental organizations. Although work has been delayed because of lack of funds, it is expected that the database and the final report will be completed in 2005.

### **Safe motherhood newsletter**

On the basis of a readers' survey, the content, layout, and format of the *Safe Motherhood newsletter* were updated and one issue focusing on success stories from countries was published in 2003. Current circulation figures exceed 20 000, and the readers' survey indicates that one copy serves 10 readers. The next edition to be published in 2004 will discuss care of the newborn with special needs, e.g. newborn and protection for malaria, prevention of mother-to-child transmission of HIV, and management of complications at birth.

### **Fistula management**

The Department is active in the partnership "Global initiative on fistula", which also includes UNFPA, EngenderHealth, FIGO and others. It is a member of the 'Fistula working group' and has committed to be the secretariat for the *Fistula management manual* Steering Committee. Work on the manual began in 2003 and a first draft is planned for mid-2004.

### **Essential reproductive health medicines and commodities**

During 2003, the Making Pregnancy Safer team worked in close collaboration with the WHO Department of Essential Drugs and Medicines Policy to finalize the interagency list of essential reproductive health medicines and commodities.

### **Operational research**

#### *Birth asphyxia*

The Department and Save the Children, USA are starting a collaborative project on birth asphyxia focusing on developing and validating an instrument for the identification of this condition both at the district hospital and at the community level. This work will be fundamental for future studies on the epidemiology of birth asphyxia in developing countries and

for the correct outcome definition in studies of risk factors for birth asphyxia and clinical trials testing the effectiveness of interventions to prevent and treat this condition. A technical meeting to finalize the research protocol is planned for 22–23 January 2004. The study will be implemented in Ethiopia, India and South Africa, and will last one year.

### *Human resources alternative strategies: assistant medical officers in Mozambique*

The Department is making efforts to increase the knowledge base and understanding on the issue of mid-level providers and skills substitution for ensuring maternal and newborn health care in less developed countries. In collaboration with the Department of Health Service Provision and the Karolinska University, Stockholm, Sweden, a research protocol is being developed to analyse the cost implications of using mid-level providers in Mozambique, as a strategy to increase access to maternal and neonatal emergency care, and to assess the legal and regulatory barriers and opportunities/levers to the use of these services, including factors for sustainability.

### *Haemoglobin colour scale*

In 2003, the Department developed an operations research proposal for the control of anaemia in pregnancy using the haemoglobin colour scale. This was to be implemented in three countries but was postponed because of funding shortages.

## **THE WAY FORWARD**

Building on current work, achievements and constraints, and on lessons learnt, and taking account of the refined and refocused Making Pregnancy Safer strategy, the Department will intensify efforts to provide technical support to assist countries in the implementation of the strategy and key interventions. It will continue to focus on areas of work which are critical for progress towards the MDGs.

Finally, it is envisaged, given the renewed attention of WHO to achieving the MDGs and its commitment to assist countries in their efforts to do so, that Making Pregnancy Safer will move forward with a strengthened global team and in close collaboration with other UN agencies and partners in maternal and newborn health.

## **Section 3**

# **Controlling sexually transmitted and reproductive tract infections**

# Controlling sexually transmitted and reproductive tract infections

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## INTRODUCTION

Sexually transmitted and reproductive tract infections (STIs and RTIs) are responsible for a considerable burden of reproductive ill-health worldwide, both directly and through their ability to enhance the risk of transmission or acquisition of the human immunodeficiency virus (HIV). Some 340 million curable STIs are estimated to occur worldwide each year, and many millions of incurable viral STIs occur annually, including an estimated five million new HIV infections. WHO's role in helping to reduce the disease burden associated with STIs and RTIs extends across all WHO core functions: advocacy, information management, research and evidence, technical cooperation and policy support, setting norms and standards, and developing new technologies, tools and guidelines.

In May 2002, the Department assumed responsibility for all WHO's STI and RTI work. This has provided the opportunity to take a coherent view of WHO's strategies and policies for STI control, including global advocacy, country support and technical issues (research, guideline development and normative functions) relative to the prevention and care of STIs, RTIs and their complications. The Department has identified the need to position STI control as a separate, though overlapping component, of a comprehensive approach to sexual and reproductive health and HIV control (Figure 3.1).

In the 1960s and 1970s, STIs were mainly considered from the point of view of infertility. During that time period, STIs were a component of family planning and reproductive health programmes. In the 1980s, STIs were identified as one of the key approaches to controlling the HIV pandemic. But as the focus of many HIV/AIDS programmes turned to other issues, such as expansion and sustainability of antiretroviral therapies and patient care, the importance of STIs became

increasingly overshadowed. The need to maintain focus on STI control is even more critical now that the expansion of antiretroviral therapy to cover three million HIV-infected patients in developing countries by 2005 (WHO's "3 by 5" target) has become a major objective of the Organization. This expansion of AIDS care must be accompanied by a complementary focus on HIV prevention, for which STI control is one of several key elements. In addition, sexual and reproductive health services provide an opportunity to provide counselling and advice on HIV prevention and to encourage men, women and adolescents to know their HIV status.

The Department's mandate in the area of Controlling Sexually Transmitted and Reproductive Tract Infections is to promote and develop guidelines and tools for STI and RTI policy, programme planning and implementation; establish the evidence for new and improved STI and RTI control strategies; conduct research on the prevention of mother-to-child transmission of HIV and other STIs; and advocate for and conduct research on the development and deployment of safe and effective microbicides. In order to fulfil this mission, the Department collaborates with a number of partners within the Organization, WHO country and regional offices, international agencies, research networks and nongovernmental organizations (NGOs).

## RESEARCH ACTIVITIES

### Female condoms

#### *Objective and rationale*

The female condom provides an additional means of protection for women when male condoms are not available or not

acceptable. The method is under the control of the woman and requires no, or little, cooperation from her male partner. WHO's female condom research addresses whether female condoms provide equivalent protection against pregnancy and STIs as male condoms.

### Progress

#### Condoms for pregnancy prevention

A contraceptive effectiveness study is being conducted in Chengdu (China), Sagamu (Nigeria), Panama City (Panama) and Durban (South Africa). Five hundred women choosing the female condom for contraception will be enrolled, with a similar number of male condom users. They will be followed monthly for six months and twice-monthly thereafter for one year. The main study endpoints are the occurrence of pregnancy or use of emergency contraception, with method discontinuation rates as secondary endpoints.

The study began in August 2002. By the end of November 2003, 1149 women had been admitted, 63% of whom chose to use the female condom. To date a total of 359 women have stopped participation in the study, with 58% of the female condom group discontinuing and 130 women switching groups (120 from female to male condoms and 10 from male to female condoms). These switches mainly occurred during the first three months of participation in the study. These rates of discontinuation or switching over from one type of condom to the other are understandable since none of the female condom users had used or even seen the device before participating in the study. In contrast, the male condom is widely available in the study sites and, with the exception of Panama where hormonal methods were the main contraceptive method, the majority of women had been using the male condom as their main method of contraception in the three months prior to enrolment. Eighty-five requests for emergency contraception—42 in the male and

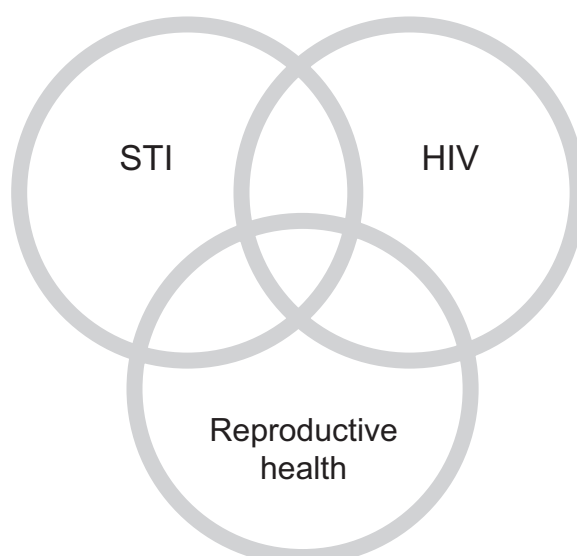
43 in the female condom group—have been reported, the main reasons being breakage (male condom group), or slip-page or incorrect insertion (female condom group). Eighteen pregnancies have been reported—nine in each condom group. Statistical analysis will be performed once follow-up of all participants is completed.

#### Condoms for STI prevention

Biological markers are an extremely sensitive method of assessing whether condoms prevent exposure to semen or STIs during intercourse. Postcoital prostate specific antigen (PSA) levels have been used to compare the efficacy of male and female condoms to prevent exposure to semen. WHO extended the concept to detect whether any exposure to sexually transmitted pathogens occurs following intercourse with an infected partner.

A study will be conducted among sex workers in the Hillbrow area of Johannesburg, South Africa, using self-administered vaginal swabs before and after intercourse, and the used condom will be assessed for the presence of STIs in the ejaculate. Pilot-projects to assess the acceptability and practicality of the study started in July 2003. A feasibility study assessed whether volunteers would be willing to participate in such a study, collect pre- and post-coital vaginal swabs and the used condoms, complete a coital diary card and report the frequency of intercourse. In addition, the prevalence of *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Trichomonas vaginalis* among the clients and partners of the study volunteers were estimated from analysis of the used condoms. A total of 15 women were recruited, underwent a full clinical examination, and were presumptively treated for STIs. After one week, nine women were excluded from the study on the basis of inconsistent condom use, failure to complete the coital diary card, moving, or acquisition of a new infection. The remaining six women collected 108 used male condoms. These demonstrated a high prevalence of STIs in

Figure 3.1. Components and areas of work in a comprehensive model of sexual and reproductive health, STI control and HIV control



male clients: 19% *Neisseria gonorrhoeae*, 11% *Chlamydia trachomatis* and 11% *Trichomonas vaginalis*. The study revealed the need to promote and train potential volunteers on use of the female condom (less than 3% of condoms used in the study were female condoms). The high prevalence of STIs among the clients means that the study will be able to assess with greater precision than anticipated the degree to which barrier methods reduce the risk of acquiring a sexually transmitted infection.

A second preparatory study assessed the performance of self-collected vaginal swabs compared with swabs collected by a clinician to detect sexually transmitted pathogens. A total of 398 self-collected vaginal swabs have been tested and compared with the corresponding clinician-collected specimens. The STI prevalence rates among the female STI patients at the Johannesburg Esselen Street clinic were 19% for *Chlamydia trachomatis*, 23% for *Neisseria gonorrhoeae* and 43 % for *Trichomonas vaginalis*. The sensitivity, specificity, positive and negative predictive values of the self-collected swabs compared with the clinician-collected swabs were 83.4%, 96.7%, 88.7% and 91.5%, respectively, for *C. trachomatis*; 89.6%, 95.7%, 90.8% and 95.1%, respectively, for *N. gonorrhoeae* and 84.3%, 99.3% 99.0% and 88.3%, respectively, for *T. vaginalis*. The confidence intervals of the performance indices are very wide. Recruitment will continue to the planned number of 810 sets of self- and clinician-collected vaginal swabs.

Information from these studies will be used to plan the main study to assess and compare the efficacy of male and female condoms to prevent exposure to sexually transmitted pathogens.

### Prevalence of STIs and RTIs

#### *Objective and rationale*

The data available to describe the etiology and prevalence of important STIs and RTIs remain limited, especially in resource-constrained settings. Additionally, requests have been received to strengthen the capacity of researchers in such settings so that countries are able to conduct high-quality STI/RTI research to target and adapt programmatic interventions. The Programme provides technical and financial support to studies on STI and RTI prevalence in the Asia-Pacific region, where this topic had been identified as a priority by the Asia-Pacific Regional Advisory Panel. This effort meets the objectives of providing high-quality, laboratory-based data for country programming, developing further the applied STI/RTI research capacity of scientists and institutes supported by the Programme, and provides data for the evidence base needed to develop and adapt tools and guidelines.

#### *Progress*

A total of nine protocols aim to assess the etiology and prevalence of STIs and RTIs in reproductive health service settings and in the community. An additional four protocols address questions related to STIs.

A study on "Prevalence of RTIs at the family planning clinic at Central Women's Hospital, Yangon" is expected to start in early 2004. The study on the prevalence of STIs and RTIs in Vientiane, Lao People's Democratic Republic, among antenatal clinic patients in two central hospitals has been completed, and the specimens transferred to Bangrak Hospital, Bangkok, Thailand, for polymerase chain reaction (PCR) analysis. The team conducting the community-based, cluster study on the prevalence of lower genital tract infections among rural women in Sichuan province, China, enrolled nearly half (1 000) of the study participants during 2003. Studies are planned in Indonesia to address the prevalence of *Chlamydia trachomatis* infection in male and female university students.

Additional STI-specific studies supported by the Programme include two protocols for studies to assess the association between *C. trachomatis* and ectopic pregnancy (to be conducted in Mongolia and Myanmar), one study to assess clinical aspects of vaginal discharge in prepubertal girls visiting the reproductive health counselling centre of the Maternal and Child Health Centre in Ulaanbataar, Mongolia, and one study to assess the performance of syphilis screening in antenatal services in selected sites in Mongolia.

The current status and future steps related to this work were to be reviewed with the Asia-Pacific Regional Advisory Panel meeting in 2003, but this was delayed until March 2004 due to funding shortages. A strategy to support small-scale studies that provide data relevant to the country as well as for global needs will be discussed.

### Incidence and risk factors for pelvic infection following induced abortion

#### *Objective and rationale*

A multicentre nested case-control study on the incidence and risk factors for postabortion pelvic infection has been embedded in a study on surgical abortion. The latter study will evaluate in a randomized double-blind trial the effect of vaginal administration of 400 µg of misoprostol prior to vacuum aspiration abortion on the incidence of complications among women seeking termination of pregnancy before 12 completed weeks of gestation. Five thousand women will be recruited in 14 centres in nine countries, and followed-up seven and 14 days after abortion. The nested study includes 11 of these sites with approximately 4000 women participating from nine countries. The incidence of postabortion pelvic infection will be obtained from follow-up in the randomized controlled trial, while the risk factors for

postabortion pelvic infections resulting from pre-existing STI/RTI will be assessed in the nested study.

### Progress

By December 2003, 10 sites were recruiting patients and the remaining site is expected to begin soon. Enrolment is expected to be completed during 2004. Laboratory specimens will be shipped to a central laboratory at the Institute for Tropical Medicine, Antwerp, Belgium, for analysis, which will be restricted to women who develop pelvic infection after abortion (cases) and a subset of women without complications (controls).

## Antiretroviral therapy, mother-to-child transmission of HIV and mother's health

### Objective and rationale

Advances have been made in recent years in ways to reduce the risk of mother-to-child transmission (MTCT) of HIV, and programmes using single-dose nevirapine to reach more pregnant women have been expanded. However, transmission rates remain persistently higher in developing than in developed countries, uptake of interventions offered by the programmes remains low, HIV-related maternal mortality remains high and infant feeding choices continue to be complex. The acceptability, safety and effectiveness of triple-combination antiretrovirals (ARVs) for the benefit of both the mother and her infant is being addressed in research conducted by the Programme.

### Progress

The protocol to study the impact of highly active antiretroviral therapy (HAART) on MTCT and mother's health was further developed in 2003, principally as a result of an agreement with the French Agence Nationale de Recherche sur le SIDA (ANRS), which had previously decided to support a closely-related project. The ANRS "projet lait" covered the postnatal period and explored the virology and immunology of breast milk, the nutritional status of infants, and anthropological issues surrounding breastfeeding by HIV-positive women. The WHO study provided the opportunity to collect such data within the context of a randomized controlled trial, thus increasing its validity. The two projects have, therefore, been combined into a single, integrated project which increases the efficiency of the study and provides synergy between the two projects. In addition to supporting the site in Bobo Dioulasso, Burkina Faso, ANRS is supporting the virology, immunology, nutrition and anthropological studies in the other study sites. Additional details were added to the protocol to conform to the requirements of the Centers for Disease Control and Prevention (CDC) Institutional Review Board and the ethical and scientific review boards at the participating sites.

The overall goal of the study is to optimize the use of ARV drugs during the antepartum, intrapartum and postpartum periods to prevent MTCT and preserve the health of the mother in settings where the majority of HIV-positive women breastfeed.

A total of 2400 HIV-positive women will be enrolled from different study sites. The multicentre study has two parts:

- Part I: a prospective cohort study of eligible HIV-positive pregnant women and their children, followed until two years after delivery/birth; and
- Part II: a nested randomized controlled trial (RCT) of eligible women enrolled in the prospective cohort study with CD4+ cell counts between 200 and 500 cells/mm<sup>3</sup>.

In the prospective cohort study (Part I), there will be two groups of women:

- Group A: Women who meet WHO criteria for HAART, i.e., CD4+ cell counts below 200 cells/mm<sup>3</sup> or with Stage 4 HIV disease, who have no contraindications to HAART, and who accept HAART. They will be offered a HAART regimen, consisting of zidovudine, lamivudine and nevirapine, to be initiated at 34–36 weeks' gestation and then continued as long as required for the woman's own health.
- Group B: Women who do not meet WHO criteria for HAART, or, although meeting criteria, have one or more contraindications to HAART, refuse HAART and/or do not agree to be randomized. These women will be offered short-course MTCT prophylaxis (see below).

In Part II of the study, those women enrolled in the prospective cohort study with CD4+ cell counts between 200 and 500 cells/mm<sup>3</sup> with no contraindication and willing to be randomized will receive one of two different regimens for the prevention of mother-to-child transmission of HIV:

- a triple-ARV regimen (zidovudine, lamivudine and nevirapine) beginning at 34–36 weeks' gestation, through delivery, until six months postpartum as long as breastfeeding continues; or
- a short-course regimen consisting of zidovudine beginning at 34–36 weeks' gestation until labour, plus one dose of zidovudine and one dose of nevirapine at the onset of labour.

All infants born to women enrolled in either part of the study will receive one dose of nevirapine within 72 hours of birth.

All mothers will receive counselling on infant feeding. Those opting for formula feeding will be provided with free formula. Those opting for breastfeeding will be counselled to stop when the child reaches six months of age.

All women enrolled in the prospective cohort study who do not meet criteria for HAART at enrolment (Part IB) whose HIV disease progresses to WHO Clinical Stage 4 or whose CD4+ count falls below 200 cells/mm<sup>3</sup> at any time within two years postpartum will be offered HAART (provided they have no contraindication to initiating therapy).

The primary objectives of the prospective cohort study are to describe the rates and correlates of AIDS-free maternal survival and HIV-free child survival among HIV-positive pregnant women and their children receiving care at participating clinical centres, and to assess the acceptability and safety of ARVs offered to these women and children according to WHO guidelines.

The primary objective of the randomized controlled trial is to assess the efficacy and safety of the triple-ARV MTCT-prophylaxis regimen compared with the short-course MTCT-prophylaxis regimen among eligible women enrolled in the prospective cohort study with CD4+ cell counts between 200 and 500 cells/mm<sup>3</sup>.

Sites identified for the study include: Department of Paediatrics, University of Nairobi, Nairobi, Kenya; The Coast Provincial General Hospital, in partnership with the International Centre for Reproductive Health, Mombasa, Kenya; The Kilimanjaro Christian Medical Centre in Moshi, Tanzania; the Centre Muraz in Bobo-Dioulasso, Burkina-Faso; and the Centre Hospitalo-Universitaire, Kigali, Rwanda. An additional sixth site to participate in the study is being identified, subject to sufficient funds becoming available. Links have been established with public and nongovernmental organizations in each of the study sites to sustain access to ARV therapy for the women and their infants beyond the end of the study.

Study instruments and procedures have been developed during 2003 and questionnaires were pre-pilot-tested in October and November 2003. The study is expected to start in 2004 in three centres following training and pilot-testing of all procedures.

The study has been given a neutral name to avoid stigma of participating in a study of HIV transmission. It is now called the Kesho Bora project, which in Swahili means "a better future".

### **Safety of antiretroviral regimens to prevent mother-to-child transmission of HIV**

#### *Objective and rationale*

Transient emergence of resistant HIV strains has been reported following use of short prophylactic regimens to prevent MTCT, particularly with single-dose nevirapine. It is not known whether this resistance has any negative impact on the efficacy of therapeutic antiretroviral regimens when such treatment is initiated months or years later.

#### *Progress*

A study protocol to assess the clinical response of women initiating combination antiretroviral therapy was developed and discussed at an expert meeting convened by the Programme in July 2003 in Geneva, Switzerland. The protocol was then revised and shared with partners. The group decided that an observational study, enrolling women who were initiating therapy in a 12-month prospective cohort study, was the easiest design to implement at this stage. Index women would be those who had been exposed to single-dose nevirapine at some time in the past, and control (non-exposed) would be those who had delivered, but had not taken any previous antiretroviral prophylaxis. Because of lack of resources in WHO, the study will be implemented by the Centres for Disease Control and Prevention (CDC), Atlanta, GA, USA, with WHO represented in the study working group. The study will be conducted at sites where MTCT-prevention interventions have been available for several years and standard first-line ARV therapies are being offered to women who require treatment as part of the CDC Global AIDS Program.

### **Safety and acceptability of cellulose sulfate**

#### *Objective and rationale*

New technologies for the prevention of HIV and other STIs are required. Microbicides, new substances that are applied vaginally and/or rectally, could empower individuals and their partners to protect themselves against STIs, including HIV. The Programme, in partnership with other agencies, is accelerating research and development of safe, effective, and affordable microbicides for use in developing countries. In collaboration with CONRAD, the Programme has completed a three-centre randomized double-blind Phase I trial of the safety and acceptability of 6% cellulose sulfate gel (CS) compared with K-Y Jelly among healthy women volunteers.

#### *Progress*

Volunteers were recruited from family planning clinics and local communities in Kampala (Uganda), Mumbai (India), and Sagamu (Nigeria). Study products were applied in 3.5 ml doses twice daily for seven consecutive days in a cohort of sexually abstinent women in each centre (cohort I), followed by a similar cohort of sexually active women (cohort II). Safety was assessed by symptoms and signs of irritation of the external genitalia, vagina and cervix, and epithelial disruption as seen on colposcopy. Product acceptability was assessed by a structured questionnaire.

Recruitment of volunteers started in December 2001 and was completed in all centres by July 2003. One hundred and eighty women (90 on CS and 90 on K-Y Jelly, equally distributed between centres and cohorts within each centre) were enrolled. Overall, two volunteers were lost to follow up; four discontinued due to onset of menses, two discontinued gel application due to product-related adverse events and one

withdrew due to personal reasons. Compliance with gel use was 94% overall. No serious adverse events were reported. Baseline characteristics of women in both gel groups were similar. In cohort I, 6 (14%) women on CS and 12 (27%) on K-Y Jelly reported genital symptoms. New colposcopy findings were detected in 4 (9%) women on CS and 9 (21%) women on K-Y Jelly in cohort I. In cohort II, two women on CS and three on K-Y Jelly reported genital symptoms. Five women (11%) in each gel group in cohort II had new colposcopy findings. Differences between gel groups were not statistically significant. Almost all women (174) who used either CS or K-Y Jelly said that the product was easy or very easy to use. The majority of women reported no problem with their product. Over 80% of volunteers said if the product was proven to work, they would buy it or recommend it to someone for prevention of pregnancy and sexually transmitted infections. In summary, this study shows that twice daily vaginal applications of 6% cellulose sulfate appear to be as safe and well tolerated as K-Y Jelly. Further studies of the effectiveness of CS to prevent HIV and pregnancy are planned.

### **Safety and acceptability study of 10% polystyrene sulfate**

#### *Objective and rationale*

Polystyrene sulfate (PSS) is a non-cytotoxic polymer with antifertility and antimicrobial effects. *In vitro* studies have shown that PSS is highly active against HIV, HSV-2, HPV, and gonococci, and moderately active against chlamydia. In a Phase I safety study conducted in the USA among healthy sexually-abstinent women, PSS was shown to be less irritating to the genital epithelium compared with a nonoxynol-9 containing gel (unpublished data). Several expanded Phase I safety trials of PSS were commissioned by CONRAD among HIV-infected women in Belgium, sexually-active women in India, and among both sexually-active and sexually-abstinent women in the USA.

#### *Progress*

In collaboration with CONRAD, WHO developed a protocol for an expanded Phase I safety and acceptability study of PSS to be implemented in Kampala, Uganda, among sexually-active women for three-times daily vaginal applications for 14 consecutive days. However, concerns about the safety of PSS have arisen from some of the preclinical toxicology studies, and all human studies with PSS have been put on hold pending review of the toxicology data by CONRAD and the US Food and Drug Administration (FDA). If the decision is taken to continue with the development of PSS, the data will be presented to the Programme's Toxicology Panel for their opinion before the study proceeds.

## **NORMS AND TOOLS**

### **Specific objectives/targets**

The objectives of the norms and tools developed by the Department are: to increase the availability of high-quality, culture- and gender-sensitive and non-stigmatizing services for the prevention, care and management of STIs and RTIs and their complications; to broaden the range of safe, effective and affordable methods to prevent and manage STIs/RTIs and MTCT of HIV and other STIs; and to contribute towards strengthening the capacity of national health systems to deliver these services.

The Department is producing and updating a series of guidelines and tools to facilitate technical support to countries and programmes for STI/RTI control. To address country needs the Department is developing a comprehensive set of guidelines, guides and tools to assist programme managers and health care providers develop and implement strategies for prevention and management of STIs and RTIs which are adapted to their own environment. These reflect a comprehensive view of STI/RTI control which is broader than just clinical management, and addresses population-level factors which impact on sexual and reproductive health and commitments made to improving reproductive health at the International Conference on Population and Development (ICPD) in 1994. The adaptation process considers the multiple elements which constitute the local environment—disease epidemiology, culture, context, social and economic factors, formal and informal health care systems, activities of other sectors and development agencies—so that strategies will have maximum benefit when adapted for local use.

### **New norms/tools developed**

#### *STI/RTI programme guidance tool*

The STI/RTI Programme guidance tool is an adaptation of WHO's Strategic Approach for contraceptive technology introduction (*Making decisions about contraceptive introduction*, WHO/RHR/02.11) to the problems of STI and RTI control and management. It considers a broad range of programmatic interventions and assists programme managers in identifying the information required for making decisions on the most culturally appropriate interventions. The tool was field-tested in Brazil, Cambodia, Ghana and Latvia, between 2000 and 2003. In March 2003, a meeting was convened in Geneva, Switzerland, with the country partners and Population Council HORIZONS Program to agree on a protocol for evaluation of the tool in the four pilot-countries and organize the evaluation research. The evaluation was conducted by external and independent consultants in April and May 2003, and the results presented to the Department in July 2003. The evaluation showed that the tool was perceived as excellent for orchestrating the interventions and actions required to improve STI/RTI control.

An STI/RTI programme guidance toolkit for programme managers has also been reviewed and finalized in 2003. It now comprises two modules: the STI/RTI programme guidance toolkit and the STI/RTI programme guidance tool country experience. The first module is an advocacy and "how to" manual and the second module describes the experience of applying the programme guidance tool in three of the four countries. For each country, the background paper, plus the results and recommendations of the rapid assessment, are included. The country experiences and evaluations were discussed and disseminated at a workshop for programme managers held during the 8th World STI/AIDS Congress in Punta del Este, Uruguay, in December. The toolkit will also be promoted through the WHO regional and country offices, partners who work with policy-makers and programme managers and through other international conferences.

### New work undertaken on norms/tools under development

#### *Supra-document*

Generic, evidence-based guidelines are now available for the prevention, detection and management of STIs and RTIs. Other guidance for assessment, design, implementation and evaluation of STI control programmes is available for programme managers.

The guides address country needs by covering seven essential elements of STI/RTI control:

1. Assessment of the epidemiological situation, the health system response and health-seeking behaviours.
2. Planning and development: prioritizing interventions, involving stakeholders, advocating and mobilizing resources.
3. Control strategies for STIs/RTIs, including targeted interventions with core groups and other vulnerable populations, case-finding and screening.
4. Clinical interventions: improving syndromic management and other reproductive health services, counselling and health education.
5. Community/population-level interventions: raising awareness, information, education and communication (IEC); influencing community norms; increasing health-seeking behaviour; and improving access to STI/RTI care.
6. Support strategies: training, laboratory, drug and commodity management improvements.
7. Monitoring and evaluation, including ongoing surveillance.

The supra-document presents in matrix form how the different guides on STI/RTI control and management interrelate.

The matrix includes the guides that are under the responsibility of the Department (Figure 3.2) but also the guides written by other WHO departments which deal with STI/RTI. This supra-document is presently in an advanced draft form and should be finalized by mid-2004.

#### *Conceptual framework for STI/RTI control*

To provide an overall picture of STI control strategies of proven effectiveness, the Department is developing a conceptual framework for STI/RTI control for programme managers. This guide, currently in draft form, covers the basic elements of an STI/RTI control strategy, together with a summary of the tools and guides available to plan how to develop and implement an STI/RTI control programme adapted to the particular social and epidemiological conditions in the country or setting. The draft framework was reviewed during a meeting in May 2003. It was noted that the conceptual framework had elements in common with the *Control of sexually transmitted diseases—a handbook for the design and management of programs* developed by AIDSCAP/Family Health International (FHI) which was due for updating. At a meeting with the editors of the FHI handbook in November 2003 it was agreed that a combined publication could meet the objectives of the conceptual framework and the handbook. Two WHO staff will join the editorial team, new chapters will be added and others updated by the end of 2004.

#### *Sexually transmitted and other reproductive tract infections: a guide to essential practice*

Clients visiting reproductive health facilities—such as family planning, antenatal care or some primary health care services—have different patterns of risk factors for, and prevalence of, STIs and RTIs than patients presenting with STI complaints or to specific STI services. The *Sexually transmitted and other reproductive tract infections: a guide to essential practice*, formerly referred to as the *Essential care practice guide*, provides a comprehensive approach to STIs and RTIs (including counselling, prevention, screening, case-finding, and management) adapted to the needs of such clients. The guide is compatible with other guides and tools developed by the Department, including the *Pregnancy, childbirth, postpartum and newborn care: a guide to essential practice*, and the *Decision-making tool for family planning clients and providers*, as well as the syndromic approach to STI management which is specifically targeted at the needs of patients presenting with complaints and/or symptoms of acute STI/RTI.

The *Sexually transmitted and other reproductive tract infections: a guide to essential practice* consists of two documents: a narrative and a pocket guide. An adaptation guide and an evidence-based document for programme managers are also being developed to assist programme managers identify and interpret national and local data on the epidemiology of STIs and RTIs and related behaviours.

The *Sexually transmitted and other reproductive tract infections: a guide to essential practice* was pre-field-tested in Brazil, China, India, Jamaica, Kenya and Latvia in January 2003 by means of a desk review by national STI/RTI and reproductive health experts, health care providers and programme managers. Comments from the pre-field-testing were reviewed in May and incorporated into a revised guide, which was discussed at a further meeting in October 2003 to agree on the optimal procedures for field-testing. Challenges included the difficulties of designing a rigorous field-testing protocol, particularly with respect to training of health care providers, the poor integration of STI services in reproductive health service settings in most of the target countries and the difficulties for a health care provider to use the guide. Advice from WHO regional office staff and other teams in the Department suggested that field-testing without a commitment for subsequent implementation could be problematic for countries. It was therefore decided that the guide should be introduced to countries through a series of regional or subregional workshops for health care providers and programme managers responsible for STIs and reproductive health services in different countries. The purpose of these workshops will be to determine: (i) whether programme managers would be interested in adopting and adapting the guide; (ii) how best to use the guide at the country level; and (iii) whether it is feasible to integrate STI services into

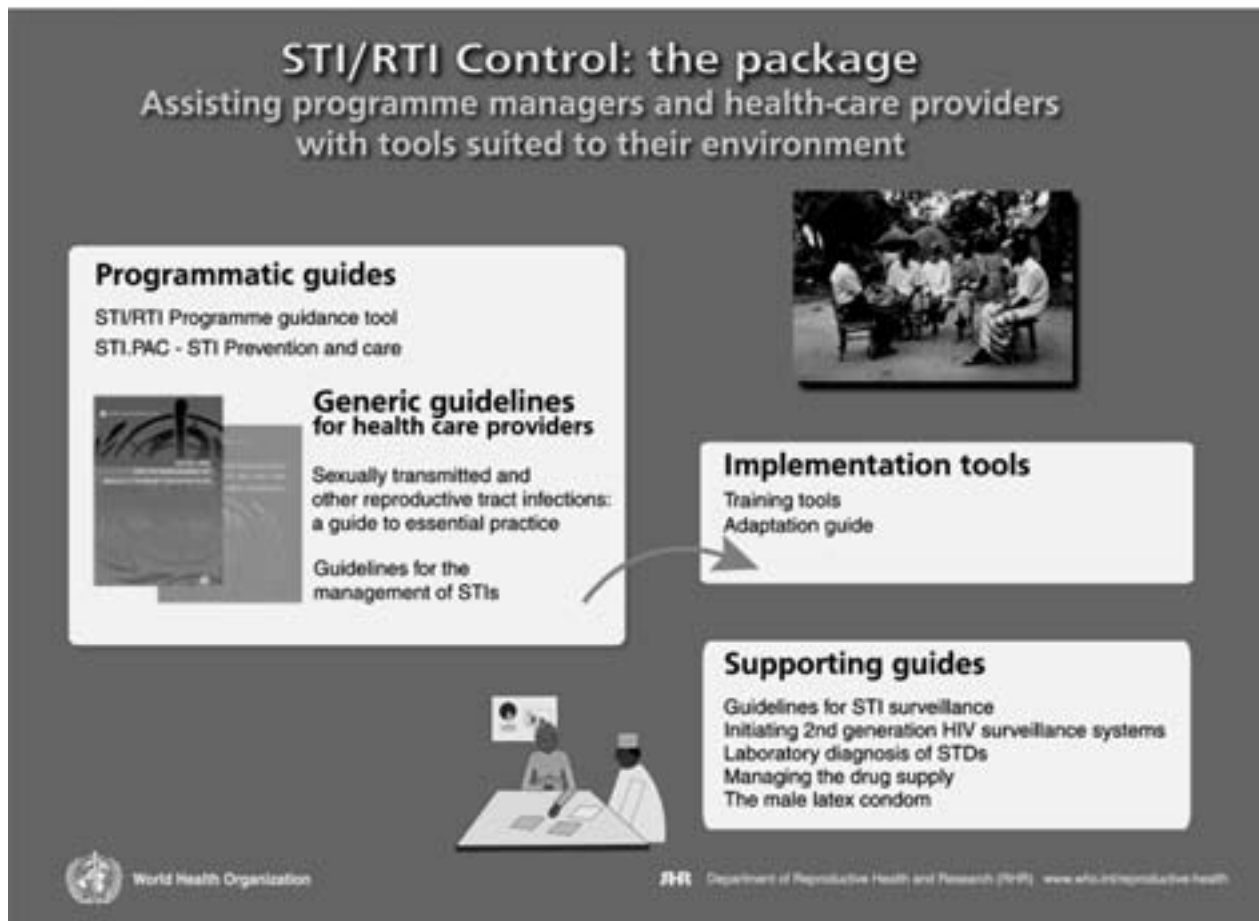
reproductive health services. In parallel with this process, the ease of use, presentation of information, and format of the guide will be evaluated by the health care providers during the workshops through a review of specific clinical scenarios. The workshops will also map out the adaptation and implementation process at country level, training needs, and a monitoring and evaluation plan. These workshops will be conducted in collaboration with WHO regional staff. Pilot introduction and adaptation will then start in countries that have identified this area of work as a priority.

Following the October meeting, the Department decided that the narrative and pocket guides should be considered generic guides for local adaptation; both would be translated into Chinese, French, Portuguese, Russian and Spanish. The adaptation guide and the document containing the evidence base have been merged into a single document which will be available for the workshops.

#### *Updated STI management guidelines*

The syndromic approach developed by WHO has been a key element in STI management in resource-limited settings. A revised version of the *Guidelines for the management of sexually transmitted infections* has been printed and is being translated into French. There are plans to have the document

Figure 3.2. Guides for STI/RTI control



translated into Portuguese and Spanish soon. The main areas of change from the previous version are the management of genital ulcer diseases (GUD) and vaginal discharge.

More data have been gathered to highlight the increase in the prevalence of sexually transmitted herpes simplex virus type 2 (HSV-2), which is rapidly establishing itself as the major cause of GUD, especially in the developing world. Recent data presented at the International Society for Sexually Transmitted Diseases Research (ISSTD) Congress in Ottawa, Canada, July 2003 showed a decline in syphilis and chancroid and an increase in HSV-2 (Figure 3.3 and Figure 3.4).

In view of these epidemiological changes in the profile of causative agents for GUD, WHO is developing and promoting appropriate adaptation of the GUD algorithm to respond effectively to the causative agents. One such strategy is the addition of acyclovir for the treatment of GUD in high-prevalence settings. This is being piloted in a number of countries, including Botswana and Sri Lanka.

*Training modules for the management of STIs*

To improve the quality of STI care at country level, WHO has developed training modules and tools for countries to use or adapt, and to train health personnel in STI management. A set of 50 modules was printed and sent to WHO regional offices and other partners and country programme managers for comment before bulk printing and distribution. Positive feedback has been received from different parts of the world.

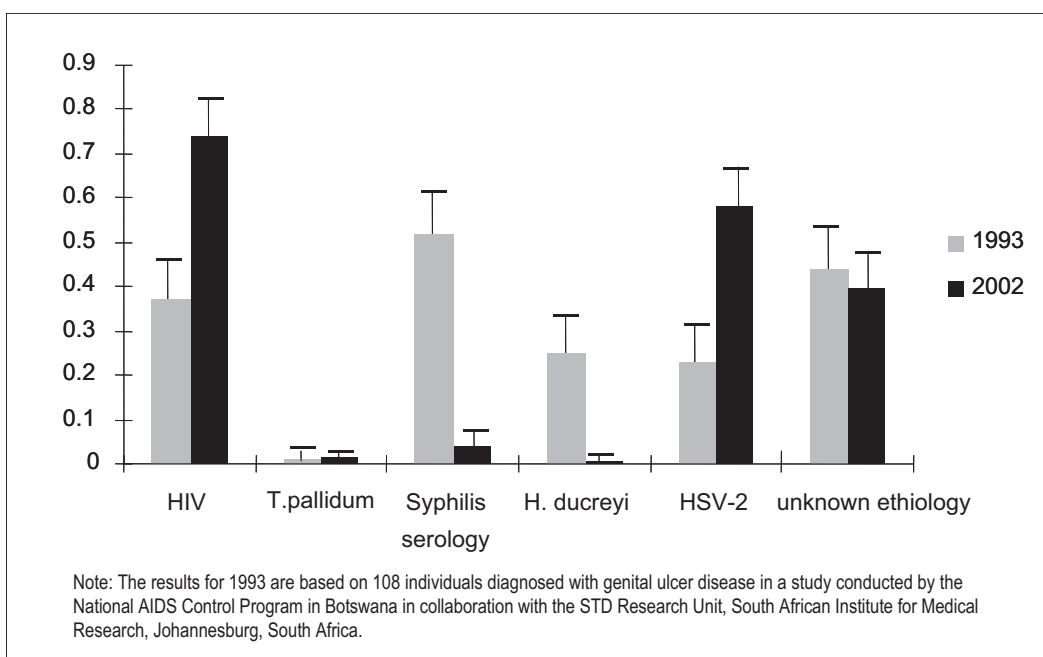
Most of the comments are being used to strengthen the training modules before publication and distribution in the first quarter of 2004. The modules will be available in modified format in a web-based and an interactive CD version.

*Elimination of congenital syphilis*

Three case studies on maternal and congenital syphilis conducted between 1999 and 2001 in Bolivia, Kenya and South Africa showed that national congenital syphilis control programmes were hampered by difficulties in operations, policy and financing. Key issues included:

- the magnitude of the problem;
- the failure of policy and programme implementation, including lack of financial, technical and operational support to programmes at country level;
- whether congenital and maternal syphilis were perceived as a problem considering that pregnant women and their newborn infants tended to be followed by different health care providers;
- the severity of the social implications of syphilis infections, and poor patient motivation;
- whether the tools available were adapted to the objectives of the programmes; and
- the effectiveness and robustness of diagnostic tools and the effectiveness of treatment.

Figure 3.3. Changes in the etiology of genital ulcer disease in Botswana from 1993 to 2002



Source: Rehman M et al. Changing patterns of STD in Botswana, 1993–2002. Ottawa, 2003 ISSTD Congress. Abstract No. 0334 (reproduced with permission).

A series of articles addressing the failures and challenges of syphilis control and elimination will be published as a special issue of the *WHO Bulletin* in time for the 2004 AIDS Conference in Bangkok.

Additionally, a draft guideline on “Maternal and congenital syphilis: an outline for prevention and control” was reviewed by an expert meeting in October 2002. The document will be shortened, updated and revised as a reference document, the key elements of which would be incorporated into the guides to essential practice under development by the Making Pregnancy Safer and the Controlling Sexually Transmitted and Reproductive Tract Infections teams in the Department. It will be presented to the Technical Advisory Group for Elimination of Congenital Syphilis in May 2004.

### New norms/tools initiated

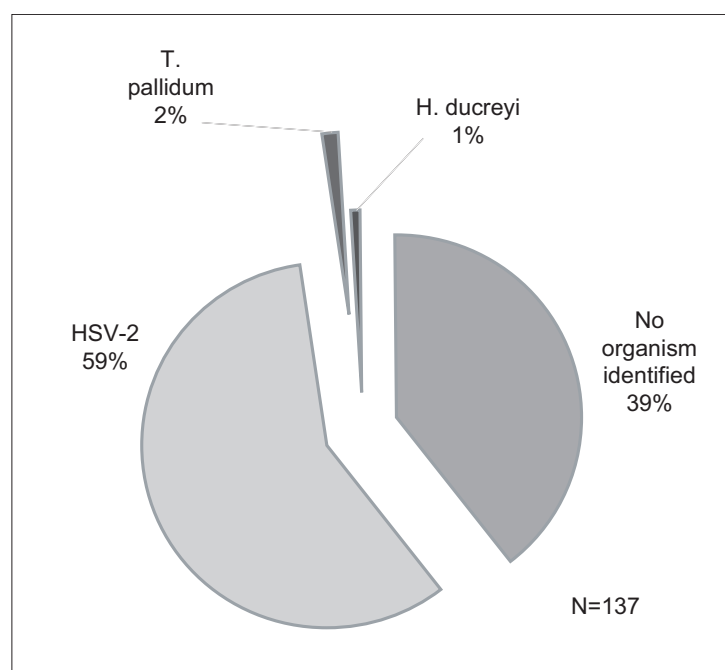
#### *Global strategy for STI prevention and control*

Work was under way to develop an updated global strategy for STI prevention and control that reflects recent evidence and experience in STI control and its impact on the HIV epidemic. A final draft document was sent to WHO regional offices and other partners such as FHI, CDC and several WHO Collaborating Centres. Feedback has been received; most of the comments have been incorporated while others have been flagged for further discussion at regional and global consultations planned for the first half of 2004.

The purpose of the strategy is to provide a framework to guide the planning and implementation of an expanded global response for the prevention and control of STIs and RTIs. In particular, this document will help to:

- ensure that limited resources are focused in priority programme areas where they are likely to have the greatest impact;
- bring together lessons learnt, developments and recommendations in the most critical areas of work in STI/RTI prevention and care, including identifying approaches and technologies that work and need to be scaled-up, as well as newer approaches and technologies that still require evaluation for effectiveness;
- leverage synergies between the human and institutional strengths and capacities of all partners to address current population coverage levels, tackle existing and emerging gaps in the response, and avoid unnecessary duplication of efforts; and
- define WHO's role within this global STI/RTI partnership and propose an operational framework for this role at the central, regional and country levels that can support a well-coordinated WHO STI/RTI programme which draws upon the strengths, resources, and comparative advantages of diverse units across the Organization.

Figure 3.4. Etiology of genital ulcer disease, Botswana, 2002



Source: Rehman M, et al. Changing patterns of STD in Botswana, 1993–2002. Ottawa, 2003 *ISSTD Congress*. Abstract No. 0334 (reproduced with permission).

The target audience for the strategy are national HIV/AIDS/STI and reproductive health programme managers, health sector stakeholders, including public and private sector providers, health ministers, policy-makers and other decision-makers in the health sector, international agencies (including WHO) and nongovernmental partners and other governmental departments and agencies.

### *Strategy for congenital syphilis elimination*

The Department's Scientific and Technical Advisory Group (STAG) endorsed in 2003 a proposal for the elimination of congenital syphilis and recommended that a detailed strategy be developed. In the Department's 2004–2009 Medium-term Programme of Work a specific goal was set to reduce the rate of congenital syphilis by 90% in four countries by 2009, as a step toward the subsequent elimination of this disease. The practicality of these goals and the strategies to achieve them were reviewed at a series of meetings within WHO to develop a 'Congenital syphilis elimination plan' together with draft advocacy and strategy documents. It was agreed that control of syphilis in the general population is necessary to sustain the elimination of congenital syphilis. The plan is being developed in partnership with the Making Pregnancy Safer initiative and the Communicable Diseases Strategy Development and Monitoring for Eradication and Elimination (CDS/CEE) unit, and may be included in the broader plan for elimination of neglected diseases.

Further work in 2004 will concentrate on the development of a fundraising strategy, adding details to the elimination plan, and initiating a series of consultations with WHO regional offices and selected countries that may be interested, and suitable to be included, in the first wave of target countries.

### *Country adaptation of global STI management protocols*

The WHO *Guidelines for the management of sexually transmitted infections* and the *Sexually transmitted and other reproductive tract infections: a guide to essential practice* reflect global recommendations for the management and control of STIs and RTIs in different health care settings. Countries are encouraged to adapt these guidelines and develop national guidelines based on available evidence and cultural norms for their country or setting. The London School of Hygiene and Tropical Medicine, London, United Kingdom, and FHI were contracted to develop the adaptation guides and an implementation process. They have produced a first draft that was discussed at a small meeting held in Geneva, Switzerland, in November 2003. The meeting also brought together other teams in the Department that are working on adaptation guides to ensure harmonization and agreement on the recommended process for adaptation at country level. The other guides are the *Adaptation guide for pregnancy, childbirth, postpartum and newborn care*, being developed by the Making Pregnancy Safer team and the *Adaptation guide for the decision-making tool for family*

*planning clients and providers*, being developed by the Promoting Family Planning team. These adaptation guides will follow a common structure—overview of the guide, the need for adaptation and how to adapt, the elements which require adaptation, and the evidence base, monitoring and evaluation of the adaptation process and utility of the guide.

Although delayed, work is continuing on the cost-effectiveness review document and a decision-making tool to help managers decide whether syndromic management of women with vaginal discharge will be cost-effective in their setting, balancing treatment costs against the benefits of prevented STIs and their sequelae (including pelvic inflammatory disease, infertility, or ectopic pregnancy). This decision-tree tool will provide managers with a rationale for adaptation, especially for the syndromic management of cervical infection in women presenting with vaginal discharge. These tools will be published and disseminated in early 2004.

In a cross-team collaborative effort, a plan of work has been developed and support from the United Nations Population Fund (UNFPA) obtained to accelerate the adoption and adaptation of these guidelines into service use in countries. The results of this effort will be seen in 2004 in terms of a number of regional workshops, technical updates, and ultimately, country introduction and adaptation.

### *Comprehensive cervical cancer control: a guide to essential practice*

One of WHO's core functions is to reduce excess mortality and morbidity, especially in poor and marginalized populations, by acting as a catalyst for change through technical and policy support and by setting standards and stimulating the development of new guidelines for disease control. Interventions to control cervical cancer are among the most cost-effective compared with almost all other cancer types. WHO advocates a comprehensive approach to cancer control including prevention, early detection, treatment and palliative care.

While there are many guidelines and reference books on the prevention and management of cervical cancer, they are not always adapted to the particular situation of low- and middle-income countries. Guides for programme managers and health care providers are particularly needed.

The objective of the joint initiative between the Department and WHO's Programme for Cancer Control (PCC) is to develop a generic guide for health care providers, consisting of a detailed guide for essential practice supplemented with a pocket guide. The guide will address all the aspects of prevention and management of cervical cancer—from prevention of human papilloma virus (HPV) infection, screening for cervical cancer to palliative care. Subsequent steps include the development of tools for adaptation, and monitoring and evaluation of the guide at country and programme levels. Assessment of the impact of the use of the guides (opera-

tional research) will be formulated as a separate project in consultation with countries and partners.

The project has been developed and will be implemented in partnership with a number of organizations and societies. It builds on the wealth of scientific knowledge and programme experience accumulated in testing new strategies for prevention, screening and management. Key partners include the Alliance for Cervical Cancer Prevention (ACCP), Engender-Health, Johns Hopkins Program in International Education for Gynecology and Obstetrics (JHPIEGO), Program for Appropriate Technology in Health (PATH), Pan American Health Organization (PAHO), WHO International Agency for Research on Cancer (IARC), the International Atomic Energy Agency (IAEA), the International Gynecologic Cancer Society (IGCS), and the International Federation of Gynecology and Obstetrics (FIGO).

The project was initiated at an 'Inter-cluster working group on cervical cancer and HPV infection' (ICCHI) in March 2003. The drafting of the comprehensive cervical cancer control guidelines started in June 2003 and is expected to be finalized by April 2005. The generic guidelines will require adaptation to the specific country epidemiology, health care facilities, structures and policies. The implementation guides and training tools will be developed in a second phase, once the guidelines for health care providers are in an advanced draft. Some training tools have been developed by ACCP. These will be adapted for use with the health care providers guide. A Technical Advisory Group to oversee and advise on the content and evaluation process will meet in February 2004. It will review the first draft of the guide and make recommendations on the next steps.

### *Quality condoms for STI/HIV prevention*

Work has continued on the technical review of the document *Male latex condom specification and guidelines for condom procurement*. The development of this document has involved an extensive consensus-building process with key stakeholders in both the private and public sectors. An external review of the document, involving over 80 respondents from both the private and public sectors, was undertaken during the first quarter of 2003. A small technical team of experts reviewed the feedback received prior to revising the document.

Publication was delayed because of new evidence which affected the initial recommendations made on stability and oxidation-testing requirements in the specification. This new information was presented at the 20<sup>th</sup> Meeting of Delegates to the International Standardization Organization Technical Committee 157 (ISO/TC/157) in June 2003. The specification was revised in accordance with key recommendations made and the Secretariat to the ISO/TC/157 issued a Technical Corrigendum to ISO Standard 4074: Male Natural Latex Condom, November 2003.

The Department is a delegate to ISO/TC/157 and participates in a number of the working groups which address issues related to stability testing, airburst testing and freedom from holes, production of guidelines, extra-strong condoms and development of a standard for male synthetic condoms. Delegates also recommended the formation of a working group involving the Department to develop a standard for the female condom. This group has not met yet.

The *Male latex condom specification and guidelines for procurement* will be a joint publication with UNFPA, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and FHI. Publication is expected in early 2004. A unique feature of this document is the establishment of an Internet-based helpline to respond to queries from the field. FHI will manage the helpline backed by a team of experts from partner agencies involved in the development of the specifications and guidelines.

In addition:

- The Department has reviewed publications prepared by UNFPA and UNAIDS on condom programming and is currently discussing a joint dissemination strategy.
- Discussions with The World Bank have led to the inclusion of training on condom quality assurance and procurement in all their global and regional commodity procurement training programmes. A draft training module has been prepared and will be further refined and field-tested before publication.
- In collaboration with Johns Hopkins Bloomberg University, Center of Communications Program and other partners, work has started on the development of an interactive training CD-ROM. This tool is being designed to make information easily accessible by defining and providing technically correct answers linked to appropriate guidelines and references for frequently asked questions from policy-makers, programme managers and procurement officers. Issues to be addressed are male and female condom safety, efficacy, effectiveness, quality, quality-assurance procedures, regulation, procurement, logistics management and programming.

### *Strategies to increase access to affordable STI drugs and commodities*

Work continued on the three-step process to increase access to STI drugs: (i) the inclusion of a greater choice of STI medicines on the WHO *Model list of essential medicines* (EML); (ii) the development of a position paper on STI drugs; and (iii) the development of a guidance tool to increase access to, and sustainability of, STI drugs at country level.

Azithromycin was successfully added to the WHO EML for the treatment of genital chlamydia infection and trachoma. Valaciclovir (a twice-daily dosage drug for the treatment of

genital herpes) on the other hand will be referred to as one of the alternatives in the same pharmacological class as acyclovir because of its high price and lack of sufficient evidence that adherence to treatment and treatment outcomes are considerably better than that with acyclovir (a five times per day dosage regimen).

A proposal for the inclusion of cefixime in the EML for the treatment of uncomplicated anogenital infections caused by *Neisseria gonorrhoeae* is in progress. This drug has the advantage that it can be used in pregnant women and has remained highly efficacious against gonococcal infections as a single-dose oral treatment.

The position paper on STI drugs discusses issues and concerns relating to the global provision of effective drugs and is being developed jointly with the WHO Regional Office for Africa (AFRO). In particular, the position paper addresses questions of availability, affordability, equity, and the use of generic drugs. AFRO has produced a draft paper that discusses issues pertaining to the African context. The paper is currently under review. Both the regional paper and the global paper will be the subject of discussion at a regional meeting in Africa planned for early 2004. Following the regional consultation, tools will be developed to assist countries to procure affordable, high-quality STI drugs—an essential element of an effective STI control strategy.

### *STI/RTI tools to adapt guidelines in country*

The second edition of the *Guidelines for the management of sexually transmitted infections* and the new *Sexually transmitted and other reproductive tract infections: a guide to essential practice* are currently available. Use of these guidelines should lead to improved quality of RTI and STI care and management in primary health care, reproductive health and STI care settings. The working groups on STIs and the guide to essential practice identified the need for simple tools to assess prevalence so that decision-makers could adapt the guidelines, since relevant local and national data are lacking. WHO is exploring the development of practical guides to assess prevalence for guideline adaptation. This work will be undertaken in parallel with the introduction (and adaptation of) guidelines into countries.

### *Colposcopy for the assessment of vaginal irritation and toxicity*

In November 2003, WHO and CONRAD convened a workshop in Punta Cana, Dominican Republic, on 'Assessing inflammation and epithelial integrity in vaginal product research'. This workshop was a follow-up to a conference held in January 1999 in Washington, DC, USA, where the role of colposcopy in assessing vaginal irritation was discussed. One outcome of the previous conference was publication of the *Manual for the standardization of colposcopy for the evaluation of vaginal products*. The main objective of the Punta Cana workshop was to evaluate colposcopy

as described in the current manual, to identify parts of the manual that require updating, and to consider progress on other technologies for assessing genital irritation. The workshop brought together 68 scientists and colposcopists involved in microbicide research from developed and developing countries. There was consensus that the manual should be updated with specific clarifications regarding the description of findings, lesion type and ectopy. It was reiterated that Pap smear should not be part of the colposcopy assessment but should be included in the general screening and health care provided to study volunteers. Whenever a Pap smear is done, at least three days should be allowed to pass before colposcopy is carried out on a particular subject. To reduce the risk of blood contamination during colposcopy, it was advised that cervical specimens should be collected last. There was a strong recommendation that the new manual should include additional photographs and be available through the web and distributed in both CD and printed versions. Other techniques that were reviewed included visual inspection, AviScope (hand-held), digital imaging, and non-visual techniques such as biopsy and cervico-vaginal lavage (CVL) for the detection of pro-inflammatory markers. Studies to determine the association between markers of cervico-vaginal inflammation and susceptibility to vaginal acquisition of HIV were encouraged.

## TECHNICAL COOPERATION WITH COUNTRIES

### **Implementation of the programme guidance tool**

Implementation of the *Programme guidance tool for sexually transmitted and reproductive tract infections* started in Guangdong and Yunnan provinces in China in April 2002, and the first assessment workshop was held in February 2003, during which time the background papers were discussed. Rapid assessments to address key gaps in knowledge were conducted in September and October 2003 and will be discussed in each province in January 2004. While representatives from the Ministry of Health at the country and provincial levels have been involved throughout, the implementation of the tool has been led by the National Population and Family Planning Commission (NPFPC). Since several recommendations concern the overlap of responsibilities between the Ministry of Health and the NPFPC, it is important that they be discussed and endorsed at the national level. A symposium to review the recommendations from the two provinces will take place in Beijing in March 2004. It is being organized jointly with the WHO Country Office, the NPFPC and the Ministry of Health.

The tool has also been implemented in Kosovo (Serbia and Montenegro) since early 2003 with the collaboration of the Kosovar Institute of Public Health, the Ministry of Health and WHO/Kosovo. The background paper was presented to key stakeholders in June 2003. The recommendations from the rapid field-assessment conducted during two weeks in

November 2003 will lead to pilot implementation projects in 2004.

### Integration of STI services into reproductive health services

As part of ongoing discussion and debate about integration of STI prevention and care into reproductive health services and the impact of such integrated services on HIV prevention and care, the Department commissioned a review of integration between STI and reproductive health services at country level and their impact (Askew and Berer, *Reproductive health matters*, 2003, 11:51–73).

Approximately 80% of HIV cases are transmitted sexually and a further 10% perinatally or during breastfeeding. Hence, the health sector has looked to sexual and reproductive health programmes for leadership and guidance in providing information and counselling to prevent these forms of transmission, and more recently to undertake some aspects of treatment. The paper reviews and assesses the contributions made by sexual and reproductive health services to HIV/AIDS prevention and treatment, mainly by services for family planning, sexually transmitted infections and antenatal and delivery care. It also describes other sexual and reproductive health problems experienced by HIV-positive women, such as the need for abortion services, infertility services and cervical cancer screening and treatment. The paper shows that sexual and reproductive health programmes can make an important contribution to HIV prevention and treatment, and that STI control is important both for good sexual and reproductive health and for HIV/AIDS control. The review concludes that more integrated programmes of sexual and reproductive health care and STI/HIV/AIDS control should be developed which jointly offer certain services, expand outreach to new population groups, and create well-functioning referral links to optimize the outreach and impact of what are, too frequently, vertical programmes with few links between different sectors. Such mutually reinforcing programmes and services are particularly important in the context of rapid expansion of HIV care and treatment through the WHO “3 by 5” initiative.

### Contribution to the HIV/AIDS 3 x 5 initiative

The Department has contributed to the WHO/UNAIDS strategy launched by the WHO Director-General in September 2003 to provide antiretroviral therapy to three million people with HIV/AIDS in developing countries by the end of 2005. The goal of the strategy is to prolong survival and restore the quality of life for individuals with HIV/AIDS by providing universal access to antiretroviral therapy to those who need it, both as a human right and within the context of a comprehensive response to HIV/AIDS. The strategic framework has five pillars:

1. global leadership, strong partnership and advocacy;
2. urgent, sustained country support;
3. simplified, standardized tools for delivering antiretroviral therapy;
4. effective, reliable supply of medicines and diagnostics; and
5. rapidly identifying and applying new knowledge and success.

The Department has been represented in three working groups, namely, the ‘Entry points to treatment’, ‘Accelerating prevention’ and ‘Country support’, that have contributed to the development of the strategic framework. The ‘Entry points to treatment’ working group developed a short paper which outlines the opportunities (or entry points) for identifying people who could benefit from treatment, by providing or facilitating the link to HIV testing and counselling and gateway to treatment services. The ‘Country support’ working group has been coordinating emergency missions to countries to assess capacity to accelerate the expansion of antiretroviral therapy and strengthen HIV prevention services. The Department developed a checklist to be used by the mission teams to assess the needs of clinical services providing STI care. In addition, the Department has developed training tools and updated the STI management guidelines that will assist in human capacity building in the context of the “3 by 5” strategy.

### Microbicides

#### *Strengthening capacity for research*

There is inadequate clinical trial capacity in developing countries to support safety and effectiveness studies of microbicides currently under development. The need exists to identify and select new clinical sites, and to strengthen the research capacity of WHO collaborating centres to implement microbicide trials. Several new sites were visited in Brazil in July 2003 and discussions have been initiated with the Ministry of Health for the final selection of centres to collaborate with the Department on microbicide development. Clinical and laboratory facilities upgrades and staff training activities are being undertaken in Ethiopia, India, Kenya, Mozambique, Nigeria and Uganda. The Department of Obstetrics and Gynaecology, Makerere University, Kampala, Uganda, acquired an extra building to develop a microbicide research clinic and laboratory. The Department is reviewing a proposal for renovating and equipping the facility, including expansion of polymerase chain reaction (PCR) capabilities and provision of digital colposcopy. In collaboration with CONRAD, one of the scientists based at the centre was trained in digital colposcopy in the USA. A PCR laboratory will be added to the facilities at the Centre for Research in Reproductive Health, Sagamu, Nigeria, following an assessment in July 2003. In

collaboration with the Department's Technical Support to Countries team, a laboratory scientist from Sagamu was trained in South Africa on PCR diagnostics and development of PCR assays for STIs and other infectious diseases.

In collaboration with the National Institute for Research in Reproductive Health (NIRRH), Mumbai, India, a proposal for conducting an epidemiology training workshop was developed. The first workshop will be held in June 2004 at the NIRRH and will involve junior scientists from clinical centres that are collaborating with the Department on microbicide research.

#### *Global advocacy and international collaboration for microbicides*

As part of global advocacy, WHO has continued to support international and regional scientific and technical meetings focusing on microbicides. The Department, in collaboration with other partners, convened a satellite session entitled 'Accelerating development and access for [sic] microbicides' during the 13<sup>th</sup> International Conference on AIDS and STIs in Africa (ICASA), on 24 September 2003, in Nairobi, Kenya. The Department has provided financial support to the secretariat for the Microbicides 2004 Conference to be held in London, United Kingdom, in March to provide scholarships to delegates from developing countries to participate at the conference.

#### *United States Food and Drug Administration (FDA) Antiviral Drugs Advisory Committee*

In August 2003, the US FDA convened a meeting of the Antiviral Drugs Advisory Committee to consider clinical trial design issues in the development of topical microbicides for the reduction of HIV transmission. Particular questions presented to the Advisory Committee included the need for placebo and no-product comparison arms in Phase III microbicide trials, the strength of evidence required before approval for licence could be considered, and the duration of follow-up of volunteers in the trial. The Department submitted written and oral evidence and comments and made the following recommendations to the Advisory Committee:

1. Not to use a no-product comparison group if an adequate control product could be used in the trial. The interpretation of data from a no-product comparison arm is complex and best avoided if possible, and conducting such a trial may be considerably more difficult.
2. Providing that the study products were indistinguishable and participants and investigators remained masked during the trial, a comparison of incidence rates between the active and placebo product groups would give a direct and unbiased estimate of product effectiveness. However, if masking is not possible, then adjustment for post-randomisation behaviours is required before an estimate of effectiveness can be derived. This is complex

and less convincing than the result obtained from a placebo-controlled, double-masked trial.

3. Although the FDA usually requires two independent trials, each significant at the  $P < 0.05$  level before giving the licence, some flexibility is necessary given the urgent need to develop and make available a product that provides protection. The strength of evidence from two such trials is equivalent to a single trial concluding with a  $P < 0.0013$  level. Moreover, it is probably not ethical to conduct two independent microbicide trials in developing-country settings to this level of significance, and local ethical review boards are unlikely to accept implementation or continuation of a second trial. However, it was recognized that a single trial significant at the  $P < 0.05$  level is unlikely to be sufficiently convincing. There was no clear answer concerning the optimal strength of evidence, particularly since the conventional  $P < 0.05$  level is an arbitrary choice in the first place. A compromise whereby a single large trial provides strength of evidence equivalent to 1½ trials ( $P < 0.008$ ), may be acceptable.

At the meeting, the FDA decided to allow an NIH- and CDC-funded trial with a no-product and a placebo-product comparison group to proceed, without requiring all trials to adopt this type of design. The strength of evidence required was not resolved, but the FDA indicated its willingness to be flexible when considering an individual trial or a series of trials.

#### *Ethical issues on clinical testing of microbicides*

The Department participated in a workshop convened by the Global Campaign for Microbicides in October in Washington, DC, USA, to discuss ethical challenges in microbicide clinical trials, in particular issues related to standards of care for trial participants, enrolling adolescents in trials, defining "fair benefits" to communities where the trials are conducted, responding to men and issues of partner consent, implications of finding a partially effective microbicide for the design of future trials, and HIV treatment in the context of microbicide trials. These issues are some of several challenges facing all teams who design and implement microbicide trials. The Department contributed to the discussion on types of trial and studies required after a first study demonstrates the product to be effective, and to the discussion on standards of care, including access to antiretroviral therapy for volunteers who become infected with HIV during their participation in the trial.

#### **Networks**

The establishment of the STI Network in Africa is in progress. The Department sponsored the attendance of the Network Task Force team and other potential network members at a meeting held during the International Conference on AIDS and STIs in Africa (ICASA) in Nairobi, Kenya, in September 2003. The Task Force team of six reported on the progress made in the previous year to establish a network of STI

experts. The team is now in a position to prepare draft terms of reference and a constitution for the network. A meeting to launch the network is planned for the first quarter of 2004.

In the WHO Eastern Mediterranean Region, preliminary training and updating of consultants was carried out in the three subregions. A meeting to train a group of consultants from each subregion is planned for the first quarter of 2004. Future plans are to establish similar networks in the WHO South-East Asia Region.

### **WHO Collaborating Centres**

WHO Collaborating Centres for Sexually Transmitted and Reproductive Tract Infections are being reviewed. Approxi-

mately eight centres have been identified for redesignation. Currently two centres are being renewed—the Division of Sexually Transmitted Diseases Laboratory Research Centre for Infectious Disease (CDC, Atlanta, GA, USA) and the Fournier Institute (Paris, France). One other centre, the Neisseria Department of the State Serum Institute (Copenhagen, Denmark) is being redesignated after an extended lapse of its designation.

The Clinical Research Unit of the Department of Infectious and Tropical Diseases of the London School of Hygiene and Tropical Medicine, London, United Kingdom, has been identified as a potential WHO Collaborating Centre and the process for its designation is in progress.

Annex 1

**STRATEGIC COMMITTEE ON CONTROLLING SEXUALLY TRANSMITTED AND REPRODUCTIVE TRACT INFECTIONS**

**Members**

Kamal Alami, STD/AIDS Control Programme Manager, Rabat, Morocco  
 Anita Albau, EASE International, Copenhagen, Denmark  
 Chitwarakorn Anupong, Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand  
 Michael Chirenje, University of Zimbabwe, Harare, Zimbabwe  
 Sinead Delaney, Reproductive Health Research Unit, Chris Hani Baragwanath Hospital, Soweto, South Africa  
 Sarah Hawkes, Population Council South and East Asia Regional Office, New Delhi, India  
 Monica Iris Jasis, Centro Mujeres A.C., Mexico City, Mexico  
 Anatoli Kamali, Medical Research Council, Kampala, Uganda  
 Philippe Mayaud, London School of Hygiene and Tropical Medicine, London, United Kingdom  
 Ibra Ndoye, National STI/HIV/AIDS Programme, Dakar, Senegal  
 Sunanda Ray, Southern Africa HIV/AIDS Information Dissemination Service, Harare, Zimbabwe  
 Adele Schwartz Benzaken, Instituto de Dermatologia Tropical e Venereologia "A", Cachoeirinha, Manaus, Brazil  
 Rachel Snow, Department of Health Behavior and Health Education, School of Public Health, University of Michigan, MI, USA

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	10	77			3	23	13
Women	5	38			2	15	7
<b>from:</b>							
AFRO	5	38					5
AMRO	2	15			1	8	3
EMRO	1	8					1
EURO					2	15	2
SEARO	2	15					2
WPRO							

**Collaborating agencies**

Sevgi Aral, Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA  
 Gina Dallabetta, Family Health International, Research Triangle Park, NC, USA  
 France Donnay, Reproductive Health Branch, United Nations Population Fund (UNFPA), New York, NY, USA  
 Caroline Ryan, Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA  
 Johannes Van Dam, Horizons Program, Population Council, New York, NY, USA  
 Lut Van Damme, CONRAD, Arlington, VA, USA

## Annex 2a

## CONTROLLING SEXUALLY TRANSMITTED AND REPRODUCTIVE TRACT INFECTIONS

## Scientists in 2003

*Principal investigators*

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 Oyunbileg Amindavaa, State Research Centre on Maternal and Child Health and Human Reproduction, Ulaanbaatar, Mongolia  
 Phan Kim Anh, Institute for the Protection of Mother and Newborn, Hanoi, Viet Nam  
 Mags Beksinka, University of Witwatersrand, Addington Hospital, Durban, South Africa  
 Olukayode Adebisi Dada, Ogun State University Teaching Hospital, Sagamu, Nigeria  
 Mohommad Dahlan Darip, West Indonesia Reproductive Health Development Centre, Medan, Indonesia  
 Zhaowen Dong, National Research Institute for Family Planning, Beijing, China  
 Manuel Gomez Alzugaray, National Institute of Endocrinology, Hospital 'Cmdte. Fajardo', Havana, Cuba  
 Aucky Hinting, Airlangga University, Reproductive Health Research Centre, Surabaya, Indonesia  
 My Huong Khanh, Institute for the Protection of Mother and Newborn, Hanoi, Viet Nam  
 Thi Ngoc Khanh, Institute for the Protection of Mother and Newborn, Hanoi, Viet Nam  
 Hendrik Koornhof, National Health Laboratory Service, Johannesburg, South Africa  
 Gunta Lazdane, Department of Obstetrics and Gynecology, Medical Academy of Latvia, Riga, Latvia  
 Liu Xiaozhang, Family Planning Research Institute of Sichuan, Chengdu, China  
 Hans Lumintang, Airlangga University, Reproductive Health Research Centre, Surabaya, Indonesia  
 Suneeta Mittal, Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi, India  
 Carlos Moreno, Centro de Investigación en Reproducción Humana, Panama City, Panama  
 Nguyen Thi Nhu Ngoc, Hung Vuong Hospital, Ho Chi Minh City, Viet Nam  
 Khin Nwe Oo, Department of Medical Research, Yangon, Myanmar  
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 Helen Rees, Reproductive Health Research Unit, Chris Hani Baragwanath Hospital, Johannesburg, South Africa  
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 Le Than Thuy, Hanoi Obstetrics and Gynaecology Hospital, Hanoi, Viet Nam  
 Francois Venter, Reproductive Health Research Unit, Chris Hani Baragwanath Hospital, Johannesburg, South Africa  
 Wu Shang-chun, National Research Institute for Family Planning, Beijing, China

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	28	88	4	13			32
Women	13	41	2	6			15
<b>from:</b>							
AFRO	6	19					6
AMRO	2	6					2
EMRO							
EURO			4	13			4
SEARO	6	19					6
WPRO	14	44					14

**Annex 2a (continued)**

*Other scientists*

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Sarah Hawkes, Population Council South and East Asia Regional Office, New Delhi, India  
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Nzambi Khonde, National AIDS Control Programme, Accra, Ghana  
David Mbirizi, Ministry of Health, Kampala, Uganda  
Kennedy Manyoni, Gedo Health, Nairobi, Kenya  
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André Meheus, Epidemiology & Community Medicine, University of Antwerp, Antwerp, Belgium  
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Guida Silva, National Coordinator STIs/AIDS, Ministry of Health, Brasilia, Brazil  
Jeffrey Smith, Johns Hopkins Program of International Education in Gynecology and Obstetrics (JHPIEGO) Corporation, Baltimore, MD, USA  
François Sobela, National SIDA 3, Lomé, Togo  
Richard Steen, Durham, NC, USA (now at WHO, Geneva)  
Giorgio Tamburlini, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Burlo Garofolo, Trieste, Italy  
Marleen Temmerman, International Centre for Reproductive Health, Ghent University, Ghent, Belgium  
Johannes Van Dam, Horizons: Global Operations Research on HIV/AIDS/STI Prevention and Care, Population Council, Washington, DC, USA  
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*Annex 2a (continued)*

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	25	61			16	39	41
Women	9	22			4	10	13
<b>from:</b>							
AFRO	16	39					16
AMRO	3	7			5	12	8
EMRO	2	5					2
EURO					11	27	11
SEARO	3	7					3
WPRO	1	2					1

**Collaborating agencies**

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Annex 2b

RESEARCH GROUP ON MICROBICIDES

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	3	100					3
Women	1	33					1
<b>from:</b>							
AFRO	2	67					2
AMRO							
EMRO							
EURO							
SEARO	1	33					1
WPRO							

Other scientists

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**Annex 2b (continued)**

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	29	60			19	40	48
Women	18	38			13	27	31
<b>from:</b>							
AFRO	15	31					15
AMRO	6	13			18	38	24
EMRO							
EURO					1	2	1
SEARO	8	17					8
WPRO							

**Collaborating agencies**

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 Lydia Antolin, CONRAD, Arlington, VA, USA  
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 Marlene Utecht, CONRAD, Arlington, VA, USA  
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Annex 2c

**MOTHER-TO-CHILD TRANSMISSION OF HIV**

**RESEARCH GROUP ON IMPACT OF HAART ON MOTHER-TO-CHILD TRANSMISSION OF HIV AND HEALTH OF THE MOTHERS**

**Scientists in 2003**

*Principal investigators*

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 John Shao, Kilimanjaro Christian Medical Centre, Moshi, United Republic of Tanzania  
 Joseph Vyankandondera, Centre Hôpitalier de Kigali, Kigali, Rwanda

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	7	100					7
Women	2	29					2
<b>from:</b>							
AFRO	7	100					7
AMRO							
EMRO							
EURO							
SEARO							
WPRO							

*Other scientists*

Céline Cames, Institut de Recherche pour le Développement, Montpellier, France  
 François Dabis, Université Victor Segalen, Bordeaux, France  
 Alice Desclaux, Laboratoire d'Ecologie Humaine et d'Anthropologie, Université Aix-Marseille, Aix en Provence, France  
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 Serge Diabougou, Centre MURAZ, Bobo-Dioulasso, Burkina Faso  
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 Esther Getambu, Provincial AIDS Control, Mombasa, Kenya  
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**Annex 2c (continued)**

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 Jean Michel Tassié, EPICENTRE, Paris, France  
 Marleen Temmerman, International Centre for Reproductive Health, Ghent University, Ghent, Belgium  
 Philippe Van de Perre, Centre Hospitalier Regional Arnaud de Villeneuve, Montpellier, France  
 Chris Verhofstede, International Centre for Reproductive Health, Ghent University, Ghent, Belgium  
 Hugo de Vuyst, International Centre for Reproductive Health, Mombasa, Kenya  
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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	16	48			17	52	33
Women	4	12			10	30	14
<b>from:</b>							
AFRO	16	48					16
AMRO					6	18	6
EMRO							
EURO					11	33	11
SEARO							
WPRO							

**Collaborating agencies**

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**Annex 3**

**PUBLICATIONS**

Anh PH et al. Prevalence of lower genital tract infections among women attending maternal and child health and family planning clinics in Hanoi, Viet Nam. *South East Asian Journal of Public Health*, 2003, 34:367–372.

Broutet N et al. Antenatal syphilis screening: has it reduced prevalence of syphilis in antenatal populations in Africa? Paper presented at ICASA congress in 2004, Kenya.

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Gaillard P et al. Use of antiretroviral drugs to prevent HIV-1 transmission through breast-feeding: from animal studies to randomized clinical trials. *Journal of Acquired Immune Deficiency Syndrome*, 2004, 35:178–187.

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## **Section 4**

# **Preventing unsafe abortion**

# Preventing unsafe abortion

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## INTRODUCTION

As early as in 1967, the World Health Assembly identified abortion as a serious public health problem. A recent estimate shows that approximately 19 million unsafe abortions occur worldwide each year. The consequences of unsafe abortion are many. In addition to some 68 000 women who die each year because of unsafe abortion, a further five million suffer temporary or permanent disability. The persistence of unmet need for family planning for an estimated 123 million women in developing countries and in the former Soviet Union continues to pose major challenges, both for ensuring access to contraceptives as well as for efforts to prevent unsafe abortion. Over 40% of couples discontinue using a contraceptive method in the first year, either because of side-effects or other reasons, or because they experience a method- or user-failure. While many of these women go on to have an unintended birth, a significant percentage report termination of pregnancy (induced or spontaneous), even in countries where abortion is legally restricted. Demographic and Health Survey (DHS) data from 16 developing countries (Bangladesh, Bolivia, Brazil, Colombia, Dominican Republic, Egypt, Guatemala, Indonesia, Kenya, Morocco, Nicaragua, Paraguay, Peru, Philippines, Turkey and Zimbabwe) indicate that over 10% of women report pregnancy termination following discontinuation of use or method- or user-failure (Figure 4.1). [Note: Among these 16 countries, abortion is available on demand only in Turkey.]

Unsafe abortion is defined by WHO as a procedure for terminating an unintended pregnancy either by persons lacking the necessary skills or in an environment lacking the minimal medical standards, or both. The Programme's work on preventing unsafe abortion is a response to recommendations of the Programme of Action adopted at the 1994 International Conference on Population and Development

(ICPD), which urges countries and organizations to address the health consequences of unsafe abortion and to ensure that, in circumstances where abortion is not against the law, the provision of abortion is safe. The overall strategy of the Programme's work in this area is: (i) to map and generate scientifically sound evidence on unsafe abortion prevalence and practices; (ii) to improve technologies and interventions to make abortion safer; (iii) to translate evidence into norms, tools and guidelines; and (iv) to assist in the development of programmes and policies to reduce unsafe abortion. This work forms an integral part of WHO's efforts to improve reproductive health and, most importantly, to reduce maternal morbidity and mortality.

## RESEARCH ACTIVITIES

### Specific objectives of research

Due to its scientific rigour, dedication to health concerns, and objectivity, the Programme has been successful in launching and supporting critically needed research in this area. The Programme conducts research to document the global dimensions of unsafe abortion by compiling and maintaining data on the incidence of unsafe abortion and unsafe abortion-related morbidity and mortality.

In 1989, the Programme undertook a pioneering effort to understand the determinants or reasons why women resort to abortion in various cultural, social, legal, and service availability contexts and the consequences they face. Evidence from 23 studies in 16 developing countries was documented. Since its inception, the Programme has also carried out systematic research for developing and improving safe and effective non-surgical methods for early termination of pregnancy. This research was crucial for the registration in 1988

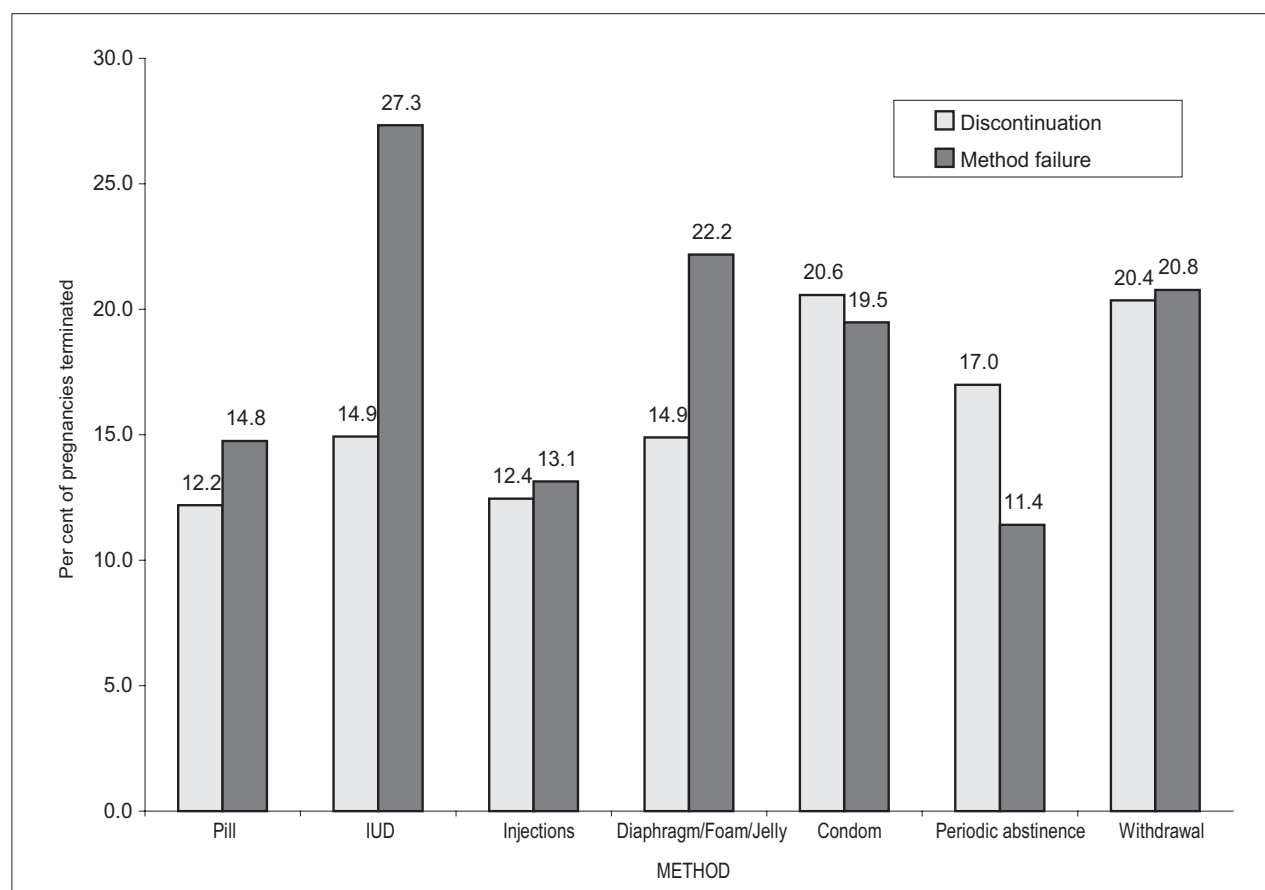
of the first non-surgical method of abortion—the sequential regimen of mifepristone followed, two days later, by a suitable prostaglandin. Subsequent research led to a simplified regimen, and investigated ways to shorten the duration of postabortion bleeding. Following two consultations on abortion in 2000 which recommended that the Programme should develop effective, safe and acceptable misoprostol-only regimens for both early first trimester as well as second trimester abortions, two multicentre studies were launched. The benefits of routine priming of the cervix with misoprostol are also being investigated in a new study to determine whether the safety of the vacuum aspiration procedure can be improved further. Another new area of research is the development of an effective non-surgical treatment for non-viable pregnancy (missed abortion).

The research by the Programme has had a major impact not only on the practices in participating hospitals, but also on policies in countries. Most centres participating in research on improved technologies are teaching hospitals in developing countries. In addition to learning how to carry out clinical research according to Good Clinical Practice (GCP) stand-

ards, the centres gain experience in improved abortion technologies that are not yet routinely available in the country. The study teams generally play a crucial role in the introduction of improved technologies and in developing guidelines, as is evident from the experience in China, Finland, India, Romania, Sweden, United Kingdom and Viet Nam. For example, in an ongoing trial of second trimester termination of pregnancy, the participating hospitals in Armenia, India, Slovenia, South Africa and Viet Nam noted that the method of abortion being tested was better than the ones they routinely used. In light of the results of the trial, these hospitals reported that they would change their methods. The Programme's clinical research also provides the high-quality scientific data required for the registration of drugs for medical abortion in countries where abortion is legally available on demand, but where these methods are not yet available.

The research generated by the Programme is used for developing norms, tools and guidelines as well as assisting countries in implementing best practices. One example of such interface is the document *Safe abortion: technical and policy guidance for health systems* published by WHO in 2003.

Figure 4.1. Per cent of pregnancies terminated following discontinuation (for reasons other than method failure) or method (or user) failure, by type of prior method used, Demographic and Health Surveys for 16 developing countries, 1990–1999



## Progress

### Mapping the evidence

To map the evidence, the Programme maintains a database on unsafe abortion and provides updated estimates periodically. Systematic reviews are also undertaken on priority issues. In 2002, estimates on the incidence of unsafe abortion, the number of unsafe abortions to 100 live births and the number of unsafe abortions per 1000 women of reproductive age became available for different regions and the world. In 2003, a number of activities were undertaken and are highlighted below.

### Mortality due to unsafe abortion

Overall, 19 million unsafe abortions are estimated to take place each year, corresponding to one in ten pregnancies

ending in an unsafe abortion or one unsafe abortion to approximately seven live births. With the availability, in 2003, of maternal mortality figures, numbers of maternal deaths due to unsafe abortion were estimated (Table 4.1). Overall, 68 000 women die each year due to unsafe abortion-related complications. Unsafe abortion continues to account for 13% of all maternal deaths. The interpretation of figures expressed as a percentage of maternal deaths is not always straightforward, however, especially for different regions. For example, when maternal mortality is relatively low and other causes of maternal deaths have already been substantially reduced, a small number of unsafe abortion-related deaths may account for a substantial percentage of maternal deaths. This is the case in Eastern Europe, where the percentage of maternal deaths due to unsafe abortion is the highest in the world even though the number of annual deaths is relatively low. In some countries in Latin America, where maternal mortality is relatively low and where abortion deaths are an important, and

Table 4.1. Global and regional annual estimates of maternal deaths due to unsafe abortion by United Nations (UN) regions, around the year 2000

	Maternal deaths (N)	% of maternal deaths	Number of deaths to 100 000 live births
<b>World</b>	68 000	13	50
More developed regions*	300	14	3
Less developed regions	68 000	13	60
<b>Africa</b>	30 000	12	100
Eastern Africa	15 000	14	140
Middle Africa	5000	10	110
Northern Africa	1000	6	10
Southern Africa	400	11	30
Western Africa	9000	10	90
<b>Asia*</b>	34 000	13	40
Eastern Asia*	—**	—**	—**
South-central Asia	29 000	14	70
South-eastern Asia	5000	19	40
Western Asia	1000	6	10
<b>Europe</b>	340	20	5
Eastern Europe	320	26	10
Northern Europe	—**	—**	—**
Southern Europe	20	13	1
Western Europe	—**	—**	—**
<b>Latin America &amp; the Caribbean</b>	4000	17	30
Caribbean	290	13	40
Central America	440	11	10
South America	3000	19	40
<b>Northern America</b>	—**	—**	—**
<b>Oceania*</b>	<100	7	20

Note: Figures may not equal totals due to rounding.

\* Japan, Australia and New Zealand have been excluded from the regional estimates, but are included in the total for developed countries.

\*\* No estimates are shown for regions where the incidence is negligible.

sometimes the main cause of maternal mortality, a similar pattern of high proportion of maternal mortality due to unsafe abortion is observed.

The unsafe abortion mortality ratio of 30 per 100 000 live births for Latin America and the Caribbean—approximately 4000 deaths—corresponds to one in five maternal deaths in the region. However, the largest number of deaths due to unsafe abortion are estimated to occur in Africa and Asia.

This update highlights that, despite a major increase in contraceptive use and the fact that unsafe abortions are entirely preventable, these abortions continue to prevail in all developing regions and remain an important cause of maternal mortality.

#### *Unsafe abortion and contraception*

In 2003, the Programme-supported review of evidence on the relationship between contraception and abortion was published. No consensus exists on the relationship between levels of contraceptive use and the incidence of induced (safe or unsafe) abortion. A careful analysis of trends in abortion and contraceptive use in seven countries with relatively reliable data shows that increased contraceptive use contributes to reducing the incidence of abortion in countries where fertility is constant. However, in countries where fertility may fall rapidly, a concurrent rise in abortion and contraceptive use can occur because the latter is unable to meet the people's growing need for fertility regulation. Thus, at the population level, the relationship between abortion and contraception can vary when fertility levels are changing.

Using data from the Programme's database on unsafe abortion, Figure 4.2 shows the percentage of couples using modern contraceptive methods, modern reversible methods

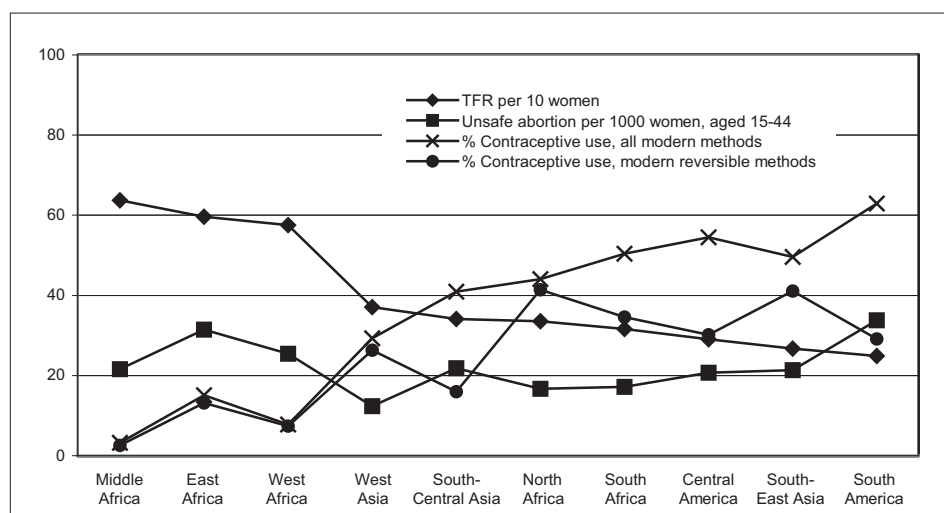
and the unsafe abortion rate, by descending level of total fertility rate (TFR). The gap between all modern methods and modern reversible methods in this figure indicates reliance on female (or, to a lesser extent, male) sterilization, which in some subregions is quite substantial.

South America has the lowest level of TFR, a subregion that is also characterized by the highest unsafe abortion rate worldwide, almost 40 unsafe abortions per 1000 women of reproductive age, together with the highest reliance on modern contraceptives. However, in this subregion, sterilization is the single most commonly used method, accounting for 54% of all use of modern methods. This may suggest that many women in this subregion turn to unsafe abortion for spacing births before terminating childbearing through sterilization. With a slightly higher level of TFR, women in South-East Asia rely more on modern reversible contraceptive methods and have two-thirds of South America's unsafe abortion rate despite a lower level of overall modern contraceptive use. Central America and South-Central Asia show a pattern similar to that for South America, but with a correspondingly higher TFR and lower contraceptive use; both subregions have quite high unsafe abortion rates of over 20. Eastern, Middle and Western Africa stand out as having the highest TFR, around six children per woman, and the lowest contraceptive use. Because of the high birth rates, these parts of Africa have modest abortion ratios of 9–16 unsafe abortions to 100 live births. These results highlight the importance of examining fertility, contraceptive method mix and unsafe abortion together to identify appropriate interventions to prevent unsafe abortion.

#### *Unsafe abortion by age*

The detailed analysis of data on unsafe abortion by age shows that two out of every three unsafe abortions occur to

Figure 4.2. Unsafe abortion, contraceptive use (all methods), and contraceptive use (modern methods) relative to the total fertility rate in developing country sub-regions



women between the ages of 15 and 30. More important from a public health perspective is, however, the observation that 2.5 million, or almost 14 % of all unsafe abortions in developing regions occur to women before the age of 20. The age pattern of unsafe abortions is markedly different from region to region (Figure 4.3). The percentage of women aged 15–19 in Africa who have an unsafe abortion is higher (26%) than in any other region, and almost 60% of unsafe abortions in Africa are among women under age 25. In Asia, half of all unsafe abortions occur in women aged 25–35. In Latin America and the Caribbean, women aged 20–29 account for about one out of every two unsafe abortions in the region.

While age patterns of unsafe abortion are critical in better understanding the barriers to access, as well as, tailoring interventions according to the region-specific pattern, prevention of unsafe abortion at all ages must remain a high priority.

*Medical methods for first trimester abortion: a systematic review*

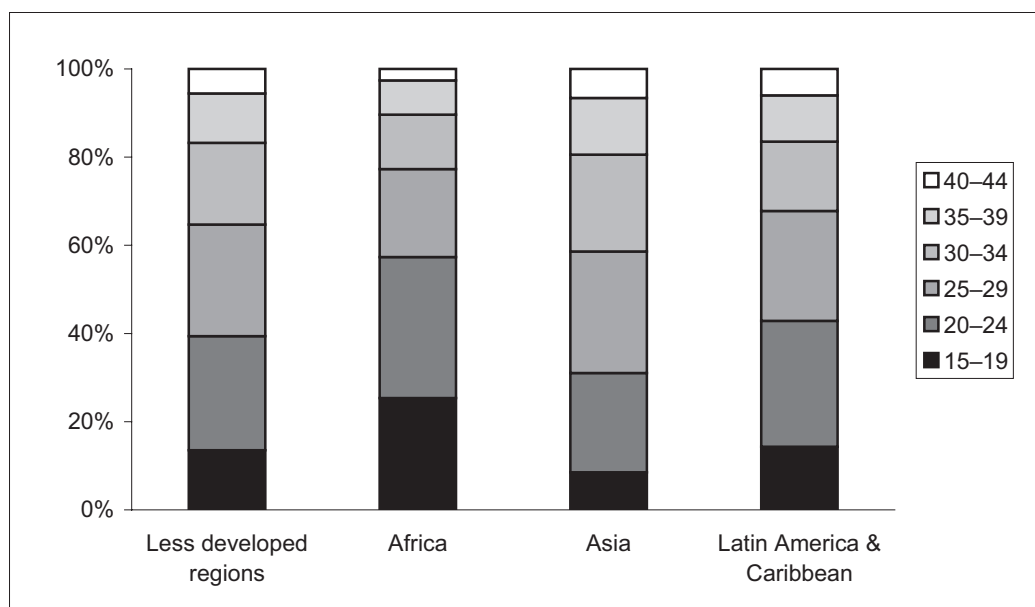
In 2003, a systematic review of medical methods for first trimester abortion, covering 39 trials, was completed. The main conclusions are as follows:

- Within the combined mifepristone-prostaglandin regimen, mifepristone 600 mg compared to 200 mg shows similar effectiveness in achieving complete abortion (four trials: RR 1.07, 95% CI:0.87–1.32). Misoprostol administered orally is less effective (more failures) than through the vaginal route (RR 3.00, 95% CI:1.44–6.24) and may be associated with more frequent side-effects such as nausea and diarrhoea.

- Mifepristone alone is less effective compared to the combined regimen mifepristone-prostaglandin (RR 3.76, 95% CI:2.30–6.15). Similarly, four of the five trials comparing prostaglandin alone with the combined regimen reported a higher effectiveness with the combined regimen. Although the results of these studies were not pooled, the RR of failure with prostaglandin alone is between 1.4 and 3.75 and the 95% confidence interval indicate statistical significance.
- In one trial comparing one dose of gemeprost 0.5 mg with misoprostol 800 µg, both combined with mifepristone, misoprostol was found to be more effective (failure with gemeprost: RR 2.86, 95% CI:1.14–7.18).
- There was no difference between using a split dose or a single dose of prostaglandin, combined with mifepristone.

In summary, effective medical methods of abortion now exist and have been tested in different populations. Combined regimens are more effective than single agents. In the combined regimen, the dose of mifepristone can be lowered to 200 mg without significantly decreasing the method effectiveness. Misoprostol taken vaginally is more effective than when taken orally. Because some of the results are based on small studies, there is greater uncertainty about these results. Also, because almost all the trials were conducted in hospital settings with good access to support and emergency services, it is not clear if the results are readily applicable to resource-poor settings where such services are lacking, even if the agents used are available.

Figure 4.3. Percentage distribution of unsafe abortion, by age and region



### *Fertility decline and the role of abortion*

An ongoing study is assessing the role of abortion in the context of West Africa where fertility has declined but increases in contraceptive prevalence are too small to account for the change. The study, conducted in Togo, a country where recourse to abortion is thought to be high, is both documenting the incidence of abortion and investigating pathways to abortion. The study includes a survey of 4500 women of reproductive age (15–49 years) to measure the prevalence of abortion and its impact on fertility levels, and uses qualitative interviews and focus group discussions to explore the pathways to abortion among women living in Lome. Currently, legislation in Togo permits abortion only in cases where it is performed to save the woman's life. Preliminary analysis was undertaken in 2003 and complete results are expected at the end of 2004.

### *Abortions in a legally restricted context: a case study of Sri Lanka*

An ongoing study in Sri Lanka, where abortion is permitted only to save the life of the woman, investigates the incidence of unsafe abortion from reports of health professionals and their perspectives on the availability of abortion services. Using self-completed questionnaires, information was sought from 67 health professionals working in Colombo district. Comparing results from various sources, the study suggests a rate of 40 abortions per 1000 women of reproductive age in this area. Results from this study were presented at the Second Asia Pacific Conference on Reproductive and Sexual Health, held in September 2003 in Bangkok, Thailand.

### *Role of men*

With the objective of reviewing the scientific literature on men's attitudes, roles and perspectives on abortion and to identify research gaps, a paper, entitled "Men and abortion: what is known and what needs researching", was completed in 2003. Using data from the World Values Survey and reviews of relevant literature, the paper synthesized the available evidence on: (i) men's knowledge about abortion; (ii) men's attitudes and motivations towards abortion; (iii) effects of partner's abortion on men; and (iv) involvement of men in the abortion process. The paper identified a number of methodological considerations and noted critical research gaps, especially for developing countries and contexts where access to abortion is restricted. Broad areas identified for future research include: (i) men's knowledge about abortion (procedures, safe vs unsafe abortion, sources of knowledge, and whether the availability of abortion influences men's motivation or behaviour regarding pregnancy prevention; (ii) the decision-making process regarding abortion (how and why do men get involved in the abortion process and in postabortion care); and (iii) the effects on men of their partner's abortion.

Research on men and abortion was identified as a high priority by two consultations held in 2000. However, the 2002 meeting of the Strategic Committee on Preventing Unsafe Abortion ranked this research low. In addition, lack of funding constrained the follow-up on this and other topics.

### *Assessing the safety and efficacy of abortions performed by mid-level providers*

In countries where abortion is permitted by law, the law generally restricts the provision of abortion to physicians and, in some cases, requires additional training and certification for the physicians. For a variety of reasons, millions of women turn to mid-level providers, or non-physicians, such as midwives, paramedics, and traditional birth attendants, who may not be clinically trained in abortion techniques. An ongoing randomized trial is investigating the safety of abortions, as measured by complications, provided by medically-trained and government-certified mid-level providers and physicians in South Africa and Viet Nam. In these countries, first trimester abortions are currently legally performed by both physicians and non-physicians. The study sample consists of providers from four clinics per country and approximately 1400 women per country. Results from the pilot phase of the study were available in 2003 for both countries. Although the number of cases in the pilot study was too small for any statistically significant conclusions, there was no difference in complication rates between the two types of providers.

In Viet Nam, 1735 subjects were recruited, and by the end of 2003, 1690 women had been followed-up. In South Africa, recruitment commenced in the second half of 2003. Results from the trial are expected by the end of 2004.

### *Medical abortion clinical trials*

#### *Non-surgical abortion using a sequential regimen*

Results were published from a randomized, placebo-controlled trial that compared sublingual and vaginal administration of 0.8 mg of misoprostol after pretreatment with 200 mg mifepristone (*Human Reproduction* 2003,18:2315–2318). The study was carried out among 224 women requesting pregnancy termination up to 63 days in Hong Kong. Complete abortion occurred in 98% (95% CI:93–99) of women in the sublingual group and in 94% (95% CI:88–97) of the vaginal administration group. There were three ongoing pregnancies in the vaginal group but none in the sublingual group. The median duration of vaginal bleeding was 17 days. There were no serious complications. Fever, chills and gastrointestinal side-effects (nausea, vomiting and diarrhoea) were significantly more common in the sublingual group. The study demonstrates the need for a larger trial to investigate whether sublingual administration is more effective. Further research is also needed to test a lower dose of sublingual misoprostol.

The results of this study are in accordance with the outcome of a uterine contractility study that was carried out in Stockholm, Sweden, comparing the sublingual and vaginal administration of misoprostol. Uterine contractility and uterine tone were both significantly better 2–4 hours after sublingual intake of misoprostol, compared with either vaginal or oral administration of the drug. Misoprostol is registered only for oral use. Sublingual administration would simplify its use and may be more acceptable to women, as several studies suggest that women prefer oral rather than vaginal administration of drugs. Therefore, sublingual administration is a promising option for the registration of the current formulation of tablets to improve the efficacy of the medical abortion regimen.

The Programme also collaborated with Chinese investigators in a multicentre trial to evaluate the efficacy and side-effects of 150 mg of mifepristone followed, two days later, by 0.4 mg misoprostol vaginally for menstrual induction among women with a menstrual delay of up to seven days. The outcome of treatment was uterine evacuation, which could mean menstruation or termination of early pregnancy. Menstrual induction refers to early uterine evacuation without laboratory confirmation of pregnancy in women with delayed menses. Mechanical aspiration is the method used in many countries but, as suggested by a pilot study, mifepristone followed by a prostaglandin analogue may be an effective alternative.

A total of 720 women were recruited. The mean delay of menstruation at recruitment was 4.9 (SD 1.7) days. Retrospective analysis of hCG from serum samples taken at admission showed that 492 (68.3%) women were pregnant at admission, and 228 (31.7%) women had delayed menstruation without pregnancy. One non-pregnant woman was lost to follow-up. Bleeding was induced in 479 (97.4%) pregnant women and in 222 (97.8%) non-pregnant women. Among the pregnant women, 455 (92.5%) had complete abortion, 12 (2.4%) had incomplete abortion and pregnancy continued in 25 (5.1%) women, including one ectopic pregnancy. Side-effects were mild and uncommon and 95.8% of the women treated had the expected outcome. However, further research is needed to compare the efficacy, safety, and acceptability of the medical regimen compared with vacuum aspiration. A rather high continuing pregnancy rate in this study was a concern. The results of this study were published in the journal *Contraception*.

Another study of medical abortion is ongoing, comparing two doses of mifepristone, 100 mg and 200 mg, followed by 0.8 mg of vaginal misoprostol either 24 hours or 48 hours later, when used for the termination of early pregnancy in women with amenorrhoea of up to 63 days from last menstrual period. The four regimens are compared with respect to the following main outcomes: effectiveness of induced complete abortion relative to the length of gestation, frequency of side-effects, and duration of bleeding. The target is to include 2184 women in 14 centres in China, Hungary, India, Mongolia, Romania, Serbia and Montenegro, Slovenia, South Africa, Sweden, Viet Nam. It is anticipated that the clinical

phase of this study will be completed in most centres by mid 2004.

### *Non-surgical abortion with misoprostol alone*

Two randomized, placebo-controlled multinational trials testing the efficacy and safety of misoprostol-alone regimens are nearing completion. The clinical phase of the study comparing four regimens in the first trimester (three doses of 0.8 mg of misoprostol, administered either sublingually or vaginally, at intervals of three or 12 hours) has been completed in nine out of 11 participating centres in Armenia, Cuba, Georgia, India, Mongolia and Viet Nam. The aim is to recruit 2068 pregnant women up to 63 days of gestation requesting legal termination of pregnancy. The four regimens are compared in respect of their effectiveness for inducing complete abortion, induction-to-abortion interval, acceptability and occurrence of side-effects.

The second study involves a total of 684 women requesting legal termination of pregnancy during the second trimester of pregnancy (14–20 weeks' amenorrhoea). Women are randomized to receive 0.4 mg misoprostol either vaginally or sublingually every three hours for up to five doses. Nine of the 11 centres in Armenia, Georgia, Hungary, India, Slovenia, South Africa and Viet Nam have completed the clinical phase of the trial.

### *Routine priming of the cervix with misoprostol*

A randomized, double-blind multicentre study is ongoing to test whether routine pre-operative treatment with 0.4 mg of vaginal misoprostol administered three hours prior to vacuum aspiration reduces complications, such as cervical injury, uterine perforation, severe haemorrhage, incomplete evacuation, pelvic infection, etc. This study will include a total of 4984 women up to 12 weeks of pregnancy, who are being recruited in 14 centres in Armenia, China, Cuba, Hungary, India, Mongolia, Romania, Slovenia and Viet Nam. It is expected that recruitment of volunteers for this study will be completed during the second half of 2004.

### *Sublingual/vaginal administration of misoprostol after mifepristone*

A randomized, double-blind study is ongoing on second trimester abortion in Hong Kong to compare the efficacy, side-effects, and acceptability of sublingual administration of misoprostol compared to vaginal administration after mifepristone pretreatment. The results of this study are expected to be available in early 2004.

## **New projects initiated during the year**

### *Assessment of postabortion care in China*

In 2003, a study was approved to assess postabortion care (PAC) in China. The main objective of the project is to provide a baseline diagnostic investigation of PAC at typical health

service settings in China. Specific objectives include the following: (i) to evaluate the existing status of equipment, supplies, infrastructure and procedures for PAC at different levels of clinical settings; (ii) to describe providers' and clients' perspectives on PAC; (iii) to assess the current quality of PAC received by clients; and (iv) to compare the quality of PAC between different health care settings, i.e. public hospitals, family planning centres, and private clinics. The study will be conducted in two cities, namely Meishan, a poor and rural area in Sichuan province in Western China, and Shenzhen, an economically booming city in Guangdong province in Southern China.

### *Medical abortion clinical trials*

Three new multicountry protocols were approved but could not be launched in 2003 due to lack of funds.

## NORMS AND TOOLS

### Specific objectives/targets

The norms and tools developed for preventing unsafe abortion, and for accessing safe abortion and postabortion care, are designed to provide policy-makers and medical practitioners with guidelines for improving the quality of care.

### Technical and policy guidance on safe abortion

*Safe abortion: technical and policy guidance for health systems* was published in English in early 2003 and released for distribution in July. Since then it has been sent to all WHO regional offices for distribution to Ministries of Health within their regions, as well as to a wide range of United Nations and other partners' agencies, professional associations, public health and research institutions, and nongovernmental organizations. Translation into Russian has been undertaken by the WHO Regional Office for Europe (EURO), and into Spanish by the WHO Regional Office for the Americas (AMRO). A Polish and a Portuguese version of the document are being prepared by nongovernmental organizations in Poland and Brazil, respectively, and the translation into French has been organized by the Department.

Dissemination of the guidance document to date has taken a number of forms. A special workshop was conducted during the meeting on "Action to reduce maternal mortality in Africa: a regional consultation on unsafe abortion", organized by Ipas in March 2003 in Addis Ababa, Ethiopia. Participants included health professionals and policy-makers from several countries in both sub-Saharan Africa and North Africa. Since then the document has been presented at a number of other international meetings, including the Interagency Group on Safe Motherhood's conference: "Saving women's lives: the health impact of unsafe abortion" held in Kuala Lumpur, Malaysia, in September 2003, and the XXth Congress of the International Federation of Gynaecology and

Obstetrics (FIGO) in Santiago, Chile, in November. It was also presented at meetings in Bucharest, Romania, and Bremen, Germany. In addition, it has been used as the basis for elaborating national guidelines in Mongolia (see Improving abortion care in Mongolia, page 137) and Nepal, and for updating guidelines in India.

As with all guidance documents, careful and targeted introduction is needed if dissemination and adoption in countries are to be successful. During 2003, the Department worked with the WHO Regional Office for Europe (EURO) and the WHO Regional Office for South-East Asia (SEARO) on plans for such a process. In EURO, a five-country workshop is planned for March 2004, which will combine introduction of the document with presentation of the Strategic Approach (see page 213) and its utilization for developing strategies to reduce the recourse to abortion and to improve the quality of care in abortion services. In all of the Russian-speaking countries of the European region, abortion is legal on a wide variety of grounds. However, many such services are being provided with outdated techniques and equipment, and are not combined with information and provision of contraception. There is, therefore, an urgent need to review and assess these services, and to update guidelines and procedures in line with WHO guidance. In Moldova, initial discussions in planning such a strategic assessment of issues related to abortion have begun, and it is anticipated that the fieldwork will be undertaken in the first half of 2004. EURO is taking the lead in this process, with technical assistance from the Programme.

A similar process for a regional workshop involving selected countries of the region is being planned with SEARO for the first part of 2004. In this region, the legal situation varies from a fairly liberal law (India) and a newly liberalised law (Nepal) to a restrictive situation in most of the other countries. The SEARO workshop will support those countries which may wish to undertake a policy and technical review of their national situation in the near future.

During 2004, the Programme will support similar regional introduction processes with the Regional Office for the Western Pacific (WPRO) and with AMRO, and will explore with the Regional Offices for Africa (AFRO) and the Eastern Mediterranean (EMRO) how to use the guidance document in countries of those regions.

### Access to abortion in the context of HIV policies and guidelines

Anecdotal information from a variety of countries and settings suggests that health services may discriminate against people known or suspected to have HIV because of fear and misinformation. Pregnant women who are infected with HIV are likely to use health services either for antenatal care and childbirth, or for abortion services. Some may find that they are infected with HIV only when they visit a health service during pregnancy.

There are currently no international guidelines regarding policies and practices relating to abortion for HIV-infected women. A few countries have made amendments to their abortion laws, while others may have elaborated explicit policies concerning indications for abortion. The WHO Department for HIV/AIDS is preparing a reference guide for HIV-related care, treatment and support of HIV-infected women and their infants, but this guide does not cover the issue of abortion in any detail. There is, therefore, an urgent need to advise on policies and practices that are appropriate (or inappropriate) and ethical for health services vis-à-vis HIV-infected pregnant women who are thinking of terminating their pregnancies or carrying pregnancy to term, in order for their reproductive rights and choices to be protected.

Following the recommendation by the Programme's Scientific and Technical Advisory Group (STAG) in 2002, the Programme has commissioned a review of existing guidelines and training materials elaborated by professional associations or Ministries of Health for the care and treatment of HIV-infected women presenting for abortion services. The review will elaborate key content points for guidelines on counselling about reproductive choices in the context of HIV and about HIV testing and counselling in the context of reproductive health. The review will also identify key gaps and challenges, including research issues that the Programme might pursue in the area of HIV and reproductive health, including abortion-seeking behaviour related to HIV status. The report is expected to be available in March 2004.

### **Bellagio consensus conference on medical abortion**

The regimens of non-surgical abortion currently provided in countries vary and do not take account of recently-compiled scientific evidence. For example, findings suggest that a lower dose of mifepristone, followed by misoprostol would be better tolerated and cheaper. An international consensus on the regimen is important, because it would help change outdated practices in countries. Also, a thorough review of misoprostol-alone regimens is needed to see whether there is enough evidence to recommend the use of a misoprostol-alone regimen in resource-poor settings, or whether more research is needed to develop an effective and safe regimen. It is also important to review issues related to service delivery of non-surgical abortion, and to agree on the minimum requirements for settings providing non-surgical abortion.

An international consensus conference on non-surgical (medical) abortion is planned at the Rockefeller Foundation's Bellagio Study and Conference Centre in November 2004 to focus on the unresolved issues related to regimens and service delivery. By that time, the Programme will have results from several ongoing trials (for example, the ongoing trial testing the efficacy of the 100 mg dose of mifepristone and the 24-hour interval between mifepristone and misoprostol). These latest results will, hopefully, contribute to the consensus at the conference.

## **TECHNICAL COOPERATION WITH COUNTRIES**

### **Improving abortion care in Viet Nam**

Following the Programme-supported national strategic assessment of issues related to abortion and abortion services, the Vietnamese Ministry of Health (MOH) began a series of activities to implement the recommendations, including the launch of a project in late 2001 known as the Comprehensive Abortion Care (CAC) project. Technical assistance for the project is provided by Ipas and the Programme. In 2003, the CAC project made major improvements in the quality of abortion services at the main CAC sites (Tu Du Hospital and the National Ob-Gyn Hospital). Providers at those hospitals participated in an advanced counselling training, which has led to private counselling prior to abortion procedures being offered to all women. A team of seven doctors and four midwives from these hospitals was trained in second-trimester abortion with dilatation and evacuation (D&E). Both hospitals have now incorporated D&E services into their routine service delivery.

The CAC project is currently expanding to the provincial level: two facilities in Dong Nai and two facilities in Hai Phong have joined the project, and they will, in turn, expand CAC to the district level. Following performance-improvement needs assessments at each site, the CAC trainers held a comprehensive first-trimester abortion training course for providers from these provinces -- helping each site transition from sharp curettage to manual vacuum aspiration (MVA), and addressing issues of counselling, infection prevention, and service management. Training activities at all levels of the CAC project will continue. Training workshops have been held for trainers from the National Ob-Gyn Hospital, Tu Du Hospital, and other sites in each of the two provinces.

Another major activity in 2003 was an assessment to prepare for the expansion of abortion methods to include medical abortion. The assessment examined the critical issues involved in moving medical abortion from research protocols to routine provision, including issues such as training needs, client information, education and communication (IEC) needs, the service delivery system, and drug availability. A report with findings of the assessment and recommendations was completed following a dissemination workshop organized by the MOH in August 2003. These findings will guide the introduction of medical abortion into abortion services at the CAC sites and, eventually, into the national reproductive health programme.

### **Improving abortion care in Romania**

In November 2001, the Programme assisted the Ministry of Health in Romania in conducting a strategic assessment of issues related to abortion, in order to identify appropriate research and programme interventions to reduce the need for abortion and to improve the quality of abortion-care services in the public and private health care sectors. The first

policy recommendation addressed was the need to develop national standards and guidelines for abortion care. Staff from the Ministry of Health and Family, the national College of Physicians, and the Society of Obstetrics and Gynaecology developed guidelines which were launched in a national meeting, "Family Planning in Romania: From Strategy to Best Practices" in March 2003.

Also in 2003, members of the assessment team submitted a proposal for a three-year project which will support the development of a model for comprehensive abortion and postabortion care services in Romania, based on the recommendations of the assessment and the new technical standards and guidelines. This model will be tested at referral and district-level hospital services in two different regions of Romania, prior to being scaled-up throughout the country. It will focus on improving the quality of existing services and will include the introduction of manual vacuum aspiration and medical abortion. The Programme will support the research component of the project, testing the impact of the comprehensive abortion care model on the quality of care in service delivery, the uptake of postabortion contraceptives, and the reduction in the incidence of repeat abortions. The assessment team is currently raising funds for the implementation component of the project.

### Improving abortion care in Mongolia

In April 2003, the Programme assisted the Ministry of Health in Mongolia in conducting a strategic assessment of issues related to abortion in order to identify appropriate research and programme interventions to reduce the recourse to abortion, to reduce abortion-related morbidity and mortality, and to improve the quality of abortion-care services which are widely available in both the public and private sectors. The assessment was conducted by a team of 18 members representing a range of national stakeholders, and covered six major regions of the country over a period of three weeks. The assessment findings and recommendations were presented in a national dissemination workshop in Ulaanbaatar in September 2003.

Recommendations from the assessment focused on policy change, implementation of pilot interventions, and action research, and included the need for:

- development and dissemination of national standards and technical and policy guidelines for high-quality, comprehensive abortion care;
- improvement of infrastructure and the development of increased training capacity at the Maternal and Child Health Research Centre, so as to serve as a model service delivery demonstration site and a locale for training of providers from across the country;
- the training of in-country master trainers to support the expanded introduction of manual vacuum aspiration, the introduction of mifepristone and misoprostol for first- and second-trimester medical abortion, as well as the introduction of D&E techniques to replace the use of the Kovacs method for second-trimester abortion;
- activities including training and the development of information, education and communication materials to support other aspects of improved abortion care, especially counselling and provision of contraceptive services;
- addressing the special needs of women and youth for comprehensive reproductive health services, including contraception, early pregnancy detection, and abortion in rural/remote communities.

Following the national dissemination workshop, the Ministry of Health submitted a proposal for Stage II follow-up activities to implement these recommendations. The project will initiate a participatory process that will guide the development, implementation, expansion, monitoring and evaluation of high-quality, comprehensive abortion care in Mongolia. Initial steps include the development and launching of national standards and technical and policy guidelines for safe abortion care; the training of national trainers; and the development of a national in-service abortion training programme based at the Maternal and Child Health Research Centre, Ulaanbaatar.

### Other country support activities

In addition to the activities described above, the Programme collaborated with the All India Institute of Medical Sciences, New Delhi, India, in organizing a Consortium Conference on "National consensus on medical abortion in India" in March 2003. The outcome of the meeting was a consensus statement on the regimen and plans for the introduction of medical abortion in India. The Programme also disseminated findings on medical abortion as well as on the incidence of unsafe abortion and related mortality at various meetings.

*Annex 1*

**SPECIALIST PANEL FOR SOCIAL SCIENCE AND OPERATIONS RESEARCH IN REPRODUCTIVE HEALTH**

**Members**

See Annex 1 of Section 1 “Promoting Family Planning”

## Annex 2

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Annex 2 (continued)

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	33	69	11	23	4	8	48
Women	18	38	4	8	2	4	24
<b>from:</b>							
AFRO	3	6					3
AMRO	3	6					3
EMRO							
EURO			11	23	4	8	15
SEARO	5	10					5
WPRO	22	46					22

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	15	65	6	26	2	9	23
Women	11	48	2	9	1	4	15
<b>from:</b>							
AFRO	2	9					2
AMRO	4	17			2	9	6
EMRO	1	4					1
EURO			6	26			6
SEARO							
WPRO	8	35					8

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**Section 5**  
**Promoting sexual and reproductive health  
of adolescents**

# Promoting sexual and reproductive health of adolescents

I.H. Shah, S. Bott, I. Warriner, H. Bathija, J. Schmidt

## INTRODUCTION

Adolescence (defined as age 10–19) is a time of transition from childhood to adulthood, during which individuals experience changes following puberty, but do not immediately assume the roles, privileges and responsibilities of adulthood. Experiences of adolescence vary by age, sex, marital status, socioeconomic status, region and cultural context. Addressing the needs of young people (defined as those in age group 10–24) in the context of rapid and profound social, economic and political changes in the developing world is undoubtedly challenging. Behaviours of young people may change faster than societal values, a disjuncture that has implications for the development of sound policies and programmes, such as appropriate family planning services for young people. These changes have enormous implications for adolescents' education, employment and marriage, but also for their sexual and reproductive health and behaviour.

The 1994 International Conference on Population and Development (ICPD) highlighted these issues and noted that “the reproductive health needs of adolescents as a group have been largely ignored to date by existing reproductive health services” (ICPD Programme of Action, paragraph 7.41; United Nations, 1998). As a group, adolescents have sexual and reproductive health needs that differ from those of adults in important ways, and which remain poorly understood or inadequately served in much of the world. Neglect of this population has major implications for the future, since sexual and reproductive behaviours during adolescence have far-reaching consequences for people's lives as they develop into adulthood.

The Department's work on promoting adolescent sexual and reproductive health concentrates on addressing these gaps, with the objective of enabling the experience of healthy sexual development and maturation and enhancing the capacity for

equitable and responsible relationships. The main focus is on supporting research that addresses policy-relevant issues and enhances the evidence base on the sexual and reproductive health situation, needs and perspectives of adolescents, including intervention research on the optimal provision of health and information services. Related to this are activities to strengthen research capacity and to disseminate findings. At the same time, technical and managerial tools and advocacy materials developed by the Department for reproductive health in the population at large are also tailored to address the unique needs of adolescents.

## RESEARCH ACTIVITIES

### Specific objectives of research

The aim of research supported by the Programme is to address factors that contribute to positive sexual and reproductive health outcomes, especially those that can be influenced by appropriate interventions in developing countries. Consequently, the focus is on behavioural research, both social science and operations.

### Progress

Most of the work in this area is supported by the ongoing social science research initiative on Adolescent Sexual and Reproductive Health (ASRH). The distribution of 43 ASRH studies by topic and country is as follows (figures in parentheses show the number of studies in the same country):

- Sexual attitudes, risk behaviours, and their determinants: Brazil, Cape Verde, China (3), Colombia, Croatia, Cuba (2), Ghana, India (2), Iran, Mexico (2), Paraguay, Peru, Poland, Syria, Tanzania, Turkey, South Africa.

- Dual protection: Colombia, Indonesia, Kenya.
- Unwanted pregnancy and its consequences: Brazil, Kenya.
- Sexual coercion: Indonesia, Nigeria, Philippines.
- Health-seeking behaviour and quality of care: Argentina, Bangladesh, Brazil, China (2), Lao People's Democratic Republic, Myanmar (2), Nepal, Thailand.
- Impact of information, education and communication (IEC) and peer education interventions: Chile, China (2).

In 2003, results from a number of studies became available. For the sake of brevity and to compare results in a broadly similar context, findings—largely from the ASRH initiative—are reported here only for Latin America.

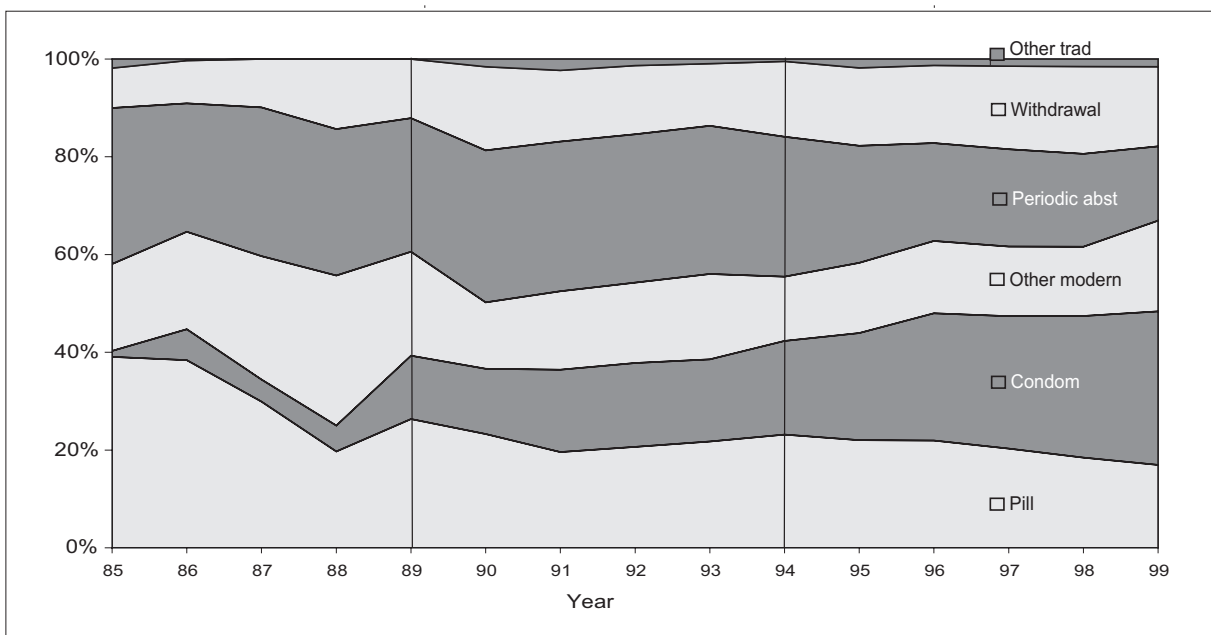
*Trends in contraceptive protection by method among never-married women aged 15–24: a case study of Colombia and Peru, 1985–1999*

In collaboration with staff of the University of London School of Hygiene and Tropical Medicine, London, United Kingdom, results from a study were published documenting yearly trends in sexual activity, contraceptive use, and subsequent reproductive outcomes among never-married women aged 15–24 in Colombia and Peru. Using ‘calendar’ data from successive Demographic and Health Surveys (DHS), the study reveals that over the period 1985–1999, young never-married women in both settings experienced profound changes

in sexual and reproductive behaviours. [Some of the results were presented in the *Annual technical report 2002*.] Further work in 2003 showed that the percentage of sexually active period protected by contraception rose in Colombia from 21% in 1985–1989, to 41% in 1990–1994 and to 49% in 1995–1999. The comparative figures for Peru were 21% in 1986–1990 and 31% in 1995–99. Figures 5.1 and 5.2 show a remarkably similar pattern of changing contribution of specific methods to overall protection among never-married young women in Colombia and Peru and the dramatic uptake of the condom. In 1989 and 1990, condom use started to rise and has continued to do so. In the most recent five-year period, condom use emerged as the most prevalent method in Colombia (providing 27% of all contraceptive protection), and in Peru it is the second method, contributing 22% of protection. No other contraceptive method has shown such a remarkable increase. In both countries, the use of periodic abstinence has declined, but it still remains a dominant method to prevent an unintended pregnancy among never-married Peruvian women.

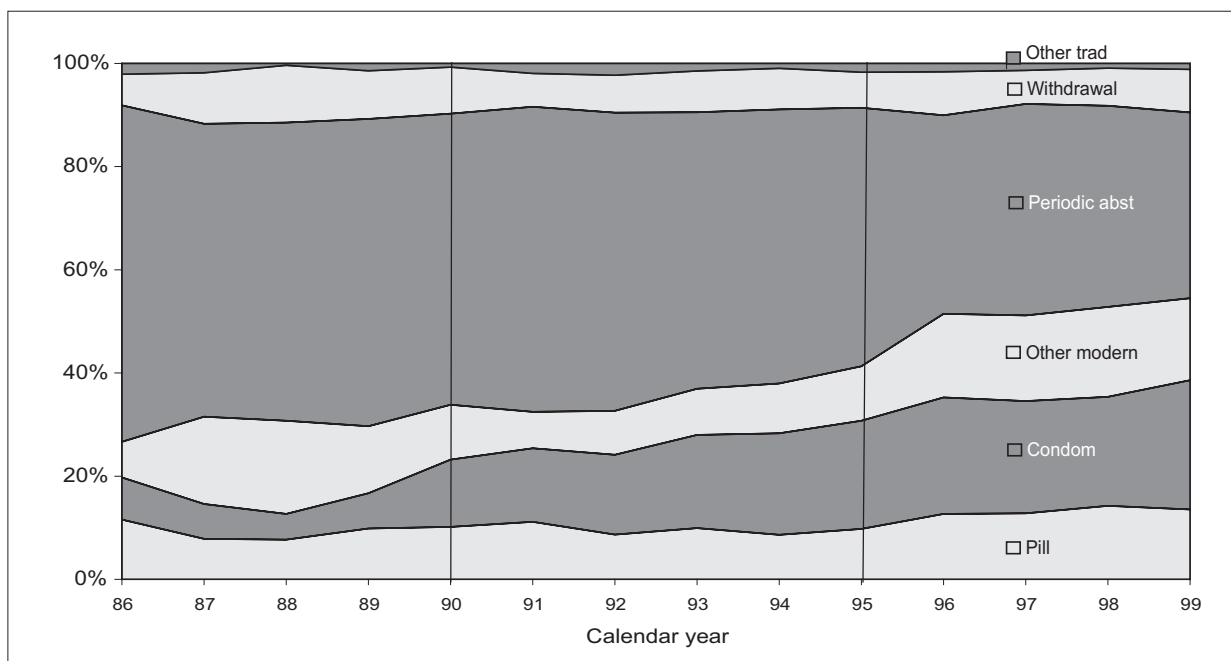
These results, together with those on sexual activity and reproductive outcomes, show that exposure to sexual activity is increasing in the two countries and outweighs the rise in contraceptive use. Therefore, programmes and policies must continue to strengthen efforts to provide appropriate information and services, as the unmet need for contraception for sexually-active young women will remain a challenge in the two countries, despite the rise in contraceptive use. In addition, these policies and programmes will have to go beyond the current focus on contraceptive use and begin to address the ever-increasing number of abortions and unwanted children born out of wedlock, for, as the studies point out, fewer

Figure 5.1. Trends in contraceptive protection by method for never-married women aged 15–24, by year, Colombia



Source: Ali, Cleland and Shah, 2003

Figure 5.2. Trends in contraceptive protection by method for never-married women aged 15–24, by year, Peru



Source: Ali, Cleland and Shah, 2003

and fewer single women in Peru and Colombia are resorting to marriage as a “coping mechanism” following pregnancy. This work also highlights the need for more focused, smaller-scale studies in order to understand better the trends and patterns which emerge from large-scale surveys.

#### *Evidence from the social science research initiative on adolescent sexual and reproductive health*

Studies supported under the ASRH initiative respond to the need for in-depth understanding of issues related to sexuality and reproduction. Qualitative studies are also helpful in identifying societal norms related to these issues as they often lag behind individual behaviours. Among the 43 ongoing studies, 13 are in countries of the Latin American region. In May 2003, 14 researchers presented papers at a meeting in Cuernavaca, Mexico. Findings from four studies in Colombia, Mexico and Peru are highlighted here. Each study used a different study design, but all explored adolescents’ perspectives about gender roles, sexual negotiation, risk perception and the implications of adolescent pregnancy. Table 5.1 summarizes the research questions, study design and selection of respondents.

#### *Views about early, premarital sex*

In all four studies, young people described double standards about socially-acceptable sexual behaviour for young women and men. In Colombia and Peru, male adolescents described social pressure to have early sexual experience—often with multiple partners—as a way to prove their virility, to fend off accusations of homosexuality and/or to enhance their prestige among male peers.

In contrast, young people interviewed in all three countries expressed disdain for girls/young women who had casual sex or multiple partners. The extent to which social norms condemn premarital sex by young women varies, however, by country, region and socioeconomic class. Adolescents in the Peruvian study expressed more judgmental attitudes about young women who have premarital sex than those from Colombia and Mexico. In Mexico, formal marriage before sex (or childbearing) appears to have more importance for upper-middle class adolescent women than for their peers from less-privileged sectors of society.

In contrast, young women interviewed in poorer communities of Colombia and Mexico spoke openly about having premarital sex for the sake of experimentation, pleasure, or emotional intimacy. Nonetheless, their narratives included concepts of purity and chastity, and they generally thought that women should have sex in the context of a stable relationship. Female respondents did not admit to having casual sexual partners, and many spoke about having to keep their sexual experience a secret from family and friends.

#### *Sexual communication and negotiation among adolescents*

In all study sites, adolescents lamented the lack of communication with parents about sex. In Peru, most young women said that the arrival of their menstrual cycles was a total surprise, as their parents had failed to talk to them about menarche before it occurred. In Colombia, adolescents described a sense of “abandonment” because of their parents’ silence about sexual matters. This inability to discuss sexual matters carried over to romantic partners, and ado-

Table 5.1. Summary of methods from each of four studies on adolescent sexual and reproductive health

Country	Primary focus of the research	Study design	Sample design	Age range and sex of respondents
Bogotá, Colombia	Risk perception and sexual negotiation among adolescents.	Qualitative design. Free-listing with 24 youth. 40 semi-structured interviews.	64 sexually-active adolescents, stratified by sex, schooling and age. Respondents were located through a convenience sample of young people identified with the help of local nongovernmental organizations.	13-19 years old, male and female. Mostly unmarried; some in stable unions.
Armenia, Colombia	Social networks, risk perception and sexual behaviour among adolescents in areas affected by natural disaster.	Primarily qualitative, with some quantitative. 68 semi-structured interviews with young people.	68 young people from a low-income urban area affected by a severe earthquake in 1999. Respondents were purposively selected and stratified by age, sex, and whether or not they were able to remain in their homes following the earthquake.	12-21 years old (10-19 years old at the time of the earthquake). Male and female.
Diverse sites in Mexico	Perceptions of adolescent pregnancy, risk factors and consequences.	Ethnographic work. Group interviews. In-depth individual interviews.	Respondents were purposively selected from different sociocultural contexts in Mexico, including a “traditional” rural community in Oaxaca, a “marginal” urban sector in Mexico City, urban “popular” sectors in two large cities, and an upper middle class sector in Mexico City.	15-23 years old male and female adolescents. Mostly unmarried; some in stable unions.
Trujillo, Huancayo and Iquitos, Peru	Perceptions of sexuality and risk, sexual negotiation.	12 Focus group discussions in each site; 120 interviews that collected in-depth qualitative data and some quantitative data.	Purposive sample of secondary school students from three cities from culturally and ecologically distinct regions of the country. The cities were Trujillo (the northern coast), Huancayo (in the central Andes) and Iquitos (in the Amazon jungle area).	13-19 years old. Male and female. Unmarried.

lescents generally suggested that it was difficult to talk about sex or protection with sexual partners.

Meanwhile, young people in all three countries described social norms that encourage young men to pressure young women to have sex using sexual seduction, verbal insistence, alcohol, and, occasionally, physical force or drugs. Most common—even routine—was the expectation that young men would use intense verbal and emotional tactics to persuade girlfriends into sex, often with threats of abandonment.

#### *Reasons for not using contraception, particularly condoms*

All four studies explored adolescents' views of contraception, particularly condoms. Adolescents generally described a youth culture in which most sex is unprotected or reliant on rhythm and withdrawal, especially at the beginning of the relationship. Use of contraception typically began only as partnerships became more stable. Adolescents did not generally perceive themselves at risk of sexually transmitted infections (STIs) with stable partners; but even with casual partners, their perceived risk of STIs failed to motivate many

young men to use condoms. One possible explanation for this was suggested by findings from Bogotá, Colombia, where many young men seemed to consider invulnerability to infection as part of their masculine identity.

In some sites (Mexico), but not others (Colombia), misinformation and lack of access to contraception (condoms) figured prominently in adolescent narratives. In fact, in Colombia, the author described an “avalanche” of information through mass media, school, peers, nongovernmental organizations (NGOs) and youth organizations, and family planning services appeared to be fairly accessible through community health promoters, NGOs and government clinics.

In all sites, adolescent narratives highlighted the extent to which taboos against open discussion of sex combined with pressure to conform to masculine and feminine ideals played a role in unprotected sex. For example, young women described social pressure to appear less sexually-experienced or knowledgeable than men and less assertive in all aspects of sexual negotiation. Lack of communication about sex and males’ tendency to use aggressive pressure tactics meant that sexual relationships were often spontaneous, unplanned, and unprotected at the beginning of a relationship. Thus, many young people used withdrawal simply because they did not have other forms of protection at the moment when they decided to have sex. In many cases, young women did not feel free to initiate discussions about protection, and young men were often unwilling to do so because they consider contraception to be the responsibility of women. Adolescent narratives in Colombia suggested that gender roles and imbalances limit women’s ability to negotiate in many other ways as well. For example, they mentioned that some women are dependent on their partners to pay for family planning services. Others felt that they could not ask a male partner to use more reliable contraception because they would insult his masculinity if they questioned his ability to control himself during withdrawal.

### *Adolescents’ perceptions about early, unplanned and/or premarital pregnancy*

These studies suggest that to understand why some adolescents have unprotected sex, it is essential to understand their views about adolescent pregnancy. For example, in Bogotá, Colombia, young people’s narratives suggested that for many, the need to use protection was mitigated because they viewed unplanned pregnancy as a manageable event. Young men, they noted, could simply refuse to take responsibility for the child if they wished, and young women could consider seeking an induced abortion, which, despite being highly restricted, was perceived to be available.

Young people in all settings acknowledged that—especially for women—early, premarital childbearing often results in criticism from family and friends, a risk of being thrown out of their parents’ house, an end to education, the loss of independence and adolescent freedoms, more limited life options

with regard to employment, and the challenge of supporting a child in the context of widespread poverty.

However, in all four studies, at least some young women suggested that marriage was not essential before sex or even childbearing. Even in the Peruvian study, in which adolescents expressed the most negative views about premarital pregnancy, some young women spoke favourably of single motherhood, as long as the young woman had finished her education and was in a position to earn an income.

Narratives of many adolescents in Colombia and Mexico reflected an idealized view of early motherhood and fatherhood. Young people often saw early motherhood or fatherhood as a way to become an adult, create a life, and/or make a partnership more secure. Women from low-income communities often have few opportunities for the future apart from becoming wives and mothers.

These views of premarital pregnancy appear to play an important role in decision-making about contraception/condoms. Throughout all four studies, young people seemed to feel that the most important condition for having sex in a “responsible” way was not necessarily to use condom (or any other contraceptive method) or to wait until formal marriage, but to wait until a woman was in a position to care for a child, either by reaching emotional maturity, earning her own income, or finding a partner willing and able to support a child.

### *Policy and programme implications*

These findings highlight the diverse social-cultural situations of adolescents in Latin America, but they also point to some broad policy and programme implications, for example:

- Because gender roles and expectations about masculine and feminine identities permeate every aspect of adolescent sexual decision-making and behaviour, programmes need to address these gender expectations and develop interventions that critically examine these beliefs and prejudices.
- Lack of communication about sex appears to be a major barrier to negotiating protected sex. Interventions to encourage young people to talk more openly about these matters—especially with sexual partners—could make it easier for women to negotiate sex and protection.
- In some settings it may be problematic for programmes to assume that all unplanned, premarital pregnancies among adolescents are unwanted—either by the father or the mother. Programmes for youth may want to address young people’s idealized images about early motherhood and fatherhood. One investigator noted that adolescents mentioned the particular value of hearing personal testimonies of adolescents who had an

unplanned child as a way to challenge these idealized views.

#### *Assessment of reproductive health needs among adolescent secondary-school students in Syria*

One of the aims of the ASRH initiative is to provide information for countries and contexts with major gaps in knowledge. As an example, a study was supported in Syria in collaboration with the WHO Regional Office for the Eastern Mediterranean (EMRO). The objective of the study was to explore, among secondary-school students, reproductive health awareness and attitudes, adolescent lifestyles and social networks, and barriers preventing adolescents from acquiring reproductive health information and care. Perspectives of both adolescents and adults on preferred ways of meeting adolescent needs were also ascertained. The study took place among secondary-school female and male students aged 15–18, and related adult gatekeepers in three major provinces of Syria (Damascus, Aleppo and Lattakia). The research design included: (i) 24 key informant interviews; (ii) 12 focus group discussion (FGDs) sessions among adolescents; and (iii) a survey, using self-administered questionnaires, conducted in a classroom setting, of 4440 (2034 boys and 2406 girls) secondary-school students drawn from 39 schools.

Results from the survey became available in 2003 and show a general lack of knowledge among adolescents surveyed on matters related to sexual and reproductive health. For example, 74% of adolescents did not know when during the menstrual cycle a woman is most exposed to the risk of pregnancy and 62% did not think that pregnancy could occur as a result of unprotected first sexual intercourse.

Findings with major policy implications include: (i) over two third (69%) of adolescents preferred to receive health care from the private sector; (ii) 42% prefer that services are delivered to them by a provider of the same sex; (iii) 72% preferred to have health services for adolescents and young people separate from those for adults; and, perhaps most importantly, (iv) there is an urgent need to provide information to young people on sexual and reproductive health.

#### *Network activities*

A network of researchers supported under the social science research initiative on adolescent sexual and reproductive health was established in 2000 to initiate a forum for exchange of ideas and information, as well as a means of providing technical support to researchers. Network activities include: regular updating of the synopsis of ongoing research supported by this initiative and the annotated bibliography of relevant materials; maintenance of a limited documentation centre, and facilities to provide researchers with materials they are unable to access; provision of core instruments (focus group discussion guidelines, in-depth interview guides and a survey questionnaire) for the study of risky sexual behaviours among adolescents, that are intended for

researchers to adapt to the thematic focus of their research and to the local context; and site visits to investigators in selected countries.

#### *Dissemination*

In addition to publication in peer-reviewed journals (see Annex 3), findings from several projects supported by the ASRH research initiative have been disseminated at seminars and conferences. For example, several papers were presented at: (i) the consultative meeting on “Non-consensual sexual experiences of young people in developing countries”, held in New Delhi, India, from 22 to 25 September 2003 and (ii) the 2<sup>nd</sup> Asia-Pacific Conference on reproductive and sexual health, held in Bangkok, Thailand, from 6 to 10 October 2003. A major highlight in 2003 was the publication synthesizing 45 major presentations and panel discussions at the international conference: “Adolescent reproductive health: evidence and programme implications for South Asia” held in Mumbai, India, in November 2000. The publication, entitled *Towards adulthood: exploring the sexual and reproductive health of adolescents in South Asia*, can also be downloaded from the Department’s web site: <[www.who.int/reproductive-health/publications](http://www.who.int/reproductive-health/publications)>.



#### *Operations research on improving reproductive health services for adolescents in French-speaking African countries*

As described in previous annual reports, an operations research project to evaluate and improve reproductive health services for adolescents has been ongoing in several French-speaking sub-Saharan countries. The project includes three phases: (i) a baseline survey of adolescents using health services and of the quality of services offered;

(ii) an intervention, informed by findings from the baseline survey, to address information needs of adolescents, training of service providers, or modification of existing services to enhance their youth-friendliness; and (iii) a post-intervention survey to evaluate the effectiveness of the intervention. The Programme facilitates and coordinates this regional initiative and provides support for research capacity strengthening, but funding for each country project is raised locally.

Since the launch of the project, the five participating countries have progressed at a different pace and the status at the end of 2003 is as follows:

- Senegal: All three stages completed and final report available.
- Guinea: Baseline study completed, interventions defined and carried out, but in a smaller scale than anticipated due to lack of funding. Evaluation initiated.
- Côte d'Ivoire: Baseline study completed, interventions defined. Progress halted due to lack of funding and political and socioeconomic instability.
- Benin: Baseline study completed, and analysis of the results in progress.
- Cameroon: Baseline study completed in 2003.

As for the ASRH initiative, this project also contributed to the development of tools, including a training manual for health professionals on adolescent health and development. These tools are now available for French-speaking countries. In addition, a network of investigators has been established to exchange information and experience as well as to discuss analysis of data and share findings.

In January 2003, an investigators' meeting was held at the Congress of the Society of African Gynaecologists and Obstetricians (SAGO) in Bamako, Mali, to review country progress and experience as well as to develop plans for future activities. Country investigators also presented their findings at the SAGO Congress. Subsequently, an electronic discussion group was developed for the participating teams and a summary report of country experiences was prepared.

Below are highlights of findings from the qualitative data gathered through in-depth interviews and focus group discussions. Comparative analysis of the quantitative data will be undertaken in 2004.

### *Access to and use of health services*

Access to health services was generally limited for similar reasons in different countries. Consultations and transportation fees posed an obstacle for many adolescents. This resulted in the use of alternative sources of health services,

such as traditional practitioners and black market medicines. Living far from health facilities was also perceived to be an obstacle for some adolescents as was inconvenient opening hours of the facilities and, in Côte d'Ivoire, health care staff not respecting the working hours was also noted as a constraint to the use of services. With regard to reproductive health services, adolescents noted: (i) the persistence of stigma against adolescent sexuality; (ii) the commonly held view that reproductive health services are for adults, married women, or for rich people only; and (iii) the negative attitudes of and treatment by health care personnel. For example, adolescents in Guinea stated that they are often insulted or mistreated by health care personnel, and particularly older staff members. However, a more positive treatment was reported at specialized private facilities, such as those run by the Red Cross and at clinics of the Association Beninoise de Planning Familial (ABPF) in Benin.

Overall, health care facilities were usually approached by adolescents only in cases of complications or other serious needs. Thus, the use of these facilities is mainly for curative and very rarely for preventive care. The most common reasons for using reproductive health facilities were related to pregnancy and prenatal care, while seeking contraceptives or information on sexual or reproductive matters are very rarely reasons for visiting a clinic.

### *Attitudes*

Parents' attitudes toward the reproductive health problems of adolescents vary by country. On the one hand, parents encouraged the use of health services by their children, but on the other hand, they were critical of the use of reproductive health services by young people. Often, parents did not approve of promoting contraception among adolescents and emphasized abstinence. Premarital pregnancy among adolescents was usually perceived negatively. For instance, the majority of parents in Guinea stated that, should their daughter become pregnant, they would send her away from home. However, parents in Senegal wanted to be more involved in the communication on adolescent reproductive health and to improve their own knowledge on such issues.

### *Communication and source of information*

Communication between parents and children on reproductive matters is often very limited. Adolescents report being "ashamed" of approaching their parents with such issues. However, when a parent is approached, it is, almost always, the mother. Information is mainly sought for curative and not preventive purposes. The most common source of information on reproduction and sexuality for adolescents was found to be friends of the same sex. Occasionally, an older family member was approached, while the use of health facilities for information remains marginal. The importance of friends as the main source of information and the first persons turned to in case of reproductive health problems suggests that peer education may be an appropriate approach in these commu-

nities. This method was adopted as part of the interventions selected in Senegal.

These results from the baseline qualitative data collection show the need for information and services for adolescent sexual and reproductive health. Information channels used by adolescents are often very informal and can pass on inaccurate or misleading information.

### *Regional research initiative on adolescent migrants and reproductive health in the Greater Mekong region*

A regional research initiative is ongoing in one major city in each of five countries of the Greater Mekong region, namely, China (Yunnan Province), the Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam. The objective is to assess the reproductive health needs of a growing but vulnerable and marginalized subpopulation—young migrants. At the same time, this initiative aims to strengthen research capacity through intraregional networking. Using qualitative research methods, the study explores risk-taking and health-seeking behaviours, and service and information needs.

In 2003, data collection in all sites was completed and focus group discussion transcripts were translated into English for comparative analysis. However, due to shortage of funds, the workshop for data analysis had to be postponed until 2004.

### *Research on pre-adolescent girls reporting vaginal symptoms*

Studies are under way in Mongolia in response to reports from providers of unusually high levels of lower genital tract infection among pre-adolescents. Symptoms may have been observed by the children themselves, or perceived by their mothers. One study explores the perceptions of about 500 mothers of these pre-adolescents concerning vaginal discharge in general and their daughter's complaint in particular. A second will examine about 500 pre-adolescents for the presence of discharge and any signs of lower genital tract infection, and screen specimens for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, *Candida* spp. and anaerobes. In 2003, data were collected from mothers and plans for the analysis were developed. Results are expected in 2004.

### *Study on bone mass and hormonal contraception*

Worldwide, over 20 million women are estimated to be currently using progestogen-only contraceptives, including injectables, implants, vaginal rings, the levonorgestrel-releasing intrauterine device and oral preparations. Concerns have been raised that progestogen-only preparations can decrease bone mineral density and thus increase subsequent risk of osteoporotic fracture. It is unclear whether any decrease noted with current use of progestogen-only contraception is transient or persistent.

Investigators at the Reproductive Health Research Unit, Durban, South Africa, are conducting a prospective study of the impact of progestogen-only contraception among women in the age groups 15–19 and 42–49 years. The younger age group covers the period of maximal bone mass acquisition, and the hypothesis is that any decrease due to progestogen-only contraception may affect the peak bone mass achieved. In the older age group, a transient decrease in bone mass with progestogen-only contraception may result in a woman starting her menopause-related decline in bone mass from a lower level.

Recruitment was completed with at least 100 women in each of eight subgroups: depot-medroxyprogesterone acetate (DMPA), norethisterone enantate (NET-EN), combined oral contraceptive (OC), and non-hormonal method users in each of two age groups (15–19 years and 42–49 years). Since most young women in South Africa are given the two-monthly injectable NET-EN, it was difficult to identify young DMPA users. All women are being followed at six-monthly intervals for up to five years. Among the younger women, body weight increased by about 2% over one year in all groups, with a greater increase among the combined OC users. There was a slight decline in bone mineral density among the OC users and an increase among the other groups. However, the differences were not significant after adjustment for difference in body weight. Interpretation of these data requires a careful scrutiny, for there are large ethnic differences in the composition of the hormonal method user groups. Results for women aged between 42–49 years are expected in 2004.

## **New projects initiated during the year**

### *Social science research initiative on adolescent sexual and reproductive health*

Two new projects were approved in 2003. The first project, "A community-based intervention study on sex/reproductive health education and services among 15–24 aged unmarried young adults in Shanghai", builds upon previous research which showed that interventions were effective and had impact in terms of increasing use of contraceptives and safe sex practices and improving knowledge with regard to sexual and reproductive health in study areas compared to the control areas. However, it remains uncertain whether such impact would sustain over time. The objective of the project is to evaluate the sustainability of a community-based sex education and reproductive health service programme among young people in Shanghai about 18 months after the end of the project. There are very few studies which evaluate the sustainability of the impact of interventions and, as such, the proposed study will fill an important gap both in terms of the methodology of impact evaluation, as well as, for programmes and policies. This information is critical for scaling-up of the intervention to other urban areas.

The second study, "Not only if, but how, condoms are used: an investigation into male condom usage by young people

in Mexico”, aims to investigate how youth (aged 16–23) use condoms—i.e., when are condoms put on and taken off, specifically. The rationale for this is that a number of STIs, both bacterial (e.g., gonorrhoea, chlamydia) and viral (e.g., genital warts and herpes simplex), can be transmitted through secondary contact or intimate skin contact. Specific objectives include: (i) whether young people use condoms correctly; (ii) the relationship between young people’s perceived risk and how condoms are used; and (iii) other factors that affect the quality of the condom use. Methodologies include the use of focus groups discussions, self-administered questionnaires, personal diaries and in-depth interviews with youth. There have been no previous studies on this topic in Mexico. Findings of the study will have major implication on the promotion of condom use among young people.

### Plans for future work

Although there is increasing evidence of risky consensual sex among young people in developing countries, non-consensual sexual experiences among them have rarely been studied. Moreover, few interventions exist that are intended to protect adolescents from unwanted sexual experiences. In this context, the Programme intends to take steps, jointly with Family Health International/YouthNet and the Population Council, to consolidate available evidence and identify and fill research gaps in the area of non-consensual sexual experiences of young people.

In September 2003, a global consultative meeting, jointly cosponsored by the Population Council, Family Health International/YouthNet and the Programme, on non-consensual sex among young people in developing countries was held in New Delhi, India. The meeting included 35 invited papers and presentations developed by some 50 experts in this field. The gathering of about 100 experts included, predominantly, researchers from all global regions, as well as legal analysts, advocates, policy-makers and young people themselves. A review of evidence from developing countries on the topic was released at the beginning of the four-day meeting. Sessions examined non-consensual sex in terms of:

- experiences of young females and males: prevalence, forms, and contexts;
- youth perspectives, through a panel of seven local youth;
- patterns of transactional sex;
- roles of the legal system;
- outcomes of coercion at the individual and community levels;
- interventions to prevent, support, and treat; and
- research methodological issues.

The meeting participants also identified a number of research gaps and potential research designs. In 2004, these recommendations will be developed into research projects. In addition, the Programme will focus on supporting interventions, as a follow-up to projects completed under the ASRH initiative which identify interventions to promote adolescent sexual and reproductive health.

## NORMS AND TOOLS

### Specific objectives

Because adolescents are more likely than adults to experience risky outcomes, and to require different approaches in terms of service and care provision, norms and tools intended to enhance reproductive health of individuals in general must be adapted to the particular situation and needs of adolescents. These issues are highlighted in guidelines and other tools for programming and capacity building developed in the Department. Other norms and tools relating to adolescent sexual and reproductive health needs are developed by the Department of Child and Adolescent Health and Development (CAH).

### Tools developed

Included in every tool developed by the Department for the promotion of reproductive health is a special section devoted to the unique needs of adolescents. For example:

- The *Pregnancy, childbirth, postpartum and newborn care: a guide to essential practice* and the forthcoming guide *Sexually transmitted and other reproductive tract infections: a guide to essential practice* include the special considerations that should be accorded when dealing with adolescents.
- The guidelines on *Medical eligibility criteria for contraceptive use* provide guidance on issues specific to adolescents, as do other tools, including the family planning practice guide, advocacy materials and guidelines on the prevention of unwanted pregnancies and unsafe abortions, and technical and managerial guidelines on management of abortion complications.
- The Department also developed specifications and procurement guidelines for the male latex condom and is working with the United Nations Population Fund (UNFPA) and the InterAgency Task Force Team on Prevention of HIV to develop condom programming guidelines, giving special consideration to the needs and situation of adolescents.
- The training curriculum *Transforming health systems: gender and rights in reproductive health* provides support for programming at national level for adolescent sexual and reproductive health in several ways. The curriculum provides case studies of adolescent sexual and

reproductive health issues which are intended to sensitize participants to address adolescent needs within their programmes and services.

- Following the publication in 2001 of *Advancing safe motherhood through human rights*, a shorter version for use by policy-makers and programme managers is now being published. This pocket guide is intended to assist national-level managers address the key human rights issues concerning adolescents and other special groups.

### TECHNICAL SUPPORT

During 2003, technical support to research investigators was provided by reviewing draft reports and papers as well as advising on the analysis of data. In addition, staff served as a resource to two international programmes on adolescent sexual and reproductive health organized by the Royal Tropical Institute, Amsterdam, Netherlands, and by the International Children Centre, Ankara, Turkey. The staff also participated in the Family Health International/YouthNet Technical Advisory Group (TAG) and was a panel member in a meeting cosponsored by the Population Council's projects, FRONTIERS and HORIZONS, and Family Health International/YouthNet on "New findings from intervention research: youth reproductive

health and HIV prevention", held in Washington, DC, USA, in September 2003.

### LINKS WITH THE DEPARTMENT OF CHILD AND ADOLESCENT HEALTH AND DEVELOPMENT

The Department continues to collaborate with the WHO Department of Child and Adolescent Health and Development (CAH) in several activities. Staff members actively participate in the working groups on 'HIV/AIDS and young people' and on 'Adolescent pregnancy'. Staff members participated in two conferences, "Meeting the Millennium Development Goals for maternal mortality reduction: where are the pregnant adolescents?" and in the Technical Consultation on "Married adolescents". The first meeting was jointly organized by CAH and the Department and the second was organized by WHO, UNFPA and the Population Council. Inputs, comments and suggestions continue to be provided on documents on adolescent sexual and reproductive health issues. As before, there has been collaboration on the operations research project assessing reproductive health services for adolescents in French-speaking sub-Saharan countries, and on the identification of general research priorities and in the review of proposals and selection of specific research projects. Collaboration has also extended to the development of norms and tools.

*Annex 1*

**SPECIALIST PANEL FOR SOCIAL SCIENCE AND OPERATIONS RESEARCH IN REPRODUCTIVE HEALTH  
IN 2003**

**Members**

See Annex 1 of Section 1 “Promoting Family Planning”

## Annex 2

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**Annex 2 (continued)**

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	52	93	4	7			56
Women	34	61	3	5			37
<b>from:</b>							
AFRO	8	14					8
AMRO	16	29					16
EMRO	3	5					3
EURO	2	4	4	7			6
SEARO	12	21					12
WPRO	11	20					11

*Other scientists*

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	13	81			3	19	16
Women	5	31			1	6	6
<b>from:</b>							
AFRO	4	25					4
AMRO	7	44			2	13	9
EMRO	1	6					1
EURO					1	6	1
SEARO							
WPRO	1	6					1

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**Section 6**  
**Gender and reproductive rights in  
reproductive health**

# Gender and reproductive rights in reproductive health

J. Cottingham, A. Martin Hilber, M. Colombini, E. Kismodi

## INTRODUCTION

Both the International Conference on Population and Development (ICPD, 1994) and the Fourth World Conference on Women (FWCW, 1995) clearly emphasized the need for promoting gender equity and equality in reproductive health policies and programmes, as well as the promotion and protection of human rights. These agreements were reinforced in the five-year reviews of both conferences, held in 1999 and 2000, respectively. Among the key issues to be given greater attention were: measures aimed at promoting and achieving gender equality and equity in a systematic and comprehensive manner (ICPD+5 paragraph 39); the incorporation of issues related to sexual and reproductive health in the work of relevant United Nations bodies on indicators for the promotion and protection of the human rights of women (ICPD+5 paragraph 40); and the protection and promotion of human rights by ensuring that all health services and workers conform to ethical, professional and gender-sensitive standards in the delivery of women's health services, including by establishing or strengthening regulatory and enforcement mechanisms (Beijing+5 paragraph 107 g). The Department's Gender and Reproductive Rights group helps to ensure that the Department's work explicitly contributes to these goals, and carries out a number of specific projects to promote gender equity and reproductive rights.

### Objectives

The Department's work in gender and reproductive rights aims to:

- identify, develop, and evaluate strategies and mechanisms for promoting gender equality and human rights in reproductive health research, programming and technical support;

- support countries to ensure that reproductive programmes and policies respect, protect, and fulfil human rights and promote gender equity and equality; and
- ensure that the promotion of gender equity and equality and human rights principles are integrated into the Department's work.

It is guided in this work by the Gender Advisory Panel (GAP), a group of independent external experts from different disciplines and regions.

## A RIGHTS-BASED APPROACH FOR LEGAL AND POLICY REVIEW

### Specific objectives

There is increasing recognition that achievement of the Millennium Development Goals, and the ICPD and FWCW targets related to sexual and reproductive rights, requires that governments take both immediate and progressive steps to respect, protect and fulfil their obligations with regard to the human rights of their population. Laws, policies, and regulations are the mechanisms which governments use to meet their human rights obligations, and a supportive legal and regulatory framework is a powerful tool for improving health as well as promoting and protecting human rights. Evidence shows that political commitment and removal of legal and policy barriers have been important factors in reducing maternal mortality in some developing countries. Yet, few countries have systematically reviewed the legal and policy environment as a central part of plans and programmes to reduce maternal mortality and morbidity and improve sexual and reproductive health more broadly. In an effort to bridge

the disciplinary boundaries and increase capacities for improving sexual and reproductive health through human rights, the Department has developed a process which can be used alongside, or as a complement to, the normative and training activities described subsequently.

The objective of this area of work is to assist countries to adapt and implement tools to review and improve the legal, policy, and regulatory environment affecting access to, utilization, use and quality of reproductive health services, using a human rights framework.

## Progress

*Policy action tool—using human rights to improve maternal and newborn health through a multisectoral approach for strengthening laws, policies and standards of care*

The policy action tool “Using human rights to improve maternal and newborn health through a multisectoral approach for strengthening laws, policies and standards of care” aims to assist countries in working towards their Millennium Development Goals and other international commitments related to maternal and neonatal health by using a multisectoral, participatory approach for considering and improving the legal, policy, regulatory and practice situations within their countries. By bringing legal and policy information together with health systems and health outcome data, the tool helps countries identify barriers and gaps in the legal, policy and normative environment related to maternal and neonatal health and health services. It uses the human rights principles of non-discrimination (including equity and equality), participation, and accountability to assess these gaps and propose solutions. The tool also allows countries, in the adaptation process, to identify specific target groups or issues that are particularly problematic in order to ensure that they are being appropriately addressed in national law, policy and practice.

Using the policy action tool in countries requires political commitment and a willingness to involve other stakeholders in the search for common solutions. Many factors affecting maternal and neonatal mortality lie outside the health sector. Included in the multi-stakeholder assessment team, representatives from the health sector, as well as other sectors such as education, environment and youth, may help to foster cross-sectoral analysis and proposals of remedies for difficult gender, cultural, institutional and infrastructural barriers. The involvement of a wide range of stakeholders, including civil society organizations and professional associations, is likely to create common commitment to national obligations to respect, protect and fulfil human rights and to meet international development goals and targets related to sexual and reproductive health.

The policy action tool will produce results on three levels, by:

1. identifying key interventions or targeted action to eliminate legal, policy or normative barriers to maternal and newborn health services;
2. facilitating the active engagement of other sectors in identifying and addressing specific, non-health sector barriers to maternal and newborn health;
3. providing data that countries can use as a basis for their human rights reports or progress reports to international Human Rights Treaty Monitoring Bodies, and other reporting processes, such as for ICPD+10.

The elaboration of the tool is new, complex and unique. The validation study, undertaken in 2002 by a multidisciplinary research team in Switzerland was completed in 2003. Results of the study informed the development of a final draft instrument, the accompanying “Guide for use in countries” and a “Question and indicator guide” for adapting the instrument to specific country situations.

A field-test began in Mozambique, and another is planned in Brazil. As part of the preparatory activities for the commencement of the field-test in Mozambique, a training workshop on human rights and maternal and newborn health was held with representatives of the Ministry of Health, the WHO Maputo Office, and staff from the United Nations Children’s Fund (UNICEF) and the United Nations Population Fund (UNFPA) working on safe motherhood. The workshop will be followed up at an orientation workshop in early 2004 with the commencement of the data collection process.

Interest in future collaboration on application of the tool in other countries has been expressed by partner agencies such as UNICEF and UNFPA with whom discussions are under way. Field-tests of the tool should be concluded by the end of 2004 and results published in early 2005.

### *Indicators for measuring fulfilment of rights*

The question of how, in practice, human rights can be integrated and used to promote health is being closely examined by WHO, and has led to an Organization-wide initiative to elaborate indicators for the right to health. The Department has been participating in a small working group convened for this purpose by the WHO Health and Human Rights focal point. Building on work done by three WHO departments—Water, Sanitation and Health; Essential Drugs and Medicines Policy; and Reproductive Health and Research—a workshop was held in May 2003 to start elaborating what kinds of key indicators would be needed to monitor governments’ progress in respecting, protecting and fulfilling their obligations towards their citizens’ right to health. This meeting included a member of the Committee on Economic, Social and Cultural Rights,

and the newly-appointed Special Rapporteur on the Right to Health. The Department presented the work on the policy action tool, which is structured to capture two kinds of indicators: “government effort” indicators related to laws, policies and the use of standards and protocols; and health outcome indicators. These in turn are organized under four groupings of rights related to maternal and newborn health: rights relating to life, survival, and security; rights relating to health and maternity; rights relating to information and education; and rights relating to non-discrimination.

The immediate result of the meeting was the inclusion of a main section on “Right to health indicators” in the first report of the Special Rapporteur to the United Nations General Assembly in October 2003. In this report, he suggests that a “right to health indicator derives from, reflects and is designed to monitor the realization or otherwise of specific right to health norms, usually with a view to holding a duty-bearer to account”. The Special Rapporteur continues, “Thus, what tends to distinguish a right to health indicator from a health indicator is less its substance than (i) its explicit derivation from specific right to health norms; and (ii) the purpose to which it is put, namely right to health monitoring with a view to holding duty-bearers to account” (UNGA 2003 document A/58/427). Structural, process and outcome indicators are described, and, most likely, will need to be used together in order to monitor governments’ progress in fulfilling the right to health.

This work will continue in 2004. It is essential that the Department ensures that indicators specifically related to sexual and reproductive health are included in what may become a “basic list” of indicators for monitoring rights.

## NORMS AND TOOLS

### Collaboration with Human Rights Treaty Monitoring Bodies to support norms and standards within the human rights framework

The United Nations Treaty Monitoring system—a key mechanism through which the United Nations (UN) promotes and protects the human rights of all individuals—has tremendous potential to advance the reproductive and sexual health and rights of all, particularly women and girls around the world. The main purpose of the treaty monitoring system is to encourage governments to comply more fully with their treaty obligations. Six of the seven international human rights treaties provide for the establishment of committees whose primary mandate is to monitor governmental progress by examining country reports (Table 6.1).

This “country reporting” process requires States to report periodically on their efforts to respect, protect, and fulfil the human rights obligations enshrined in a particular treaty. A formal meeting eventually follows the submission of a country report. This provides an opportunity for committee members—all of whom are independent experts on human rights—to discuss the content of the reports with country representatives. Furthermore, committees consider input from nongovernmental organizations and UN agencies throughout the country reporting process. These exchanges are a major strength of the reporting process and provide a great opportunity for other actors to improve governmental compliance with treaties. Committee members then issue “concluding observations” to the reporting government. Every year, these observations are compiled in a report and sent to the General Assembly of the United Nations.

Table 6.1. Key human rights treaties and their monitoring committees

Human rights treaty	Committee
International covenant on civil and political rights	Human Rights Committee (HRC)
International covenant on economic, social and cultural rights	Committee on Economic, Social and Cultural Rights (CESCR)
Convention on the elimination of all forms of discrimination against women	Committee on the Elimination of Discrimination against Women (CEDAW)
Convention on the rights of the child	Committee on the Rights of the Child (CRC)
International convention on the elimination of all forms of racial discrimination	Committee on the Elimination of Racial Discrimination (CERD)
Convention against torture and other cruel, inhuman or degrading treatment	Committee Against Torture (CAT)

Within WHO, the Health and Human Rights Team (SDE/ETH) is responsible for overall coordination of various departments' technical contributions to the treaty monitoring bodies. The Department has been taking a leading role in providing sexual and reproductive health information to the Human Rights Committee, the Committee on Economic, Social and Cultural Rights (CESCR) and the Committee on the Elimination of Discrimination against Women (CEDAW). The Department has also been working closely with the Department of Child and Adolescent Health and Development (CAH) by providing input on sexual and reproductive health to the reports submitted to the Committee on the Rights of the Child (CRC). During 2003, reports have been submitted by the Department to the different committees on the following countries:

- CESCR: Lithuania, Russia, Slovakia, Yemen.
- HRC: Colombia, Mali, Philippines, Sri Lanka.
- CEDAW: Ethiopia, Nepal.
- Contribution to CRC reports: Bangladesh, Morocco, Sri Lanka.

These countries are selected by WHO on the basis of various criteria, including the maternal mortality ratio and the legal and policy environment.

The compiling of all these reports—which are usually limited to 10–15 pages including questions and recommendations—is done in close consultation with WHO country and regional offices. Their concerns and recommendations are essential for this process. The Department also works closely with CAH, the Department of Gender and Women's Health and the HIV/AIDS Department. The Department also consults with UNFPA on the preparations of the reports.

Because international human rights treaties have the force of law, countries are legally bound to work towards implementing the concluding observations of the committees. By carefully selecting the countries it reports on, the Department can subsequently use treaty bodies' concluding observations to strengthen the technical support given to countries.

During 2004–2005 the Department will work closely with selected countries to ensure that concluding recommendations are fully understood, and a plan made for their implementation. In order to facilitate this process, the Department, together with CAH, plans to organize regional and country-based workshops to improve understanding of the Treaty Monitoring Bodies process and its importance for advancing sexual and reproductive health and rights. To continue the reporting process, up to eight reports will be submitted to the Treaty Monitoring Bodies. The countries will be selected in consultation with the technical units of the departments and regional offices.

The Department continues to work closely with all the Treaty Monitoring Bodies and the Office of the High Commissioner for Human Rights. In 2004, further lunchtime seminars will be conducted with treaty monitoring bodies to improve their understanding of sexual and reproductive health as a key to fulfilment of human rights.

## TECHNICAL COOPERATION WITH COUNTRIES

### Training on gender and rights in reproductive health

The Department, together with regional partners, has played a key role in elaborating a training curriculum and course for health managers in which gender and rights analysis is integrated into policy development and health service planning.

Of the five institutions which have run the course, the Key Centre for Women's Health in Society, Victoria, Australia and the Centre for African Studies, Nairobi, Kenya, ran the course for the fifth time each in 2003. The Women's Health Project at the University of the Witwatersrand, Johannesburg, South Africa, ran its seventh course in October 2003. All three courses were well received. The Centre for the Study of State and Society (CEDES), Buenos Aires, Argentina and the Yunnan Reproductive Health Research Association (YRHRA), Kunming, China, both expect to run the course in 2004.

#### *Expansion of the training to other regions*

On the recommendation of the Gender Advisory Panel, the Department has expanded outreach of the course to new regions. In particular, it is providing technical assistance to two new centres to carry out the course in 2004: the Kazakhstan School of Public Health in Almaty, Kazakhstan, which plans to run an adapted form of the course in Russian for countries of Central Asia; and the Ahfad Women's University in Khartoum, Sudan, which intends to run an adaptation of the course for selected countries of the WHO Eastern Mediterranean Region. In addition, the University of the Philippines in Manila, Philippines, has expressed interest in running a two-week course in South-East Asia. The Department is also exploring the possibility of running a course in Burkina Faso for the French-speaking African countries.

#### *Kazakhstan and Central Asia*

The Kazakhstan School of Public Health, a WHO collaborating centre for the region, plans to run the WHO course on gender and rights in reproductive health for three years (starting in September 2004). This course is one part of Kazakhstan's broader national reproductive health strategy adopted in 2003 as part of a joint workplan between the Ministry of Health and the WHO Regional Office for Europe.

In October 2003, as part of the preparatory process, the Department sponsored a workshop for trainers on the training curriculum, which was hosted by the Kazakhstan School of Public Health in Almaty. Twelve participants (eight from Kazakhstan and four from Kyrgyzstan) attended the workshop. The aim of the workshop was: (i) to provide potential course-trainers with an understanding of the perspectives that have guided the construction of the training course; (ii) to introduce them to the course content and methodology; and (iii) to provide an opportunity for practice in facilitating and teaching.

The Department is currently assisting the Kazakhstan School of Public Health with the regional adaptation of the course and an adapted version of the curriculum in Russian will be used for the two-week course for Central Asian countries scheduled in September 2004.

### *Sudan and countries of the Eastern Mediterranean Region*

The Institute for Women, Gender & Development Studies at Ahfad University for Women in Khartoum, Sudan, plans to run a regionally-adapted training course, using the WHO curriculum, for selected countries of the WHO Eastern Mediterranean Region at the end of November 2004. In September 2003, as an initial step, the Department, in collaboration with the WHO Country Office, visited the Ahfad University for Women to begin planning how such a course might be shaped, organized and supported. As part of the preparatory phase, the Department will organize a "training of trainers" workshop to be hosted at the Ahfad University for Women at the end of March 2004.

### *Myanmar*

In December 2003, upon request from the Ministry of Health of Myanmar, the Department collaborated with the WHO Country Office in Yangon, Myanmar, and the WHO Regional Office for South-East Asia in the running of a two-week national level course in Yangon for senior health managers from the Ministry of Health, the Ministry of Social Welfare, the Ministry of Education and nongovernmental partners. The overall evaluation of the course indicated that all participants felt they had gained important analytical skills for applying gender analysis in their work. Some planned to integrate gender components into their own training programmes, health research and projects.

### *Adaptation for use in other courses and curricula*

In the field of medical education, the Department has been approached by a number of medical schools and those involved in elaborating medical curricula for guidance in integrating gender and rights into these curricula. During 2003, the Department collaborated with the Department of Gender and Women's Health and the WHO Regional Office for South-East Asia to support representatives from other coun-

tries in the region to participate in two workshops organized by the Achutha Menon Centre for Health Science Studies in Trivandrum, India. During the first workshop in January 2003, a syllabus for a two-week training course on gender and medical education was elaborated for medical educators, health service managers and policy-makers with the aim of introducing gender and rights sensitivity into medical curricula. During the second workshop in November 2003, the training module, which drew substantially from the WHO manual, was field-tested and adapted for medical educators.

The Achutha Menon Centre for Health Science Studies in Trivandrum, India, has also adapted parts of the modules on gender, social determinants and policy for integration into its Masters of Public Health programme.

### *Promotion of the training curriculum*

Dissemination and promotion of the curriculum has continued throughout 2003.

At the beginning of 2003, a CD-ROM version of the curriculum in English became available (3 000 copies). CD-ROM versions in other languages will be prepared as the texts become available. The production of an interactive electronic version for use on the web is planned for 2004–2005.



In August 2003, the Spanish version of the training manual was published and launched by CEDES, in Buenos Aires, Argentina. In May 2003, the Chinese translation, prepared by YRHRA, was completed and the Chinese version will be published in early 2004. Both these centres will run the course in their regions in 2004. The possibility of producing a French version is being explored with several centres in Africa, particularly in Burkina Faso. Presentations of the curriculum were made at the Second Asia-Pacific Conference on Sexual and Reproductive Health in Bangkok, Thailand (October 2003), and the WHO/PAHO Pre-Congress Workshop just prior to the Congress of the International Federation of Gynecologists and Obstetricians (FIGO) in Santiago, Chile (November 2003).

### Future plans

Over the next biennium, the Department plans to:

- encourage and give technical support to the centres in Kazakhstan and Sudan to run the course for countries in their respective region;
- give continued technical support to those centres already running the course, as requested; and
- give guidance and technical support for the development of short-course adaptations for use with specific countries or organizations.

## OTHER AREAS OF WORK

### Sexual and reproductive health of refugees

The Department has expanded its work in the area of gender-based violence, particularly in conflict areas. In October 2003, it took part in the organization of the ninth Inter-Agency Working Group on Reproductive Health in Refugee Situations (IAWG), which took place on 9–10 October 2003. Gender-based violence was among the key areas of coordination and collaboration for 2003–2004, identified during the group work of the IAWG meeting.

In June 2003, the Department, in collaboration with the Gender and Women's Health Department, UNFPA and the United Nations High Commissioner for Refugees (UNHCR), began an evaluation of the implementation of the *Clinical management of rape survivors* guide in refugee settings into site-specific protocols, in order to elaborate specific elements on human rights to be incorporated into the guide. As an outcome of this activity, a joint workplan for follow-up was developed and an evaluation questionnaire was sent out to the field.

In 2003, the Department, the WHO Regional Office for Africa (AFRO) and the Departments of Gender and Women's Health, Violence and Injury Prevention, and Health Action

in Crisis undertook collaborative activities on gender-based violence in conflict areas. The aim of this interdepartmental effort for crisis management is to assist survivors of gender-based violence in two African countries—Liberia and the Democratic Republic of Congo. A joint plan of work was developed by the Department and the Department of Gender and Women's Health to provide technical support for specific crisis management activities to be carried out during 2004.

Future plans are to:

- continue evaluation and updating of the *Clinical management of rape survivors* guide;
- provide technical support to AFRO to carry out crisis management activities concerning gender-based violence in Liberia and Democratic Republic of Congo.

### Informed consent research

Following the completion of three pilot-studies on the informed consent process in Brazil, Chile and Mexico, both the Gender Advisory Panel and the Scientific and Technical Advisory Group have encouraged the Department to continue such research. The aim is to assess research participants' understanding of the informed consent process in a multicountry study (if possible) in order to improve and optimize the process in different cultural settings.

Over the past year, the project has progressed slowly because of the difficulty in identifying an appropriate study on to which the informed consent study could be "piggy-backed". A Phase I clinical trial on the microbicide polystyrene sulfonate appeared to be the only study about to begin which could be deemed favorable to adding a component on informed consent. The study involves both women and their partners, and thus presents a good opportunity to assess the differences in perceptions as well as the challenges of partner notification and agreement. Because it is a placebo-controlled, randomized, triple-masked study, ensuring participants' full understanding will be an important challenge. However, as described earlier (page 107), this microbicide study is currently on hold pending review of toxicological data.

Annex 1

**GENDER ADVISORY PANEL IN 2003**

**Members**

Babatunde Ahonsi, Ford Foundation, Lagos, Nigeria  
 Soledad Diaz, Chilean Institute of Reproductive Medicine (ICMER), Santiago, Chile  
 Amal El-Hadi, New Woman Research Centre (NWRC), Cairo, Egypt  
 Thein Thein Htay, Ministry of Health, Department of Health, Yangon, Myanmar  
 Sharad Iyengar, Action Research and Training for Health (ARTH), Udaipur, India  
 Borbala Koo, Society for Education on Contraception and Sexuality, Bucharest, Romania  
 Karen Newman, Consultant, London, United Kingdom  
 Maria Isabel Plata (*Chairwoman*), PROFAMILIA, Bogota, Colombia  
 Raffaella Schiavon, Population Council, Mexico City, Mexico  
 Rashidah Shuib, Universiti of Sains Malaysia, Kelantan, Malaysia  
 Sheila Tlou, Department of Nursing Education, University of Botswana, Gaborone, Botswana  
 Zhang Kaining, Yunnan Reproductive Health Research Association (YRHRA), Kunming, China

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	10	83	1	8	1	8	12
Women	7	58	1	8	1	8	9
<b>from:</b>							
AFRO	2	17					2
AMRO	3	25					3
EMRO	1	8					1
EURO			1	8	1	8	2
SEARO	2	17					2
WPRO	2	17					2

**SCIENTISTS IN 2003**

Sofia Gruskin, François Xavier Center for Health and Human Rights, Harvard School of Public Health, Boston, MA, USA  
 Sundari Ravindran, Achutha Menon Centre for Health Science Studies, Trivandrum, India

## **Section 7**

# **Promoting sexual health**

# Promoting sexual health

A. Martin Hilber and J. Cottingham

## INTRODUCTION

The Programme of Action of the International Conference on Population and Development (ICPD, 1994), adopted by 184 countries, emphasized a broad-based concept of reproductive health, which is defined, in part, as the ability to have a satisfying and safe sex life and includes sexual health.

In order to achieve sexual and reproductive health, people must be empowered to exercise control over their sexual and reproductive lives and gain access to related health services. While these rights, and the ability to exercise them, constitute an important value in themselves, they are also a condition for well-being and development. The neglect and denial of sexual and reproductive health and rights are at the root of many health-related problems around the world, such as unwanted pregnancies, unsafe abortion, maternal mortality, sexually transmitted infections (STIs) including the human immunodeficiency virus (HIV infection), infertility, discrimination, coercion and violence.

In addressing these problems, it is imperative to give explicit attention to sexuality, sexual health and safer sex, and not only to reproductive health issues. The HIV/AIDS pandemic demonstrates the importance of addressing sexual behaviour and stigma, and preventing and managing STIs. Unwanted pregnancies, which have devastating effects on women's health and socioeconomic opportunities, are associated with sexual coercion and lack of access to information and services regarding sexuality and fertility regulation. Gender power imbalances are an important underlying cause of many of these problems; these and other contextual factors influence women's, men's, and young people's ability to practise safe sex. Discussing sexual matters between partners (or between service providers and clients) is often

problematic since sex remains taboo in many cultures, especially when considered separately from reproduction. While ICPD has done much to increase the importance of sexual health on an advocacy level, implementation has received little attention, especially in terms of services.

The linkages between sexual and reproductive health problems and people's ability to have a safe and satisfying sexual life require that a wider spectrum of health care needs is recognized and provided for. However, how to address sexuality and specific sexual health issues in the public health care system, including sexual dysfunction and sexual violence, remains a challenge. Sexual health concerns are often dealt with by the private sector because few resources are publicly available. As a result, there is little evidence available on how sexuality and sexual health problems (other than HIV/STI prevention and treatment) have been specifically implemented and scaled-up in countries. This may be because, in resource-constrained settings, dealing with sexuality and different aspects of sexual health often appears as a luxury—despite its fundamental relevance for sexual and reproductive health. Without such evidence, few recommendations can be made on how to programme sexual health interventions in an integrated manner at country level.

As decided by the Department's Scientific and Technical Advisory Group (STAG) and the Programme's Policy and Coordination Committee (PCC) in 2003, sexual health will be a new thematic area of work for the Department beginning in 2004. Thus, in 2003, the Department continued its preparatory work in this new area of work. Following the meeting of the Strategic Committee on Sexual Health in October 2002, the Department prepared a Medium-term Programme of Work on Sexual Health that focuses on building the evidence base related to sexual health.

## Goal and objectives

The goal of the new cross-cutting area of work on sexual health is to promote optimal sexual health and an affirmative view of sexuality for women, men and young people.

The objectives are:

- to build the evidence base for high-quality, non-discriminatory, acceptable and sustainable sexual health education and service programmes; and
- to increase knowledge and understanding of the social and cultural factors related to harmful sexual practices in order to develop strategies to abolish these practices.

## RESEARCH ACTIVITIES

Based on recommendations from the Strategic Committee, STAG, the Department's Gender Advisory Panel (GAP) and PCC, the Department's work on sexual health will focus its research activities on building the evidence base related to programming, service delivery and educational interventions.

A priority of the planned future work on sexual health is the promotion of essential, integrated sexual health interventions in countries. To date, however, there is insufficient information or consensus on which key interventions to promote. In order to begin to collect the evidence on key sexual health interventions, the Department began a partnership with the Royal Tropical Institute (KIT) of Netherlands, whereby the Institute will dedicate significant staff time in the coming biennium to work on this activity. During the course of 2003 and culminating in a planning meeting in December in Amsterdam, a workplan was developed for the evidence-building activities that are scheduled to begin in early 2004 and continue until 2006.

In 2003, the Department continued to convene the inter-departmental working group on sexual health to coordinate activities and collaborate on various projects. To assure consensus and clarity of concepts and scope of the work area, the Department commissioned the development of a conceptual framework for working on sexual health. The framework, currently being developed by the Thomas Coram Research Unit of the Institute of Education, at the University of London, United Kingdom, is based on a review of the current evidence and in-depth interviews with WHO colleagues both at Headquarters and in regional offices currently working on aspects of sexual health. This review will be the first in a new sexual health document series the Department will launch in 2004.

A second document, "Integration of sexual health into reproductive health services: needs, evidence and implications" was also finalized in 2003 with the technical assistance of a senior scientist from the London School of Tropical Medicine

and Hygiene, London, United Kingdom and KIT. It will be jointly published by the Department and KIT, and will appear in the planned sexual health document series in 2004.

To contribute to the knowledge base on the meaning, context, and prevalence of specific vaginal practices, the Department began work on a protocol for a planned multi-country research on gender, sexuality and vaginal practices in South-East Asia (Indonesia and Thailand) and Southern Africa (Mozambique and South Africa). In October 2003, a preliminary planning meeting on research methods was held just prior to the Asia-Pacific Conference on Sexual and Reproductive Health held in Bangkok, Thailand, to share national data and methodologies used to investigate dry sex and other vaginal practices, and to begin to define common ethnographic and survey methods for the planned research. In the beginning of 2004, a meeting will be held in Jakarta, Indonesia, to finalize a common protocol for Departmental technical and ethical review in 2004.

## NORMS AND TOOLS

The Department focused on integrating sexual health issues (e.g. promoting healthy sexuality throughout the life cycle, addressing sexual violence in various health services, and improving counselling on sexuality) into tools being developed by the Department and others, both within WHO and internationally.

### Medical curricula on human sexuality

The Department sent out a questionnaire to over 1500 medical schools around the world asking whether and how human sexuality and gender are addressed in the medical school curricula. The questionnaire received a 60% response rate. This was done in collaboration with the International Society of Impotence and Sexual Research (ISISR), Copenhagen, Denmark, to review whether sexuality and sexual health is being dealt with in training materials and curricula being used in medical education around the world. On the basis of this review, new training materials or curricula will be developed for training health providers to address more effectively sexuality and sexual health related issues in the course of their duties. In the coming year, an expert group will review the findings in order to decide whether generic training modules on human sexuality (including gender issues) should be developed in the coming years by the Department and partners.

### HIV in pregnancy

Responding to a request from the HIV Department, the Department assisted in the conceptualization and drafting of a chapter on sexual health and another on sexual violence in the upcoming "Guidelines on HIV-related care, treatment, and support for HIV-infected women and their children in resources constrained settings" that will be published in 2004

by WHO, the United Nations Children's Fund (UNICEF), the United Nations Population Fund (UNFPA), The World Bank, the Joint United Nations Programme on HIV/AIDS (UNAIDS), Family Health International (FHI) and the United States Centers for Disease Control and Prevention (CDC).

### **TECHNICAL COOPERATION WITH COUNTRIES AND REGIONS**

As part of its mandate to promote sexual health more broadly, the Department continued to build mechanisms and partnerships both within WHO and externally. This work involved participating in the development of regional networks in the African and European regions, assisting in the conceptualization of regional meetings in the African and Eastern Mediterranean regions, and exploring partnership initiatives to provide training on sexuality and sexual health in the Eastern Mediterranean and South-East Asian regions. In addition, the Department continued to participate and strengthen its collaboration with other initiatives and organizations working on sexuality and sexual health, including the Ford Foundation sexuality resources centres, the International Association for the Study of Sexuality, Culture and Society (IASSCS), the International Society of Impotence and Sexual Research (ISISR), SHARENET of the Netherlands, and the World Association of Sexology (WAS).

### **FUTURE PLANS**

In 2004, the Department will commence its Mid-term Programme of Work for 2004–2009. Planned activities for 2004–2005 include:

- a multicountry study on gender, sexuality, and vaginal practices to discern the role they play in relation to people's vulnerability and risk to sexual ill-health;
- a comprehensive review of best practices in a wide range of sexual health services, including counselling in family planning and antenatal care, HIV/STI/RTI prevention and care, prevention of gender-based violence, and elimination of harmful sexual practices such as female genital mutilation, will be carried out to assess whether an integrated sexual health service package can and should be offered in both primary and reproductive health care services settings;
- a review of the Global Burden of Disease (GBD) related to sexual health that will complement the ongoing work of the Department in assessing the GBD related to reproductive health;
- participation in a multi-institutional effort to review existing curricula on sexuality education for health providers to assess current needs and develop appropriate curricula that can be adapted by countries and regions;
- support for regional efforts to improve the definition and promotion of healthy sexuality and sexual health in countries;
- continued research into female genital mutilation (FGM).

Two research studies will be conducted in six African countries that will focus on (i) decision-making processes and behaviour models that lead to abandonment of FGM, and (ii) understanding the relationship between sexuality and FGM. A third study, an operations research study, will assess the factors that underlie effective intervention programmes. Findings will be analysed, tested, and if successful, promoted as learned lessons for use in national settings by policy-makers.

## Annex 1

## SCIENTISTS IN 2003

Peter Aggleton, Thomas Coram Research Unit, Institute of Education, University of London, London, United Kingdom

Eli Coleman, World Association of Sexology, Minneapolis, MN, USA

Gary Dowsett, Australian Research Centre in Sex, Health and Society, La Trobe University, Melbourne, Australia

Sarah Hawkes, London School of Hygiene and Tropical Medicine, London, United Kingdom

Terrence Hull, Australia National University, Canberra, Australia

Korrie de Koning, KIT (Royal Tropical Institute), Amsterdam, Netherlands

Anke van der Kwaak, KIT (Royal Tropical Institute), Amsterdam, Netherlands

Herman Ormel, KIT (Royal Tropical Institute), Amsterdam, Netherlands

Marian Pitts, Australian Research Centre in Sex, Health and Society, La Trobe University, Melbourne, Australia

Maria-Pia Waelkens, KIT (Royal Tropical Institute), Amsterdam, Netherlands

Gorm Wagner, International Society of Impotence and Sexual Research (ISISR), University of Copenhagen, Copenhagen, Denmark

Kate Wood, Thomas Coram Research Unit, Institute of Education, University of London, London, United Kingdom

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members					12	100	12
Women					6	50	6
<b>from:</b>							
AFRO							
AMRO					1	8	1
EMRO							
EURO					8	67	8
SEARO							
WPRO					3	25	3



## **Section 8**

# **Technical cooperation with countries**

## Overview of activities—interregional activities and collaboration with regional offices

A. Ntabona, M. Mbizvo

The main objective of the Department in Technical Cooperation with Countries (TCC) is to assist countries in enhancing their capacity to develop and implement national and regional research and programmatic activities aimed at improving reproductive health. The specific aims are to:

- assist developing countries in identifying priority areas where research is required to address reproductive health needs;
- support national planning and programming, including the introduction of reproductive health technologies and the adaptation and application of practice guidelines essential for improving reproductive health;
- provide assistance to developing countries to strengthen their capacity to undertake research, and to disseminate and apply results of reproductive health research; and
- collaborate with countries in the monitoring of effects of policies and initiatives related to health sector reforms on reproductive health programmes and outcomes.

The present overview of progress in the year 2003 includes: collaboration with WHO regional offices and partner agencies, support to national reproductive health research, research capacity strengthening, and reproductive health programme development. Across the regions, specific support was provided as follows:

- Overall 27 institutions (or national research coordinating committees) were receiving support through institu-

tional development grants and resource maintenance grants. In addition, 24 scientists from these institutions were receiving research training grants; most of these researchers were receiving training within their respective regions;

- With support from the Programme and national and international sources, up to 761<sup>1</sup> research projects were initiated or ongoing in these institutions and a total of 736<sup>2</sup> research articles were published and/or disseminated through congress abstracts presented at national, regional and international scientific events held in the regions.

In addition, several research and programmatic activities were supported jointly by different thematic groups within the Department and the TCC team in selected countries as an entry point for strengthening research capacity and programme development in the areas of family planning, maternal and newborn health, sexually transmitted and reproductive tract infections, field-testing of new tools, evidence-based medicine and implementing best practices, programme planning and evaluation.

### INTRODUCTION

The Department continued to cooperate with WHO regional and country offices, governments, nongovernmental organizations (NGOs) and other partners, with the objective of addressing reproductive health needs through intraregional and national research, and research and technical capacity strengthening.

<sup>1</sup> Years 2002 and 2003 combined.

<sup>2</sup> Years 2002 and 2003 combined.

## HIGHLIGHTS OF PROGRESS IN INTER-REGIONAL ACTIVITIES DURING 2003

### Enhancing utilization of reproductive health research findings

At a meeting organized in 2001 in Nairobi, Kenya, policy-makers, reproductive health programme managers and heads of research institutions (receiving grants for research capacity strengthening) urged the Programme to develop guidelines for converting research into action. In 2003, the Programme convened a technical consultation to initiate the development of guidelines to help countries utilize research findings in policy-making and developing and strengthening sexual and reproductive health programmes. An outline of the guidelines was developed and agreed upon based on experiences in selected countries, and it is hoped that they will complement the existing guidelines of the Programme on development of research proposals. The final version is expected to be published during 2004.

### Collaboration between WHO and UNFPA: the UNFPA-funded Strategic Partnership Programme

Bilateral discussions between the Department and the United Nations Population Fund (UNFPA) continued in 2003 regarding the establishment of the UNFPA-funded Strategic Partnership Programme (SPP)—the successor to the inter-agency Technical Advisory Programme (TAP). An SPP proposal was submitted to UNFPA to achieve jointly the objective of supporting the dissemination, adaptation and adoption of the Department's tools and guidelines, and strengthening the technical capacity of countries in reproductive health programme development through the UNFPA country support teams (CSTs). Initial funding was approved with effect from October 2003, and workplans have been drawn and agreed for the period up to December 2005. The main expected outcome is to have jointly contributed to improvement of quality of care of sexual and reproductive health services, particularly in the areas of family planning and control of sexually transmitted infections (STI) and reproductive tract infections (RTI), through the adoption and up-scaling of evidence-based practices in selected countries. The Department will work with, and provide support to, the CSTs, whose task is to advise governments on population and development issues, including the development of policies and programmes for improving sexual and reproductive health.

### Global and regional courses on health sector reforms, reproductive health and poverty

The Department continued to collaborate in the organization and delivery of the global course offered by the World Bank Institute since 1998 which aims at, *inter alia*, (i) improving the understanding on how the changing international environment impacts upon the work in reproductive health, and (ii) increasing the strategic thinking and ability of various stake-

holders to ensure that health sector reforms help, rather than hinder, improvements in population and reproductive health outcomes in the countries concerned. A customized format of the course has been offered annually since 2001 for the French-speaking countries in West Africa and has been successfully used to establish a network of selected training institutions based in Africa and in Canada and USA. This has resulted in building the capacity to deliver the programme at the regional level through local institutions, so as to phase out the use of international/Western experts and ensure sustainability. The course is targeted at teams made up of persons involved in financing, planning, implementation and evaluation of sexual and reproductive health services, who are well-placed to act as agents of change in their countries. These include high-level officials from public sector ministries, policy-makers, private sector professionals, academics and researchers, representatives of donor agencies and local or international nongovernmental organizations. Based on the lessons learnt from the three-year experience in West Africa, necessary steps have been taken to use the same approach for expanding the course and the institutional networking in 2004 to the English-speaking countries in Africa and, possibly, to other regions.

### Collaboration with WHO regional offices

The main collaborative activity with all regional offices in 2003 consisted of a series of consultations to elicit the inputs into the paper requested by the World Health Assembly (WHA55.19) for the design of a global strategy for accelerating progress towards achievement of the international development goals and targets related to reproductive health. The strategy documents the major discrepancies between global goals and realities, and describes the principal barriers to progress, particularly the inequities due to gender, poverty and exposure to risks in adolescents. It highlights the care aspects of reproductive and sexual health services and suggests actions for countries and WHO to develop innovative approaches for accelerating progress. In addition, collaborative activities were undertaken with each of the WHO regional offices, in line with joint biennial plans of action developed in early 2002. Table 8.1 provides highlights of a few collaborative activities with WHO regional offices in 2003.

### WHO Collaborating Centres in reproductive health

During 2003, there were 53 officially designated WHO Collaborating Centres for Research and Technical Cooperation in Human Reproduction: seven of these have been redesignated for another 4-year period and 10 others are still to complete the redesignation process. Two new centres, one from the Americas and one from Europe, were granted the official designation status in 2003; they will be directly monitored by the respective regional offices. One additional centre in Europe is in the final stage of the screening process and will receive the designation status in early 2004. In addition, there was cooperation with 26 centres which are not officially designated.

### Collaboration in the interagency and interdepartmental activities on reproductive health in crisis situation and displacement

The main objective of this work area is to ensure that reproductive health issues receive appropriate attention during emergency and crisis situations. The Department participated (as a member of the Steering Committee) in the global evaluation led by the United Nations High Commissioner for Refugees (UNHCR) in 39 countries on reproductive health of refugees and internally displaced persons. The Department reviewed the documentation and assisted with the evaluation components of the "minimum essential service package" and "reproductive health kits of medicines and commodities", as well as the component on available financial resources for reproductive health care of persons in crisis situations. The evaluation led to holding of a consultation to revise the content of the UNFPA document *Manual of reproductive health kits for crisis situations*, which in turn resulted in the agreement to include HIV post-exposure prophylaxis (PEP) for survivors of rape and to add STI and PEP drugs for children. The reports on the evaluation and the consultation will be made available in 2004.

In collaboration with UNFPA, the Department organized the 9th Annual Inter-Agency Working Group (IAWG) on reproductive health in refugee settings (Brussels, Belgium, 9–10 October 2003). The meeting was attended by 45 IAWG members. The main outcome consisted of a coordinated action plan for 2003–2004 based on a set of revised terms of reference and a joint plan for meeting the training needs of programme coordinators, policy-makers and programme managers. Other related activities included participation in the preparation of guidelines for the management and prevention of HIV/AIDS in emergencies; the development of protocols for PEP for STIs/HIV after rape; and fundraising for field-based technical support activities.

### Interagency collaboration on essential reproductive health medicines and commodities

Following a recommendation from the Inter-Agency Working Group on Commodity Security, a draft list of medicines and commodities was published in collaboration with UNFPA in early 2003 and is currently under review. Furthermore, the Department collaborated with the WHO Department of Essential Drugs and Medicines Policy (EDM) and prepared the background documents upon which the evidence-based list of reproductive health essential medicines is defined: (i) 122 essential medicines and supporting policies, guidelines and prescribing practices were reviewed; (ii) discrepancies/contentious issues were identified through technical reviews; and (iii) the evidence base for selection of a list of essential medicines was completed through Cochrane reviews. A project was planned in two phases. The first phase will be the development of a consensus-driven evidence-based list of reproductive health medicines and commodities, and the second phase will focus on building capacity in countries for

ensuring access to quality reproductive health medicines and commodities. Another important activity in this area was the interagency consultation held in November 2003 on the 'Selection and delivery of essential medicines and commodities'. This meeting brought together representatives from key Departments within WHO, United Nations Children's Fund (UNICEF), Joint United Nations Programme on HIV/AIDS (UNAIDS), Department for International Development (DFID) of the United Kingdom, Deutsche Gesellschaft für Technische Zusammenarbeit (GTZ) of Germany, Family Health International (FHI) [also representing United States Agency for International Development (USAID)], John Snow International (JSI) and Program for Appropriate Technology in Health (PATH). The participants recommended, *inter alia*, that the Department: (i) review available evidence and prepare proposals to solve the current inconsistencies between the existing lists; and (ii) include a comprehensive list of contraceptives in the *WHO Model list of essential medicines* in accordance with the recommendations of the *Medical eligibility criteria for contraceptive use*. The final background for the technical basis for the list will be presented at another interagency meeting in 2004 and the proposals for new items will be submitted to the EDM Expert Committee in 2005.

### PLANNED ACTIVITIES

- The SPP implementation phase is proposed to begin in early 2004 by familiarizing the CST regional advisers with the new/updated guidelines on family planning and control of RTI/STI and developing plans for introducing and adopting these guidelines in selected countries in all regions.
- Further work on reproductive health research utilization is planned with partner agencies for 2004. It is proposed to convene a workshop with researchers and programme managers which will use selected case studies to demonstrate pathways and barriers towards utilization of research to improve reproductive health.
- Support to the World Bank Institute programmes will continue through the co-facilitation of the courses offered at regional and global levels, with particular emphasis on the initial implementation of the programme for the English-speaking countries in the African region.
- In view of the trends in humanitarian crises globally, and subject to availability of funds, the Department could be required to increase its capacity to respond to regional and country requests for assistance in 2004.
- The work on essential reproductive health medicines and commodities will be pursued, in collaboration with EDM and PATH; a system will be established to maintain a continued consultation with other partners and stakeholders to ensure consistency with the *WHO Model list of essential medicines*.

Table 8.1. Collaboration with WHO regional offices, 2003

Region	Collaborative Activity
Africa	<ul style="list-style-type: none"> <li>• The Department and the WHO Regional Office for Africa (AFRO) convened a meeting of investigators to finalize the protocol and develop instruments for the proposed intra-regional study on community and facility interventions to improve maternal health.</li> <li>• AFRO established a Regional Reproductive Health Task Force whose mandate includes, <i>inter alia</i>, to provide guidance to AFRO on issues relevant to WHO Member States in the implementation of the regional reproductive health strategy, advise on programmatic directions most likely to impact positively on service delivery, and mobilize resources. The Department participates actively in the meetings of the Task Force.</li> <li>• The Department collaborated with AFRO in identifying centres and areas of cooperation within the proposed grants to 'Service Guidance Centres'.</li> <li>• The Department collaborated with AFRO and the Commonwealth Regional Health Community Secretariat (CRHCS) through:                         <ul style="list-style-type: none"> <li>i) participation in the 38<sup>th</sup> Health Ministers' Conference whose 2003 theme was "Strengthening and scaling up health interventions in east, central and southern Africa: the role of human resources for health (HRH)";</li> <li>ii) membership of the Steering Committee of the CRHCS Family and Reproductive Health Programme and the HIV/AIDS Experts.</li> </ul> </li> <li>• The Department facilitated a Regional Course in Reproductive Health Research Methodology.</li> </ul>
Americas	<ul style="list-style-type: none"> <li>• Collaborative activities between the WHO Regional Office for the Americas (AMRO) and the Department embraced the areas of improving maternal and perinatal health, introducing emergency contraception, defining programmes for constructive involvement of men, improving adolescent sexual and reproductive health, and the application of the Strategic Approach to increase access to quality reproductive health services.</li> <li>• Membership of the Advisory Group for the Global Conference on Reaching Men to Improve Reproductive Health for all.</li> </ul>
Eastern Mediterranean	<ul style="list-style-type: none"> <li>• The Department is supporting the Regional Office in the preparation of a directory of reproductive health research institutions (five countries).</li> <li>• After helping with its planning, the Regional Office is assisting the Department in the follow up of the research initiative on adolescent reproductive health (three centres).</li> </ul>
Europe	<ul style="list-style-type: none"> <li>• With support from the Department and FRONTIERS, EURO is organizing training courses in reproductive medicine, operations research and reproductive biology.</li> </ul>
Asia and the Pacific	<ul style="list-style-type: none"> <li>• SEARO and WPRO are collaborating with the Department in the systematic introduction of essential care practice guides.</li> <li>• The Department supported the participation of experts from the region (identified by SEARO) in the 2<sup>nd</sup> Asia-Pacific Conference on Reproductive and Sexual Health.</li> </ul>

# The WHO Regions of Africa and the Eastern Mediterranean

H. Bathija, D. Chikamata, A. Fahmy

## INTRODUCTION

The main objective of the Department in Technical Cooperation with Countries (TCC) is to pursue the strengthening of research capacity of institutions in the African and Eastern Mediterranean regions in order to enhance their potential to implement reproductive health research relevant to national and regional needs and to facilitate their participation in the global research effort.

The strategy continues to focus on the strengthening of selected institutions and stimulation of interest in reproductive health research in various countries.

The main elements of this strategy are as follows:

1. development of subregional "centres of excellence", which are capable of assisting weaker centres, especially those in least developed countries (LDCs);
2. promotion of networks through "South-to-South" and "South-to-North" links;
3. improvement of research protocol development, research management and scientific writing;
4. promotion of intraregional training;
5. stimulating donor interest in the LDCs, French-speaking Africa and the Eastern Mediterranean regions;
6. promoting resource mobilization for research capability strengthening activities in the region;
7. strengthening research skills in the social sciences;

8. promoting "targeted" research on major reproductive health problems and on the needs of LDCs.

Collaboration with institutions such as the Geneva Foundation of Medical Education and Research (GFMER), Geneva, Switzerland, the International Centre for Reproductive Health (ICRH), Ghent, Belgium, the National Institute of Health and Medical Research (INSERM), Paris, France, the Free University of Brussels, Belgium, and Oxford University, Oxford, United Kingdom, continues to be an important way to support these strategies.

## RESEARCH ACTIVITIES

### Overall research output

The 10 centres supported with long-term institutional development grants or resource maintenance grants are involved in projects that address regional and national reproductive health priorities. From a total number of 129 studies, 16 projects (12%) were implemented with support from the Programme and 71 projects (55%) were carried out with support from national sources. The institution-strengthening efforts deployed by the Programme in these regional centres have enhanced their capacities for fundraising from other international agencies and addressing topics of global or local relevance: 42 projects (33%) received support from international agencies other than WHO.

About one-third of the projects were in the area of epidemiology or social science research, whereas 49% related to clinical research. Ten projects (8%) were basic science studies and eight (6%) were using operations research designs with different types of methodologies. All thematic areas were

studied, but the highest number of projects were in the area of maternal health (61), family planning (17) and HIV/AIDS (13). Many projects had multiple themes.

## Regional research initiatives

### *Research on female genital mutilation*

The Programme's current work in this field aims to provide solid evidence on the obstetric complications of female genital mutilation (FGM), in order to improve advocacy and community-based programmes and to encourage the development of counselling and training manuals for managing such complications.

Research on the obstetric sequelae of FGM is undertaken as a multicountry, multicentre prospective cohort study, based at certain maternity units and obstetrics departments in Burkina Faso (5 sites), Ghana (3 sites), Kenya (3 sites), Nigeria (6 sites), Senegal (13 sites) and Sudan (3 sites). The study's primary objectives are to estimate the incidence of obstetric complications among women with FGM giving birth in hospital and to evaluate the relationship between different types of FGM and obstetric complications. A subsidiary objective is to obtain clinical information relevant to the prevention and treatment of obstetric complications in women with FGM.

All women with singleton pregnancies admitted to the participating centres for delivery are approached for possible recruitment into the study. Those who accept undergo an examination to determine their FGM status prior to delivery and are included in the study. They are then followed through labour and delivery up until six weeks after their discharge from hospital. Information is also obtained regarding the health and anthropometric measures of infants born to these women.

The study is observational in nature, with no active interventions expected on the part of the staff, apart from examining women and gathering information. A total of 29 700 women were enrolled and data collection was completed in May 2003. Data analysis is ongoing and a study report will be available in 2004.

Another current focus of the work of the Programme with regard to FGM are the sociocultural determinants of the practice. Although there is growing information on the cultural context in which FGM is practised, much of this information is fragmentary and from secondary sources. There is, therefore, a need for an in-depth study to understand the sociocultural diversity and complexity of the practice, in order to design culturally meaningful and workable programmes for advocacy and intervention strategies.

In response to this need, the Department developed a call for proposals for studies examining these aspects. In 2002, the call for proposals was sent out to over 200 persons, groups

or institutions. A total of 30 research protocols were received and nine were selected for further development and eventual funding. To date, three protocols have been approved and are expected to start in 2004. They address the links between gender relations and FGM in Gambia, the persistence of the practice among some ethnic communities in Kenya, and the issue of FGM among displaced southern Sudanese women in Khartoum.

The Programme is making plans to support research examining the decision-making process with regard to FGM and the relation between sexuality and FGM, and an intervention programme aiming to plan, implement and evaluate innovative community-based programmes using a combination of different successful models. Six countries will be participating: Burkina Faso, Djibouti, Gambia, Mali, Senegal and Uganda. Development and technical supervision of these activities will be carried out by the International Centre for Reproductive Health (ICRH), at the University of Ghent, Ghent, Belgium.

### *Operations research on improving reproductive health services for adolescents*

In 2003, the operations research project to evaluate and improve reproductive health services for adolescents continued in five French-speaking sub-Saharan countries: Benin, Cameroon, Côte d'Ivoire, Guinea and Senegal. While the Programme is facilitating and coordinating this regional initiative and is providing support for the research capacity strengthening aspects of the project, funding for most country projects is being raised locally. A characteristic feature of the project has been its implementation by multidisciplinary research teams, with the active participation of youth representatives in each team.

In Senegal, the Programme is collaborating with the Population Council's FRONTIERS project. FRONTIERS has assumed funding responsibility for formative and interventions research, whereas the Programme contributed financially to the evaluation phase that was completed in 2002. Final results were published in 2003.

More details on this project are given in the chapter on Promoting sexual and reproductive health of adolescents (see page 149).

### *Adolescent reproductive health in the Eastern Mediterranean region*

In response to the recommendations of the intercountry workshop on adolescents' needs and perspectives in reproductive health in the Eastern Mediterranean region, held in Tunisia in 1999, the Programme, in collaboration with the WHO Regional Office for the Eastern Mediterranean has, since 2000, given technical support for the development of research proposals in the Islamic Republic of Iran, Oman and Syria.

These studies are in progress and explore the reproductive knowledge, attitudes and behaviour of 15–18 year old boys in Teheran, and of adolescents in secondary schools (Oman, Syria).

The findings of the Syria study are reported in more detail in the chapter on Promoting sexual and reproductive health of adolescents (see page 149).

### *Operations research on community and facility interventions towards improving maternal and newborn health*

Of all the regions of the world, sub-Saharan Africa has the highest maternal mortality ratio, estimated to be 920 per 100 000 live births. This study proposes to undertake an intervention towards improving maternal and newborn health by identifying and utilizing community- and health-facility based interventions that involve pregnant women, their partners, their families, community leaders, health providers and policy-makers in facilitating access of pregnant women to health care.

The study will be conducted in three phases: pre-intervention assessment, intervention and evaluation phases. Interventions at community level and at the health facility will be developed and implemented based on the findings of the pre-intervention assessment phase. The impact of the interventions will be evaluated by comparing pre- and post-intervention indicators. The study will take place in Ethiopia, Nigeria, South Africa and Uganda.

During the pre-intervention assessment phase, community members of the selected catchment areas, namely, women (currently pregnant and women who delivered within the last 12 months), male partners, health personnel and community leaders will be interviewed. Data collection will also include reviews of delivery and antenatal care records. Health facilities will be assessed in terms of training for improvement of skills for health care workers, provision of equipment, drugs and other supplies to ensure that women receive high-quality maternity care.

If the effectiveness of community- and facility-based interventions in improving access to health care is confirmed, the Department will develop and circulate recommendations for incorporation of these interventions into routine obstetric care.

### **National studies**

#### *A randomized, double-blind study to compare two regimens of levonorgestrel in emergency contraception in Nigeria*

The objective of this project is to compare the efficacy and side-effects of two treatments: (i) levonorgestrel administered in two doses of 0.75 mg at 24-hour interval; and (ii) levonorg-

estrel administered in one dose of 1.5 mg. It would be a major practical advantage if levonorgestrel could be given in a single dose up to 120 hours after unprotected intercourse. This would simplify the treatment and increase compliance and acceptability. In addition, the project is being used for training in clinical research carried out according to Good Clinical Practice guidelines and for developing a network of clinical research centres in Nigeria. Finally, the project will contribute to making emergency contraception known in various areas in Nigeria and to collecting national data on the use of levonorgestrel for emergency contraception. The study is being conducted in seven centres and is being coordinated by the Centre for Reproductive Health Research in Sagamu.

The recruitment of 3150 women into the study started in June 2002 but was slowed down by a strike action in the family planning clinics including those participating in the study. It is now anticipated that recruitment will be completed in 2004.

## **DEVELOPMENT OF HUMAN RESOURCES**

### **Workshops and short courses**

#### *Research synthesis and systematic reviews workshop by the Effective Care Research Unit, University of Witwatersrand, East London, South Africa*

In June 2002, a research methods training workshop was run by the Effective Care Research Unit, University of Witwatersrand, East London, South Africa. It was attended by all unit members, participants from other disciplines in the university, and researchers from Gambia, Mozambique and Zambia, as well as Programme staff.

In June 2003, the course focused on learning the fundamentals and practical skills for conducting randomized clinical trials and systematic reviews. It included self-directed pre-course preparation, hands-on computer sessions, a multiple choice examination and individual mentoring. Course materials sent to the participants in advance of the course included lecture notes on the course topics; the Cochrane Collaboration Open Learning materials; RevMan software; and Epi-Info 2002 software. Participants were from Gambia (1), Nigeria (3), Saudi Arabia (1) and South Africa (23).

#### *WHO-sponsored international semenology workshop*

Since 1997, the Department of Obstetrics & Gynaecology, Tygerberg Hospital, Cape Town, South Africa, has organized, in conjunction with the Programme, semenology workshops for health care providers from collaborating research centres in Africa. A total of 78 individuals have been trained and enrolled in a quality-control programme for sperm morphology. The quality-control programme has been extremely successful and has led to the establishment of satellite laboratories in various centres. One example is the Centre

for Research in Reproductive Health in Sagamu, Nigeria, which has initiated a local training course and gives guidance to multiple individuals in semenology, thus contributing directly to the capacity development of the area. Currently, 61 participants from 11 African countries, namely; Benin (3), Democratic Republic of Congo (1), Ethiopia (1), Kenya (17), Nigeria (8), South Africa (10), Tanzania (1), Tunisia (1), Uganda (8), Zambia (4), and Zimbabwe (7) are enrolled in the quality control programme for sperm morphology. The data from the quality control project have been used to develop a unique statistical model for laboratory directors to distinguish between individual laboratory technicians. Using the data from the quality control programme, all the participants (trainees) have been classified as having excellent reading skills (83%), good reading skills (11%) and marginal reading skills (6%).

#### *Cervical cancer screening by visual inspection with acetic acid (VIA) workshop*

In 2001, at a regional symposium for policy-makers, the Department of Obstetrics and Gynaecology, University of Harare, Harare, Zimbabwe, presented the results of a field-based study in which they demonstrated that visual inspection with acetic acid (VIA) was a promising screening approach for identifying women with high-grade precancerous lesions of the cervix. A number of directors from collaborating centres in Africa expressed interest in conducting similar projects. In 2002, the Regional Advisory Panel (RAP) at its Sixth Meeting approved a proposal to conduct a workshop to train physicians from district hospitals in seven countries in VIA for screening and cryotherapy treatment. In addition, the physicians were to develop demonstration project proposals to integrate VIA in reproductive health services in district hospitals.

The workshop took place in October 2003 in the Department of Obstetrics and Gynaecology, Harare, Zimbabwe. Eight participants from district hospitals in Nigeria, Tanzania, Uganda, Zambia and Zimbabwe attended the workshop. The didactic sessions provided background information needed to do VIA competently. The practical sessions took place at two gynaecological and one family planning clinics in Harare. During the workshop the participants prepared draft proposals for demonstration projects to pilot-test integration of VIA into existing reproductive health services in their hospitals.

#### *Regional training course in research methodology for French-speaking countries in Africa*

Training researchers in the development of research proposals in the area of reproductive health through short courses has been one of the capacity building activities of the Programme in French-speaking countries of the African and Eastern Mediterranean regions. In order to guarantee sustainability of these short courses at country or regional level, it has become important to develop "ready-to-use" modules, which include lectures, overhead transparencies,

handouts to students and exercises that can be used by trainers to increase the critical mass of trained researchers. A follow-up plan to these modules which are being tested in the field will be the training of trainers who are likely to use these modules.

A meeting was held at WHO headquarters in Geneva, in March 2003, to plan the process for developing the teaching manual for research methodology training for French-speaking African countries. It was agreed to follow a process that builds on the materials developed over the years by WHO and other agencies, but also, and more importantly, draws on the expertise of the French-speaking reproductive health professionals from Europe and Africa who have used these and other materials in teaching research methodologies. Unfortunately, the financial difficulties of the Programme prevented carrying out these plans.

#### *Workshops on ethical issues in research in reproductive health*

A regional workshop on ethical issues in research in reproductive health was planned for French-speaking countries of Africa. Unfortunately, the funding situation did not permit to hold it. Similarly, workshops planned for Egypt and Tunisia had to be postponed to 2004. A session on ethical issues was held during the operations research training course in Bamako, Mali (see below).

#### *Regional workshop on infertility management*

In response to the recommendation by the RAP, the Department of Obstetrics and Gynaecology, University of Nairobi, Nairobi, Kenya, organized a workshop on management of infertility in February 2002. The Department of Obstetrics and Gynaecology is currently in the process of producing the proceedings of the workshop and the Programme will contribute a chapter summarizing WHO's work in the area of infertility in the last two decades. It was planned that the practice guide *Prevention and management of infertility: a guide for reproductive health workers*, describing management of infertility in resource-poor settings would be revised and field-tested in two centres, one in Africa and the other in the Eastern Mediterranean region in 2003. However, this had to be postponed due to funding constraints.

#### *Operations research training*

The Department, the United States Agency for International Development (USAID), and the Population Council's FRONTIERS project signed a Memorandum of Understanding (MOU) in 2001 to collaborate in operations research activities. Improving the capacity of developing countries to conduct and utilize operations research has become an important part of this collaboration. One of the main concerns with capacity building efforts has been to institutionalize training in universities and research organizations in order to ensure local capacity for producing better-trained managers and researchers.

A special initiative for developing an operations research training centre for French-speaking Africa was planned in 2002 in collaboration with FRONTIERS and with WHO's Regional Office for Africa (AFRO). The Centre de Recherche sur la Population et le Développement (CERPOD) in Bamako, Mali, was selected to become the training centre for French-speaking countries.

The first workshop took place in September 2003 in Bamako. Seventeen high-level policy-makers, programme managers and researchers from six French-speaking countries (Benin, Chad, Mali, Mauritania, Niger, and Senegal) attended this orientation workshop, where they agreed on three themes for the operations research projects to be developed in future training workshops: maternal health (especially the low rates of skilled attendants at birth); family planning (the low and stagnating contraceptive prevalence rates in rural areas); and adolescent reproductive health (the high abortion mortality as well as the high rates of sexually transmitted infections).

While the Department committed itself to providing training and technical support, and FRONTIERS is contributing technically, a source of funding for the research projects themselves needs to be identified.

*Reproductive Health Research Methodology Course in the Reproductive Health Research Unit, Chris Hani Baragwanath Hospital, Soweto, Johannesburg, South Africa*

The Reproductive Health Research Unit in Chris Hani Baragwanath Hospital, Soweto, in collaboration with the Medical Research Council of South Africa and the Department, has been conducting annually, since 1997, the Reproductive Health Research Methodology Course in Johannesburg, South Africa. The main aim of the course is to support and improve reproductive health policy and programme planning in Africa by building capacity in reproductive health research skills and intervention strategies. In 2003, 21 participants from 10 countries in sub-Saharan Africa attended the course. The participants received bursaries for the course from WHO, the Wellcome Trust, Ford Foundation, the United Kingdom's Department for International Development (DFID) and the Comprehensive International Programme for Research into AIDS (CIPRA).

To date, 190 participants from 17 countries in sub-Saharan Africa have attended this course. Of these, 113 were females and 77 males. The majority of participants were reproductive health advisors, project managers, medical officers and nurse-midwives from government, nongovernmental organizations and research institutions.

### Research training grants

In 2003, five researchers were studying under a grant from the Programme: one from Nigeria was being trained in the

technique of polymerase chain reaction in the University of Witwatersrand Molecular Diagnostic Laboratory, Johannesburg, South-Africa; one from Ethiopia was reading a Master's course in reproductive and sexual health research at the London School of Tropical Medicine and Hygiene, London, United Kingdom; one from Côte d'Ivoire and one from Tunisia were reading a Master's course on health systems research at the Free University of Brussels, Brussels, Belgium; and one from Kenya was enrolled in a Master's course in reproductive health at the University of Edinburgh, Edinburgh, United Kingdom (the grant provided by the University of Edinburgh was negotiated by the Programme). The difficult financial situation of the Programme prevented consideration of new applications.

### M.Sc. course in biostatistics, University of Ibadan, Ibadan, Nigeria

Since 1998, the Programme has provided support to an M.Sc. Course in Biostatistics at the University of Ibadan, Ibadan, Nigeria. The course is organized by the Department of Epidemiology, Medical Statistics and Environmental Health, College of Medicine, University of Ibadan. This course aims to train professional biostatisticians. The Programme's support to this course includes building capacity to strengthen the academic staff and enhancing computer facilities and library resources. Due to the late start of the course, the eight students who enrolled in the academic year 2002/2003 will complete the programme in March 2004.

Since its inception, the Programme has supported the training of 42 professional biostatisticians and epidemiologists. Of these, five were foreign students, all others were Nigerians. As part of follow-up activities, the Programme has compiled a directory of all graduates of the course and there are plans to form an Association of Biostatisticians for the African region.

### Training provided by the centres

Overseas training of staff from centres supported by the Programme was complemented by training programmes organized by the centres themselves for professional and technical staff from national institutions, including service providers. The 10 centres receiving research capacity strengthening support provided individual training to 77 staff from other institutions. A total of 291 fellows participated in formal courses and 672 persons attended short, group-learning activities, such as seminars and workshops, organized by these centres.

## DISSEMINATION OF RESEARCH FINDINGS

The Department sponsored a session on "Selected aspects of WHO's work in combating the HIV epidemic" at the 28<sup>th</sup> Congress of the South Africa Society of Obstetricians and Gynaecologists in Durban, South Africa, in April 2003. Three papers were presented, one on guidelines on HIV counsel-

ling and testing, one on microbicide research and development, and the third paper was on the management of STIs to reduce the risk of HIV/AIDS.

With the Programme's financial support, the African Reproductive Health Research Network (RESAR) organized a workshop on electronic communications in July 2003 in Lomé, Togo. Twenty-two participants, representing members of six national chapters of RESAR (Benin, Burkina Faso, Cameroon, Democratic Republic of Congo, Niger and Togo), were trained in techniques of electronic communications and data bases, creating web sites, electronic publishing and bibliographic search. As a major outcome, the RESAR web site was updated and an electronic journal "*Cahiers du RESAR*" was created.

During the reporting period, a total of 45 research articles (35 original papers and 10 review articles) were published and 14 books or book chapters were authored by staff from the 10 centres receiving research capacity strengthening support. Likewise, 40 presentations were made in national, regional or international scientific events.

## SUMMARY OF COUNTRY ACTIVITIES

During 2003, the Department collaborated with 47 institutions or research groups in 28 countries of the African and Eastern Mediterranean regions. A brief description of the main activities at country level is given in Table 8.2.

### Regional directories of reproductive health

An informal consultation on a reproductive health research directory in the Eastern Mediterranean region was held in WHO's Regional Office for the Eastern Mediterranean (EMRO) in August 2001. It was attended by the country coordinators of Egypt, Iran, Lebanon, Saudi Arabia and Syria, a representative of the United Nations Population Fund (UNFPA) and WHO secretariat from EMRO and headquarters. The data collection and the follow-up activities have been hampered by the insufficiency of funds. However, some activities were carried out in 2003. A reproductive health research network web site was created under the web site of EMRO. It aims to facilitate exchange of information and research-related experiences in the field of reproductive health between and within countries.

The design of the reproductive health research network consists of two components:

1. a comprehensive directory of governmental, private and nongovernmental institutes, scientific bodies, research agencies, advocacy groups, and organizations concerned with and involved in reproductive health research in countries of the Eastern Mediterranean region;

2. a searchable database about research activities conducted over a specified period of time (1995 to present).

### The African Reproductive Health Research and Training Network

A feasibility study conducted in 2001 identified the need to establish an African Reproductive Health Research and Training Network (ARHRTN). This would serve as an umbrella regional network that will link, coordinate and strengthen existing reproductive health research networks for the purpose of improving reproductive health in Africa. The African Network is affiliated with the African Health Research Forum and other relevant bodies.

In 2002, the Programme supported an interim Steering Committee meeting of African experts in the field of reproductive health to draft a constitution and a three-year workplan. The Steering Committee has 18 members representing the eastern, northern, southern and western regions in Africa and special groups. The Secretariat is based in the Reproductive Health Research Unit of the University of Witwatersrand in Johannesburg, South Africa.

Unfortunately, due to lack of funds, most of the activities planned for 2003 could not be implemented, and priority was given to fundraising activities.

## HIGHLIGHTS OF JOINT ACTIVITIES ON PROGRAMME ISSUES

A number of activities that were carried out in collaboration with other partners either within the Department or other international agencies are summarized in Table 8.3 below. Details of these activities are given in other chapters of this report.

## PLANNED ACTIVITIES

Activities planned for 2004 can be summarized under the following main lines of work:

- Through institutional development grants, support and maintain institutions currently collaborating with the Programme to enable them to undertake research projects relevant to their identified reproductive health needs and priorities.
- Promote and further strengthen regional research networks involved with such key issues as maternal health, adolescent reproductive health, FGM, infertility, cervical cancer and HIV/AIDS.
- Promote dissemination and utilization of tools developed by the Department through the Implementing Best

Practices initiative and the engagement of collaborating centres.

- In collaboration with other partners, continue and increase efforts to institutionalize operations research training in the African region.
- In collaboration with the Department of Health Action in Crises and other partners, continue to develop approaches for assisting countries in crisis.

Table 8.2. Summary of country activities in the WHO regions of Africa and Eastern Mediterranean

Country	TCC support and activities in the research centres
Benin	<p>Operations research on adolescents<sup>1</sup></p> <p>Team (Ministry of Health, research institution and WHO country office) participates in the operations research training initiative<sup>1</sup></p> <p><i>Small grant</i><sup>2</sup>—The Centre for Research in Human Reproduction and Demography (CERRHUD) of the Department of Obstetrics and Gynaecology, University of Benin, Cotonou:</p> <ul style="list-style-type: none"> <li>• provides statistical support to adolescent study in other countries<sup>1,2</sup></li> </ul>
Burkina Faso	<p>Team (Ministry of Health, research institution and WHO country office) participates in the operations research training initiative<sup>1</sup></p> <p>Obstetric sequelae of female genital mutilation (FGM)<sup>1</sup>—Centre Hospitalier National Yalgado Ouedraogo, Ouagadougou</p>
Cameroon	<p>Operations research on adolescents<sup>1</sup></p> <p><i>Small grant</i><sup>2</sup>—WHO Centre for Research in Human Reproduction, Université de Yaoundé, Faculté de Médecine et Sciences Biologiques, Yaoundé</p> <p>The African Network for Research in Reproductive Health (RESAR): organizes research methodology courses and develops manuals for French-speaking countries<sup>1</sup></p>
Chad	<p>Team (Ministry of Health, research institution and WHO country office) participates in the operations research training initiative<sup>1</sup></p>
Côte d'Ivoire	<p>Operations research on adolescents<sup>1</sup></p> <p><i>LID grant 1998–2002</i>—National Research Cellule on Reproductive Health in the National Institute of Public Health in Abidjan, member of RESAR:</p> <ul style="list-style-type: none"> <li>• collaborates actively with many national agencies on issues such as validating research protocols and planning courses on reproductive health</li> <li>• participated in the organization of an international symposium on “Gender, population and development in Africa”</li> </ul>
Egypt	<p><i>LID grant 1992–2002</i>—The Egyptian Fertility Care Society (EFCS) is an affiliate of the Egyptian Medical Association and its research network includes all University and Ministry of Health teaching hospitals</p>
Ethiopia	<p><i>LID Grant 1990–1994. New LID grant approved for 2003–2007</i>—Department of Obstetrics and Gynaecology, University of Addis Ababa, Addis Ababa:</p> <ul style="list-style-type: none"> <li>• organized a stakeholders meeting to identify national reproductive health research priorities</li> <li>• planning participation in project “Operations research on community and facility interventions towards improving maternal health”<sup>1</sup></li> <li>• preparatory work to participate in a multicountry research project on microbicides</li> </ul>
Ghana	<p>Obstetric sequelae of FGM<sup>1</sup>—Rural Help Integrated, Bolgatanga</p>
Guinea	<p>Operations research on adolescents<sup>1</sup></p> <p><i>LID grant approved for 2003–2007</i>—The Reproductive Health Research Cellule (CERREGUI) is part of the African Network for Research in Reproductive Health (RESAR):</p> <ul style="list-style-type: none"> <li>• the Partogram study “Impact of the use of partograph on the reduction of labour complications in rural area in the health centres of the administrative region of Kankan, in Republic of Guinea” was completed and the data analysis is ongoing</li> </ul>

<sup>1</sup> Activity reported in detail elsewhere in the report.

<sup>2</sup> Awarded, but not executed due to lack of funds.

Table 8.2. Summary of country activities in the WHO regions of Africa and Eastern Mediterranean (continued)

Islamic Republic of Iran	<p>Research on adolescent reproductive health<sup>1</sup>, Ministry of Health</p> <p><i>Small grant</i><sup>2</sup>—National Research Centre for Reproductive Health of Deputy Ministry for Research Affairs of Ministry of Health and Medical Education, Tehran</p>
Kenya	<p>Obstetric sequelae of FGM<sup>1</sup>—Kenyatta National Hospital, Nairobi</p> <p><i>Small grants</i><sup>2</sup>—National Centre for Research in Reproduction (NCRR) is composed of four units: the Department of Obstetrics and Gynaecology, University of Nairobi; the Reproductive Biology Unit in the Department of Animal Physiology, also at the University of Nairobi; the Institute of Primate Research of the National Museums of Kenya; and the Reproductive Health Research Unit (RHRU) of the Kenya Medical Research Institute (KEMRI)</p> <p>The Department of Obstetrics and Gynaecology, University of Nairobi:</p> <ul style="list-style-type: none"> <li>• is preparing proceedings of the 2002 regional workshop on “Management of infertility in developing countries”</li> <li>• participates in the “WHO Global Survey on Maternal and Perinatal Health”</li> </ul> <p>The Institute of Primate Research (IPR), Nairobi, submitted a proposal on a baboon model for HIV and steroid contraception, which was approved by the Programme, but could not be funded</p> <p>Re-entry grant for research project “Production and characterization of monoclonal antibodies against Baboon Endogenous Virus (BaEV) and retroviral-related antigens expressed in baboon placental villous tissue”, Institute of Primate Research (IPR), Nairobi</p>
Malawi	<p>The Centre for Reproductive Health, College of Medicine, University of Malawi, submitted an institutional profile with a view to applying for a LID grant</p>
Mali	<p>The Centre for Research on Population and Development (CERPOD) organized the operations research training programme for French-speaking countries, 2003–2005<sup>1</sup></p>
Mauritania	<p>Team (Ministry of Health, research institution and WHO country office) participates in the operations research training initiative<sup>1</sup></p>
Niger	<p>Team (Ministry of Health, research institution and WHO country office) participates in the operations research training initiative<sup>1</sup></p>
Nigeria	<p>Obstetric sequelae of FGM<sup>1</sup>—National Hospital for Women and Children, Abuja and University of Benin City Hospital, Benin City</p> <p><i>Small grants</i><sup>2</sup>—Department of Obstetrics and Gynaecology, University of Ibadan, Ibadan; Department of Obstetrics and Gynaecology, University of Benin, Benin City; Department of Obstetrics and Gynaecology, University of Jos, Jos; Department of Obstetrics and Gynaecology, University of Lagos, Lagos</p> <p><i>LID grant 1999–2003</i>—Centre for Research in Reproductive Health, College of Health Science, Ogun State University Teaching Hospital, Sagamu:</p> <ul style="list-style-type: none"> <li>• conducts community-based research in reproductive health</li> <li>• coordinates an ongoing national multicentre study to compare two doses of levonorgestrel for emergency contraception</li> <li>• conducted three workshops on andrology, operations research and research methodology</li> </ul> <p>Centres in Jos and Benin City are planning to participate in the project on “Operations research on community and facility interventions towards improving maternal health”<sup>1</sup></p> <p>M.Sc. course in Biostatistics<sup>1</sup>—Ibadan Department of Epidemiology, Medical Statistics and Environmental Health</p> <p>Emergency contraception study ongoing<sup>1</sup>—the seven collaborating centres are the Departments of Obstetrics and Gynaecology in the university teaching hospitals in Benin City, Enugu, Ibadan, Jos, Lagos, Port Harcourt and Sagamu (coordinating centre)</p> <p>Workshop on “Ethical issues in reproductive health”<sup>1</sup>, Department of Obstetrics and Gynaecology, University College Hospital, Ibadan</p>

<sup>1</sup> Activity reported in detail elsewhere in the report.

<sup>2</sup> Awarded, but not executed due to lack of funds.

Table 8.2. Summary of country activities in the WHO regions of Africa and Eastern Mediterranean (continued)

Oman	<p>Support for research on adolescent reproductive health, Ministry of Health, Muscat<sup>1</sup></p> <p>Support for Ministry of Health proposal development on “Integrated management of maternal and child health”</p> <p>Strategic Approach on a birth spacing programme<sup>1</sup></p>
Pakistan	<p><i>Small grants</i><sup>2</sup>—National Research Institute of Fertility Care (NRIFC), Ministry of Population Welfare, Government of Pakistan, Karachi; Reproductive Physiology Laboratory, Department of Biological Sciences, Quaid-I-Azam University, Islamabad</p>
Senegal	<p>Operations research on adolescents<sup>1</sup></p> <p>Obstetric sequelae of FGM<sup>1</sup>—Cheick Anta Diop University, Dakar</p> <p><i>LID grant for 1999–2003</i><sup>2</sup>—The Department of Obstetrics and Gynaecology at Le Dantec Hospital, University of Dakar, Dakar, and the International Centre for Training and Research in Reproductive Health (CEFOREP), which is attached to the Department:</p> <ul style="list-style-type: none"> <li>• continued research on postabortion care and on natural family planning</li> <li>• organized a research methodology course and a scientific writing workshop for its staff</li> <li>• CEFOREP provided support for statistics for the study “Operations research on improving reproductive health services for adolescents” in Cameroon</li> </ul> <p>Team (Ministry of Health, research institution and WHO country office) participates in the operations research training initiative<sup>1</sup></p>
South Africa	<p><i>Small grant</i><sup>2</sup>—Reproductive Health Research Unit (RHRU), Chris Hani Baragwanath Hospital, Johannesburg</p> <p>Research methodology course<sup>1</sup>—RHRU, Johannesburg</p> <p>Semenology course and quality control programme<sup>1</sup>—University of Stellenbosch, Cape Town</p> <p>Planning participation in “Operations research on community and facility interventions towards improving maternal health”<sup>1</sup>—RHRU, Durban</p> <p><i>LID grant 2001–2005</i>—Effective Care Research Unit (ECRU) in the Department of Obstetrics and Gynaecology of the East London Hospital complex which consists of Cecilia Makiwane Hospital in Mdantsane and Frere Hospital in East London:</p> <ul style="list-style-type: none"> <li>• focuses on clinical trials designed to answer questions of relevance to reproductive health</li> <li>• conducted workshops for labour ward staff in 24 districts of Eastern Cape on “Better Births” initiative to promote evidence-based, humane maternity care</li> <li>• prepared and continues to update more than 30 systematic reviews published in the Cochrane Library</li> <li>• participated in review and editorial work of <i>The WHO Reproductive Health Library (RHL)</i></li> <li>• contributed to the production of two teaching videos included in RHL</li> </ul>
Sudan	<p><i>Resource maintenance grant</i>—The Department of Obstetrics and Gynaecology, University of Khartoum, Khartoum:</p> <ul style="list-style-type: none"> <li>• has an active endocrinology/microbiology laboratory</li> <li>• published a book of abstracts of the clinical obstetrics and gynaecology theses of the postgraduate students</li> <li>• published proceedings of a workshop on “Women’s sexual and reproductive rights”</li> </ul> <p>Obstetric sequelae of FGM<sup>1</sup>—University of Khartoum, Khartoum.</p>
Syria	<p>Support for research on adolescent reproductive health, Ministry of Health<sup>1</sup></p>

<sup>1</sup> Activity reported in detail elsewhere in the report.

<sup>2</sup> Awarded, but not executed due to lack of funds.

Table 8.2. Summary of country activities in the WHO regions of Africa and Eastern Mediterranean (continued)

United Republic of Tanzania	<p><i>LID-grant 2003–2007</i><sup>2</sup>—The Kilimanjaro Christian Medical Centre, Centre for Reproductive Health Research (KCRHR), Moshi:</p> <ul style="list-style-type: none"> <li>• participates in study on “Impact of HAART during pregnancy and breastfeeding on MTCT and mothers’ health” (support provided for the research capacity component of the study)</li> </ul>
Togo	<p><i>Cellule de Recherche (CRESAR)</i> hosted the RESAR workshop on electronic communication<sup>1</sup> at the Centre SYFED, structure of the University Agency of the Francophony (AUF) situated at the University of Lomé</p>
Tunisia	<p><i>LID grant for 1998–2002</i>—The Centre for Research in Human Reproduction, Tunis, part of the National Office of Family and Population (ONFP):</p> <ul style="list-style-type: none"> <li>• initiated a project on diagnosis and management of high-risk pregnancy</li> </ul>
Uganda	<p><i>Resource maintenance grant</i>—The Department of Obstetrics and Gynaecology, Makerere University, Kampala:</p> <ul style="list-style-type: none"> <li>• collaborated extensively with many institutions at international level</li> <li>• planning participation in project “Operations research on community and facility interventions towards improving maternal health”<sup>1</sup>—Department of Obstetrics and Gynaecology, Mulago Hospital, Kampala</li> <li>• project “The Release Trial: a randomized trial of umbilical vein oxytocin versus placebo for the treatment of retained placenta”, postponed due to lack of funds—Department of Obstetrics and Gynaecology, Mulago Hospital, Kampala</li> <li>• planning to host the launch of the Implementing Best Practices initiative in East Africa</li> </ul>
Zambia	<p><i>Small grant</i><sup>2</sup>—The Department of Obstetrics and Gynaecology, University of Zambia, based in the Teaching Hospital in Lusaka:</p> <ul style="list-style-type: none"> <li>• submitted a proposal to conduct training of trainers workshop in 2004 using <i>The WHO Reproductive Health Library</i></li> </ul>
Zimbabwe	<p><i>Resource maintenance grant</i>—The Department of Obstetrics and Gynaecology, University of Zimbabwe, Harare:</p> <ul style="list-style-type: none"> <li>• organized a scientific-writing workshop for 10 participants from five countries in the region</li> <li>• conducted two workshops for multicountry project on cervical cancer screening by visual inspection with acetic acid</li> </ul>

<sup>1</sup> Activity reported in detail elsewhere in the report.

<sup>2</sup> Awarded, but not executed due to lack of funds.

Table 8.3. Activities carried out in collaboration with other teams within the Department or other international agencies

Department thematic group or collaborating agency	Activity	Countries participating in the activity
Controlling STIs/RTIs	Capacity strengthening in microbicide research	Ethiopia, Nigeria, Uganda
	Expanded safety and acceptability study of 6% cellulose sulfate	Nigeria
	Multicentre study on impact of HAART on mother's health and MTCT of HIV	Burkina Faso, Kenya, Tanzania
Making pregnancy safer	Making Pregnancy Safer initiative focus countries	Ethiopia, Mauritania, Mozambique, Nigeria, Sudan, Uganda
	Use of misoprostol in the third stage of labour	Egypt, Nigeria, South Africa
	Follow-up study of children whose mothers participated in the trial on "Magnesium sulphate for management of pre-eclampsia (MAGPIE)"	Nigeria (Ibadan and Sagamu)
	Preparation for Essential Care Practice Guide (ECPG) validation study. The study will be conducted in March 2004.	Sudan, Uganda
	WHO Global Survey on maternal and perinatal health	Algeria, Angola, Democratic Republic of Congo, Ethiopia, Kenya, Niger, Nigeria, Uganda
	Perinatal and neonatal mortality database	South Africa
Promoting family planning	Multicentre clinical trial on two implantable contraceptives for women: Jadelle and Implanon	Zimbabwe
Implementing Best Practice initiative (IBP)	Preparations are in progress for the launch of IBP in Africa in June 2004, in Kampala, Uganda	Ethiopia, Kenya, Tanzania, Uganda, Zambia
Preventing unsafe abortion	Proposals submitted to the Social Science Specialist Panel by various researchers from different institutions	Pakistan
WHO's Department of Health Action in Crises	Collaboration on various proposals relating to reproductive health in countries in crisis	Afghanistan, Democratic Republic of Congo, Iraq, Liberia
WHO Country Focus Initiative	Planning of Country Cooperation Strategies (CCS)	African and Eastern Mediterranean regions
Planning and programming in collaboration with AFRO	A training initiative in evidence-based reproductive health care	African region
Policy and programmatic Issues	Cofacilitation of the World Bank Institute (WBI) Programme in West Africa, including the preparation and delivery of the regional course on reproductive health and health reforms	Burkina Faso
	Participation in the expansion of the WBI Programme to English-speaking African countries	Ethiopia, Kenya, South Africa, Tanzania, Uganda, Zambia, Zimbabwe
	WHO Strategic Approach to reproductive health: Stages I, II and III	Ethiopia, Oman, South Africa, Zambia
	Planning for a follow-up to the English-speaking Africa regional workshop to disseminate information on the WHO Strategic Approach to improving the quality of care of reproductive health services	Malawi, Nigeria, Tanzania

Annex 1

**REGIONAL ADVISORY PANEL FOR THE AFRICAN AND EASTERN MEDITERRANEAN REGIONS IN 2003**

Asya Al-Riyami, Department of Research and Studies, Ministry of Health, Muscat, Oman  
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 Boniface Nasah, Society of African Gynaecologists and Obstetricians (SAGO), Buea, Cameroon  
 Babatunde Osotimehin, Social Science and Reproductive Health Network, University College Hospital, Ibadan, Nigeria  
 Christine Sekadde-Kigundu, Department of Obstetrics and Gynaecology, University of Nairobi, Kenyatta National Hospital, Nairobi, Kenya (*Chair*)  
 Christiane Wellfens-Ekra, Department of Obstetrics and Gynaecology, University Hospital Yopougon, Abidjan, Côte d'Ivoire

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	13	100					13
Women	6	46					6
<b>from:</b>							
AFRO	9	69					9
AMRO							
EMRO	4	31					4
EURO							
SEARO							
WPRO							

**Collaborating agency scientists**

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## Annex 2

**SCIENTISTS COLLABORATING IN 2003****African region**

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Emmanuel O. Wango, Reproductive Biology Unit, University of Nairobi, Nairobi, Kenya

K. Monique Wasunna, Centre for Clinical Research, Kenya Medical Research Institute, Nairobi, Kenya

**Eastern Mediterranean region**

Badar Uddin Abbasi, National Research Institute of Fertility Control, Karachi, Pakistan

Rim Ben Aissa, Research Centre for Human Reproduction, National Office for Family and Population, Tunis, Tunisia

Abdulaziz S. Gerais, Department of Obstetrics and Gynaecology, University of Khartoum, Khartoum, Sudan

Ezzeldin O. Hassan, Egyptian Fertility Care Society, Cairo, Egypt

Samina Jalali, Department of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan

Mohamed El Fadil Saad, Faculty of Medicine, University of Khartoum, Khartoum, Sudan

Sami Said, Department of Obstetrics and Gynaecology, Shatby Maternity Hospital, Alexandria, Egypt

Fahimeh Ramezani Tehrani, National Research Centre in Family Planning, Ministry of Health and Medical Education, Tehran, Islamic Republic of Iran

Annex 2 (continued)

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	37	100					37
Women	9	24					9
<b>from:</b>							
AFRO	29	78					29
AMRO							
EMRO	8	22					8
EURO							
SEARO							
WPRO							

# The WHO Region of the Americas

E. Ezcurra

## INTRODUCTION

Strengthening the research capacity of institutions in the WHO Region of the Americas was undertaken to enhance further their potential to implement reproductive health research relevant to national and regional needs and to facilitate their participation in the global research effort.

The main goals established by the Regional Advisory Panel (RAP) for the 2002–2003 biennium were: (i) to continue strengthening research capacity in Programme-supported collaborating institutions in the Americas region, by promoting and supporting the implementation of well-designed research projects in topics relevant to national and regional reproductive health problems; and (ii) to promote the dissemination and utilization of relevant research findings.

The fundamental strategies selected for attaining this goal are:

- implementation of regional and national reproductive health research and participation in the global research effort, particularly by strengthening regional and national research networks in basic reproductive biology, clinical/epidemiological investigations and the social sciences;
- development and strengthening of human resources; and
- increased dissemination of relevant research results to facilitate their adaptation and utilization in reproductive health programmes and services.

The main activities implemented under these strategies are described in the following sections.

## RESEARCH ACTIVITIES

The seven centres supported with research capacity-strengthening grants are involved in projects that address regional and national priorities. During the 2002–2003 biennium, from the overall number of 187 studies, 10 projects (5%) were implemented with support from the Programme's capacity building grants. A total of 97 projects were carried out at the centres with support from national sources (52%). The participation of the regional centres in the global research effort is exemplified by the 18 projects (10%) conducted in these collaborating institutions with support from thematic groups of the Department. Likewise, the institutional strengthening efforts deployed by the Programme in its regional centres have enhanced their ability to procure funding from other international agencies to address topics of global or local relevance. During 2002–2003, 62 projects (33%) carried out in these regional centres received support from international agencies other than WHO.

With respect to capacity developed to address research issues from different methodological approaches, it is worth noting that in 2002–2003, out of 187 research studies, 101 (54%) were epidemiological or social science projects. This is the first time ever that these types of projects account for more than half of all those undertaken at the centres being supported.

Ongoing projects supported by long-term institutional development grants include basic science work in the area of male fertility, an assessment to identify priority interventions that would improve access to and quality of family planning services, research on maternal and neonatal health care, and social science research in the area of male involvement in reproductive health. Maternal/infant health, family planning and sexual and reproductive health of adolescents were the

main thematic areas covered by projects being implemented in centres receiving resource maintenance grants.

### DEVELOPMENT OF HUMAN RESOURCES

Basic resources for training grants (BRT) were awarded to the Institute of Nutrition in Mexico City, Mexico, to the National Institute of Public Health, Cuernavaca, Mexico, and to the Centre for the Study of the State and Society (CEDES), Buenos Aires, Argentina, to support regional postgraduate courses in reproductive biology, in reproductive epidemiology and in the social sciences, respectively. In terms of individual support, 19 scientists from regional centres received grants in 2002–2003 to undergo training in different areas relevant to reproductive health. Table 8.4 summarizes the overall number of training grants awarded in 2002–2003 which were supported with funds from the regional budget. Among the 19 fellows who received grants for short- and long-term training, 15 (79%) were women and the training took place mostly (i.e. in the case of 10 trainees—53%) in centres located in Latin America.

Training abroad of staff from the supported centres was complemented by extensive training programmes organized by the centres themselves for professional and technical staff from national institutions, including service providers. In 2002–2003, the seven centres provided individual training to 847 staff from other local institutions. A total of 62 fellows completed formal postgraduate courses and 4006 attended short, group-learning activities such as seminars and workshops organized by the centres receiving research capacity strengthening support.

Table 8.4. Research training grants awarded in 2002–2003

Type of grant	Area	Number of trainees		Females		Males	
		2002	2003	2002	2003	2002	2003
M.Sc. Course	Reproductive epidemiology	1	1	1			1
M.Sc. Course	Social sciences	1				1	
M.Sc. Course	Health systems	1				1	
Diploma Course	Reproductive biology	3	2	3	2		
Workshop	Programme evaluation	2		1		1	
Workshop	Communication	1	3	1	3		
Workshop	Health sector reform and reproductive health		1		1		
Course	Molecular biology	1	2	1	2		
	<b>Sub-total</b>	<b>10</b>	<b>9</b>	<b>7</b>	<b>8</b>	<b>3</b>	<b>1</b>
	<b>Total</b>		<b>19</b>		<b>15</b>		<b>4</b>

### DISSEMINATION AND UTILIZATION OF RESEARCH FINDINGS

#### Scientific publications

During 2002–2003, a total number of 299 research articles (268 original papers and 31 review articles) were published and 77 books and book chapters were authored by staff from the seven centres receiving capacity strengthening support. Likewise, 467 presentations were made in national, regional or international scientific events and 43 official reports were presented to national and international authorities and agencies. Figure 8.1 shows the distribution of publications and presentations in national/regional and international journals and meetings.

#### Facilitating enhanced utilization of research findings

A national workshop on utilization of research findings took place in Buenos Aires, Argentina, on 9–10 December 2003. It brought together policy-makers, programme officers from federal and provincial levels, directors of the main maternity hospitals of the country and investigators from four Argentinean research institutions. The latter have a long-standing history of involvement in reproductive health research at national and international levels as well as an outstanding record of collaboration with the Department. The overall objectives of the workshop were:

- to optimize quality of services provided within the framework of the national reproductive health law;
- to promote evidence-based interventions in sexual and reproductive health services that also take into account the rights of women and men to receive information, in order to make informed decisions about their health without any coercion or violence;

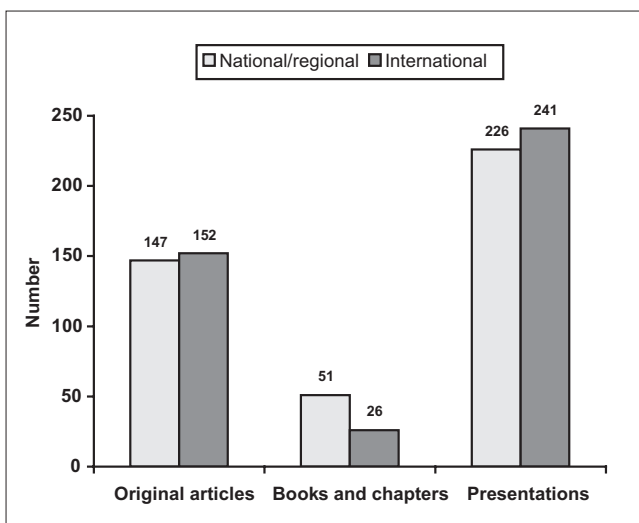
- to facilitate a closer interaction between researchers, policy-makers and heads of maternal and child services of hospitals from all over the country, in order to optimize the use of research results by programmes and services and to make researchers aware of what constitutes programmatically relevant research, within the context of national and local sexual and reproductive health needs.

The workshop, inaugurated by the Minister of Health of Argentina, was attended by 58 participants—47 health officers and 11 directors of maternity hospitals from all over the country, particularly areas where maternal mortality rates are high. Also present were a group of 15 Argentinean researchers from local WHO collaborating institutions and representatives from the regional and local staff of the Pan American Health Organization.

Given that reduction of maternal mortality and morbidity is of priority interest to the country, discussions centered on research results presented by local researchers who addressed the two main contributors to maternal mortality: hypertensive disorders of pregnancy and postpartum haemorrhage. The need to utilize a gender- and rights-based approach in sexual and reproductive health service provision was also highlighted and national research and research training experiences in this area were shared.

In-depth discussions were undertaken in plenaries and in small groups to identify barriers and facilitators to the use of evidence-based practices in the management of eclampsia, pre-eclampsia and postpartum haemorrhage. With the support of the Ministry of Health, a permanent line of communication between researchers and hospital directors, and sharing of electronic and printed information between participants, researchers and representatives of PAHO and WHO will be fostered. A follow-up plan was agreed upon that will assess in eight months' time the utilization of recommended practices by those participating in the workshop and the degree to which services offered to pregnant women have been optimized in these hospitals.

Figure 8.1. Publications and presentations in 2002–2003



## SUMMARY COUNTRY REPORTS

In 2002–2003, the Department collaborated with 18 institutions in ten countries of Latin America: Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Guatemala, Mexico, and Peru. A brief description of the main developments at country level follows.

### Argentina

Support has continued to the Centre for Perinatal Studies (CREP) in Rosario. CREP conducts research in the areas of maternal and infant health, adolescent health and reproductive health epidemiology, and serves as a training and research methodology referral centre for the country and the region. CREP staff has worked closely with Ministry of Health authorities to facilitate the utilization of research results by programmes and services.

The Centre for Population Studies (CENEP) in Buenos Aires was the coordinator and one of the study sites of the regional multicountry social science study on “Men’s perceptions and behaviour with respect to decision-making processes affecting sexual and reproductive health”. CENEP has also developed concept papers for future initiatives on other relevant topics.

The Institute for Experimental Biology and Medicine in Buenos Aires continues to develop basic sciences research in the field of male fertility.

The Centre for the Study of the State and Society (CEDES) in Buenos Aires organized the MSc Course in Social Sciences and is involved in several global research projects supported by the thematic groups of the Programme.

### Bolivia

Bolivian investigators associated with the Centre for Social Research, Appropriate Technology and Training (CISTAC), La Paz, participated in the four-country research initiative on “Men’s perceptions and behaviour in respect of decision-making processes affecting sexual and reproductive health”. The final country report was completed in February 2002 and plans for information dissemination and utilization are expected to be implemented in 2004.

### Brazil

The Centre for Research and Control of Maternal and Infant Disease (CEMICAMP) of the University of Campinas, Campinas, has been the main recipient of Programme support in the country. Grants cover work undertaken on training in research methodology and on research dealing with clinical epidemiology and social science issues relevant to contraceptive introduction and other aspects of women’s reproductive health. In 2003, CEMICAMP completed a Programme-supported study on counselling in family planning services.

## Chile

Two institutions in Santiago continued to receive support from other thematic areas of the Department: the Institute of Maternal and Child Health Research (IDIMI) and the Unit of Reproductive Biology and Development at the Catholic University of Chile. These centres participate in Programme-supported biomedical research on the mechanisms of action of emergency contraception preparations.

## Colombia

The Centre at the University del Valle in Cali received support from the Programme to take part in follow-up of children of mothers who took part in the "Magpie" Trial coordinated by Oxford University, Oxford, United Kingdom, that evaluated the use of magnesium sulfate for the treatment of pre-eclampsia.

## Costa Rica

The Central American Population Centre of the University of Costa Rica organized workshops on "Improving communication skills of researchers" and on "Programme evaluation", in which several fellows from Programme-supported centres in Latin America participated.

## Cuba

Support to activities in Cuba is channelled through the National Coordinating Network for Research in Human Reproduction, comprised of the National Institute of Endocrinology, the Hospital America Arias, the Ramon Gonzalez Coro Hospital and the National Centre for Sex Education (CENESEX).

The National Institute of Endocrinology's Social Sciences Unit implemented the four-country regional research initiative on "Men's perceptions and behaviour in respect of decision-making processes affecting sexual and reproductive health" and is also active in global research in the field of adolescent reproductive health. Dissemination of the findings of the study on men and plans for its utilization will be undertaken in 2004.

The Institute and the two Obstetrics-Gynaecology Hospitals that are members of the Network, are participating in two clinical trials concerned with improved non-surgical methods for pregnancy termination.

## Guatemala

The Guatemalan Research Group in Reproductive Health based at the San Juan de Dios Hospital, Guatemala City, received support mainly to develop a reproductive health research programme focused on the country's research priorities. During the reporting period, the final report of a strategic assessment which identifies priority interventions that would improve access to and quality of family planning,

maternal and neonatal care in Guatemala was produced. A draft proposal for Stage II action-research based on these findings was submitted for review.

## Mexico

The Department of Reproductive Biology in the National Institute of Medical Sciences and Nutrition, Mexico City, is the main recipient of Programme support in the country. The Institute is actively involved with the various thematic groups of the Department and other international funding agencies. In 2002–2003, the Institute continued to receive a basic resources for training grant to partially support its extensive participation in research training, particularly the Diploma Course on Reproductive Biology.

Another grant supports the two-year M.Sc. Degree programme in Reproductive Epidemiology organized by the National Institute of Public Health at its centre in Cuernavaca. Over the past 10 years, course graduates include students from Programme-supported centres in Argentina, Chile, Cuba, Guatemala, Mexico, Panama, Peru and Venezuela.

## Peru

The Programme supported two centres affiliated to the Peru University Cayetano Heredia in Lima which serves as a resource and training centre in reproductive health. Research carried out by the Institute of Research on Altitude, presently receiving a resource maintenance grant, includes studies in the areas of reproductive health of adolescents, reproduction at high altitude, and reproductive immunology.

The Faculty of Public Health was one of the sites of the four-country, regional social science research initiative on "Men's perceptions and behaviour in respect of decision-making processes affecting sexual and reproductive health". The study was completed and a national dissemination workshop is planned to take place early 2004. The Faculty also organized, for the first time in 2002, a Master's Degree Course in Sexual and Reproductive Health which was attended by national and foreign students.

## HIGHLIGHTS OF JOINT ACTIVITIES ON PROGRAMME ISSUES

A number of activities that were carried out in collaboration with other partners either within the Department or other international agencies are summarized in Table 8.5 below. Details of these activities are given in other chapters of this report.

## PLANNED STRATEGIES

One strategy identified as a top priority for the immediate future is the need to develop mechanisms to conduct research capacity strengthening activities in the least devel-

oped countries in the Americas. Follow-up activities to a site visit conducted in Paraguay in December 2002 advanced the implementation of the Strategic Approach (see page 213) in this country, effective in 2004, with support from an research capacity strengthening grant.

At its November 2002 meeting, the Americas Regional Advisory Panel awarded small grants to centres in El Salvador, Honduras and Nicaragua. Unfortunately, due to the Programme's financial constraints, these grants could not be implemented in 2003.

Special emphasis will continue to be placed on the dissemination and utilization of research findings, particularly of those resulting from national and regional research initiatives. Activities planned for Bolivia, Cuba and Peru in this area were postponed to 2003 due to the funding problems, but are expected to be re-initiated in 2004.

At the same time, if funding becomes available, the regional and subregional networks will launch new initiatives on topics of relevance to countries and to the region. One project, already at the stage of proposal review, is a study that explores providers' knowledge and attitudes on emergency contraception in Barbados and in Jamaica.

Table 8.5. Activities carried out in collaboration with other teams within the Department or other international agencies

Department thematic group or collaborating agency	Activity	Countries participating in the activity
Controlling RTIs/STIs	Study on contraceptive effectiveness of female condoms	Panama
	Field testing of STI/RTI Programme Guidance Tool	Brazil
Making pregnancy safer (MPR)	Follow-up study of children whose mothers participated in the trial on "Magnesium sulphate for management of pre-eclampsia (MAGPIE)"	Argentina, Colombia, Cuba
	The WHO randomized double/blind controlled trial of calcium supplementation during pregnancy of the prevention of pre-eclampsia	Argentina, Peru
	Preparatory activities of the WHO Global survey on maternal and perinatal health	Argentina, Brazil, Cuba, Ecuador, Mexico, Nicaragua, Paraguay, Peru
	Introduction of new WHO antenatal care model	Argentina, Brazil, Bolivia, Cuba, El Salvador, Haiti
	Randomized controlled trial evaluating strategies for routine screening and treatment of urinary tract infections during pregnancy	Argentina
	Validation studies of the "rapid assessment" and the "newborn examination chart" of the <i>Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice</i>	Brazil
Promoting sexual and reproductive health of adolescents	Participation in social sciences research initiative on this topic	Argentina, Brazil, Chile, Colombia, Cuba, Mexico, Paraguay, Peru
Promoting family planning	Multicentre clinical trial on two implantable contraceptives for women: Jadelle and Implanon	Brazil, Chile, Dominican Republic
	Phases I and II field testing of <i>Decision making tool for family planning clients and providers</i>	Mexico, Trinidad and Tobago
	Studies on mechanism of action of emergency contraceptives	Chile
	Study on HIV and steroid contraception	Brazil
Implementing Best Practices	Randomized controlled trial to evaluate evidence-based medicine based on the WHO Reproductive Health Library	Mexico
Preventing unsafe abortion	Randomized study of routine priming of the cervix with misoprostol prior to vacuum aspiration	Cuba
	Efficacy and safety of non surgical abortion with misoprostol	Cuba
Policy and Programmatic Issues	Strategic approach to reproductive health : Phases I, II and III	Bolivia, Brazil, Chile, Guatemala, Paraguay

Annex 1

**REGIONAL ADVISORY PANEL FOR THE AMERICAS IN 2003**

**Members**

Carlos Cáceres, REDESS Jovenes, Lima, Peru  
 Stella Campo, Hospital de Niños, Buenos Aires, Argentina  
 William Fraser, Laval University, Quebec, Canada  
 Ana Cristina González, Santafé de Bogotá, Bogota, Colombia  
 Sylvia R. Guendelman, School of Public Health, University of California, Berkley, CA, USA (*Chairperson*)  
 Luis Rosero Bixby, Universidad de Costa Rica, San Jose, Costa Rica  
 Silvia Salinas, La Paz, Bolivia  
 Jim Trostle, Trinity College, Hartford, CT, USA

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	5	63			3	38	8
Women	3	38			1	13	4
<b>from:</b>							
AFRO							
AMRO	5	63			3	38	8
EMRO							
EURO							
SEARO							
WPRO							

**Collaborating agency scientists**

Luis Bahamondes, Latin American Programme for Research and Research Training in Human Reproduction, Mexico City, Mexico  
 Roberto Rivera, Family Health International, Research Triangle Park, NC, USA  
 Raffaella Schiavon, The Population Council, Mexico City, Mexico

## Annex 2

## PRINCIPAL INVESTIGATORS OF CENTRES IN 2002-2003

Stella Campo, Endocrinology Research Centre (CEDIE), Buenos Aires, Argentina  
 Guillermo Carroli, Centre for Perinatal Studies (CREP), Rosario, Argentina  
 Horacio Croxatto, Chilean Institute of Reproductive Medicine (ICMER), Santiago, Chile  
 Patricia Cuasnicú, Institute for Biology and Experimental Medicine (IBYME), Buenos Aires, Argentina  
 Luigi Devoto, Institute for Maternal and Child Health Research (IDIMI), Santiago, Chile  
 Oscar Díaz, National Institute of Endocrinology, Havana, Cuba  
 Franklin García, Centre for Social Research, Appropriate Technology and Training (CISTAC), La Paz, Bolivia  
 Gustavo Gonzales, Peru University Cayetano Heredia, Lima, Peru  
 Ellen Hardy, Centre for Research and Control of Maternal and Infant Disease (CEMICAMP), Campinas, Brazil  
 Bernardo Hernández, National Institute of Public Health, Cuernavaca, Mexico  
 Edgar Kestler, Epidemiologic Research Centre, Guatemala City, Guatemala  
 Fernando Larrea, National Institute of Nutrition, Mexico City, Mexico  
 Carlos Moreno, Centre for Research in Human Reproduction, Panama, Panama  
 Edith Pantelides, Centre for Population Studies (CENEP), Buenos Aires, Argentina  
 Silvina Ramos, Centre for the Study of the State and Society (CEDES), Buenos Aires, Argentina  
 Oscar Rojas, University of Valle, Cali, Colombia  
 María Serón-Ferré, Pontifical Catholic University, Santiago, Chile

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	17	100					17
Women	6	35					6
<b>from:</b>							
AFRO							
AMRO	17	100					17
EMRO							
EURO							
SEARO							
WPRO							

# The WHO Regions of South-East Asia and the Western Pacific

K. Ba-Thike

## INTRODUCTION

In 2002, while endorsing research capacity-strengthening programmes at the various centres, the Regional Advisory Panel for Asia and the Pacific recommended a strategic shift away from encouraging basic research in reproductive health to promoting regional initiatives and networking among national centres. The objectives for 2003 were to strengthen the regional initiatives aimed at promoting the three main priorities set for the region: reducing maternal mortality, preventing unsafe abortion and addressing sexually transmitted and reproductive tract infections. The programme of work was guided by the framework set by the Regional Advisory Panel. However, some of the planned activities were postponed due to funding constraints.

## ACTIVITIES IN INSTITUTIONS RECEIVING RESEARCH CAPACITY STRENGTHENING GRANTS

Linkages were further strengthened between the Department and institutions in the Asian and Western Pacific region that have received research capacity strengthening grants over the years. In 2003, six centres in five countries received long-term institutional development grants. Also, four countries were awarded resource maintenance grants, which were to be shared by 13 institutions in those countries. One of the aims of institutional strengthening is to support the researchers and develop the institutions to reach a stage where they can generate research proposals independently and can compete effectively for funding from national and international sources.

The institutions that received these grants can be divided into two groups. The first category comprises those that have received substantial assistance and have collaborated with

the Programme for several years: these institutions can now be considered as mature centres. Many of them have been designated as WHO Collaborating Centres. Centres in China and India belong to this category, and both programme sustainability and financial viability have been demonstrated by these centres. The second group consists of institutions that are still in the phase of developing their capacities.

## Countries undergoing institutional capacity strengthening

The "developing" centres are at different stages of enhancing their capacity for research and training. Table 8.6 summarizes current activities in centres that are receiving their first or second cycles of research capacity-strengthening grants. The projects listed are those funded by the Programme. Some centres also conduct research in reproductive health supported by the Ministries of Health or other international sources, e.g. the Department of Medical Research, Myanmar, collaborates with the Population Council, Thailand, and the University of Colombo, Sri Lanka, collaborates with the Universities of Leeds and Sheffield, United Kingdom. The number of ongoing research projects related to reproductive health in each centre ranges from five to 15.

## China

Through the National Coordinating Board, eight centres received a resource maintenance grant. These are: the National Research Institute for Family Planning, Beijing; the Shanghai Institute of Planned Parenthood Research, Shanghai; the Peking Union Medical College Hospital, Beijing; the Institute of Population Research, Beijing; the Tianjin Municipal Research Institute for Family Planning, Tianjin; the Family Planning Research Institute of Zhejiang, Hangzhou; the Family Planning Research Institute of Sichuan, Chengdu;

Table 8.6. Summary of activities in institutions in the WHO South-East Asian and Western Pacific regions receiving research capacity-strengthening grants<sup>1</sup>

Country	Grants, institutions and activities
Indonesia	<p><i>First cycle LID grant</i>—Western Indonesia Reproductive Health Development Centre (WIRHDC), Faculty of Medicine, University of North Sumatra, Medan:</p> <ul style="list-style-type: none"> <li>• conducts research on emergency obstetric care in North Sumatra</li> <li>• participates in regional research initiatives</li> <li>• organized workshop on hormonal assay in infertility</li> </ul> <p><i>First cycle LID grant</i>—Reproductive Health Research Centre (RHRC), Airlangga University, Surabaya:</p> <ul style="list-style-type: none"> <li>• conducts research on: <ul style="list-style-type: none"> <li>– “Chlamydial lower genital tract infections in female adolescents in Surabaya”</li> <li>– “Chlamydial urethral infections in adolescent males in Surabaya”</li> </ul> </li> </ul>
Lao People’s Democratic Republic	<p><i>Second cycle LID grant</i>—Maternal and Child Health Centre (MCHC), Ministry of Health, Vientiane:</p> <ul style="list-style-type: none"> <li>• conducts research on prevalence of reproductive tract infections (RTIs) in antenatal clinic patients in two central hospitals in Vientiane</li> </ul> <p>Participation in regional research initiatives on adolescent reproductive health</p>
Mongolia	<p><i>Second cycle LID grant</i>—State Research Centre on Mother and Child Health and Human Reproduction, Ulaanbaatar:</p> <ul style="list-style-type: none"> <li>• conducts research on: <ul style="list-style-type: none"> <li>– incidence and risk factors for pelvic inflammatory disease following induced abortion</li> <li>– clinical aspects of vaginal discharge among prepubescent girls visiting the outpatient clinic of the Maternal and Child Health Hospital, Ulaanbaatar</li> <li>– mothers’ knowledge, perception and health-seeking behaviour related to their pre-pubertal daughters’ vaginal discharge</li> <li>– incidence of ectopic pregnancy in Ulaanbaatar and its association with chlamydial antigen in tubal tissues</li> <li>– performance of antenatal care syphilis screening</li> </ul> </li> </ul> <p>Participation in regional research initiatives on cesarean section and multicentre trials coordinated by the Programme</p>
Myanmar	<p><i>Second cycle LID grant</i>—Department of Medical Research, Lower Myanmar, Yangon:</p> <ul style="list-style-type: none"> <li>• conducts research on: <ul style="list-style-type: none"> <li>– non-ulcerative sexually transmitted diseases (STDs) among married women in selected urban and peri-urban areas in Yangon</li> <li>– social and behavioural dimensions of sexually transmitted infections (STIs) among adolescent clinic attendees</li> <li>– prevalence of reproductive tract infections (RTIs) at the family planning clinic at Central Women’s Hospital, Yangon</li> <li>– <i>Chlamydia trachomatis</i> and ectopic pregnancy in Yangon</li> </ul> </li> </ul> <p>Participation in regional research initiatives on cesarean section</p> <p>National workshop on research methodology for epidemiological research</p>
Sri Lanka	<p><i>RMC grant</i>—through National Coordination Committee for Research on Reproductive Health, Colombo, to Task Forces based in Universities of Colombo, Peradeniya and Ruhuna</p> <p>Five workshops organized to identify current research priorities in reproductive health and develop research project proposals and laboratory techniques in andrology</p>

<sup>1</sup> Research capacity strengthening grants were also awarded to some institutions in China and India.

Table 8.6. Summary of activities in institutions in the WHO South-East Asian and Western Pacific regions receiving research capacity-strengthening grants (continued)

Viet Nam	<p><i>RMC grant</i>—National Obstetrics and Gynaecology Hospital, Hanoi</p> <p>Participation in regional research initiatives on cesarean section and multicentre trials coordinated by the Programme</p> <p><i>Second cycle LID Grant</i>—Hung Vuong Hospital, Ho Chi Minh City:</p> <ul style="list-style-type: none"> <li>• conducts research on: <ul style="list-style-type: none"> <li>– prevalence of RTIs among women attending the family planning clinic of Hung Vuong Hospital, Ho Chi Minh City</li> <li>– prevalence of gonococcal, chlamydial, hepatitis B and syphilis infection among pregnant women attending Hung Vuong Hospital, Ho Chi Minh City</li> </ul> </li> </ul> <p>Participation in regional research initiatives on cesarean section, adolescent reproductive health and multicentre trials coordinated by the Programme.</p>
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and the National Evaluation Centre for the Toxicology of Fertility Regulation Drugs, Shanghai. The first seven centres are designated WHO Collaborating Centres. The focus of research in these centres has broadened from development of contraceptives and evaluating their safety and efficacy to other components of reproductive health and issues related to quality of care. These centres have conducted basic research on monoclonal antibodies, gene function, luteinizing hormone-releasing hormone antagonists; clinical research on reproductive tract infections, development of injectable contraceptives for men, vaginal ring, implant, and immunocontraception; qualitative research on sexual and reproductive health of adolescents and unmarried young adults; and social science research on informed choice and quality of care in family planning/reproductive health. In addition to research of national relevance, they collaborated in multicentre trials coordinated by the Programme. These centres serve as service guidance centres, and have participated in systematic reviews of commonly used oral contraceptives and currently used IUDs in China. They also offer Master's and Doctoral-level courses in reproductive health topics.

The Shanghai Institute of Planned Parenthood Research collaborated with the Department for the translation of *The WHO Reproductive Health Library*, to be further developed into a CD-ROM. The Department supported the National Coordinating Board in the implementation of the National Comprehensive (Reproductive Health) Programmes which comprise four comprehensive community-based components: (i) improving the quality of contraceptive care; (ii) reproductive tract infections interventions; (iii) healthy baby promotion; and (iv) integrated reproductive health services in Western China.

## India

In addition to research and training, the All India Institute of Medical Sciences (AIIMS), New Delhi, has coordinated activities on emergency contraception. Following the establishment of a consortium to obtain national consensus on

emergency contraception, training of trainers on emergency contraception was conducted in July 2003. The 73 trainers from 24 states will provide further training in their respective states.

Linkages were re-established with two centres in India, the National Institute for Research in Reproductive Health (NIRRH), Mumbai, and the Department of Obstetrics and Gynaecology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh. NIRRH conducts research on: safer fertility-regulating technologies, including medical methods for pregnancy termination; infertility; prevention of reproductive tract infections (RTIs) including sexually transmitted infections (STIs); maternal health; and menopause. It also offers Doctoral and short training courses. AIIMS and NIRRH participate in several multicentre trials coordinated by the Programme.

PGIMER conducts training on high-risk pregnancies and assisted reproductive techniques. In addition to reproductive health research, PGIMER carries out studies on herbal products for their microbicidal properties.

## Monitoring of research capacity strengthening activities

An evaluation was conducted of the Western Indonesia Reproductive Health Development Centre (WIRHDC), Faculty of Medicine, University of North Sumatra, Medan, and the network of centres in Sri Lanka (Universities of Colombo, Peradeniya and Ruhuna in Colombo, Kandy and Galle, respectively). A site visit was made to the National Institute for Research in Reproductive Health, Mumbai.

The following are some of the key recommendations made on the modalities of future assistance by the Programme. For WIRHDC, an 18-months "bridge grant" was recommended, which would be followed by an assessment of the Centre's work towards the end of 2004, to determine subsequent support. Another suggestion was that the Centre conducts

research focusing on a few national and regional priority areas already identified, namely maternal health and reproductive tract infections.

For Sri Lanka, the Programme will initiate the process of research capacity strengthening activities for new medical faculties in the Universities of Kelaniya and Sri Jayawardenapura and resume support to the University of Jaffna through the National Coordination Committee. A general recommendation was to use in-country expertise for technical assistance, both in the development of proposals and in conducting research. Identifying national consultants who could serve as “mentors” would be a practical and cost-effective alternative to external consultants.

Although site visits to some centres were postponed, monitoring of, and support to, centres was achieved, to a certain degree, through electronic communication. This was accomplished by the timely submission of reports by the institutions and through discussions with WHO country representatives, regional office reproductive health advisers and scientists from centres, both in-country and during meetings in Geneva.

## RESEARCH INITIATIVES

### National studies

National research initiatives have been conducted on the identified priority areas: reducing maternal mortality, preventing unsafe abortion, and controlling sexually transmitted infections and reproductive tract infections. The studies have been discussed in the previous section.

### Regional research initiatives

Regional research initiatives have been undertaken with the objectives of fostering multidisciplinary and/or multicentre scientific collaboration between centres, enhancing capacity building in reproductive health by incorporating research-based training in priority areas, and promoting networks and other arrangements to strengthen the centres' ability to enhance their effectiveness and efficiency.

The project on “Adolescent migrants and reproductive health in the Greater Mekong Region” was conducted in suburban areas of Kunming, Yunnan, China; Bangkok and its vicinity, Thailand; urban districts in Vientiane, Lao People's Democratic Republic; and Ho Chi Minh City, Viet Nam. A data

Table 8.7. Centres collaborating in the regional reproductive epidemiology research, “Patterns and predictors of Caesarean section in Asia”

Country	Institution
Bangladesh	Bangladesh Institute of Research for Promotion of Essential and Reproductive Health and Technologies, Dhaka
China	Family Planning Research Institute of Sichuan, Chengdu
Indonesia	Western Indonesia Reproductive Health Development Centre, University of North Sumatra, Medan Universitas Andalas, Padang, Sumatra
Mongolia	State Research Centre for Maternal and Child Health and Human Reproduction, Ulaanbaatar
Myanmar	Department of Medical Research, Lower Myanmar, Yangon
Nepal	Department of Community Medicine and Family Health, Institute of Medicine, Tribhuvan University, Kathmandu
Philippines	Philippine Heart Centre, Manila
Sri Lanka	The University of Kelaniya, Colombo
Thailand	Faculty of Medicine, Khon Kaen University, Khon Kaen Department of Obstetrics and Gynaecology, Prince of Songkla University, Hat Yai
Viet Nam	The National Obstetrics and Gynaecology Hospital (formerly Institute for Protection of Mother and Newborn), Hanoi Hung Vuong Hospital, Ho Chi Minh City

analysis workshop will take place in early 2004 and regional and national dissemination of results has been planned to ensure translation of findings into policies and programmes.

Data collection on the reproductive epidemiology project "Patterns and predictors of Caesarian section in Asia" has been completed in nine out of 13 centres (Table 8.7), and a data analysis workshop is planned in 2004.

### Multicentre studies

Research institutions in some countries in the region, notably, collaborating centres in China and India, and others in Thailand, have contributed significantly to the global research effort. In the past few years, institutions in Mongolia, Philippines and Viet Nam have collaborated with various teams from the Department. The body of research work falls into priority areas of the region, as well as those of the Department. Research projects include pregnancy-related research, including "Calcium supplementation for the prevention of pre-eclampsia among low-calcium-intake women", "Vitamins in pre-eclampsia: a multicentre randomized clinical trial of vitamins C and E supplementation in pregnancy for the prevention of pre-eclampsia", and "A double-blind, placebo-controlled, randomized trial to evaluate the effectiveness of a one-day versus seven-day regimen for the treatment of asymptomatic bacteriuria in pregnancy". Seven centres have

participated in research on post-ovulatory methods for fertility regulation that include comparisons of different routes, intervals, and regimens of misoprostol.

The centres have also been involved in the work of the Policy and Programmatic Issues group, i.e. the dissemination and utilization of the WHO Strategic Approach (see page 213) for specific areas of reproductive health.

The collaboration is summarized in Table 8.8. Other centres in the region from China, India, Philippines, Thailand and Viet Nam, that do not currently receive research capacity grants are also participating in these activities (not shown in the table).

## DEVELOPMENT OF HUMAN RESOURCES

### Research training grants

Research training grants have been awarded with the objective of strengthening institutions or centres in the development of human resources necessary to undertake research in priority areas in reproductive health, and to build up a critical mass of researchers who can address priority issues, needs and necessary interventions in reproductive health, and, thus, contribute to this field. All 10 mid-level trainees

Table 8.8. Collaboration between thematic areas and centres receiving research capacity strengthening grants

Thematic area	Topic	Countries (number of centres participating in the activity)
Promoting family planning	Intrauterine devices	China (6), Thailand (2)
	Methods for the regulation of male fertility	China (2)
Controlling STIs/RTIs	Safety and acceptability of 6% cellulose sulfate	India (1)
Preventing unsafe abortion	Post-ovulatory methods for fertility regulation	China (2), India (2), Mongolia (1), Viet Nam (3)
Making pregnancy safer	Pre-eclampsia	Viet Nam (2)
	Asymptomatic bacteriuria	Thailand (1)
Adolescent reproductive health	Reproductive and sexual health issues in adolescent and young adults, including migrant population in China	China (3)
Policy and programmatic issues	Stage I - Strategic assessment	Lao People's Democratic Republic (1), Myanmar (1), Mongolia (1), Viet Nam (1)
	Stage II - Testing of interventions	
	Stage III - Scaling-up of findings for policy development and wider implementation	

(four women, six men) who received grants returned to their institutions in 2002–2003 and are participating in current research at their respective institutions.

### Training programmes

Training programmes were also organized by the centres for programme staff and researchers from national institutes. The “mature” centres conduct training programmes for national and international trainees in their respective areas of expertise, ranging from reproductive toxicology, cellular and molecular biology, laboratory techniques, to reproductive endocrinology, to name a few. In China, in 2002, a total of 36 workshops and 13 small-group training activities were organized while 49 and 17 trainees were registered for Master’s and Doctoral courses, respectively. In 2003, a total of 41 workshops and 31 small-group training activities were conducted by all the centres.

## NETWORKING AND PARTNERSHIPS

In addition to the national and regional networks described previously, partnerships were promoted to strengthen centres developing their research capacity.

### Partnerships

Partnerships were forged between the Department and the Forum for Ethical Review Committees in Asia and the Western Pacific (FERCAP) for training researchers in ethical issues in research with a view to developing a group of regional trainers. Collaboration with the Population Council, Regional Office, India, was established for operations research training. Partnerships were initiated between the Department, the Fudan University School of Public Health, Shanghai, China, and the Geneva Foundation for Medical Education and Research, Geneva, Switzerland, to conduct training courses on reproductive health in China.

Controlling STIs and RTIs is a priority for the Asia-Pacific region, although there is limited in-country research capacity and data availability. Partnerships between six centres receiving research capacity-strengthening grants, and the Department and WHO Collaborating Centres were established to support STI/RTI prevalence studies in various settings. The objectives of this activity are to generate reliable laboratory-based data and to promote use of the data for decision-making. This will inform in-country programmes and services, help in the adaptation of WHO STI and RTI care guidelines and provide inputs for national estimates.

North-to-South networks were also maintained between the Prince Henry’s Institute of Medical Research, Melbourne, Australia, and the Shanghai Institute of Planned Parenthood Research, Shanghai, China. Collaboration for research training was initiated between the University of Ruhuna, Galle, Sri

Lanka, and the Institute of Reproductive Medicine, Westfalian Wilhelms University, Münster, Germany.

### Collaboration with WHO regional offices

A joint workplan between WHO headquarters and the WHO Regional Office for South-East Asia (SEARO) and the WHO Regional Office for Western Pacific (WPRO) was developed for 2003, but could not be fully implemented. The recommendation of the External Evaluation of the Programme—to involve the regional offices and utilize their resources and capacities—has been reflected in the workplan for 2004 which includes conducting site visits by the headquarters area manager and regional reproductive health advisers for the monitoring and evaluation of centres receiving support. To enhance translation of research findings into policies and programmes, the Department and the regional offices will jointly support workshops for the training of trainers for pregnancy, childbirth, postpartum and newborn care, and for regional workshops on the *Medical eligibility criteria for contraceptive use*. WPRO is coordinating the development of a proposal on ‘Risk factors and characteristics of women presenting with complications of abortion (Cambodia, Philippines, and Viet Nam)’. Collaboration with the Research, Policy and Co-ordination (RPC) Team from SEARO was established for the training of researchers in ethical and legislative aspects of international collaborative research organized by the National Institutes of Health (NIH), Bethesda, MD, USA, RPC/SEARO and the Indian Council of Medical Research (ICMR).

## FACILITATING UTILIZATION OF RESEARCH FINDINGS

As difficulties remain in implementing research findings in programmes, a recommendation by the External Evaluation of the Programme was to strengthen further efforts to ensure that research results are known to national and international policy-makers.

Research findings were disseminated to peers, programme managers and policy-makers through conferences, seminars and annual meetings of medical or obstetric and gynaecological societies, publications in local languages, and national and international journals. Some of the centres have been very successful in disseminating their research results. For example, between 2001 and 2002, research findings emanating from work at NIRRH were disseminated through 23 publications in international and national peer-reviewed journals, six presentations at international conferences and symposia, and 53 presentations at national meetings.

In 2002, the Chinese centres published 182 original articles in national journals, 16 articles in international journals, and 15 reviews; staff from these centres presented 64 papers at seminars. In 2003, centres in China published 219 original

articles in national journals and 46 in international journals. During the same year the three institutions in India had a total of 45 international and 22 national publications. This reflects the mature status of the institutions in China and India. Centres in other countries of the region, however, are still in the process of development and need continued assistance. The combined output of these centres for 2002 was six original publications (national), five original publications (international), 43 presentations (national), eight presentations (international) and one report. In 2003, these centres produced 57 original national publications and seven international publications.

Highlights of some of the activities related to dissemination of research findings in 2003 include:

- A symposium on Adolescent Reproductive Health was organized in Shanghai on 15–17 October to disseminate findings of projects on the reproductive and sexual health of youth and adolescents, including migrants. Policy-makers, managers, researchers, educators and journalists from different provinces and cities came to a consensus on the important and urgent need to provide sexual and reproductive health education and services for adolescents and unmarried youth.
- An international symposium on Expanding Contraceptive Choices: International and Indian Experiences and their Implications for Policies and Programmes was held in Mumbai, India, from 7–10 December by NIRRH.

### PROPOSED ACTIVITIES FOR 2004

Proposed activities for 2004 include:

- In collaboration with the Population Council, Regional Office, Asia, an operations research training workshop will be conducted for national teams of programme managers and researchers in order to enhance the linkage between research and programmes and to provide greater support to the health systems.
- In partnership with the Forum for Ethical Review Committees in Asia and the Western Pacific (FERCAP) researchers will be trained in ethical issues in research.
- Support will be provided to regional research projects with an emphasis on an equitable framework for cooperation between institutions involved in research.
- Assistance will be provided in the development of an enabling environment at country level to facilitate dissemination of research findings through conferences and symposia to promote and enhance the utilization of research results.

## Annex 1

## REGIONAL ADVISORY PANEL FOR ASIA AND PACIFIC IN 2003

## Members

Diana L.C. Galwaduge, Office of the Provincial Director of Health Services, Sangaraja Mawatha, Kandy, Sri Lanka

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Matthews Mathai, Christian Medical College Hospital, Vellore, Chennai, India

Than Than Tin, Central Women's Hospital, Yangon, Myanmar

Bencha Yoddymnern-Attig, Institute for Population and Social Research, Mahidol University, Nakhon Pathom, Thailand

Zheng Xiao Ying, Institute of Population Research, WHO Collaborating Centre for Reproductive Health and Population Science, Peking University, Beijing, China

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	7	88			1	13	8
Women	5	63					5
<b>from:</b>							
AFRO							
AMRO							
EMRO							
EURO							
SEARO	4	50					4
WPRO	3	38			1	13	4

## Temporary advisers

Azrul Azwar, Director-General, Community Health, Ministry of Health, Jakarta, Indonesia

Tran Thi Phuong Mai, Deputy-Director of Reproductive Health Department, Ministry of Health, Viet Nam

Takako Yasukawa, Health Specialist, Social Sectors Division, East and Central Department, Asian Development Bank, Manila, Philippines

Annex 2

**HEADS OF CENTRES FOR ASIA AND PACIFIC IN 2003**

**China**

Gao Ersheng, Shanghai Institute of Planned Parenthood Research, Shanghai  
 Ge Qingsheng, Peking Union Medical College Hospital, Beijing  
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**Indonesia**

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 Djafar Siddik, Western Indonesia Reproductive Health Development Centre, Medan

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**Mongolia**

Janchiv Radnaabazar, State Research Centre on Mother and Child Health and Human Reproduction, Ulaanbaatar

**Myanmar**

Soe Thein, Department of Medical Research, Lower Myanmar, Ministry of Health, Yangon

**Sri Lanka**

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**Viet Nam**

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 Nguyen Duc Vy, National Obstetrics and Gynaecology Hospital, Hanoi

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	19	100					19
Women	8	42					8
<b>from:</b>							
AFRO							
AMRO							
EMRO							
EURO							
SEARO	7	39					7
WPRO	12	63					12

# Central and Eastern Europe, including the Newly Independent States and Central Asian Republics

A. Ntabona

## INTRODUCTION

According to recent surveys<sup>1</sup>, women and men in most countries in the European region enjoy relatively low reproductive health risk. However, there are striking disparities between the market economies of the West and the transitional economies of the East. Some of the common features of countries of Central and Eastern Europe (CCEE) and Newly Independent States (NIS) include: (i) relatively early marriage and childbearing compared with women in Western Europe; (ii) reliance on repeat abortions (e.g. total abortion rate by age 45 up to 3.7 per woman in Georgia) as the means of preventing births, although there has been a recent decline in this practice as a result of the increased use of modern contraception; (iii) persistently high unmet needs for modern contraception, ranging between 22% of married women aged 15–49 in Kazakhstan and 53% in Azerbaijan; (iv) levels of maternal deaths up to five times higher than in the West, despite a universal coverage of care during pregnancy and childbirth, with complications from unsafe abortions being among the leading causes; and (v) emerging HIV/AIDS epidemic resulting from the explosion of sexually transmitted infections, intravenous drugs use, and an increasing transmission through sexual contact among young people and the growing number of sex workers. Growing concerns are expressed about the stalling or shrinking population size due to very low birth rates, ranging from 1.2 children per woman in Ukraine to 2.9 births per woman in Turkmenistan. As a result, some policy-makers consider family planning unnecessary or counterproductive. Most countries have undertaken some forms of policy reforms aimed at improving the responsiveness and stewardship of the health system by turning over parts of it to the private sector or to national insurance agencies. However, this resulted in some popula-

tion subgroups being either uninsured or left with minimal benefits. The impact of such measures on the effectiveness and quality of reproductive health services is under study.

## OBJECTIVES

The main objectives of the Department in the European region are:

- to strengthen national capacity in reproductive health research, with a particular focus on providing training opportunities for CCEE, NIS and Central Asian Republics (CAR);
- to assist the WHO Regional Office for Europe (EURO) in providing technical support to countries to implement their reproductive health programmes.

In this regard, among other major steps, the Regional Advisory Panel for the European region was formally established in 2001. It is responsible for fostering, guiding, monitoring and evaluating the technical cooperation activities supported by the Department and the Reproductive Health Programme in EURO with a view to strengthening the capabilities for research and programme development in reproductive health in the European member countries.

## PROGRESS

### Third meeting of the Regional Advisory Panel for Europe, 27–29 August 2003, Tallinn, Estonia

The deliberations of this third meeting evolved around three major issues: (i) research and research capacity building

<sup>1</sup> *Reproductive health trends in Eastern Europe and Eurasia*. Population Reference Bureau. Washington, DC, Policy Brief, 2003.

in the region; (ii) continued advocacy and information dissemination on sexual and reproductive health through the Regional Magazine *Entre Nous*; and (iii) support to EURO for the implementation of the regional strategy for sexual and reproductive health, including planning for the adaptation of the WHO course on *Transforming health systems: gender and rights in reproductive health*.

#### *Research development and research training*

The Panel commended EURO and the Department for organizing the first operations research training course for Russian-speaking countries in Almaty, Kazakhstan, in April 2003, in collaboration with the Population Council's FRONTIERS Project. The 20 participants in the course came from 10 countries: Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Ukraine and Uzbekistan.

Six proposals prepared as part of the research training were further refined and submitted to the RAP for review. The research themes included: audit in maternal and perinatal health; promotion of healthy behaviour in sexual and reproductive health for young people; fertility regulation methods; early detection of cervical cancer; and health systems policies. Three of these proposals were recommended to the Department for further review through the established mechanisms and possible funding.

#### *Reproductive health advocacy tool: regional magazine "Entre Nous"*

Inputs were requested from RAP on ways to ensure continued adequate funding for the regional magazine *Entre Nous* which, reportedly, has had significant impact on the dissemination of information on sexual and reproductive health in the region. The magazine has been published since 1982, three times a year, in six languages (average of 10,000 copies produced per issue); it is now available in English on the web. Until 2003, this project was mostly funded by the United Nations Population Fund (UNFPA). WHO funded the Russian edition, whereas the Bulgarian, Hungarian, Portuguese and Spanish versions were prepared and distributed by other donors, including Ministries of Health.

RAP proposed, and it was agreed, that the Editorial Advisory Board of the magazine should be expanded to include not only technical representatives from sponsoring agencies (WHO, UNFPA, the International Planned Parenthood Federation—IPPF), but also other people who may be willing to promote the magazine and give technical and substantive advice to its editors. RAP further encouraged the Secretariat to seek diversified sources of funding to keep the magazine alive.

#### *Programmatic issues*

RAP reviewed the progress reports on technical support provided by EURO to the implementation of the following regional priorities:

##### *Making Pregnancy Safer*

EURO continues to place emphasis on building capacity for adoption and adaptation by countries of WHO evidence-based policies and standards for maternal and newborn care. In this regard, model training courses for trainers were undertaken in Moldova, the Making Pregnancy Safer spotlight country in the European region. Selected health professionals currently involved in the development of clinical guidelines were introduced to the concept of evidence-based medicine in order to stimulate their skills in finding and critically appraising relevant research papers and in evaluating their implication for changing organizational and clinical practices. The adaptation of these concepts, using local languages such as Romanian, Russian, and others, remains a major challenge for the expansion of the model course.

##### *Gender and reproductive health*

Progress on gender mainstreaming in reproductive health and regional programmes was reviewed. Preparatory activities have been undertaken to adapt and organize the course on gender and rights in reproductive health (see chapter on Gender and reproductive rights in reproductive health). RAP suggested that this course should be used as an appropriate channel for raising awareness and providing guidance on how to address the serious and complex issue of women trafficking, in partnership with other United Nations agencies and one nongovernmental organization already working in this area in Eastern Europe, i.e. The Baltic Network Against Sexual Trafficking.

##### *Training in reproductive health*

Pending completion of the inventory of training institutions that offer courses on reproductive health in the region (delayed due to financial constraints), RAP reviewed and strongly supported the proposal submitted by the WHO Collaborating Centre in Uppsala University, Uppsala, Sweden, to establish an Internet-based distance-learning programme on "Quality improvement in perinatal care for Eastern Europe". This course could become a powerful tool for information exchange and sharing of experiences in the region.

#### **Capacity building in operations research in CCEE, NIS & CAR**

This is a collaborative initiative between the Department and FRONTIERS aimed at bringing research into reproductive health programme management in these countries. Continued support will be provided to investigators throughout all the research steps up to the reporting and dissemination

of findings. RAP recommended that one additional session of the operations research training course be organized for another group of Russian-speaking countries. A course evaluation could be carried out thereafter, to assess the course's effectiveness in shifting research approaches in beneficiary institutions/countries and its impact on the career development of former trainees. Opportunities would be sought for linking this initiative with the application of the WHO Strategic Approach (see page 213) for strengthening reproductive health policies and programmes in selected countries and, possibly, stimulate interest for undertaking programmatic research in the priority areas identified by RAP. These are: (i) sexual and reproductive health for young people; (ii) maternal and perinatal mortality and morbidity, including unsafe abortion; (iii) planning of families in the changing European environment; (iv) sexual violence; and (v) quality of care and gender mainstreaming as cross-cutting issues.

### **Postgraduate training course on reproductive medicine and reproductive biology, University of Geneva—WHO Collaborating Centre**

As in previous years, the Department co-organized the 11<sup>th</sup> session of the Postgraduate Training Course offered annually by the WHO Collaborating Centre, University of Geneva, Geneva, Switzerland. Thirty-one participants took part in the course. The stand-out innovation of this session is that the WHO Non-Communicable Diseases Cluster has joined as a new partner in the course. The first module on research methodology was given to all participants, who then chose one of two tracks depending on their interest, i.e. chronic diseases or reproductive health. Modules in the reproductive health track include, among others: basic sciences, genetics, family planning, infertility, gynaecological cancers, gender and ethics. The participants are requested to undertake a bibliographic search on selected topics, make an oral presentation and answer multiple-choice questions for the final

test. The Collaborating Centre is also exploring the possibility of decentralizing the course to places in Eastern Europe, Africa and Asia, through distance-learning.

## **PLANNED ACTIVITIES FOR 2004**

### **Research development**

In the follow-up to an initial review by RAP, at least three out of six proposals emanating from the Operations Research Course held in Almaty, Kazakhstan, will be submitted to the Programme for further review through existing mechanisms and approval for funding. Five of them have already been translated into English to facilitate the review process.

### **Research training**

Building on the experience gathered by the core group of trainers that facilitated the Kazakhstan course in April 2003, a second operations research training course will be organized for another group of Russian-speaking countries in 2004. Two to three candidates, including one scientist with a track record in research and one programme manager from central or district level, will be selected from each country.

### **Postgraduate course for training in reproductive medicine and reproductive biology, University of Geneva, Switzerland.**

Support to this course will continue in 2004, including the planned decentralization of the course to other regions through the adaptation of learning materials and distance-learning. Discussions are already ongoing between the University of Geneva and selected centres in Benin, Cameroon and China as partners for implementing this innovation.

## Annex 1

## REGIONAL ADVISORY PANEL FOR THE EUROPEAN REGION IN 2003

## Members

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Mihai Horga, Ministry of Health, Bucharest, Romania

Helle Karro, University of Tartu, Estonia (*Chair*)

Evert Ketting, Netherlands School of Public Health, Utrecht, Netherlands

Gunta Lazdane, Family Planning Association, Riga, Latvia

Alfred Merkle, Deutsche Gesellschaft für Technische Zusammenarbeit (GTZ), Eschborn, Germany

Saule Nukusheva, School of Public Health, Almaty, Kazakhstan

Petr Velebil, Research Institute for Maternal Health, Czech Republic

	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	1	11	6	67	2	22	9
Women	1	11	4	44			5
<b>from:</b>							
AFRO							
AMRO							
EMRO							
EURO	1	11	6	67	2	22	9
SEARO							
WPRO							

# Policy and programmatic issues

P. Fajans

## INTRODUCTION

The objectives of the Policy and Programmatic Issues Group are to review, develop and test methodologies for the planning and implementation of reproductive health services and to assist countries in the strengthening of their reproductive health policies and programmes. Central to this work is the testing, refinement and promotion of the strategic planning method known as the "Strategic Approach". This process has three stages.

Stage I is a strategic assessment based on a systems framework of (a) the needs and perspectives of current and potential users, (b) the extent of coverage, quality of care and capacity of the service delivery system, and (c) the mix of technologies and other reproductive health interventions. These assessments use a qualitative methodology and a field-based, participatory approach, involving programme managers, service providers, researchers, and others, including women's and youth organizations, which have an interest in improving reproductive health. A variety of recommendations emerge from a strategic assessment. Stage II is a means of testing, on a limited scale, the recommendations for policy change or other interventions to improve access, utilization and quality of care in service delivery. The purpose of Stage III is to disseminate and apply the findings from the Stage II action research for policy development and planning for wider implementation. The Strategic Approach has been used by 22 countries to address a variety of different reproductive health issues. In five of these countries, the process has been used more than once to address additional issues.

## MAIN AREAS OF WORK

Main areas of work on the Strategic Approach during 2003 included the dissemination and support for utilization of the strategy by countries, adaptation of the Strategic Approach to other areas of reproductive health and an increased focus on Stage III scaling-up of activities.

### Dissemination, advocacy and capacity building

A field guide entitled *Making decisions about contraceptive introduction: a guide for conducting assessments to broaden contraceptive choice and improve quality of care* was published in 2002. During 2003, work began on a new "core" document that will provide an overview of the underlying philosophy and framework of the Strategic Approach, in addition to guidance for generic implementation of all three stages of the approach. This will be supplemented by a series of shorter companion guides which will provide more focused information on adaptation of the methodology to address different specific issues in reproductive health. An initial draft of a companion guide on adaptation to address adolescent sexual and reproductive health was developed and will be field-tested in Nigeria.

In previous years, regional workshops to advocate for the utilization of the Strategic Approach and to train national experts in implementation of strategic assessments were implemented in collaboration with regional partners in Latin America, Asia and Africa. A comprehensive report of the African workshop was published in 2003. A similar workshop for countries in the European region was planned, but has been delayed until 2004 due to a shortage of available funds.

### Adaptation of the Strategic Approach

Work is continuing on the adaptation of the Strategic Approach to address other reproductive health issues. The Department has continued working with the Population Council's HORIZONS Project on the "Programme guidance tool for sexually transmitted and reproductive tract infections", an adaptation of the Strategic Approach to address policy and programme development related to reproductive tract infections (RTI) and sexually transmitted infections (STI) (see page 107). In 2003, a strategic assessment of issues related to abortion took place in Mongolia, while Stage II projects addressing abortion care, including postabortion contraception were developed in Romania, and were ongoing in Viet Nam. A strategic assessment addressing community-level issues in family planning and maternal and newborn health has been planned in Paraguay, while Malawi and Nigeria are planning to assess and revise their strategies on adolescent sexual and reproductive health services.

There is a growing recognition of the need for a methodology and tools to assist countries in strategic planning and programming for comprehensive integrated reproductive health services. In the past, strategic assessments that addressed a broad range of reproductive health concerns had been conducted in Ethiopia, Myanmar, and the Lao People's Democratic Republic. During 2002–2003, the Department, in collaboration with the International Council for the Management of Population Programmes (ICOMP) and the Population

Council office in Bangkok, Thailand, tested further modifications of the methodology in supporting a comprehensive reproductive health assessment that focuses on access and use of services by the poor in Yunnan, China. Planning with partners also continued in Rajasthan, India, to implement, in early 2004, a similar strategic reproductive health assessment focusing on the poor.

### Stage III: replication and scaling-up

In April 2003, a conference titled "From pilot projects to policies and programs: strategies for scaling-up innovations in health service delivery" examined and attempted to synthesize knowledge gained about the determinants of successful scaling-up of service delivery innovations from action research to broader policy and programme development. The conference discussed a background review of the literature and country case studies, highlighting lessons learnt about scaling-up from countries implementing the Strategic Approach. Discussions also centered on experience gleaned from projects in China and Ghana which had focused on studying scaling-up of pilot interventions. An overview of the discussions and the conference papers are being published in a volume which will provide input for programme managers and donors to help facilitate the scaling-up of pilot projects and other service delivery innovations. In addition, during the conference the participants formed a new network entitled "ExpandNet" which will bring together policy-makers, programme managers, researchers, and technical experts

Figure 8.2. Countries implementing the Strategic Approach (supported by WHO and by other partners) by end 2003



who will share experiences focusing on scaling-up activities. ExpandNet will provide technical support and promote research to understand better how to implement successful scaling-up of reproductive health innovations and interventions.

## COUNTRY EXPERIENCES DURING 2003

### Ongoing activities in the WHO African and Eastern Mediterranean regions

#### *Ethiopia*

The first of several planned Stage II activities has been the development of a project to test strategies to expand access to coitally-dependent methods of contraception and dual protection for youth. The project is being implemented by the Family Guidance Association of Ethiopia (FGAE), and is a response to findings from the assessment that sexually-active youth were not interested in using routine contraceptives, but desired coitally-dependent methods. The study is using the introduction of the female condom and emergency contraception, as well as the promotion of the male condom and vaginal foaming tablets, as a means for strengthening the overall quality of youth-centred services.

The positive results of a rapid evaluation of the project in 2003 has led FGAE to decide to use their own funds to continue repackaging and marketing emergency contraception tablets together with condoms and to expand key project activities into the control sites of the study. In 2004, FGAE will disseminate its experience within the context of a new initiative to mainstream emergency contraception services across Africa. Sponsored by the Population Council with funding from the Hewlett Foundation, the initiative will establish stakeholder groups in six African countries (including Ethiopia), each of which will develop strategies for introducing and/or mainstreaming emergency contraception availability. The groups will conduct strategic assessments focusing on the introduction of emergency contraception, and developing strategies and action plans for expanding access in their respective countries.

#### *Oman*

The Ministry of Health is leading the implementation of a strategic assessment intended to develop strategies to improve the quality of care in family planning services. The assessment field work will take place in early 2004.

#### *Zambia*

A Stage II study tested interventions to enhance contraceptive choice and quality of care in 11 rural health centres, located in three districts in the rural Copperbelt province of Zambia. The project introduced injectable contraceptives and emergency contraception, and offered training for providers in

all the available contraceptive methods and in the treatment of RTIs. This was supported by the development of provider self-training manuals, and newsletters to share management interventions and successful innovations among participating districts and health centres. An end-of-project evaluation showed that providers in project sites had better technical skills and provided more information to clients, resulting in a doubling of the number of new acceptors each month and a broadening of the method mix in the intervention health centres, as compared to baseline and to control sites.

In late 2002, a Stage III project to replicate the strategy and the lessons learnt in all health centres in all of the districts in the Copperbelt province commenced with funding from the United States Agency for International Development (USAID) and WHO and technical support from the Population Council office in Nairobi. The project, entitled "Pilots to regional programs (PRP) initiative," is utilizing innovative strategies to scaling-up that support the development of the districts' capacity to formulate individual implementation plans for introducing a common package of interventions developed in the Stage II project.

Thus far, PRP has seen major progress in each of its three key intervention areas: expanding contraceptive choice; applying innovative training approaches; and strengthening community/health sector linkages. In the case of expanding contraceptive choice, injectable contraception, female condom, emergency contraception and the new Standard Days™ approach to natural family planning have been introduced throughout the target area. PRP has also introduced a new tool to assist providers in standardizing criteria to monitoring the use of dual protection method.

For training purposes, PRP has implemented traditional "training of trainers," as well as a new self-directed learning curriculum. The curriculum is a distance-learning approach that health care providers, particularly rural providers, can use to master the key elements of family planning and reproductive health service provision. A comprehensive review of the curriculum and course found levels of provider performance to be equal to or better than graduates of the classroom course and the costs of the self-learning method to be 66% lower.

PRP has also forged new linkages between health centres and the communities they serve. These have included the establishment of community health committees, as well as groups of young people, unmarried women, and men who are not typically served through static facilities. Finally, PRP has involved respected community leaders as promoters of recommended health-seeking behaviours. These leaders include local chiefs, traditional marriage counsellors, and traditional healers.

In November 2003, the PRP initiative moved into its second phase, designed to allow each of the eight districts to assess their initial experience with PRP, and to plan for the scaling-

up of intervention activities during a third phase, to begin in 2004. All of the districts have undertaken "local" strategic assessments in which they: identify their strategic goals; identify and prioritize PRP interventions to realize these goals; formulate implementation plans for scaling-up relevant interventions; and identify the technical/financial support needed from the project to carry out implementation plans. The results of the assessments are being incorporated into each district's 2004 Action Plan, reflecting the district's operational priorities and unique circumstances.

### Ongoing activities in Asia

#### *China*

In 2001, the Department supported the implementation of a strategic assessment in Chongqing, China, that addressed the issue of contraceptive introduction, with an emphasis on intrauterine device (IUD) technologies available in the national family planning programme. Numerous important findings and recommendations emerged, including the need to: (i) strengthen providers' capacity to provide all contraceptive methods with improved quality of care and informed choice; (ii) reduce the number of types of IUDs provided in the programme and improve aspects of care related to both insertion and removal; and (iii) review the contraceptive products available with regard to their efficacy, the quality of their manufacture and/or their long-term safety.

Follow-up activities continued in 2003 with the conduct of systematic reviews of available data on the safety and efficacy of IUDs and hormonal contraceptive methods provided through the national programme. The results of these systematic reviews will be presented to national policy-makers in early 2004 to support their decision to select a reduced number of the safest and most effective products for provision. A proposal for a Stage II project to test a package of interventions recommended by the assessment to improve informed choice and quality of care for all methods has been developed and is undergoing review and refinement, prior to implementation in 2004.

In late 2002, the Yunnan Reproductive Health Research Association led a team representing a broad range of provincial-level stakeholders in the implementation of an assessment that addressed a range of reproductive health issues, with a focus on developing strategies to improve access, utilization and quality of services for the poor and marginalized groups, including ethnic minorities and urban migrants in Yunnan province. The findings and recommendations of the assessment team were presented and discussed at a dissemination workshop in early 2003. The findings highlighted the challenges resulting from the unexpected impact of recent health reforms on access to and utilization of reproductive health services both by the rural poor as well as by urban migrants from rural areas.

Based on the recommendations, proposals for three Stage II projects are being developed. The first will develop and test a model for the provision of quality comprehensive reproductive health services for urban migrants. The second will address STI/HIV/AIDS prevention for rural cross-border migrants, while the third project will test a revised version of the rural health insurance scheme in isolated rural communities so as to improve access to reproductive health services, including maternal health care for the poor. Technical support for these activities is being provided by ICOMP, the Population Council office in Bangkok and WHO, with financial support from WHO and the Rockefeller Foundation.

#### *Lao People's Democratic Republic*

In 1999, the Ministry of Health led a strategic assessment focusing on strengthening integrated reproductive services. Since then, many of the recommendations have been implemented with the support of a variety of international organizations, including the development of a Stage II research project that explores how reproductive health outreach services can be strengthened. In 2003, the project was initiated by the Maternal and Child Health Centre (MCHC). Activities include development of an integrated outreach plan, training of providers in the components of the outreach package, which includes contraception, maternal health care, the promotion of use of the newly developed maternity waiting homes and the strengthening of the capacity of the village health team. The activities include a research/evaluation component and complement and inform the WHO maternal waiting home and essential obstetric care project being implemented in two districts. Activities commenced in October 2003 with research-capacity building and data collection of baseline information.

#### *Mongolia*

During 2003, the Ministry of Health led the conduct of a strategic assessment of issues related to abortion in Mongolia. This activity is described in the chapter on Preventing unsafe abortion (see page 137).

#### *Myanmar*

An ongoing Stage II research project is developing and testing a district-level model for improving the quality of care of family planning and other reproductive health services. Project activities include: development of new information, education and communication (IEC) materials; curricula development and training for public sector health staff, private general practitioners, drug shop staff; a community advocacy component; and efforts to strengthen district-level health staff's management capabilities related to planning, supervision and logistics. The project is being implemented in two districts with differing geographical conditions, ethnic composition and reproductive health needs.

In late 2001, a mid-project evaluation was conducted, resulting in revisions to project training materials, as well as scaling-up of activities prior to the completion of the project. During 2002 and 2003, refresher training was provided to health staff in both the public and private sectors, including drug shop and pharmacy staff in the project districts. District staff has been engaged in reproductive health advocacy activities with community members in their villages. In addition, the provider training curriculum developed by the project has been used by the Ministry of Health (MOH) for training health staff in eight of the 17 States and Divisions of Myanmar. This was accomplished with UNFPA and WHO Myanmar project support. The Myanmar Medical Association has also used the curriculum to provide training to private general practitioners in 25 additional districts. The revised IEC materials developed by the project are also being adopted by the Ministry of Health and UNFPA for use in their project districts. The final component of the project currently being implemented is the development of a management training curriculum which will be tested in two project districts prior to its broader usage in other UNFPA-supported districts.

### *Viet Nam*

Viet Nam has gone through the three stages with regard to its initial activities concerning contraceptive introduction. A Stage II study assisted the Government to develop a strategy for introducing the injectable contraceptive depot-medroxyprogesterone acetate (DMPA), while at the same time strengthening the quality of family planning services for all methods. A Stage III project replicated the interventions tested, initially in 21 provinces, but by the end of the project, activities had expanded with Government support to over 50 provinces. During 2003, expansion reached all provinces in Viet Nam.

The Ministry of Health is also implementing a project to follow up the recommendations of a second strategic assessment, which focused on issues related to reducing the recourse to abortion and improving the quality of abortion care. This project is described in the chapter on Preventing unsafe abortion (see page 136).

## **Ongoing activities in Eastern Europe**

### *Romania*

Activities are focusing on reducing the recourse to abortion and improving the quality of care of family planning and abortion services. They are described in the chapter on Preventing unsafe abortion (see page 136).

### *Moldova*

The Ministry of Health in Moldova has requested technical assistance in conducting a strategic assessment of issues related to abortion care in 2004. Country activities are expected to be funded by the Open Society Institute, New York, NY, USA.

## **Ongoing activities in Latin America**

### *Bolivia*

A Stage II study attempted to strengthen family planning and related reproductive health service delivery, while introducing DMPA, in the Departments of La Paz and Santa Cruz. Interventions focused on provider training, strengthening the management of services, and the development of community participation in guiding service delivery.

Lessons learned and materials developed through the project are now being used by the Ministry of Health in the broader introduction of DMPA, supported by the United Kingdom Department for International Development (DFID), with technical assistance provided by the Population Council office in Brazil. In a closely linked activity, the "Reprolatina project," a partnership between the nongovernmental organization Reprolatina, the University of Michigan and the Population Council office in Brazil with funding from the Bill and Melinda Gates Foundation, is assisting the Ministry of Health in developing training capacities in the Department of Santa Cruz as a model to support expansion and scaling-up of project activities focusing on improving quality of care throughout the country. All Strategic Approach partners have been providing technical assistance to WHO-supported Strategic Approach activities in Latin America since their inception.

### *Chile*

A previous strategic assessment focusing on the need for contraceptive introduction in Chile demonstrated that although overall reproductive health indicators were relatively good, the service system was weak in various dimensions of quality of care and lacked training capacity in contraceptive and related reproductive health services. During 2003, the Reprolatina Project collaborated with the Ministry of Health in building training capacity through the creation of three training centres which are expected to provide regional training in reproductive health service systems and, subsequently, to other regions of the country.

### *Brazil*

The Brazil Stage II project had demonstrated that expansion of reproductive choice could be undertaken at the municipal or district level within existing resource constraints. The Stage III project tested the replicability of activities in four additional municipalities. Efforts to expand and replicate activities in 12 additional municipalities in the North and South of the country are continuing through the Reprolatina Project. The project concentrates on building training capacity through the establishment of training and educational centres. Such centres have thus far been created in eight municipalities. The adolescent programme of the Reprolatina Project, developed during the Stage II research phase, has now expanded to a second municipality in 2003.

### Guatemala

The Ministry of Public Health and Social Welfare of Guatemala had previously collaborated with the Department to implement a strategic assessment to identify priority interventions that would improve access to and quality of family planning and maternal health services, with emphasis on emergency obstetric care. The assessment report was published by the Pan American Health Organization (PAHO) in 2003 and a proposal for action research to test interventions to improve access to and quality of family planning and other reproductive health services is under development.

### Paraguay

A team led by the Ministry of Health developed plans for a strategic assessment of issues related to maternal and neonatal health and family planning, with a focus on the community level. A proposal was approved but the assessment fieldwork was subsequently postponed due to the unavailability of funds. The fieldwork is now scheduled for early 2004 and will be supported by the Department, in collaboration with the Reprolatina Project and PAHO.

## EXTERNAL QUALITY ASSESSMENTS OF REPRODUCTIVE HEALTH SERVICES

A background document reviewing lessons learnt in the implementation of External Quality Assessments (EQAs), as a means to improve and ensure the quality of care of reproductive health services, was completed. A consultant reviewed the literature on the utilization of external and/or independent assessment processes, including accreditation, for quality improvement of reproductive health services. Twelve case studies of reproductive health services which had undergone an EQA process using explicit standards and indicators were also developed to offer insight into the use and impact of EQAs from the perspectives of service providers, clients and stakeholders. In 2004, discussions with the WHO regional offices and with the Department of Health Service Provision (OSD) will take place, so as to gain further understanding of such processes and to support the use of such processes and tools for improving the quality of reproductive health services.

## UNFPA/WHO/ILO-STEP/ UNICEF PROJECT ON QUALITY OF CARE

The Department has continued to be a partner in the UNFPA/WHO/UNICEF/ILO-STEP project "Improving the quality of sexual and reproductive health care through empowering users". The project is addressing whether the organization of community demand can influence the quality of reproductive health care and, if so, what mechanisms can be used to increase effectively the capacity of communities to influence the way reproductive health care is delivered.

The project is ongoing in six countries: India, Kyrgyzstan, Mauritania, Nepal, Peru and Tanzania. In each country, action research projects are examining the impact of different approaches, including empowerment of women's groups and development of community insurance schemes, on strengthening demand for quality reproductive health services. The Department is providing technical assistance to activities in Kyrgyzstan and Nepal.

In Kyrgyzstan, the pilot study began in 2003 in nine villages in two districts. The project has provided training for service providers at all levels in the two districts, created community initiative groups in the nine villages, and provided basic equipment and supplies to village health centres and the community groups. It developed a curriculum on reproductive health, counselling, communication and relationship skills, and action plans and proposals. This curriculum was then used to train health providers, teachers and community groups. Community dialogue on sexual and reproductive health began in each of the project sites, as did the development of community self-help initiatives.

In Nepal, the project assisted the Government in the development of a national strategy for the quality of care of reproductive health services. Following a needs assessment in Saptari district in eastern Nepal, a pilot intervention study began in five villages. The project has begun training health care providers in the provision of reproductive health services and is developing mechanisms for dialogue and action between community groups, service providers and the district health management system.

## THE IMPACT OF HEALTH REFORMS ON REPRODUCTIVE HEALTH

In recent years, health reforms have been promoted as means of improving effectiveness, efficiency, quality, equity, and financial soundness. Typically, reforms have involved significant changes in the financing, payments, organization, and regulation of health systems. These broad system changes can have important influences on sexual and reproductive health programmes and pose challenges to the development of interventions to promote and ensure reproductive health. There is a need to understand better the impacts of various types of health reforms on access to, utilization of and quality of reproductive health services, as well as on reproductive health outcomes and on the sexual and reproductive health rights of individuals. This increased understanding is critical to providing proper guidance to countries undertaking reforms of their health systems. A three-year research initiative to examine the interaction between health reforms and reproductive health was developed to begin implementation in 2003.

The first phase of this initiative was to undertake a review of existing knowledge and identification of existing key gaps. This has been undertaken in collaboration with a South

African nongovernmental organization, the Women's Health Project of the University of Witswatersrand, in their project entitled "Sexual rights and reforms". This project brings together members of nongovernmental women's health organizations from Africa, Asia and Latin America. This initiative aims to strengthen understanding among activists and decision-makers of the role of health sector reform in facilitating or undermining efforts to achieve sexual and reproductive rights and health policies and programmes. It also aims to identify and advocate for strategies to improve outcomes with regard to sexual and reproductive health and services. The project has developed regional and global reviews of the literature and experiences on a series of key issues concerning the impact of health reforms on sexual and reproductive health and rights. The reviews were presented and discussed at an expert consultation, so as to identify knowledge gaps and develop an agenda for research and advocacy on these issues. During 2004, WHO will support limited research to address key priority issues identified in the literature reviews and in the consultation.

## POVERTY AND REPRODUCTIVE HEALTH

The Department has continued work documenting the relationships between poverty and reproductive health. Initial activities have focused on efforts to document the relationships between poverty and maternal and neonatal health, described more fully in the chapter on Making Pregnancy Safer (see page 91). In addition, efforts are under way to adapt the Strategic Approach methodology to focus on policy and programme development to promote access to and utilization of quality services for the poor. Initial testing of this approach is ongoing in Yunnan (People's Republic of China) and Rajasthan (India).

## Annex 1

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	10	100					10
Women	6	60					6
<b>from:</b>							
AFRO	2	20					2
AMRO	1	10					1
EMRO							
EURO							
SEARO	3	30					3
WPRO	4	40					4

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	30	57	12	23	11	21	53
Women	20	38	5	9	5	9	30
<b>from:</b>							
AFRO	6	11					6
AMRO	6	11			9	17	15
EMRO	1	2					1
EURO			12	23	2	4	14
SEARO	5	9					5
WPRO	12	23					12

**Annex 2**

**PUBLICATIONS IN 2003**

Population Council. Africa regional workshop on the WHO strategic approach to improving the quality of reproductive health care services. Nairobi, 2003.

Romanian College of Physicians and Romanian Society of Obstetrics and Gynaecology. *Standards and practice recommendations for performing elective pregnancy termination*. Bucharest, Romanian Ministry of Health and Family, 2003.

# Implementing best practices

M. Gülmezoglu, M. Usher-Patel, J. Villar, A. Shah, S. Monaghan

## INTRODUCTION

The Department publishes many evidence-based guidance documents and the challenge is not only to generate and synthesize evidence, but also to find innovative ways of translating this knowledge into practice in resource-constrained settings. Changing practice requires a systematic approach that involves health professionals in the decision-making process and enables them to drive change from within the system. Moreover, there is a need to support consistently the transfer and exchange of explicit evidence-based knowledge. However, new knowledge must be easily accessible and presented in a way that builds on previous experience. The Department works with countries to design approaches that support access to knowledge, so they can adapt and apply the knowledge to meet their specific needs. This requires systems that increase in-country capacity to access, interpret, critically appraise and apply the evidence.

The communication of research findings and evidence-based guidance to target populations for uptake and utilization is a major challenge. Strategies that support the transfer of knowledge and bring change in practice are of particular importance in this context. These strategies are often complex interventions where a series of activities are packaged together to address the different institutional, organizational and individual barriers-to-change with the aim of improving practices and the quality of reproductive health.

To address the issue of knowledge generation, synthesis, dissemination, access and utilization, the Department is working on two major projects:

1. The “Programme to Map Best Reproductive Health Practices” aims to generate up-to-date good quality evidence through rigorously conducted research, summarize it through systematic reviews, disseminate it and build capacity in evidence-based medicine in countries to enable decision-makers to make the best use of it.

*The WHO reproductive health library (RHL)* is a major component of this project. It is recognized as the leading resource for evidence-based reproductive health knowledge.

2. The WHO-led “Implementing Best Practices (IBP) initiative” is a global collaborative effort, involving 20 partner agencies, to support the development of local strategies to disseminate, adapt and use evidence-based practices, materials and tools. IBP partners work with country teams of health professionals from the Ministry of Health, international and local nongovernmental agencies, grass roots organizations, the public sector and professional bodies to support the transfer and exchange of evidence-based information and the sharing of country experience and lessons learnt.

The initiative responds to the information needs of key stakeholders in each country to work out how they can build on existing programmes, harmonize approaches, and reduce duplication of effort and work collaboratively to introduce best practices that will accelerate progress towards the common reproductive health goals.

## THE WHO PROGRAMME TO MAP BEST REPRODUCTIVE HEALTH PRACTICES

### Research activities

#### Objectives

The overall objective of this activity is to generate evidence to guide future strategies to improve practices. Specifically, the aim is to determine whether electronically-provided, up-to-date information on the effectiveness of health care interventions presented through an active dissemination strategy actually changes clinical practice.

#### Progress

The randomized controlled trial to evaluate a programme promoting evidence-based medicine based on *The WHO reproductive health library* (RHL) has been completed. Data entry, queries and data cleaning are ongoing and the final analysis will be completed by mid 2004. A manuscript describing the methodology of the trial is in press and another describing baseline clinical practices is being prepared. A meeting to discuss the initial analysis of results is scheduled for early 2004.

The Department is participating in several knowledge management and utilization projects within and outside WHO. In 2003, a survey of major health care journals was conducted in collaboration with the Population Council to evaluate the possibility of bias in publishing studies reported from developing countries.

### Research synthesis

#### Objectives

Systematic reviews locate, appraise and synthesize evidence from scientific studies in order to provide informative empirical answers to scientific research questions. In addition, by identifying what is known and not known, they are an invaluable first step before carrying out new primary research. Systematic reviews on the effectiveness of practices are conducted through the Collaborative Review Groups of the Cochrane Collaboration, while those addressing other epidemiological questions are conducted independently.

#### Progress

In 2003, systematic reviews were conducted in all major areas of reproductive health (Table 8.9).

The Department continues to work closely with Cochrane Review Groups and Cochrane Centres in both Cochrane systematic reviews and capacity strengthening activities by providing technical support to reviewers. The Department is initiating a plan of work to harmonize the *WHO List of Essential Medicines* and the list of essential reproductive health medicines agreed by the Department and the United Nations Population Fund (UNFPA) through appraisal of existing evidence; the Department is also conducting systematic reviews where necessary.

### Dissemination of evidence-based reproductive health care information: *The WHO reproductive health library*

#### Objectives

*The WHO reproductive health library* (RHL) aims to provide health care workers in developing countries with a free-of-



Figure 8.3. RHL in English and Spanish

Table 8.9. Distribution of systematic reviews by topic area (2003)

Topic area	New reviews	New protocols	Updated reviews
Maternal and perinatal health	-	5	10
HIV/AIDS/STI	1	-	1
Fertility regulation (including unsafe abortion)	2	-	2
<b>Total</b>	<b>3</b>	<b>5</b>	<b>13</b>

charge source of up-to-date evidence-based synthesized information on reproductive health care interventions (Figure 8.3). Published as an annual electronic review journal, RHL focuses on global reproductive health problems of high priority. It includes Cochrane systematic reviews, each supplemented by commentaries (including advise/opinion on practice implications of findings of each review); the commentaries are prepared by experts from developing countries or individuals with extensive knowledge of the conditions of practice in those countries. RHL is the product of collaboration between the Department and the Cochrane Collaboration.

*Progress*

*Contents*

In 2003, RHL No. 6 was published in English and Spanish. The contents were expanded significantly. Highlights are:

- Updates: 14 Cochrane reviews were updated together with their corresponding commentaries and practical aspects.
- New reviews: 10 new reviews were included, bringing the total to 79.
- The research and research synthesis methodology section included an article on advantages of large, simple, randomized controlled trials and an entire section on the conduct and analysis of randomized controlled trials published in *The Lancet* earlier in 2002.
- Implementation aids: These are tools to facilitate the implementation of effective, beneficial practices. In addition to two videos—one on the technique of external cephalic version and the other on the benefits of companionship during labour—a detailed description of how to implement the new WHO Antenatal Care Model and a presentation on how to administer magnesium sulfate to women with eclampsia are included. Links to the documents used in the Better Births initiative, including a PowerPoint presentation about the project, are also included in this issue. In 2003, a video describing Caesarean section techniques was recorded and will be published in RHL No. 7 in 2004.

A small questionnaire was inserted in the CD-package of RHL 6 in an attempt to assess the usefulness of the contents. Between April and November 2003, 219 responses were received. In general, systematic reviews, commentaries and implementation aids are regarded as “most useful”.

*Dissemination*

*Subscriptions and other mail distribution:* Initially, RHL was mailed to selected groups in the Department’s and the WHO library’s newsletter mailing lists, encouraging the recipients to subscribe to ensure continued access. These general

mailings have been gradually reduced and currently the majority of RHL users are subscribers. The free-subscription system has substantially facilitated access to RHL in developing countries. The print run of the CDs (Figure 8.4) and the number of subscribers (Figure 8.5) continue to increase.

*Active dissemination:* Conference presentations and WHO meetings serve the purpose of raising awareness about RHL and evidence-based medicine. RHL presentations and workshops are conducted by the Department, RHL regional editors and collaborators within the Programme’s Maternal and Perinatal Health Research network. Table 8.10 shows the list of presentations/workshops conducted in 2003.

*Translations*

The Centre Rosarino de Estudios Perinatales (CREP) in Rosario, Argentina, has produced state-of-the-art translations of RHL. CREP developed a translation model that can be duplicated for other languages as well. The high-quality translation software allows the combination of human translation skills with leading translation memory technologies.

The Shanghai Institute of Planned Parenthood Research (SIPPR), Shanghai, China, was requested in 2002 to develop the Chinese version of RHL. Unfortunately, the work by SIPPR to publish RHL in Chinese during 2003 had to be postponed due to the Programme’s financial difficulties. However, efforts to raise funds to complete the Chinese version as well as to produce a French version of RHL are continuing.

**Capacity building in evidence-based reproductive health care**

In Africa, a “Making evidence-based decisions in reproductive health care” training programme was initiated jointly with the WHO Regional Office for Africa (AFRO) and the South African Cochrane Centre (SACC) in Cape Town, South Africa.

Figure 8.4. RHL print volume since 1997

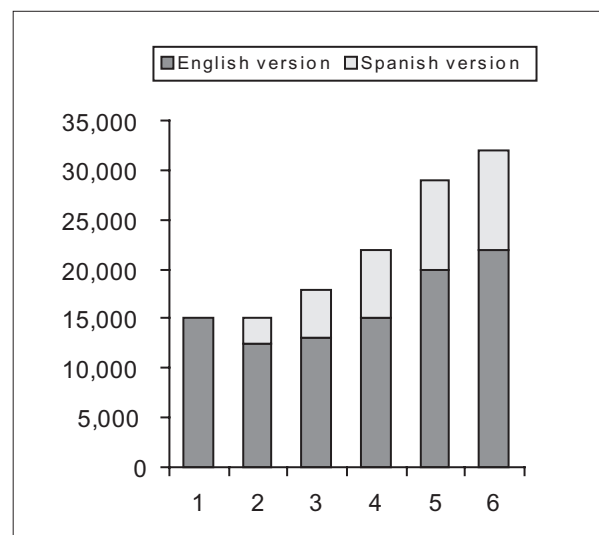
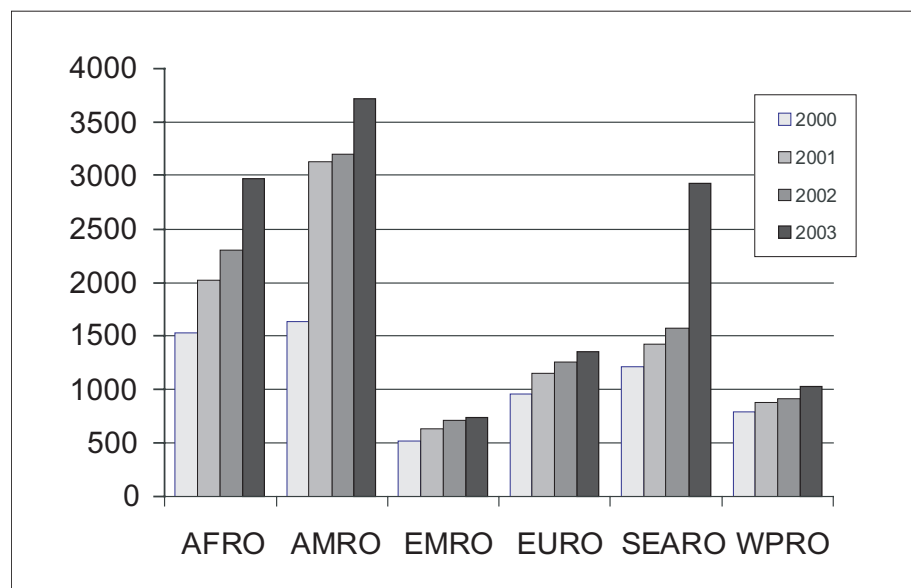


Figure 8.5. RHL subscription status (2000–2003)



A 4-day training package that includes manuals for workshop facilitators, participants and a monitoring and evaluation module was developed. This interactive course uses different techniques such as role plays, case studies and an innovative learning tool in the form of a board game. The manuals



were printed in 2003. A workshop to adapt and utilize the same programme in South-east Asia was conducted in Hat Yai, Thailand, in 2003.

The Department is working with an international group developing a system to grade research evidence to assist decision-making. In 2003, a workshop for WHO staff was

conducted and another workshop for Department staff is scheduled for early 2004.

### Knowledge access and utilization

The Programme to Map Best Reproductive Health Practices and the Implementing Best Practices (IBP) initiative are recognized as important knowledge management projects within and outside WHO. The RHL trial referred to above (see Research activities on page 224), the research synthesis programme and the structured dissemination activities generate important empirical evidence in this field. The Mapping and Implementing Best Practices team collaborates with relevant groups within and outside WHO, and has contributed to the activities outlined below:

1. WHO Task Force on Knowledge Access and Sharing. First meeting held in December 2003 addressing prospective registration of controlled trials and different research information access models.
2. WHO Task Force on Innovations and Evidence-based Applications for Health Systems Development. First meeting held on 3 December 2003.
3. World Report on "Knowledge for Better Health". The Department has been collaborating with the Department of Research Policy and Cooperation in the preparation of this report that will be published in 2004. Part of this report will include case studies on the Programme-supported research leading to the development and introduction of copper-releasing intrauterine devices.
4. WHO-Cochrane Collaboration scoping study. A survey to identify the extent of Cochrane Collaboration involve-

Table 8.10. RHL presentations coordinated by the Department in 2003

WHO Regions	Workshops /presentations	Attended/trained
Africa	10	704
Americas	16	4310
Eastern Mediterranean	4	600
Europe	10	533
South-East Asia	27	3133
Western Pacific	4	830
Headquarters	6	139
<b>Total</b>	<b>77</b>	<b>10 249</b>

ment and knowledge in WHO (WHO headquarters and regional offices) will be conducted in 2004. This survey will be supported by the Cochrane Collaboration.

- The HRP Controlled Trials Register is being updated regularly and linked to the meta-register of controlled trials (web site: <www.controlled-trials.com>).

### Future challenges

RHL has become a recognized source of evidence-based, up-to-date information in reproductive health. RHL is incorporated into the medical curricula of several institutions and universities, such as the Khon Kaen University in Thailand, Universities of Pretoria and Witwatersrand in South Africa, Rosario University in Argentina. It is also an important resource for postgraduate training and college membership examinations. Furthermore, the RHL trial will provide useful insights into changing behaviour of health care professionals in under-resourced settings. As activities related to RHL, systematic reviews and capacity building in evidence-based reproductive health care decision-making expand and become more widely known, new challenges will emerge. The future challenges for the "WHO Programme to Map Best Reproductive Health Practices" include:

- how best to generate evidence for knowledge management and utilization globally;
- how the Department can best ensure that its recommendations for practices and implementation are based on best available evidence from systematic reviews;
- finding the best ways of working with partners of the Implementing Best Practices initiative in order to expand the content of RHL to cover: systematic reviews of observational studies to map the burden of reproductive ill-health, materials and tools for improving management and performance in health care, training programmes,

videos and other tools to facilitate the implementation of effective practices;

- finding cost-effective ways of maintaining and improving the quality of RHL;
- finding the most cost-effective and efficient ways of creating a critical mass in developing countries of scientists who are well informed and competent in critically appraising and preparing systematic reviews in reproductive health;
- developing an Internet version of RHL in 2004-2005 (consultations are currently under way to identify appropriate partners for launch of an Internet version of RHL in 2005).

## IMPLEMENTING BEST PRACTICES

### The goal of the Implementing Best Practices initiative

The Implementing Best Practices (IBP) initiative is a growing collaborative network of 20 partner agencies dedicated to working with regional and country networks of key stakeholders to exchange information and use a systematic process to introduce, adapt and apply evidence-based best practices.



**"20 partners work collaboratively with countries to support knowledge-sharing strategies to introduce, adapt and apply evidence-based practices, materials and tools to improve reproductive health"**

**Country Action - Jordan Team, April 2002:**

Since attending the IBP meeting in Egypt, in 2002, the Jordan country team has continued to work together in collaboration with the Ministry of Health to:

- a) Use the *Medical Eligibility Criteria for Contraceptive Use* and other technical guidance documents produced by the Department as the basis for modifying national reproductive health/family planning standards of care.
- b) Develop an integrated comprehensive Reproductive Health/Family Planning counselling training curriculum.

The Ministry of Health has approved the training curriculum and reproductive health standards and in 2003, implementation started in all districts.

The goal of the IBP initiative is to help countries access the latest available evidence-based information so that they can select the interventions, materials and tools that need to be adapted and applied to improve access to and quality of reproductive health (refer to Annex 4 for list of IBP partners).

The partners have signed a Memorandum of Understanding to form the IBP Consortium and have committed to work collaboratively with countries to:

- disseminate and promote the use of research findings and evidence-based materials and tools relevant to the identified needs of countries;
- disseminate and promote the use of existing materials and tools produced by partner agencies that support the development of enabling environments and practices in areas including management and leadership, performance improvement, supply chain and logistics management, client/provider interaction, informed choice, organization of work, education and training, and monitoring and evaluation;
- harmonize messages and approaches and reduce duplication;
- work with country teams to select evidence-based interventions, materials and tools that can be used to update national guidelines and adapted/applied at programmatic levels to improve the quality of specific areas of reproductive health services; and
- support the development of a mentorship and follow-up programme to provide countries with ongoing support to implement plans to adapt and apply best practices.

**Progress**

*IBP Consortium*

Over time, the membership of the Consortium is expected to expand to include a wide variety of stakeholders from country programmes in developing and developed countries. Partners function on a cost-sharing basis and provide technical expertise to support the development of the IBP initiative. EngenderHealth have accepted the Chair of the IBP Consortium for 2003–2004.

*Regional and country activities*

Since 2000, the IBP initiative has been successfully launched through regional meetings in Nepal and Egypt and country meetings in China. In 2003, the IBP initiative was launched in four states in India and activities are being undertaken to launch the IBP initiative in five countries in East Africa in 2004.

*IBP India intracountry activities*

The IBP initiative was launched in India in September 2003 for the states of Uttar Pradesh, Jharkhand, Andhra Pradesh and Uttaranchal. IBP partners prepared the launch in collaboration with the IBP India Steering Committee, consisting of representatives from the Ministry of Health, WHO Regional Office for South-East Asia (SEARO), the WHO Country Office in India, seven nongovernmental agencies, the United States Agency for International Development (USAID) in India and the United Nations Population Fund (UNFPA). The IBP India Steering Committee defined the technical theme of the meeting “To create enabling environments to prevent unwanted pregnancy and the transmission of STIs/HIV”.

Over 280 senior health officials from the Ministry of Health, international and nongovernmental agencies, research institutes, professional bodies and local grass roots organizations, sponsored by IBP partner organizations, were involved in the launch of the IBP initiative. The meeting was highly interactive and an excellent example of collaboration between international and country partner agencies. Each state selected different reproductive health goals and developed action plans that focused on introducing evidence-based interventions to accelerate reaching their common goal (Table 8.11). All participants were provided with sets of technical and managerial guidelines, manuals and tools, and IBP partners committed themselves to providing support to the implementation of the action plan.

Since the launch of the IBP initiative, the Joint Secretaries, Ministry of Health and Family Welfare, have written to the Department and to their counterparts in each state to support the IBP mentorship and follow-up programme. All state teams have been followed up electronically by the IBP Secretariat and visited by their local follow-up facilitators. The feedback from all state teams reporting action taken to implement their activity plans is encouraging.

Table 8.11. Selected programmatic goals of state teams

Team	Goal
Andhra Pradesh	To increase the use of temporary contraceptive methods by 2% over existing levels in eight districts within 18 months.
Jharkhand	To re-organize services at the primary health care level to increase the quality of services and be responsive to the needs of pregnant and post-pregnant women.
Uttaranchal	To support each other and improve quality and increase coverage of antenatal care by 30%.
Uttar Pradesh	To improve the quality of service delivery to increase access to and acceptance of family planning services at all sites

### *IBP launch in Africa*

Activities are being undertaken in collaboration with WHO's Regional Office for Africa (AFRO), the Regional Advisory Panel (RAP) for Africa, AFRO's Regional Reproductive Health Task Force, the Reproductive Health Research and Training Network and IBP partner agencies to launch the IBP initiative in Africa. A small team from the region attended the IBP India meeting, both to observe the methodology and to initiate the planning process. Ethiopia, Kenya, Tanzania, Uganda, and Zambia will be the first countries to be involved in the initiative and initial country visits have been undertaken. The Regional Centre for Quality Health Care, Makerere University in Kampala, Uganda, will host the meeting, due to be held in June 2004. The meeting will focus on issues related to repositioning family planning in the context of the HIV/AIDS epidemic.

### *Knowledge sharing and management*

An electronic communication and management system, based on knowledge management principles, is being designed as an important part of the IBP initiative. This is being developed in collaboration with the WHO Department of Information Technology and Telecommunications, IBP partners and the Johns Hopkins Bloomberg School of Public Health INFO project. It is designed to encourage international and country health professionals to share ideas, opinions, experiences and lessons learnt in reproductive health. By providing easy-to-use electronic communication tools and alternatives for those with limited technological resources, users can access evidence-based tools and collaborate with colleagues and experts to innovate and learn from others. The system will support such activities as knowledge sharing, on-line meetings, access to health materials, regular technical and managerial updates, links to web sites, etc.

### *Other key accomplishments*

- The Department has supported a literature review on knowledge management, which will be used as a basis for improving further the IBP methodology.

- Plans are currently being made to build on the current three-year programme of work and develop further the IBP strategic plan for 2004–2007.
- A technology café brochure of available web sites, CD-ROMs and resource centres, an advocacy kit and a CD-ROM tool kit of evidence-based technical materials and tools and practices have been developed to support IBP activities.
- IBP partners have followed up and mentored individuals and agencies involved in IBP activities. The IBP Secretariat is in the process of compiling a document of success stories of action taken after an IBP launch.
- The Department's strategic planning process for the years 2004–2009 has enabled the IBP team to integrate IBP activities within the programme of work of other teams within the Department. The UNFPA Strategic Partnership Programme is an example of employing an integrated approach to converting evidence into practice.
- The USAID-supported Population Leadership Program has funded a fellow to work with the Department for two years to support the development of the IBP initiative.

### **Future plans**

The plans for the IBP initiative for 2004 and beyond are to:

- backstop and support the India Steering Committee to follow up the IBP initiative, explore the feasibility of expanding to other states and encourage a locally-led initiative by each state team to diffuse the IBP process down to district-level managers;
- work in collaboration with country task teams to prepare, implement and follow up the meeting planned for five countries in Africa and prepare to support other regions to introduce the IBP initiative;
- field-test the electronic communication and management system in India and in African countries, including

the provision of materials and tools produced by IBP partners;

- develop a process to grade the evidence of managerial and performance improvement practices that can be recommended to countries;
- update the IBP strategic plan for 2004–2007 and capture the lessons learnt in knowledge management systems for application to reproductive health;
- ensure that the IBP initiative is linked to other programmes within the Department and with all partners for greater cohesiveness and the practical application of harmonized approaches;
- support the implementation of the UNFPA Strategic Partnership Programme project proposal for the dissemination, adaptation and application of evidence-based practices;
- formulate an evaluation framework for the entire IBP initiative, prepare a progress report, identify funding sources and expand the network to include additional agencies and professional bodies; and
- initiate action to develop a repository of resource materials in French and Spanish.

## Annex 1

## WHO PROGRAMME TO MAP BEST REPRODUCTIVE HEALTH PRACTICES

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	6	86			1	14	7
Women	3	43					3
<b>from:</b>							
AFRO	1	14					1
AMRO	2	29			1	14	3
EMRO							
EURO							
SEARO	2	29					2
WPRO	1	14					1

Annex 2

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	Developing countries		Countries in transition		Developed countries		Totals
	Number	% of total	Number	% of total	Number	% of total	
Members	60	68	1	1	27	31	88
Women	16	18			6	7	23
<b>from:</b>							
AFRO	25	28					25
AMRO	18	20			8	9	26
EMRO	3	3					3
EURO			1	1	17	19	18
SEARO	11	13					11
WPRO	3	3			2	2	5

Annex 3

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**Annex 4**

**IMPLEMENTING BEST PRACTICES (IBP) INITIATIVE**

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**Section 9**  
**Monitoring and evaluating  
reproductive health**

# Monitoring and evaluating reproductive health

M. Gülmezoglu, A. Betran, L. Say

## INTRODUCTION

The objective of this area is to monitor progress towards reproductive health-related goals and targets, including the Millennium Development Goals (MDGs) of improving maternal health and reducing under-five child mortality.

Improved knowledge of the magnitude/burden of leading causes of maternal and newborn morbidity and mortality is needed for evaluation purposes. This information needs to be reliable, up-to-date and generated and summarized using rigorous methodology. In addition to the need for improved assessment on leading morbidities such as eclampsia, haemorrhage and low birthweight, other conditions which affect large numbers of women, but remain neglected, require attention, such as genital prolapse, incontinence and depression. Reliable information on these morbidities will complement the MDGs and will point to areas for more intensive action.

Indicators are needed for monitoring reproductive health. Unfortunately, there is a discrepancy between locally relevant indicators and those that are useful for global monitoring purposes. Global indicators obscure differences in health status within countries among populations differing in socio-economic status, rural and urban residence, age and ethnic groups. Furthermore, there is limited experience with some of the reproductive health indicators that have been agreed upon. Therefore, it seems that more research and capacity strengthening efforts are needed to make optimal use of those indicators. There is also a need to communicate the monitoring and evaluation activities and develop tools to provide access to and training in reproductive health indicators.

## EPIDEMIOLOGY OF REPRODUCTIVE ILL-HEALTH

### Objectives

The overall goal is to map reproductive morbidities and mortality in a comprehensive and systematic manner. Mapping will provide support for identifying priorities for future research on practices to prevent these morbidities and assist implementation of evidence-based country programmes and advocacy. The specific objective is to calculate the prevalence/incidence, case fatality rates, sequelae and attributable fractions of pregnancy-related and reproductive morbidities from systematic reviews of published or unpublished studies and data sets.

### Progress

#### *Maternal morbidity and mortality: a systematic review*

The primary objective of the systematic review is to obtain prevalence/incidence estimates for maternal morbid conditions and mortality worldwide. In 2003, data extraction, entry and descriptive analysis for the systematic review were completed. Over 60 000 citations identified through a comprehensive search strategy were initially screened by evaluating titles and/or abstracts. More than 4500 deemed to be potentially relevant were retrieved for full text evaluation. Out of these, 2351 that fulfilled predetermined inclusion criteria were included in the review and 1920 were excluded. The remaining 346 are in the process of retrieval and evaluation.

By November 2003, data extraction and entry was complete for 1269 reports. The distribution of these reports according to the study designs, characteristics of the participants

and settings are presented in Figure 9.1. Figure 9.2 shows the regional and development status (United Nations classification) of the countries where the reported studies were conducted.

Where possible, the data were disaggregated by study periods, age groups, ethnic groups, settings and interventions used (i.e. different arms of randomized controlled trials) and entered in the database as separate data sets. These sets from the 1269 reports include data on maternal mor-

tality ( $n=335$ ) and a variety of morbidities ( $n=3215$ ) which include major conditions such as hypertensive disorders of pregnancy, haemorrhage, abortion and sepsis, as well as other important but neglected disorders such as depression, urinary/faecal incontinence and perineal tears.

A manuscript discussing the methodological issues of the systematic review was prepared and submitted for publication. In 2004, individual reports will be prepared on the morbidities covered in the systematic review.

Figure 9.1. Characteristics of reported studies ( $n = 1269$ )

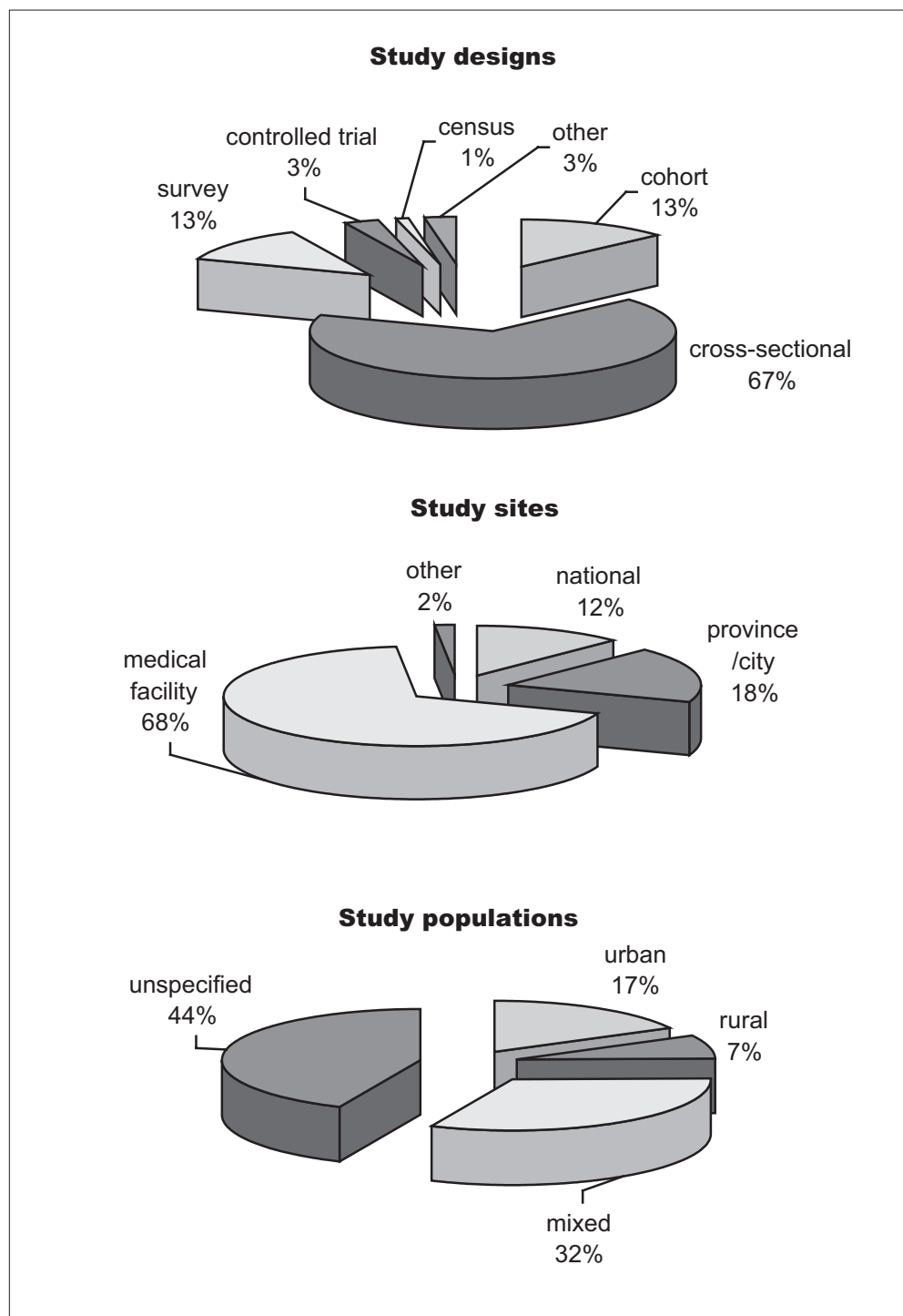
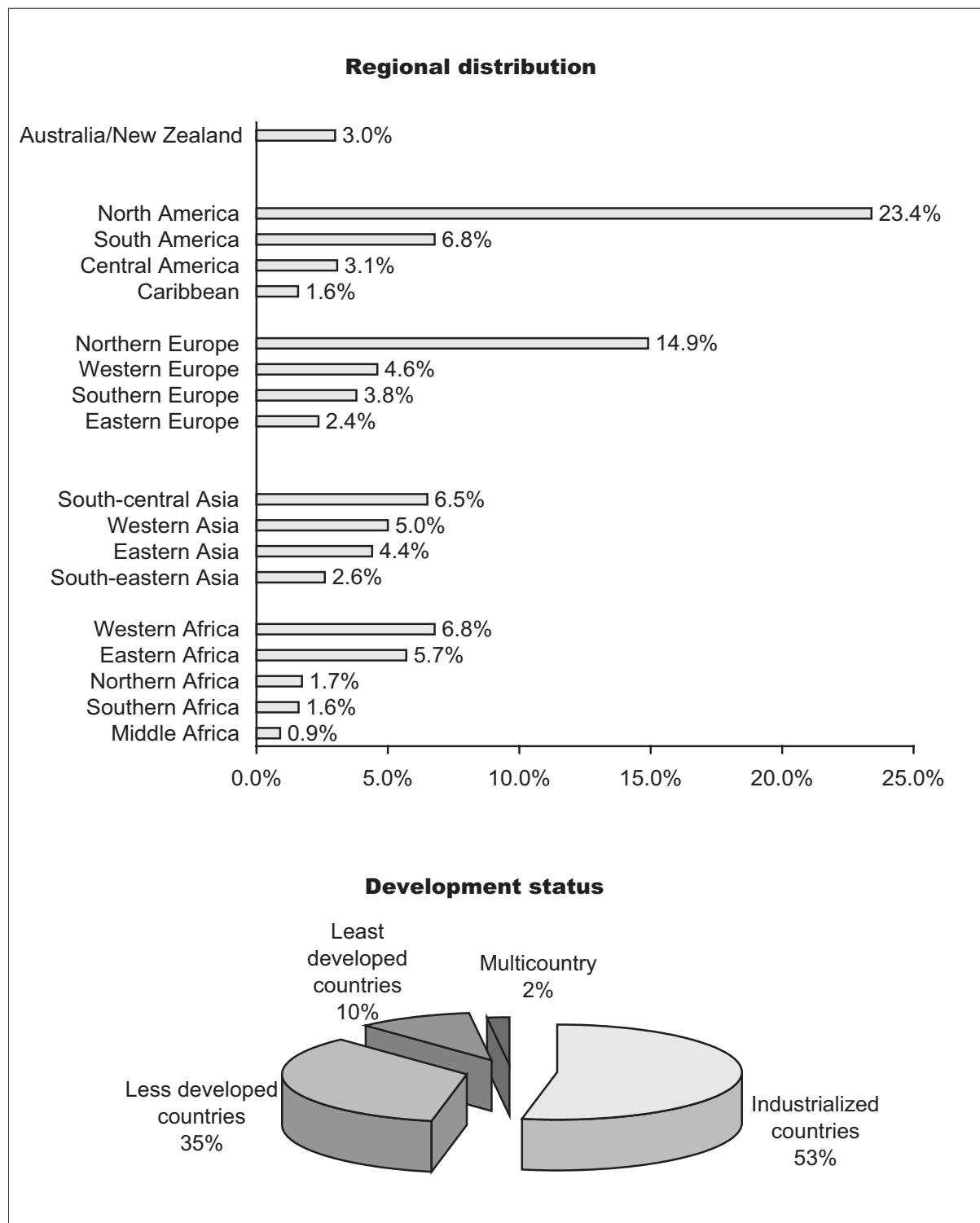


Figure 9.2. Distribution of reported studies by region and development status



*Maternal mortality estimates*

Reduction of maternal mortality is one of the major goals agreed to at several recent international conferences (such as the Millennium Conference). However, due to the difficulties and complexity of measuring maternal mortality, reliable information on the extent of the problem is not easily

available. WHO, together with the United Nations Children's Fund (UNICEF) and the United Nations Population Fund (UNFPA), has developed an approach to estimate maternal mortality at global, regional and national levels. National estimates were reviewed with countries and the maternal mortality estimates for 2000 released in October 2003 <[http://www.who.int/reproductive-health/publications/maternal\\_mortality\\_2000/index.html](http://www.who.int/reproductive-health/publications/maternal_mortality_2000/index.html)>.

The estimated number of maternal deaths in 2000 for the world is 529 000, of which 95% occurred in Africa and Asia. Only less than 1% occurred in more developed countries. Women living in sub-Saharan Africa have a one in 16 risk of dying in pregnancy or childbirth, whereas this risk is one in 2800 for women living in more developed regions.

### *Skilled attendant at delivery*

Because of the difficulties in measuring maternal mortality and the wide margins of uncertainty associated with these estimates, monitoring of trends relies, to a large extent, on process indicators. The most widely used of these process indicators is the proportion of women who deliver with the assistance of a trained health care provider (skilled attendant at delivery), which has been included as a key indicator for tracking progress in reducing maternal mortality in the MDGs. Since 2000, the Department has been updating global and regional estimates for this indicator and providing country-level data. The 2003 estimates are available through the Department's web site and they will be updated in early 2004: <[http://www.who.int/reproductive-health/global\\_monitoring](http://www.who.int/reproductive-health/global_monitoring)>.

### *Systematic review on genital prolapse*

A systematic review, started in 2002 to estimate the prevalence, associated factors and consequences of genital organ prolapse, is now complete and the report will be published in 2004.

### *Perinatal mortality and low birthweight estimates*

Estimates for perinatal mortality and low birthweight have been developed and reports are being prepared.

### *Unsafe abortion*

Estimates of maternal mortality due to unsafe abortion were completed (see the chapter on Preventing unsafe abortion on page 130).

### *Antenatal care*

An analysis of trends, levels and differentials in antenatal care during 1990–2001 in developing countries was prepared and published.

## REPRODUCTIVE HEALTH INDICATORS

### Objectives

There are 17 global reproductive health indicators that have been agreed upon by international agencies. The Department's work on mapping the epidemiology of reproductive ill-health will improve the knowledge base for these indicators globally. Development of tools to compile available information aims to facilitate the use of the indicators as needed.

## Progress

### *Reproductive health indicators database*

In 2003, a database was developed which provides up-to-date information (broken down by national, regional and global figures) of the 17 reproductive health indicators (plus an additional five) and 16 socioeconomic and demographic indicators. It is available electronically through the Department's web site at <[http://www.who.int/reproductive-health/global\\_monitoring/database.html](http://www.who.int/reproductive-health/global_monitoring/database.html)>. This database allows queries by country or region and generates tables and graphs accordingly (Figure 9.3). It will be updated annually.

### *Measuring access to reproductive health services*

At the International Conference on Population and Development (ICPD) in 1994, and its five-year follow-up in 1999, governments pledged to provide access to reproductive health services to all individuals of appropriate ages by 2015. The World Health Assembly, in resolution WHA55.19 of May 2002, declared that "increased access to good quality primary health care information and services, including reproductive health, is critical for attainment of the development MDGs. However, there is a lack of agreement on the most appropriate indicators of access to monitor progress made by countries on the ICPD recommendation.

The Department and UNFPA organized a meeting in December 2003 and agreed on a set of four indicators to represent the "access to reproductive health services" goal and to provide a MDG-type framework for reporting progress.

## FUTURE CHALLENGES

Future challenges in the area of monitoring and evaluation are as follows:

1. Dissemination of information obtained through the systematic review of maternal mortality and morbidity. Significant information on the prevalence/incidence of important maternal morbidities and mortality from a variety of countries, settings and population groups has been compiled with the systematic review. This information needs to be summarized and presented in a logical and useful manner. Although reviews of observational studies exist in the literature, this review is probably the largest in addressing prevalence/incidence and poses new challenges in quantifying and summarizing the burden of ill-health.
2. Reproductive health indicators. Empirical work on the usefulness of the global reproductive health indicators remains to be conducted. The gap between global goals and locally relevant and operational indicators is a challenge for international agencies to address. In doing so, equity in access to services needs to be measured as well. The morbidity differentials among population

Figure 9.3. A sample table created using the Reproductive Health Indicators database

Department of Reproductive Health and Research (RHR), World Health Organization


email this country report

Last update: 15 March 2004 Reproductive Health Indicators for **Afghanistan**

**Socio-Economic and Demographic:**

Total population (x 1000)	21391	2000	Infant mortality rate (per 1000 live births)	167	1995-2000
Population growth rate (%)	2.14	1995-2000	Child mortality under 5, male (per 1000 live male births)	250	2002
Urban population (%)	21.9	2000	Child mortality under 5, female (per 1000 live female births)	256	2002
Sex ratio (males per 100 females)	107	2000	Life expectancy at birth, male (years)	41.9	2002
Females aged 15-49 (x 1000)	4700	2000	Life expectancy at birth, female (years)	43.4	2002
Females aged 15-19 (x 1000)	1081	2000	Net primary school enrolment ratio, male (%)	42 (a)	1997-2000
Births per year (x 1000)	1044	2000	Net primary school enrolment ratio, female (%)	15 (a)	1997-2000
Crude birth rate (per 1000 population)	47.7	1995-2000	Gross national income per capita (US\$)	nd	
Crude death rate (per 1000 population)	22.3	1995-2000			

**Maternal Mortality:**

Maternal deaths	20000	2000	Lifetime risk of maternal death (1 in)	8	2000
Maternal mortality ratio (per 100 000 live births)	1900	2000	Proportion of maternal deaths (%)	46	2000



3. Improvement of the methods used to measure maternal mortality at country level. A major challenge is to develop mechanisms to promote and facilitate the implementation of reliable methods of measuring deaths and their causes.
4. Systems for global monitoring. The systematic review mentioned above will reveal gaps in data with regard to different morbidities. The next step will be to implement systems to collect these data in a more reliable way through prospective studies. The work on a system for routine monitoring of important health conditions and for conducting prospective research on emerging issues is ongoing.

**Annex 1****PUBLICATIONS IN 2003**

Turan JM et al. Community participation for perinatal health in Istanbul. *Health Promotion International*, 2003, 18:25–32.

Turan JM, Say L. Community-based antenatal education in Istanbul, Turkey: effects on health behaviours. *Health Policy and Planning*, 2003, 18:391–398.

Villar J et al. WHO leads global effort on systematic reviews. *International Journal of Epidemiology*, 2003, 32:164–165.

Villar J et al. Eclampsia and pre-eclampsia: a worldwide health problem for 2000 years. In: Critchley HOD et al., eds. *Hypertension in pregnancy*. London, Royal College of Obstetricians and Gynaecologists Press, 2003:189–207.

Villar J et al. Methodological and technical issues related to the diagnosis, screening, prevention and treatment of pre-eclampsia and eclampsia. *International Journal of Gynecology and Obstetrics* (in press).



## **Section 10**

# **Communication, advocacy and information**

# Communication, advocacy and information

J. Khanna, C. Hamill, S. Kolev, J. Maurice

## INTRODUCTION

The Communication, Advocacy and Information group (CAI) aims to facilitate access to reproductive health information—within and outside the Department—in support of the WHO mandate and objectives in improving global reproductive health. The main objectives are:

- to develop a strategic, proactive and cost-effective programme for the dissemination and communication of reproductive health knowledge to target audiences and stakeholders;
- to facilitate the transfer of reproductive health information through appropriate strategies and media, focusing on participatory communication;
- to initiate, develop and manage a communication research programme to evaluate the impact of dissemination activities and to strengthen dissemination/communication strategies; and
- to initiate advocacy and public relations interventions.

## PROGRESS

### Production of documents and publications

The following publications/documents were produced and distributed in 2003:

#### *Progress in reproductive health research*

The Programme's newsletter *Progress in reproductive health research* continues to serve as a key instrument for dissemi-

nation of research information to policy-makers, programme managers, scientists and the general public. Four issues of the newsletter were published in 2003. *Progress* continues to be translated into Chinese and is published on the Department's web site.

#### *Annual technical report 2002—CD-ROM*

Along with the Department's *Annual technical report 2002*, this CD-ROM contains other key documents on the work of the Department, including the entire contents of the Department's Internet web site as of 1 June 2003. Some 2500 copies of the CD-ROM had been distributed by December 2003, primarily to scientists and national and international policy-makers. In addition, print copies of the *Annual technical report 2002* were also produced and distributed.

#### *Safe motherhood—A newsletter of worldwide activity*

The Safe Motherhood initiative is a global effort to reduce maternal mortality and morbidity. As part of its contribution to the initiative, WHO began publishing *Safe Motherhood—a newsletter of worldwide activity* in 1989. In 2003, one issue of the newsletter was published, covering the topic of success stories in safe motherhood.

#### *Other information materials*

A total 28 information materials (including different language versions and promotional materials) were produced and distributed (see Table 10.1).

#### *Video—Evidence-based Caesarean section*

To help train physicians in evidenced-based techniques of Caesarean section, a new video was produced by the

Department. This video will be included in the No. 7 (2004) issue of *The WHO reproductive health library*.

no Internet access to have all information materials of the Department in searchable electronic form.

### Reproductive health web site

The web site of the Department continues to expand and serve as an excellent communication tool. Almost all documents and publications are now posted to the web site four to six weeks before they are available in printed format. More than two and a half million hits were recorded during 2003, which corresponds to over half a million visitors downloading over one million files. Twice during the year, the web site was made available on CD-ROM allowing those with poor or

A notable highlight of the site during 2003 was the publication of the on-line version in French of *Managing complications in pregnancy and childbirth: a guide for midwives and doctors [Prise en charge des complications de la grossesse et de l'accouchement: guide destiné à la sage-femme et au médecin]*. Published in html format with all cross-references hyperlinked, this version enables the user to find any information in the book instantly. Work is under way to make other selected pages of the site available in French.

Table 10.1. All information materials produced in 2003

#### Newsletters

1. Progress in Reproductive Health Research (four issues)
2. Safe Motherhood (one issue)

#### Electronic documents on CD-ROM

3. Annual technical report 2002
4. The WHO Reproductive Health Library, No.6
5. Publications, documents and web site with special focus on Making Pregnancy Safer

#### Printed documents

6. Annual technical report 2002
7. Safe abortion: technical and policy guidance for health systems
8. Towards adulthood: exploring the sexual and reproductive health of adolescents in South Asia
9. Antenatal care in developing countries: promises, achievements and missed opportunities
10. Kangaroo mother care: a practical guide
11. Expanding capacity in operations research in reproductive health. Summary report of a consultative meeting.
12. HIV-infected women and their families: psychosocial support and related issues
13. HRP proposed programme budget 2004–2005
14. RHR proposed programme budget 2004–2005
15. Managing newborn problems. A guide for doctors, nurses and midwives
16. Maternal mortality in 2000: estimates developed by WHO, UNICEF and UNFPA
17. Summary report: WHO/CONRAD technical consultation on Nonoxynol-9
18. Working with individuals, families and communities to improve maternal and newborn health
19. UNFPA/WHO bilateral consultation on collaborative activities
20. High-level consultation between WHO and UNFPA

#### Language versions other than English

21. *Prise en charge des complications de la grossesse et de l'accouchement*
22. *Une sélection de recommandations pratiques relatives à l'utilisation de méthodes contraceptives*

#### Revised field-testing version

23. Sexually transmitted and other reproductive tract infections: a guide for essential practice
24. Sexually transmitted and other reproductive tract infections: a pocket guide for essential practice

#### Promotional materials

25. Highlights of 2002
26. HRP External evaluation 1990–2002: executive summary
27. Sexual and reproductive health: publications and documents, October 2003

#### Video

28. Evidence-based Caesarean section

### **The WHO reproductive health library: dissemination of No. 6 and production of No. 7**

The No. 6 issue of the electronic journal *The WHO reproductive health library (RHL)* was published in February 2003. Later in the year, a Spanish version was also published. A total of 22 000 copies of the English version and 10 000 copies of the Spanish version were produced. By December 2003, all 20 000 copies of the English version and all 10 000 copies of the Spanish version had been distributed. Subscriptions to RHL continued to rise, and by December 2003, there were more than 13 000 addresses in the mailing list for the English and Spanish versions. During 2003, work was under way to produce RHL No. 7, and plans were made to produce an Internet version of the RHL.

#### **Press release**

The Department issued one press release in October 2003. Entitled *Maternal deaths disproportionately high in developing countries*, this press release drew attention to the newly published (on the Internet) global report on *Maternal mortality in 2000: estimates developed by WHO, UNICEF and UNFPA*. The press release received widespread attention from the media.

### **Strengthening the capacity for communication and information dissemination of the Programme's collaborating centres—Scientific writing workshops**

The Programme's scientific writing workshops focus on the skills involved in writing a scientific research paper and aim to encourage scientists in the Programme's collaborating centres to publish more papers, especially in international peer-reviewed journals. (A detailed description of the scientific writing workshops can be found in the Programme's *Annual technical report 1995*.)

#### *New research proposal writing component added to the scientific writing workshop*

In 2003, a scientific writing workshop was conducted at the Research Institute for Health Sciences, in Chiang Mai, Thailand. A total of 37 Thai researchers were trained.

In response to requests from many institutions, for the first time a newly developed half-day component on how to write a research project proposal was included in this workshop.

Based on the participants' comments about this component, it was felt that the new session had been very successful and would be suitable for further development. Given the overlap between the skills needed for writing scientific research papers and research project proposals, the two could be conducted together with minimum changes to the overall structure of the scientific writing workshop. On the other hand, if needed, the project proposal component could also be conducted independently.

#### *New scientific writing workshop developed for social scientists*

In 2003, together with FRONTIERS, the Programme developed a new dedicated scientific writing workshop for social scientists. The exercises and other training materials developed for this purpose were tested in a workshop conducted in Washington, DC, USA, especially for Population Council social scientists. The 12 participants in the workshop rated it very highly, requesting further assistance from the Programme in helping them to become trainers themselves so that they could train other social scientists.

A short training session on writing project proposals and research papers was conducted at the 13<sup>th</sup> Postgraduate Course for Training in Reproductive Medicine and Reproductive Biology at the WHO Collaborating Centre in Geneva, Switzerland. It was attended by 32 participants.

#### **Collaboration**

The Department of Communication, Cornell University, Ithaca, NY, USA, collaborates with the Programme in a variety of activities including the conduct of communication workshops for scientists. The Programme is also collaborating with FRONTIERS on scientific writing workshops for social scientists.

### **PLANNED ACTIVITIES**

In 2004, the Department will continue to produce its usual serial and non-serial publications, disseminate appropriate public relations material and conduct its scientific writing, communication and information management workshops. Plans are also under way to conduct scientific writing workshops in Indonesia, Myanmar and Sri Lanka. There are plans for communication workshops in Romania and India, as well.

# **Section 11**

## **Clinical trials and informatics support**

# Clinical trials and informatics support

O. Ayeni, G. Piaggio, A. Peregoudov, S. Landoulsi

## INTRODUCTION

The Clinical Trials and Informatics Support group provides technical support in statistics and data processing to the Department.

Technical support to research activities includes statistical advice in the review and development of research projects and responsibility for the management and analysis of some single-centre and nearly all multicentre studies carried out by the Programme. The group also coordinates the implementation of Good Clinical Practice (GCP) guidelines in all of the Programme's research activities. In the area of Technical Support to Countries, the group assists in the formulation, execution and review of institution strengthening policies in statistics and data processing, and in the organization and conduct of workshops and training courses in these areas for scientists from collaborating institutions. Staff of the group provide on-the-project training in research data management and statistical analysis to staff of countries participating in some multicentre studies or carrying out their own single-centre trials. Professional staff of the group contributes to the development of appropriate techniques for the conduct, management and analysis of multicentre research projects in reproductive health in developing countries. The group also provides local informatics support to the administrative management of the Department.

The group's strategy is to coordinate international multicentre studies from Geneva while continuing to enhance the ability of individual centres to handle their own single-centre and national multicentre studies.

## SUPPORT TO RESEARCH ACTIVITIES

### Specific objectives

The objectives are to provide high-quality and efficient statistical and data-processing support to all research conducted by the Programme and to ensure statistical and methodological rigour, including adherence to Good Clinical Practice guidelines (GCP), for all such support.

### Progress

#### *Support to research projects*

Activities carried out by the group in 2003 in support of research projects included technical advice in research development and review; statistical design; assistance with project organization; data processing, monitoring and management; data analysis and preparation of statistical reports; and participation in the writing of scientific papers resulting from the projects. A total of 64 research projects were supported. The distribution of these projects by their stage of support at the end of 2003 is shown in Table 11.1.

In addition, the group provided support to the Department's thematic areas in the form of technical review of projects submitted to them for funding and making arrangements for logistic support to projects before launching. Technical reviews focused mainly on the biostatistical and data processing aspects of protocols, while logistic support included site visits to the participating coordinating centres to review facilities and data collection mechanisms.

During 2003, the group organized and conducted a three-week training workshop for all of its headquarters' data management staff in Geneva. The objectives were to introduce a new, portable data-management system—DMS/3—devel-

oped by the group during the year, and to refresh the data management skills of staff members to enable them to provide up-to-date technical support to research projects.

### *Implementation of Good Clinical Practice guidelines in research*

During the year, efforts continued to implement formally WHO Good Clinical Practice research guidelines throughout the Programme's research activities. Editing of the new, as well as revision of the existing Standard Operating Procedures (SOPs), was completed. A workshop to introduce the SOPs and train Programme research staff in their use is planned for early 2004. A consultant with experience in human research quality assurance and harmonization of regulatory quality assurance, who has been involved in the SOP review and editing, is being contracted for this purpose.

### *Development of methodological tools*

The group continued collaboration on the extension of guidelines for clinical trials with the group on Consolidated Standards of Reporting Trials (CONSORT) of the London School of Hygiene and Tropical Medicine, United Kingdom. In May 2003, a staff member participated in the CONSORT group meeting in Château Montebello, Quebec, Canada to formulate and recommend guidelines for the reporting of clinical trials using various designs and the reporting of safety data in randomized trials. Work is ongoing on the methodology of meta-analysis of observational studies.

## **SUPPORT TO INSTITUTION STRENGTHENING ACTIVITIES**

### **Objective**

The objective of these activities is to strengthen the statistical and data-processing capabilities of selected developing-country institutions so that they can support their own research work.

## **Activities**

The following are the highlights of activities during 2003.

### *Site visits*

Staff of the group continued on-site training of staff in collaborating centres participating in international multicentre trials. The purpose of such site-visits included supervision of data collection, management of data queries, assessment of data quality and monitoring of studies in progress. Centres in East London and Johannesburg, both in South Africa, as well as Assiut and Cairo in Egypt, were visited to help review outstanding data problems in the study on calcium supplementation for the prevention of pre-eclampsia. A staff member also visited Khartoum, Sudan, to review queries concerning data quality for the study on the obstetric sequelae of female genital mutilation.

### *Training courses, seminars and workshops*

A staff member of the group gave lectures on community interventions and equivalence trials and on strategies for data analysis of randomized clinical trials and community interventions at the 13<sup>th</sup> Postgraduate Course for Training in Reproductive Medicine and Reproductive Biology at the WHO Collaborating Centre in Geneva, Switzerland. The course was attended by 32 participants.

### *Attendance at professional/scientific meetings*

A staff member of the group made a presentation on "Ethical aspects and stopping rules in equivalence trials: two case studies" at the Third Joint Meeting of the International Society for Clinical Biostatistics and the Society for Clinical Trials in London, United Kingdom. Another staff member presented the paper, "Contraception and conception among young single women: an international comparison" at the annual meeting of the Population Association of America in Minneapolis, MN, USA. This staff member also attended the symposium, "Expanding contraceptive choices: international and Indian experiences and their implications for policies and programmes," that took place in Mumbai, India, in December 2003. There, he presented the paper, "Contraceptive choices and use dynamics among single people: evidence from developing countries".

Table 11.1. Number of studies by stage of support (December 2003)

In the planning stage or just starting: protocol preparation, forms design, data management systems design, supplies distribution	22
Ongoing studies: data validation, data quality control, study monitoring, interim analysis	17
Final analysis: final data cleaning, preparation of final analysis	8
Statistical report drafted, manuscript in preparation, revisions and/or additions to final analysis	7
Final analysis completed	10
<b>TOTAL</b>	<b>64</b>

## Annex 1

## PUBLICATIONS IN 2003

- Ali MM, Shah I, Cleland JG. Trends in reproductive behaviour among young single women in Colombia and Peru 1985–2000. *Demography*, 2003, 40:659–673.
- Ali MM, Blacker J, Jones G. Annual mortality rates and excess deaths of children under five in Iraq, 1991–1998. *Population Studies*, 2003, 57:217–226.
- Ali MM, Cleland JG, Shah IG. Condom use within marriage: a neglected HIV intervention. *Bulletin of the World Health Organization*, 2004, 82:180–186.
- Ali MM, Cleland JG. Sexual and reproductive behaviour among single women aged 15–24 in eight Latin American countries: a comparative analysis (submitted).
- Che Yan, Cleland JG, Ali MM. Periodic abstinence in developing countries: an assessment of failure rates and consequences. *Contraception*, 2004, 69:15–21.
- Cleland JG, Ali MM. Reproductive consequences of contraceptive failure in nineteen developing countries (submitted).
- Cui N, Tang G, Li M, WHO Task Force on Methods for the Natural Regulation of Fertility. The impact of breast-feeding pattern on the duration of lactational amenorrhoea in Chengdu, China. *Journal of Reproduction and Contraception*, 2002, 13:98–109.
- Dada OA et al. Infant feeding and lactational amenorrhoea in Sagamu, Nigeria. *African Journal of Reproductive Health*, 2002, 6(2):39–50.
- D'Arcangues C et al. Effectiveness of Vitamin E and low-dose aspirin, alone or in combination, on Norplant-induced prolonged bleeding (accepted).
- Donner A, Piaggio G, Villar J. Meta-analyses of cluster randomization trials: power considerations. *Evaluation & the Health Professions*, 2003, 26:340–351.
- Gülmezoglu AM et al. Cluster randomized trial of an active, multifaceted information dissemination intervention based on The WHO Reproductive Health Library to change obstetric practices: methods and design issues (submitted).
- Hill ZE, Cleland JG, Ali MM. Religious affiliation and extra-marital sex in Brazil. *International Family Planning Perspectives* (accepted).
- Hofmeyr GJ et al. Effect of misoprostol on profuse blood loss after birth: an exploratory study of data from the WHO randomized trial of misoprostol in the third stage of labour (submitted).
- Piaggio G. Contraceptive research. In: Machin D, Day S, Green SB, eds. *Textbook of clinical trials*. John Wiley & Sons (accepted).
- Piaggio G, et al. The reporting of methods for reducing and detecting bias: an example from the WHO Misoprostol Third Stage of Labour equivalence randomized controlled trial. *BiomedCentral Medical Research Methodology*, 2003, 3:19.
- Piaggio G, Elbourne D, Altman D for the CONSORT Group. CONSORT: extension to equivalence trials (submitted).
- Piaggio G et al. Combined estimates of effectiveness of mifepristone 10 mg in emergency contraception. *Contraception*, 2003, 68:439–446.
- Piaggio G, von Hertzen H, Elbourne D, on behalf of the WHO Post-Ovulatory Research Group. Ethical aspects and stopping rules in equivalence trials: two case studies. *Controlled Clinical Trials*, 2003, 24(Suppl.):90S.
- Piaggio G et al. Meta-analysis of randomized trials comparing different doses of mifepristone in emergency contraception. *Contraception*, 2003, 68(6):447–452.
- Stephenson JM et al. A randomized intervention trial of pupilled sex education in England (RIPPLE) (submitted).
- Villar J et al. Eclampsia and pre-eclampsia: a health problem for 2000 years. In: Critchley H et al., eds. *Pre-eclampsia*. London, Royal College of Obstetricians and Gynaecologists Press, 2003, 189–207.
- Villar J et al. Heterogeneity of perinatal outcomes in the preterm delivery syndrome. *Obstetrics and Gynaecology* (accepted).
- von Hertzen H et al. WHO multinational study of three misoprostol regimens after mifepristone for early medical abortion: I. Efficacy. *British Journal of Obstetrics and Gynaecology*, 2003, 110: 808–818.
- von Hertzen H et al. WHO Multinational study of three misoprostol regimens after mifepristone for early medical abortion: II. Side-effects and acceptability (submitted).
- von Hertzen H, Piaggio G. Levonorgestrel and mifepristone in emergency contraception. *Steroids*, 2003, 68:1107–1113.

**Annex 1 (continued)**

WHO Task Force on Long-acting Systemic Agents for Fertility Regulation. Comparative study of the effects of two once-a-month injectable contraceptives (Cyclofem® and Mesigyna®) and one oral contraceptive (Ortho-Novum 1/35®) on coagulation and fibrinolysis. *Contraception*, 2003, 68:159–176.

Xiao B et al. Menstrual induction with mifepristone and misoprostol. *Shengzhi Yixue Zazhi* [Journal of Reproductive Medicine], 2003, 12:137–145.

Xiao B et al. Menstrual induction with mifepristone and misoprostol. *Contraception*, 2003, 68:489–494.

Xiao B et al. Postcoital treatment with mifepristone and misoprostol for prevention of pregnancy. *Contraception* (accepted).

Xiao B et al. Expanded clinical trial of emergency contraception with 10 mg mifepristone. *Contraception*, 2003, 68:431–437.

# Appendix 1

## Staff of the Department, December 2003

Paul Van Look, Director

### Programme Management

- <sup>1</sup> Anne Allemand, Administrative Assistant
- <sup>1</sup> Luc Bernier, Reproduction Equipment Operator
- <sup>1</sup> Catherine d'Arcangues, Medical Officer
- <sup>1,2</sup> Manjula Lusti-Narasimhan, Technical Officer
  - Barbara Kayser, Secretary
  - Craig Lissner, Technical Officer
  - Michael Mbizvo, Scientist
  - Bérengère Nail, Secretary
- <sup>1</sup> Corinne Penhale, Administrative Assistant
- <sup>1,2</sup> Lihong Su, Programme Assistant
- <sup>1,2</sup> Claire Tierney, Secretary
- <sup>1</sup> Hazel Ziaei, Administrative Assistant

### Promoting Family Planning Team

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- <sup>1</sup> Sybil De Pietro, Secretary
- <sup>2</sup> Mary Gaffield, Technical Officer
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- <sup>1</sup> Maud Keizer, Secretary
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  - Gloria Lamptey, Secretary
- <sup>1</sup> Lynda Pasini, Secretary
  - Herbert Peterson, Coordinator
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### Making Pregnancy Safer Team

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- <sup>1,2</sup> Mario Meriardi, Medical Officer
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- <sup>2</sup> Archana Shah, Technical Officer
- <sup>2</sup> Della Sherratt, Midwife
- <sup>1</sup> José Villar, Medical Officer
- <sup>2,3</sup> Juliana Yartey, Technical Officer
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- <sup>1</sup> Katherine Ba-Thike, Scientist
- <sup>1</sup> Jennifer Bayley, Secretary
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